



ENCYCLOPEDIA OF

Pestilence, Pandemics, and Plagues



Edited by Joseph P. Byrne • Foreword by Anthony S. Fauci, M.D.

Encyclopedia of Pestilence, Pandemics, and Plagues

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Volume 1, A–M

Edited by
JOSEPH P. BYRNE

Foreword by
Anthony S. Fauci, M.D.



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Contents

List of Entries	vii
Guide to Related Topics	xiii
Foreword by Anthony S. Fauci, M.D.	xix
Preface	xxi
Introduction	xxiii
The Encyclopedia	1
Glossary	801
Bibliography	813
About the Editor, Advisory Board Members, and Contributors	827
Index	843

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List of Entries

- AIDS in Africa
- AIDS in the United States
- AIDS, Literature, and the Arts in the United States
- Air and Epidemic Diseases
- Animal Diseases (Zoonoses) and Epidemic Disease
- Animal Research
- Antibiotics
- Apothecary/Pharmacist
- Armstrong, Richard
- Astrology and Medicine
- Avian Flu. See Influenza.
- Avicenna (Ibn Sina)
- Ayurvedic Disease Theory and Medicine

- Babesiosis
- Bacterium/Bacteria
- Bartonella* Diseases
- Behring, Emil von
- Biblical Plagues
- Bimaranistan/Maristan
- Biological Warfare
- Bioterrorism
- Black Death (1347–1352)

- Black Death and Late Medieval Christianity
- Black Death, Economic and Demographic Effects of
- Black Death, Flagellants, and Jews
- Black Death: Literature and Art
- Black Death: Modern Medical Debate
- Bubonic Plague
- Bubonic Plague in the United States

- Capitalism and Epidemic Disease
- Chadwick, Edwin
- Children and Childhood Epidemic Diseases
- Chinese Disease Theory and Medicine
- Cholera
- Cholera before the Pandemics
- Cholera: First through Third Pandemics, 1816–1861
- Cholera: Fourth through Sixth Pandemics, 1862–1947
- Cholera: Seventh Pandemic, 1961–Present
- Cinema and Epidemic Disease
- Colonialism and Epidemic Disease
- Conjunctivitis

- Contagion and Transmission
Contagion Theory of Disease,
Premodern
Cordon Sanitaire
Corpses and Epidemic Disease
- Demographic Data Collection and
Analysis, History of
Diagnosis and Diagnostic Tools
Diagnosis of Historical Diseases
Diet, Nutrition, and Epidemic Disease
Diphtheria
Disease in the Pre-Columbian
Americas
Disease, Social Construction of
Disinfection and Fumigation
Drug Resistance in Microorganisms
Dysentery
- Early Humans, Infectious Diseases in
Ectoparasites
Ehrlich, Paul
Empiric
Encephalitis
Encephalitis, Epidemic Outbreaks
in the Twentieth Century
Enders, John Franklin
Enteric Fevers
Environment, Ecology, and Epidemic
Disease
Epidemic and Pandemic
Epidemiology
Epidemiology, History of
Ergotism
- Farr, William
Fernel, Jean
Flight
Folk Medicine
Fracastoro, Girolamo
Frost, Wade Hampton
- Galen
Geopolitics, International Relations,
and Epidemic Disease
Germ Theory of Disease
Gonorrhea and Chlamydia
- Gorgas, William Crawford
Greco-Roman Medical Theory
and Practice
- Haffkine, Waldemar Mordechai
Hansen, Gerhard Armauer
Hemorrhagic Fevers
Hemorrhagic Fevers in Modern Africa
Henderson, Donald Ainslie
Hepatitis
Hereditry and Epidemic Disease
Hippocrates and the Hippocratic Corpus
Historical Epidemiology
Hospitals and Medical Education in
Britain and the United States
Hospitals in the West to 1900
Hospitals since 1900
Human Body
Human Immunity and Resistance to
Disease
Human Immunodeficiency
Virus/Acquired Immune Deficiency
Syndrome (HIV/AIDS)
Human Papilloma Virus and Cervical
Cancer
Human Subjects Research
Humoral Theory
- Immunology
Industrialization and Epidemic Disease
Industrial Revolution
Influenza
Influenza Pandemic, 1889–1890
Influenza Pandemic, 1918–1919
Insect Infestations
Insects, Other Arthropods, and Epidemic
Disease
International Health Agencies and
Conventions
Irish Potato Famine and Epidemic
Disease, 1845–1850
Islamic Disease Theory and Medicine
- Jenner, Edward
Kitasato, Shibasaburo
Koch, Robert

- Latin America, Colonial: Demographic
 Effects of Imported Diseases
 Laveran, Charles Louis Alphonse
 Leeuwenhoek, Antony van
 Legionnaires' Disease
 Leprosarium
 Leprosy
 Leprosy in the Premodern World
 Leprosy in the United States
 Leprosy, Societal Reactions to
 Literature, Disease in Modern
 London, Great Plague of (1665–1666)
 Lyme Disease

 Magic and Healing
 Malaria
 Malaria and Modern Military History
 Malaria in Africa
 Malaria in Medieval and Early
 Modern Europe
 Malaria in the Americas
 Malaria in the Ancient World
 Mallon, Mary
 Malthusianism
 Manson, Patrick
 Mather, Increase and Cotton
 Measles
 Measles, Efforts to Eradicate
 Measles Epidemic in Fiji (1875)
 and Eugenics
 Measles in the Colonial Americas
 Medical Education in the West,
 1100–1500
 Medical Education in the West,
 1500–1900
 Medical Ethics and Epidemic Disease
 Meningitis
 Microscope

 Napoleonic Wars
 Neolithic Revolution and Epidemic
 Disease
 News Media and Epidemic Disease
 Nicolle, Charles Jules Henri
 Non-Governmental Organizations
 (NGOs) and Epidemic Disease
 Nurses and Nursing

 Paleopathology
 Panspermia Theory
 Paracelsianism
 Paracelsus
 Pasteur, Louis
 Penicillin
 Personal Hygiene and Epidemic Disease
 Personal Liberties and Epidemic
 Disease
 Pest Houses and Lazarettos
 Pesticides
 Pettenkofer, Max Josef von
 Pharmaceutical Industry
 Physician
 Pilgrimage and Epidemic Disease
 Plague and Developments in Public
 Health, 1348–1600
 Plague: End of the Second Pandemic
 Plague in Africa: Third Pandemic
 Plague in Britain, 1500–1647
 Plague in China
 Plague in East Asia: Third Pandemic
 Plague in Europe, 1500–1770s
 Plague in India and Oceania:
 Third Pandemic
 Plague in Medieval Europe,
 1360–1500
 Plague in San Francisco, 1900–1908
 Plague in the Contemporary World
 Plague in the Islamic World,
 1360–1500
 Plague in the Islamic World,
 1500–1850
 Plague Literature and Art, Early
 Modern European
 Plague Memorials
 Plague of Athens
 Plague of Justinian, First Pandemic
 Plagues of the Roman Empire
 Plagues of the Roman Republic
 Pneumonic and Septicemic Plague
 Pneumonic Plague in Surat, Gujarat,
 India, 1994
 Poison Libels and Epidemic Disease
 Poliomyelitis
 Poliomyelitis and American Popular
 Culture

- Poliomyelitis, Campaign Against
Popular Media and Epidemic Disease:
Recent Trends
Poverty, Wealth, and Epidemic
Disease
Protozoon, -zoa
Public Health Agencies in Britain
since 1800
Public Health Agencies, U.S. Federal
Public Health Boards in the West
before 1900
Public Health in the Islamic World,
1000–1600
Public Health Posters
- Quacks, Charlatans, and Their Remedies
Quarantine
- Race, Ethnicity, and Epidemic Disease
Reed, Walter
Relapsing Fever
Religion and Epidemic Disease
Rhazes
Ross, Ronald
Rush, Benjamin
- Sabin, Albert
St. Vitus's Dance
Salk, Jonas E.
Sanatorium
Sanitation Movement of the
Nineteenth Century
Scapegoats and Epidemic Disease
Schaudinn, Fritz Richard
Schistosomiasis
Scientific Revolution and Epidemic
Disease
Semmelweis, Ignaz
Severe Acute Respiratory Syndrome
(SARS)
Sexuality, Gender, and Epidemic
Disease
Sexual Revolution
Simond, Paul-Louis
Simpson, William John Ritchie
Slavery and Epidemic Disease
Sleeping Sickness
- Smallpox
Smallpox and the American Revolution
Smallpox Eradication
Smallpox in Canada and the United
States since 1783
Smallpox in Colonial Latin America
Smallpox in Colonial North America
Smallpox in European Non-American
Colonies
Smallpox in Premodern Europe
Smallpox in the Ancient World
Snow, John
Social Psychological Epidemics
Sulfa Drugs
Surgeon
Sweating Sickness
Sydenham, Thomas
Syphilis
Syphilis in Sixteenth-Century Europe
- Theiler, Max
Thirty Years' War
Trade, Travel, and Epidemic Disease
Tuberculosis
Tuberculosis and Romanticism
Tuberculosis in England since 1500
Tuberculosis in North America
since 1800
Tuberculosis in the Contemporary
World
Typhoid Fever in the West since 1800
Typhus
Typhus and Poverty in the Modern
World
Typhus and War
- Urbanization and Epidemic Disease
- Vaccination and Inoculation
Venereal Disease and Social Reform in
Progressive-Era America
Virchow, Rudolf
Virus
- War, the Military, and Epidemic Disease
Water and Epidemic Diseases
West Nile Fever

Whooping Cough
Wu Lien Teh

Yellow Fever
Yellow Fever Commission, U.S.
Yellow Fever in Colonial Latin America
and the Caribbean

Yellow Fever in Latin America and the
Caribbean, 1830–1940
Yellow Fever in North America to
1810
Yellow Fever in the American South,
1810–1905
Yersin, Alexandre

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Guide to Related Topics

Biological, Physiological, and Medical Theories

Air and Epidemic Diseases
Astrology and Medicine
Ayurvedic Disease Theory and Medicine
Chinese Disease Theory and Medicine
Contagion Theory of Disease
Disease in the Pre-Columbian Americas
Disease, Social Construction of
Folk Medicine
Germ Theory of Disease
Greco-Roman Medical Theories
and Practices
Humoral Theory
Islamic Disease Theory and Medicine
Magic and Healing
Malthusianism
Panspermia Theory
Paracelsianism

Biomedical Research into Disease Causes, Prevention, and Treatment

Animal Research
Antibiotics

Avicenna (Ibn Sina)
Behring, Emil von
Drug Resistance in Microorganisms
Ehrlich, Paul
Enders, John Franklin
Fernel, Jean
Fracastoro, Girolamo
Galen
Haffkine, Waldemar Mordechai
Hansen, Gerhard Armauer
Henderson, Donald Ainslie
Hippocrates and the Hippocratic Corpus
Human Subjects Research
Jenner, Edward
Kitasato, Shibasaburo
Koch, Robert
Laveran, Charles Louis Alphonse
Leeuwenhoek, Antony van
Manson, Patrick
Microscope
Nicolle, Charles Jules Henri
Paracelsus
Pasteur, Louis
Pettenkofer, Max Josef von
Poliomyelitis, Campaign Against
Reed, Walter

Rhazes
Rush, Benjamin
Ross, Ronald
Sabin, Albert
Salk, Jonas E.
Schaudin, Fritz Richard
Scientific Revolution and Epidemic
Disease
Semmelweis, Ignaz
Simond, Paul-Louis
Simpson, William John Ritchie
Sydenham, Thomas
Theiler, Max
Wu Lien Teh
Yellow Fever Commission, U.S.
Yersin, Alexandre

Biological Causes of Disease

Bacterium/Bacteria
Ectoparasites
Insects, Other Arthropods, and
Epidemic Disease
Protozoon, -zoa
Virus

Colonial Experience and Disease

Colonialism and Epidemic Disease
Latin America, Colonial: Effects of
Imported Diseases
Leprosy, Societal Reactions to
Measles in the Colonial Americas
Slavery and Disease
Smallpox in Colonial Latin America
Smallpox in Colonial North America
Smallpox in Europe's Non-American
Colonies
Yellow Fever in Colonial Latin America
and the Caribbean

Cultural and Societal Effects of Epidemic Disease

AIDS, Literature, and the Arts in the
United States

Black Death and Late Medieval
Christianity
Black Death, Economic and
Demographic Effects of
Black Death, Flagellants, and Jews
Black Death: Literature and Art
Cinema and Epidemic Disease
Corpses and Epidemic Disease
Disease, Social Construction of
Flight
Latin America, Colonial: Effects of
Imported Diseases
Leprosy, Societal Reactions to
Literature, Disease in Modern
Personal Liberty and Public Health
Plague Literature and Art, Early Modern
Plague Memorials
Poison Libels and Epidemic Disease
Poliomyelitis and American Popular
Culture
Popular Media and Epidemic Disease:
Recent Trends
Scapegoats and Epidemic Disease
Tuberculosis and Romanticism
Venereal Disease and Social Reform in
Progressive-Era America

Diseases

Animal Diseases and Epidemics
Babesiosis
Bartonella Diseases
Bubonic Plague
Cholera
Conjunctivitis
Diphtheria
Disease in the Pre-Columbian Americas
Dysentery
Early Humans, Infectious Diseases in
Encephalitis
Enteric Fevers
Ergotism
Gonorrhea
Hemorrhagic Fevers
Hepatitis
Human Immunodeficiency Virus
(HIV)/AIDS

Human Papilloma Virus and
Cervical Cancer
Influenza
Legionnaires' Disease
Leprosy
Lyme Disease
Malaria
Measles
Meningitis
Pneumonic and Septicemic Plague
Poliomyelitis
Relapsing Fever
St. Vitus's Dance
Schistosomiasis
Severe Acute Respiratory Syndrome
(SARS)
Sleeping Sickness
Smallpox
Social Psychological Epidemics
Sweating Sickness
Syphilis
Tuberculosis
Typhus
West Nile Fever
Whooping Cough
Yellow Fever

Drugs and Pharmaceuticals

Antibiotics
Penicillin
Pharmaceutical Industry
Sulfa Drugs
Vaccination and Inoculation

Epidemics and Other Historical Disease Outbreaks

AIDS in Africa
AIDS in the United States
Armstrong, Richard
Biblical Plagues
Black Death (1347–1352)
Black Death: Modern Medical Debate
Bubonic Plague: Third Pandemic in
East Asia

Bubonic Plague: Third Pandemic in India
and Oceania
Bubonic Plague in the United States
to 2000
Cholera: First through Third Pandemics,
1816–1861
Cholera: Fourth through Sixth
Pandemics, 1863–1947
Cholera: Seventh Pandemic, 1961–Present
Diagnosis of Historical Diseases
Encephalitis, Epidemic Outbreaks in the
Twentieth Century
Gorgas, William Crawford
Hemorrhagic Fevers in Modern Africa
Historical Epidemiology
Influenza Pandemic, 1889–1890
Influenza Pandemic, 1918–1919
Insect Infestations
Irish Potato Famine and Epidemic
Diseases, 1845–1850
Leprosy in the Premodern World
Leprosy in the United States
London, Great Plague of (1665–1666)
Malaria in Africa
Mather, Increase and Cotton
Measles Epidemic in Fiji (1875)
and Eugenics
Measles in the Colonial Americas
Plague: End of the Second Pandemic
Plague in Africa: Third Pandemic
Plague in Britain (1500–1647)
Plague in China
Plague in East Asia: Third Pandemic
Plague in Europe, 1500–1770s
Plague in India and Oceania:
Third Pandemic
Plague in Medieval Europe, 1360–1500
Plague in San Francisco, 1900–1905
Plague in the Contemporary World
Plague in the Islamic World, 1360–1500
Plague in the Islamic World, 1500–1850
Plague of Athens
Plague of Justinian, First Pandemic
Plagues of the Roman Empire
Plagues of the Roman Republic
Pneumonic Plague in Surat, Gujarat,
India, 1994

Smallpox in Canada and the United States since 1783
 Smallpox in Colonial Latin America
 Smallpox in Colonial North America
 Smallpox in Europe's Non-American Colonies
 Smallpox in Premodern Europe
 Smallpox in the Ancient World
 Syphilis in Sixteenth-Century Europe
 Tuberculosis in England since 1500
 Tuberculosis in North America since 1800
 Tuberculosis in the Contemporary World
 Typhoid Fever in the West since 1800
 Yellow Fever in Colonial Latin America and the Caribbean
 Yellow Fever in Latin America and the Caribbean, 1830–Present
 Yellow Fever in North America to 1810
 Yellow Fever in the American South, 1810–1905

Epidemiology

Chadwick, Edwin
 Contagion and Transmission
 Contagion Theory of Disease
 Demographic Data Collection and Analysis, History of
 Epidemic
 Epidemiology
 Epidemiology, History of
 Farr, William
 Frost, Wade Hampton
 Historical Epidemiology
 Immunology
 Measles, Global Effort to Eradicate
 Paleopathology
 Poliomyelitis, Campaign Against
 Snow, John
 Virchow, Rudolf

Factors in Disease Outbreaks

Air and Epidemic Diseases
 Capitalism and Epidemic Disease

Children and Childhood Epidemic Diseases
 Contagion and Transmission
 Corpses and Epidemic Disease
 Diet, Nutrition, and Epidemic Disease
 Disease, Social Construction of
 Drug Resistance in Microorganisms
 Environment, Ecology, and Epidemic Disease
 Personal Hygiene and Epidemic Disease
 Geopolitics, International Relations, and Epidemic Disease
 Heredity and Epidemic Disease
 Human Immunity and Resistance to Disease
 Industrialization and Epidemic Disease
 Industrial Revolution
 Mallon, Mary
 Neolithic Revolution
 Personal Hygiene and Epidemic Disease
 Poverty, Wealth, and Epidemic Disease
 Race, Ethnicity, and Epidemic Disease
 Sexual Revolution
 Sexuality, Gender, and Epidemic Disease
 Slavery and Disease
 Trade, Travel, and Epidemic Disease
 Typhus and Poverty in the Modern World
 Urbanization and Epidemic Disease
 Water and Epidemic Diseases

Institutions

Bimaristan
 Hospitals and Medical Education in Britain and the United States
 Hospitals since 1900
 Hospitals to 1900
 Leprosarium
 Pest Houses and Lazarettos
 Sanatorium

Medical Personnel

Apothecary/Pharmacist
 Diagnosis and Diagnostic Tools

Empiric
 Medical Education in the West,
 1100–1500
 Medical Education in the West,
 1500–1900
 Hospitals and Medical Education in
 Britain and the United States
 Medical Ethics and Epidemic Disease
 Nurses and Nursing
 Physician
 Quacks, Charlatans, and Their Remedies
 Surgeon

Public Health

Cordon Sanitaire
 Demographic Data Collection and
 Analysis, History of
 Disinfection and Fumigation
 Farr, William
 Frost, Wade Hampton
 Gorgas, William Crawford
 International Health Agencies and
 Conventions
 Non-Governmental Organizations
 (NGOs) and Epidemic Disease
 Personal Liberty and Public Health
 Pesticides
 Plague and Developments in Public
 Health, 1348–1600
 Public Health Agencies in the West
 before 1900
 Public Health Agencies in Britain since
 1800
 Public Health Agencies, U.S. Federal
 Public Health in the Islamic World,
 1000–1600
 Public Health Posters
 Quarantine
 Sanitation Movement of the Nineteenth
 Century
 Smallpox Eradication
 Snow, John
 Vaccination and Inoculation
 Virchow, Rudolf

Religion

Biblical Plagues
 Black Death and Late Medieval
 Christianity
 Black Death, Flagellants, and Jews
 Islamic Disease Theory and Medicine
 Leprosy, Societal Reactions to
 Magic and Healing
 Pilgrimage and Epidemic Disease
 Religion and Epidemic Disease

Slavery

Colonialism and Epidemic Disease
 Civil War, American
 Latin America, Colonial: Effects of
 Imported Diseases
 Measles in the Colonial Americas
 Race, Ethnicity, and Epidemic Disease
 Scapegoats and Epidemic Disease
 Slavery and Disease
 Smallpox in Colonial Latin America
 Smallpox in Colonial North America
 Smallpox in Europe's Non-American
 Colonies
 Yellow Fever in Colonial Latin America
 and the Caribbean
 Yellow Fever in North America to 1810
 Yellow Fever in the American South,
 1810–1905

War

Biological Warfare
 Bioterrorism
 Colonialism and Epidemic Disease
 Malaria and Modern Military History
 Napoleonic Wars
 Smallpox and the American
 Revolution
 Thirty Years' War
 Typhus and War
 War, the Military, and Epidemic
 Disease

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Foreword

Pandemics, epidemics, and infectious diseases have long been the deadliest challenges to human existence, greatly outstripping wars, accidents, and chronic diseases as a cause of mortality. They have filled history books and have been woven into the fabric of popular and religious culture: examples include the Pharaonic “plagues” of the Old Testament and the many later “plagues” of ancient Greece and Rome; the writings of Boccaccio, Machaut, and Petrarch about the Black Death; Daniel Defoe’s long-running 1722 best seller memorializing London’s 1665 plague epidemic, *A Journal of the Plague Year*; and the dying consumptive heroines of Dumas and Murger, widely read and then reimagined operatically in *La Traviata* and *La Bohème*.

Much about infectious diseases has changed in the modern era, with the availability of vaccines, antimicrobial therapy and other interventions; however, much remains eerily familiar. We still face the unpredictable appearance of new diseases such as SARS, H5N1 avian influenza, and HIV/AIDS. We still read and see and listen to the plague artistry of earlier times, with the same morbid fascination, but we also find and cherish contemporary “plague art.” Popular histories about epidemics continue to become best sellers, such as John Barry’s *The Great Influenza*, about the 1918–1919 pandemic. *Outbreak*, a film about a deadly viral pandemic threat, has been seen by millions of people and remains popular more than a decade after its 1995 release. “Andromeda strain,” taken from the title of a 1969 book about a potentially world-ending pandemic, has even entered the standard English vocabulary.

Although a deep-seated public fascination with plagues, pestilences, and pandemics is obvious, many encyclopedic works on the subject already sit on library shelves. Is there anything new to say in 2008 that has not already been said countless times before? I think the answer is a resounding Yes. Our understanding of infectious diseases has grown steadily in the past two decades, thanks in large part to the new tools of molecular biology. Much of this new knowledge is incorporated into the entries in this encyclopedia.

Let us put this new knowledge into perspective. More than a century ago, Robert Koch's 1876 publication on anthrax, the first fully characterized infectious disease, was followed by an explosion of microbiological knowledge. A new "microbial era" quickly produced passive immunotherapies, vaccines, and antimicrobials. Long before 1900, scientists began to predict the eventual eradication of infectious diseases. Unfortunately, optimism was premature: old epidemic diseases such as tuberculosis and dengue fever simply refused to go away, and more than 30 new ones have been recognized in the past four decades alone.

The U.S. Institute of Medicine's influential 1992 report—*Emerging Infections: Microbial Threats to Health in the United States*—took a new approach, one that profoundly impacted our thinking about "newly emerging" and "reemerging" infectious diseases. Since that report, it has become more widely recognized that men and microbes exist in complex dynamic ecosystems that are continually perturbed and unsettled not only by interactions between the microbes and humans themselves, but also by human movement, crowding, climate, environmental damage, and many other interrelated factors. With their superior ability to adapt to new ecologic opportunities by rapid replication and genetic change (e.g., by mutation), microbes always threaten to gain the upper hand over their slowly evolving human counterparts. Such microbial genetic advantages must be offset by human ingenuity and by a broader understanding of infections in their total context. This includes not only variables of the microbial agent, the human host, and the environment, but also the impact of societal choices, behaviors, and policies on disease emergence, spread, and control. Addressing the problem in this way requires not only the efforts of basic scientists, epidemiologists, and physicians, but also entomologists, environmental specialists, policy makers, bioinformatics experts, and many others, working together in interdisciplinary partnership.

Pestilence, pandemics, and plagues have always been among the greatest challenges to continued human existence. In learning about them we learn about who we are and about our human history, and we make connections across millennia that reinforce our identity, our heritage, and our shared human experience. The more we learn about emerging infectious diseases, the more we understand how deadly and persistent the challenge is and will remain, and the better able we will be to respond to future challenges that the microbial world is certain to present to us.

Readers should find this encyclopedia stimulating and informative. There are many lessons to be learned, but among the most important is this: the next pandemic waits in the wings for some convergence of critical determinants not yet imagined by any of us. How we respond may make a difference not only for ourselves, but for the rest of the world as well.

Anthony S. Fauci, M.D., Director of the National Institute of Allergy
and Infectious Diseases of the National Institutes of Health

Preface

This encyclopedia of infectious diseases in history grew out of a proposal for an encyclopedia of the Black Death that followed two volumes I wrote for Greenwood Press on the second plague pandemic. Greenwood's editors were correct to suggest a much broader, interdisciplinary work, given that existing works on the history of epidemic disease tended to be either chronological or topical by disease, or topical by place. Given the opportunity, I engaged a truly first-rate editorial board of medical historians, M.D.s, a microbiologist, and medical history librarians.

With their indispensable help, I crafted a list of entries that would take the nonspecialist advanced high school or college student from the basics of bacteria and viruses, through the intricacies of the human body and immunity to disease, to the major infectious diseases (and some others of growing relevance). Historical outbreaks constituted a second category of entries. We chose the major pandemics of plague, influenza, and cholera, of course, but we also included more tightly focused outbreaks that allowed for a closer analysis of the phenomena, their impacts, and the ways people dealt with them. A third major group of articles, we felt, needed to discuss the range of care-giving and treatments that developed independently of or in response to the great disease outbreaks. Physicians, nurses, pharmacists, hospitals, leprosaria, sanatoria, as well as sulfa drugs and antibiotics found their places in these pages. Related to these entries are those outlining major theories of disease and medicine that dictated cultural responses to epidemic disease. Desiring to be synthetic as well as specific in coverage, we decided to commission a series of longer entries on historical (and contemporary) factors that have affected the emergence and spread of epidemic diseases. Some of these are natural (air, water, the environment) but many are social, economic, and political: colonialism, war, poverty, urbanization, and the sexual revolution, for example. A final broad category covers effects or responses to disease, including media and artistic responses, international health organizations, and effects on personal liberties. We chose these categories and topics with a view

to both the basics and to geographical and chronological diversity. We make no claims of completeness or comprehensiveness but do hope that we have provided a variety of materials that will stimulate and aid research, both informing and leading the reader to other fruitful sources.

To aid internal searching, we have provided an alphabetical list of all entries in the front matter, as well as an index at the end of Volume 2. Each entry includes a list of related entries under “See also,” while terms with their own entries that appear in the text are boldfaced for easy identification.

Arcing across the nearly 300 articles are certain themes that should serve a student well: colonialism, war, the development of Western medicine, the roles of migration and modern globalization, and the continuing plight and challenges of much of the underdeveloped world in the face of established and emerging diseases. We have chosen some of these themes and grouped relevant entries in the Guide to Related Topics that follows the List of Entries in the front matter. Entries have been written and edited for use by students with minimal backgrounds in biology, and a glossary of predominantly biomedical terms has been appended. Each entry has a list of suggested readings, and many have useful Websites. A broad bibliography of Websites, books, and articles appears at the end of Volume 2.

In acknowledging my own debts to those who made this work possible, I would like to begin with the 101 authors from around the world who lent this project their time and expertise. The outstanding credentials of our editorial board members—Ann Carmichael, Katharine Donahue, John Parascandola, Christopher Ryland, and William Summers—are listed elsewhere, but let me assure the reader that without their contributions from conception to final editing, these volumes would have but a fraction of their merit. Each has gone well beyond any contractual obligations, each in his or her own ways, and any and all flaws are mine alone. Greenwood Press has provided me with a very helpful and supportive editor in Mariah Gumpert who has overseen this work from start to finish. I also wish to acknowledge the local efforts of Sarah Bennett, who developed the illustration program for the encyclopedia, Rebecca and Elizabeth Repasky who compiled the glossary and edited portions of the text, and Elizabeth Schriener who gathered many of the Website citations scattered about these pages. Finally, I wish to thank Belmont University, my home institution, for providing me with the academic leave and many of the means necessary to pull this project together.

Introduction

In *War of the Worlds*, English novelist H. G. Wells presented the gravest of imaginable threats to human life on earth: bellicose extraterrestrial invaders. Humanity laid prostrate, our weapons useless, our future bleak. The final outcome reflected Wells's genius as well as his time: simple terrestrial germs killed off the mighty aliens, and the war was won. What caused humans mere mild discomfort proved fatal to the beings whose bodies were not prepared for the microbial onslaught. Of course, this has long been part of the human condition on our own planet. Epidemiologists call this phenomenon a “virgin-soil epidemic,” and throughout history human populations have lost their battles with “simple terrestrial germs.” Plague killed perhaps 40 percent of the Western world in the late 1340s; Mayas and Aztecs fell by the tens of thousands to the measles and smallpox brought by European colonists; and in the nineteenth century, Africa's pathogen-rich environment earned it the fitting nickname “white man's graveyard.”

We literally swim in a sea of germs, and our bodies are coated inside and out with a wide range of bacteria, viruses, mites, fungi, and other tiny hitchhikers. Most are benign, many helpful, and some potentially harmful. But add the wrong microbe into the mix, and the mighty human organism, like Wells's Martians, shudders and halts—and may shut down altogether.

When these microbes can be transmitted to other people, we call the resulting illnesses infectious disease. When the same disease extends across a broad population, we call it an epidemic. Anthropologists generally agree that humans became susceptible to epidemics when we settled in large villages and early cities in the later Neolithic period of human prehistory. Our own “war of the worlds”—the human organism vs. deadly microorganisms—has thus been going on for thousands of years, and until recently we have unvaryingly lost. And although modern science has reduced many former scourges to minor threats, we remain locked in mortal combat with many—both old and new—and in apprehension of the next wave of pathogenic assault. The

founders of the scientific method noted that we have to understand nature and its processes before we can control them, but knowledge about microbes came very recently and still does not ensure victory.

Thirty years before this writing, scientists, policy-makers, doctors, volunteers, nurses, donors, and civil servants finally eliminated deadly smallpox from nature. But though it was the first, it is still the only human disease to be eradicated, despite the best intentions and efforts of experts, technicians, officials, and men and women of good will. Each year the World Health Organization and the U.S. Centers for Disease Control and Prevention monitor the fluctuating incidence of a long list of diseases and the lives they take. Old standards such as malaria, tuberculosis, and polio beef up the statistics, as do recent arrivals such as AIDS, Lyme disease, and West Nile Fever, and reemerging conditions such as cholera and Hansen's disease (leprosy). Footnotes account for the patterns of flux: wars, changing economic and social conditions, new encroachments on virgin natural areas, human migration, and natural processes such as genetic mutation and environmental change. Through jet travel, a minor, local outbreak of an exotic disease can find its way into dozens or hundreds of human communities within days. The "war" is far from over.

There is an ongoing flow of books that tell the story of "man vs. microbe," or narrow parts of it, and many of these are listed at the end of entries or in the bibliography at the end of these two volumes. These serve the general reading public as well as the historian and student of medical history. The present work cannot replace a ripping good medical yarn, and its editor and his collaborators have no intention of trying to do so. Instead we seek to place in the hands of the interested lay reader or student a collection of thought-stimulating and question-answering essays that will complement deeper research or merely provide accurate, condensed information to the curious. The fact that sites on the Internet seem capable of doing just this may seem to make a work like ours, or any reference book, rather quaint and clumsy by comparison. In fact, each of our contributors has taken the Web, as well as other publications, into account in preparing the present articles. The result is a sound, authoritative source covering a very wide and interdisciplinary range of topics connected to the history and science of infectious disease.

As I edited each entry and added the bolding to cross-listed terms, and compiled the "see also" lists, I was struck by and increasingly satisfied with the rich texture of interrelationships among the entries. Each reader, each student preparing to write on a relevant topic, should make use of the several tools that we have provided to help one profit from this texture. Each entry mentions related entries and provides recent or classic books and/or articles on its topic. The List of Entries—and, even better, the Guide to Related Topics—goes further in suggesting relationships between subjects. The index gives a quick overview of topics that go beyond the entry titles, and provides a clear gauge of the depth of coverage in these two volumes.

The types of discussion that fall under the broad heading of infectious disease are far more varied than may first seem evident. If I consider my senior year in high school, I can imagine using this volume in English Lit (seventeenth-century plague literature); U.S. History II (Spanish Flu in 1918 to 1919); Advanced Biology (any given disease); fourth-year German (Thomas Mann and his tuberculosis); and Religion (comparative religious theories of disease). At the other end, our essays on topics such as "News Media and Epidemic Disease," "War, the Military, and Epidemic Disease," "Colonialism and Epidemic Disease," or "Urbanization and Epidemic Disease" could spawn and help shape senior or

even masters-level university theses. Teachers preparing units or professors preparing courses on medical history or disease in history will find our content stimulating and relevant, and, we believe, written at a level appropriate to our students. As I stated in the Preface, this work is by no means comprehensive or definitive, nor is it meant to be. If the reader is patient and systematic, however, I firmly believe it will prove to be very useful indeed.

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A

ACQUIRED IMMUNE DEFICIENCY SYNDROME. See Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS).

AIDS. See Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS).

AIDS IN AFRICA. Over 25 years have gone by since the onset of the **Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome**, or HIV/AIDS, **pandemic** in the world, and yet the syndrome continues to take lives throughout the developing world, particularly in Sub-Saharan Africa. In the 10 worst affected countries, all of them in eastern and southern Africa, rates of HIV infection range from 16 percent to over 40 percent. Estimates by United Nations AIDS (UNAIDS) indicate that at the end of the year 2007, 22.5 million people were living with HIV in Africa, and that approximately 1.7 million additional people were infected with HIV during that year. During the same year, over 1.6 million people were estimated to have died from this syndrome. Since its onset in the 1980s, well over 11 million **children** on the continent have been orphaned by AIDS.

Initial Response to the Epidemic. Given these staggering statistics, many have observed that the human and social ramifications of AIDS are complex and wide-ranging. They threaten stability, exacerbate inequalities within and between countries, undermine previous gains in development, and harm children. At the onset of the **epidemic** in the early 1980s, initial responses were often guided by fear and ignorance. At that time, AIDS evoked intense fear in the United States, where many began a clarion call for **quarantine**—which historically has been the usual method of dealing with epidemics. The call for quarantine was made in spite of the fact that previous efforts to control epidemics such as **leprosy, cholera, tuberculosis**, and drug addiction through quarantine of large numbers of people were never successful. Association of the disease with homosexuality and Afro-Caribbeans from Haiti added layers of stigma to both victims and the disease itself.

By the mid-1980s, the disease was reported in Rakai District in Uganda, as well as other central African countries. Although the geographic origins of AIDS may never be known, at that time many Western scholars, including prominent geographers in the United States, began to point a finger at Africa as the origin of the **virus**. Indeed, the complex but hypothetical map drawn by Gary Shannon, Gerald Pyle, and Rashid Bashshur in 1991, showing the routes that the epidemic took to diffuse from Central Africa via Europe and Haiti to America, became accepted as the truth rather than as mere speculation on the part of these authors. This unleashed hysteria throughout the developed world. Specifically, Belgium began testing African students for the virus, arguing that it was useless to invest scholarships in students who were ill and were soon going to die. Similarly, the U.S. government under President Ronald Reagan (1911–2004) advocated the quarantining, deportation, or denial of entry visas to those with the virus.

As the pandemic began to spread rapidly in the late 1980s in Sub-Saharan Africa among men and women (i.e., heterosexual as opposed to homosexual transmission), some scholars began to offer prejudiced explanations as to why it was spreading so rapidly. They stated that the virus had jumped from monkeys to humans because Africans were having sex with monkeys. Others stated that it had jumped to humans through the peculiarities of African culture in which Africans applied monkey blood to their genitals as an aphrodisiac. Since the disease in the United States was initially found among homosexual men, some scholars set out to uncover homosexuality in Africa, even when the facts failed to support their paradigm. Indeed, on the assumption that homosexuality is a universal phenomenon, scholars looked across the continent to find homosexual populations, gay bathhouses, and other elements of a homosexual cultural landscape. Failing to find this evidence, they concluded that African homosexuality must be carefully concealed.

These ethnocentric and racist explanations from the developed countries, combined with the fear of stigmatization, denial of entry visas by Western countries, and the possible loss of the lucrative tourist **trade**, resulted in vehement denials by many African leaders about the existence of the epidemic in their countries. Some counteracted the accusations by claiming that AIDS was a disease of white people. For example, President Daniel arap Moi of Kenya (b. 1924) spent the first four years of the growing pandemic denying that there was any HIV in his country and ascribing reports of it to a deliberate hate campaign against his country. He threatened to remove the visas and deport any foreign journalist reporting AIDS and waited until 1986 before allowing even the most innocuous “AIDS guidelines” to be published. Meanwhile, he instructed the Ministry of Health to under-report the known cases, on the grounds that many of those with AIDS were “not Kenyans.” While this was going on, the seropositivity rate of commercial sex workers in Nairobi rose from 17 percent to almost 100 percent by 1990. A similar story of denial was repeated in other countries such as Malawi, Tanzania, Zambia, and South Africa. It was not until 1990 that African governments reluctantly started to acknowledge that the disease was spreading widely throughout their countries. This acknowledgment came too late to launch an effective AIDS control program. The damage was already done.

Even in the early 2000s, many African leaders continued to be in denial and questioned the existence, cause, and treatment of AIDS. For example President Thabo Mbeki (b. 1942) of South Africa stunned the AIDS industry and its critics in February of 2000 when he announced that he would host an international panel of experts to examine the science of AIDS, its treatment, and the role of the **pharmaceutical** companies. The panel

that met in Pretoria in May 2000 included both supporters and critics of the “HIV-causes-AIDS model.” At this panel “HIV-causes-AIDS” critics embraced the opportunity to participate in an open exchange of scientific ideas, whereas proponents of the notion that HIV causes AIDS expressed indignation, not-so-veiled threats, and insults. Thabo Mbeki, the first head of state to rethink the HIV-causes-AIDS issue, was and remained suspicious of the idea of a single virus causing AIDS. Although Mbeki was ridiculed in the media as being out of touch with reality, his call for a reconsideration of the epidemic was soon being taken seriously. Mbeki’s debate received great attention, and a number of issues emerged from the debate, including the recognition of **poverty** as an issue in HIV/AIDS infection. Other African leaders have propagated the story that HIV/AIDS was created in U.S. labs and exported to Africa to kill Africans. Rumors are rife in many African settings that even the condoms touted to stop the **transmission** of AIDS are already tainted with the virus at manufacturing plants in Western countries and then exported to Africa to infect Africans. It is within this context that the lukewarm response of African leaders to tackling the disease needs to be understood. Without this context, it is difficult to understand why African governments and peoples are often skeptical of receiving or implementing HIV prevention programs from developed countries.

Geographic Spread. Regarding the geographic spread of the epidemic in Africa, John Iliffe, in his book *The African AIDS Epidemic* (2006), masterfully synthesizes the plethora of studies that have been conducted from the 1980s to the present, tracing the geographic beginnings and spread of AIDS throughout the continent. Iliffe weaves together a story that attempts to explain the origins, nature, and spread of the virus from its detection in the early 1980s to its current progression throughout the continent. He places the origins of the disease somewhere in central Africa, where it spread slowly to East Africa. In the 1990s, the disease moved to southern Africa, where it has wreaked havoc and where the pandemic remains the most intense. Using sentinel surveillance data that began to be collected in the mid-1980s, along with advanced mapping techniques, Ezekiel Kalipeni and Leo Zulu traced the geographic trajectory of the disease. Their findings, as shown in the accompanying maps, support Iliffe’s picture and clearly delineate the progression of the disease from somewhere in central Africa, to eastern Africa, and finally to southern Africa.

The maps show interpolated HIV prevalence rates and the spatial-temporal progression of HIV/AIDS across Sub-Saharan Africa for the years 1986, 1990, 1994, 1999, and 2003. These maps show that southern Africa has consistently had HIV prevalence rates in excess of 5 percent since 1986, and parts of North and West Africa have generally had the lowest prevalence, below 5 percent. However, over time the epicenter of HIV/AIDS (10 to 20 percent prevalence) located in the Great Lakes region of East Africa (Burundi, Rwanda, Tanzania, and Uganda) and an isolated pocket in West Africa (Guinea-Bissau) in 1986 had by 1990 expanded in both prevalence level and spatial extent within the Great Lakes region and had developed a second nucleus in the southern Africa region (Zimbabwe, Zambia, Mozambique, and Malawi). By 1994 a more intense (15 to over 30 percent) southern Africa epicenter had expanded to include Botswana and parts of South Africa, whereas the Great Lakes nucleus had broken down into isolated pockets, and a new nucleus had developed over Ethiopia/Eritrea. The years 1999 and 2003 saw an even more intense southern Africa expansion to include Namibia, South Africa, Swaziland, and Lesotho, with isolated, less intense pockets in the East Africa region (Kenya, Uganda, Tanzania, and Ethiopia) and in Cameroon and Côte d’Ivoire in West Africa. The spatial-temporal trends

so vividly brought out by these maps largely conform with UNAIDS estimates of an escalating epidemic in southern Africa and with signs of stabilization or decline in the East African region. In the early 2000s, southern Africa remained the worst-affected subregion in the world, with HIV prevalence rates in excess of 25 percent, a sharp rise from around 5 percent in 1986. In short, these maps lend credence to the saying that “there is not just one epidemic in Africa, but many.” West Africa and North Africa have consistently experienced lower rates than the other regions, although in some countries in West Africa, the epidemic is creeping up. Even within the other high-risk regions, some areas have lower rates than others.

Causes and Consequences. Once the disease was established in Africa in the early 1980s, it found fertile ground and began to spread like wildfire. The causes of the rapid spread are many and complex. There are both macro- and micro-level dimensions that put African peoples at very high levels of vulnerability to this disease. These dimensions are rooted in the history of the continent, especially its colonial interlude. The historical context of **colonialism** and its economy based on labor migration, contemporary gender issues, **poverty** and disease burden, global forces, government commitment, and the cultural context have all intertwined in complex ways to put peoples of Sub-Saharan Africa at risk of contracting HIV. It must be understood that while people’s behavior and actions are inherently important factors in determining vulnerability to HIV, the context is even more critical. Thus, any assessment of HIV vulnerability has to include global, national, regional, and community factors that influence or exacerbate personal vulnerability. Thus the political, cultural, social, and economic contexts—and particularly the colonial economy based on labor migration—made Sub-Saharan Africa susceptible to the rapid spread of the epidemic. These factors result in situations of powerlessness of individuals and communities at large.

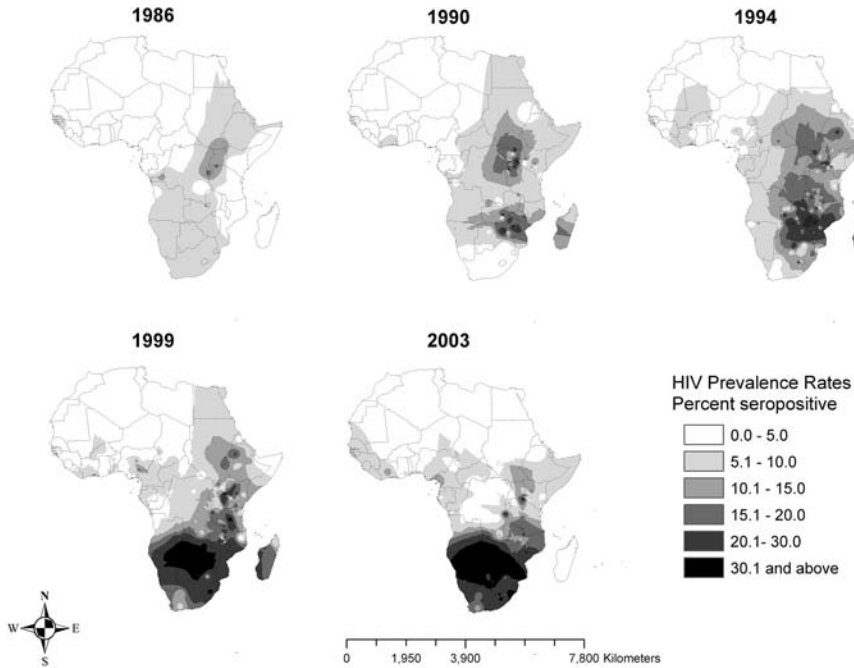
The impacts of HIV/AIDS on the critical infrastructures that sustain the security, stability, and viability of modern nation-states are manifold. For the African peoples, the consequences have been tragic. In Africa, HIV/AIDS continues to undermine education and health systems, economic growth, micro-enterprises, policing and **military** capabilities, political legitimacy, family structures, and overall social cohesion. The initial impact of AIDS is the suffering of individuals and their immediate families. But a more insidious impact is its threat to the development gains of communities and nations. African countries are hard-pressed to provide health care, treatment, and support to a growing population of people with HIV-related illnesses. In times of ongoing economic and political turbulence, African governments are finding it difficult to launch costly aggressive campaigns to reduce the increasing annual toll of new HIV infections by enabling individuals to protect themselves and others. It is further estimated that, so far, over 20 million people in Africa have died from this epidemic, leaving behind millions of orphans and other survivors. This has put further strain on communities and on national development. In the worst-hit countries, life expectancy has declined significantly. Average life expectancy in Sub-Saharan Africa is now 47 years, when it could have been 62 without AIDS.

The Way Forward. Yet in spite of the tragic consequences that have been brought upon the peoples of Africa by this epidemic, there is light at the end of the tunnel. Belatedly, the international community has been begun to galvanize itself in providing life-saving antiretroviral medications. Although the number of people receiving these vital medications is minuscule in comparison with the need, the efforts at providing such medications at subsidized rates or for free are commendable. Governments in the West, in

cooperation with international pharmaceutical corporations, are also in the process of supporting the ongoing research on vaccine development. Other positive trends are the growth of grassroots political activism in Africa and the emergence of compassionate organizations such as The AIDS Support Organization (TASO) in Uganda, and Treatment AIDS Campaign (TAC) in South Africa. These are all signs of the local and international cooperation necessary to at least stabilize but possibly even reverse the patterns of the pandemic disease.

Indeed, there is growing evidence that in some countries the epidemic has leveled off. In others it is actually on the decline (e.g., Uganda), and in still others, where government commitment was strong immediately after the epidemic was recognized, the prevalence rates have been kept at very low levels (e.g., Senegal). Although the epidemic continues to ravage the continent, Uganda and Senegal appear to have implemented successful and sustainable efforts to combat the HIV/AIDS crisis. In Uganda, HIV prevalence and incidence rates that were on the increase in the 1980s began to decline significantly during the 1990s. In Uganda's capital city, Kampala, the prevalence rate in 1992 was as high as 20 percent among pregnant women visiting prenatal clinics; today it is about 7 percent. In other sites in Uganda, mostly rural, this rate was 9 percent, whereas today it is about 4 percent. Seroprevalence among 15- to 19-year-old pregnant women, which is believed to be reflective of HIV incidence, fell sharply from the early 1990s until 1996, and since then has remained low. In the case of Uganda, success stems from the fact that although most African governments buried their heads in the sand, the government of Uganda acknowledged the AIDS crisis as early as 1986 and began mobilizing both domestic and international support to combat it. In addition to high-level political support with multi-sectoral response, Uganda's prevention efforts included a range of social strategies. These included raising the legal age for sexual intercourse; social mobilization that reduced stigmatization and discrimination; decentralized planning and implementation for behavior change communication (BCC), which reached the general population and key target groups; confidential voluntary counseling; social marketing and use of condoms; increased emphasis on control and prevention of sexually transmitted infections; and a decrease in multiple sexual partnerships.

The second success story is Senegal, which acted early enough to tackle the disease before it had spread widely in the general population. Whereas politicians in some other countries ignored the threat of AIDS for fear of alienating conservative supporters by initiating a discussion about safe sex, politicians in Senegal vigorously supported efforts to confront the epidemic. The government of Senegal mobilized its meager resources to set up an ambitious program to stop HIV in its tracks. Senegal's program hinged on strong political leadership that was willing to work hand in hand with religious and community leadership, and on mobilization of the young, including sex workers and their partners, to practice safe sex. Whereas it is true that Sub-Saharan Africa remains by far the worst affected region in the world, these two examples of success offer a sign that it is possible to stem the tide of the epidemic if governments and concerned communities work together. *See also* AIDS in the United States; Animal Diseases (Zoonoses) and Epidemic Disease; Hemorrhagic Fevers in Modern Africa; Hospitals since 1900; International Health Agencies and Conventions; Non-Governmental Organizations (NGOs) and Epidemic Disease; Personal Liberties and Epidemic Disease; Poison Libels and Epidemic Disease; Popular Media and Epidemic Disease: Recent Trends; Race, Ethnicity, and Epidemic Disease; Sexuality, Gender, and Epidemic Disease; Vaccination and Inoculation.



HIV/AIDS Prevalence Rates for Selected Years. Courtesy Ezekiel Kalipeni and Leo Zulu. Adapted from Kalipeni, E. and Zulu, L. 2008. "Using GIS to Model and Forecast HIV/AIDS Rates in Africa, 1986–2010." *Professional Geographer* 60(1).

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EZEKIEL KALIPENI

AIDS IN THE UNITED STATES. Acquired immunodeficiency syndrome (AIDS) was first recognized in American medical literature in mid-1981. It was named just over a year later to describe the multiple symptoms seen in patients that were the result of an underlying immune deficiency caused by infection with the **human immunodeficiency virus (HIV)**. In the United States, AIDS was discovered in major homosexual communities of large cities and often initially called “gay-related immune deficiency (GRID)” or “gay cancer.” By 1983 medical practitioners and the public came to realize that AIDS could and did affect many others, especially intravenous drug users who shared needles and those who received tainted blood products during medical procedures. The U.S. Food and Drug Administration approved the first successful drug therapy, AZT, in 1987. While AIDS activist groups protested the supposed lack of government interest in AIDS and AIDS-related research, laboratories developed multi-drug “cocktails” with varying levels of effectiveness, releasing the first in 1993. In recent years, AIDS has become entrenched in marginalized communities where preventive and therapeutic interventions have been unavailable or have not been adopted.

Recognition of AIDS as a New Disease. Medical research studies indicate that the first, unrecognized cases of AIDS probably occurred in West Africa, where the causative virus mutated from a form that infected monkeys to one that could infect humans. Why, then, was AIDS first recognized as a new disease in the United States? The answer lies in the differences between the ways in which medicine is practiced by **physicians** and experienced by patients in Africa and in the United States. Individuals in Africa who succumbed to AIDS in the decades before 1981 were most often poor, rural people who rarely consulted physicians practicing Western medicine. Conversely, such physicians, upon seeing an African with a fever and wasting, would likely attribute the symptoms to any of a host of diseases present in tropical countries. The earliest AIDS patients in the United States, in contrast, were largely Caucasian, upper-middle-class people with health insurance who regularly consulted physicians when they fell ill. Their physicians recognized a disruption in the medical history of their patient populations that led them to question idiosyncratic diagnoses and wonder about the possibility of a novel disease process.

Specifically, in the late 1970s, U.S. dermatologists began seeing young men with rare cancerous lesions (Kaposi’s sarcoma) normally found on elderly Mediterranean men. In early 1981, infectious disease physicians encountered patients with infections, especially *Pneumocystis carinii* pneumonia (PCP), associated normally with patients whose immune systems had been compromised because of cancer treatments. In June 1981, the cases seen in Los Angeles were described in a short paper in the *Morbidity and Mortality Weekly Reports*, a weekly publication issued by the U.S. **Centers for Disease Control and Prevention** (CDC) in Atlanta. Additional papers followed in July and August, all of which observed that the affected patients were previously healthy homosexual men living in gay communities in large cities.

By June 1982, cases of AIDS outside gay communities had been observed, including cases in newborn babies, heterosexual patients who had undergone surgery, Haitian immigrants, and persons who regularly received blood products to treat their

hemophilia (a genetic disease characterized by the inability to clot blood). AIDS became known at this time as the “4-H” disease because it had been observed in homosexuals, heroin addicts, Haitians, and hemophiliacs. Epidemiologists understood, however, that these categories of patients also suggested a blood-borne cause. If AIDS were transmitted by blood, the nation’s supply of whole blood and blood products was at risk, a finding that many people, including those who managed blood banks, did not want to believe. Hemophiliacs previously tolerated the possibility of infection with **hepatitis B** virus because the value of the clotting factor produced from pooling serum outweighed that risk. Hemophiliacs and their families were horrified, however, by the prospect that the lifesaving blood product might harbor a lethal disease agent. After 1983, when the virus was first isolated in the Paris laboratory of Dr. Luc Montagnier, HIV was demonstrated to be the cause of AIDS. By mid-1984 transfusion-transmitted viruses were no longer considered acceptable risks in reaping the benefits of blood products. An enzyme-linked, immunosorbent assay (ELISA) for antibodies to HIV, developed for use in laboratory research on the etiology of AIDS, was adapted in 1985 as a screening test for blood and blood products. In 1987 the U.S. Food and Drug Administration (FDA) issued regulations requiring such screening, and in 1988 the FDA began inspecting 100 percent of FDA-regulated blood and plasma donor facilities to enforce screening regulations.

Another consequence of the development of sensitive **diagnostic** tests for HIV was the transformation of the definition of AIDS. Between 1981 and 1986, the CDC issued successive statements about which opportunistic infections and cancers could be used as the basis for a diagnosis of AIDS. Diseases such as *Pneumocystis carinii* pneumonia, candidiasis (a yeast-like infection) of the esophagus or lungs, toxoplasmosis of the brain, and Kaposi’s sarcoma were included early. General wasting symptoms, such as ongoing diarrhea and severe pelvic inflammatory disease in women, were less clearly a part of the “syndrome” caused by the acquired immunodeficiency. Details about the various diagnoses mattered because health insurers and the U.S. federal government based reimbursement payments and access to clinical trials on such information. In August 1987, the CDC revised its definition of AIDS from a list of particular illnesses to any illness that resulted from a long-term infection with HIV. Since that time, the name used for the disease has been “HIV/AIDS.”

Social, Religious, and Political Reactions to AIDS. The social stigma carried by AIDS as a sexually transmitted disease resulted in what some public health leaders called “a second **epidemic** of fear.” From 1983 to 1987, when public fear and panic were at their most destructive, some religious groups proclaimed that AIDS was God’s vengeance on the gay community for violating what they viewed as **biblical** prohibitions against homosexuality. Injecting drug abusers were also viewed as people who made wrong “lifestyle” choices that led to disease. Hemophiliacs, surgery patients who received infected blood, and women who were infected by their spouses, in contrast, were viewed as “innocent” victims of AIDS. This division of people with AIDS into guilty and innocent categories led advocates of conservative views to support research on drugs to treat AIDS but to oppose any public expenditure for condom distribution or needle exchange programs for drug addicts. Teaching personal responsibility—through sexual abstinence and “just say no” to drugs campaigns—was their preferred approach to AIDS prevention efforts. Social and religious reluctance to discuss **sexuality** in any public setting exacerbated the obstacles to effective public education about AIDS.

Individuals diagnosed with AIDS or as having antibodies to HIV were sometimes fired from their jobs. Police officers, firefighters, ambulance personnel, and other health-care workers occasionally refused to take care of AIDS patients. Young Ryan White (1971–1990) in Indiana and three brothers—Ricky (1977–1992), Robert (1978–2000), and Randy (b. 1979) Ray—in Florida, all hemophiliacs who contracted AIDS from contaminated blood products, were denied entrance to schools. Even as medical research demonstrated that AIDS was not transmissible through casual contact, the epidemic of fear moved an arsonist in Arcadia, Florida, to set fire to the Ray brothers' house and the school board in Kokomo, Indiana, to insist that Ryan White take classes over the telephone to avoid accidentally touching his classmates.

The most important tool used by public health leaders to counter this fear was accurate communication about AIDS. Sharing new information as soon as it became available often made the difference between keeping and losing staff at hospitals, firehouses, police departments, and other public service agencies. A concerted education program about AIDS and how it was transmitted helped to diffuse fear in school systems. On the national level, U.S. Surgeon General C. Everett Koop (b. 1916) issued an informational report on AIDS in 1986 and two years later mailed a flier titled "Understanding AIDS" to every household in the United States.

October 2, 1985, marked a turning point in the history of AIDS in America. On that date, Hollywood actor Rock Hudson (1925–1985) died of AIDS. Hudson's death seemed to bring home the point to a broad public that anyone, even a movie star, could contract AIDS. The publicity surrounding Hudson's death motivated the U.S. Congress to appropriate significantly more money for AIDS research than it had been willing to commit previously. During the 1990s, other celebrities with AIDS—including the tennis player Arthur Ashe (1943–1993) and Elizabeth Glaser (1947–1994), wife of actor Paul Michael Glaser—as well as others without AIDS, such as Elizabeth Taylor (b. 1932), became public spokespersons for raising money to combat AIDS and raising awareness that people with AIDS should be treated fairly and with compassion.

Throughout the 1980s within the gay community, AIDS activists worked from the earliest years of the epidemic to provide care for sick individuals, to raise money for foundations, to lobby the federal government to increase research, and to make possible therapies available more quickly than the traditional drug approval process would allow. To draw attention to their cause, some of the activists staged public demonstrations, or "street theatre," designed to attract national media attention. In 1987 the organization AIDS Coalition To Unleash Power (ACT UP) was formed by activists in New York City with the initial goal of gaining the release of experimental drugs. Soon ACT UP expanded to advocate for other AIDS issues as well. ACT UP's numerous protests were so successful that they became a model for advocates for other diseases.

A more politically vexed public health policy was the decision about whether to close bathhouses in the gay communities of San Francisco, Los Angeles, and New York. The bathhouses represented for many in the gay community a civil rights triumph. After years "in the closet" for fear of losing jobs or being physically attacked, they could openly declare their gay identities and socialize in public at gay bathhouses and bars. They argued that bathhouse clients were intelligent enough to begin protecting themselves once informed of the need for safe sex, and that because they were the principal population at risk for AIDS, conducting AIDS prevention education at the bathhouses would lower the rate of **transmission** of the virus in the entire community. Others in the gay community, bolstered by some public health

**“BATHHOUSES REFLECT AIDS CONCERNS,”
NEW YORK TIMES, OCTOBER 14, 1985**

Attendance has declined at the 10 homosexual bathhouses in New York since the onset of the AIDS epidemic, according to the city’s Department of Health. But some of the owners report that business remains profitable despite mounting public pressure that the baths be closed.

“I’ve gone through my own particular moral crisis with this,” said Bruce Mailman, a homosexual and a Lower East Side real-estate entrepreneur who owns the St. Marks Baths, as well as the Saint, a homosexual discotheque. “Am I profiting from other people’s misery? I don’t think so. I think I’m running an establishment that handles itself as well as it can under the circumstances.”

Mr. Mailman reports a 50 percent decline in attendance since 1982, while Jim Schwartz, who describes himself as a minority stockholder at the East Side Sauna, one of the city’s smaller bathhouses, said business had declined 25 percent, from nearly 2,000 customers a week to about 1,500.

Neither of the owners was willing to describe his profits in detail, but both said that if they were not making money they would close their doors, as five other local bathhouses have done in recent years.

FORUMS FOR EDUCATION

With nearly 14,000 cases of AIDS reported nationwide, 6,700 in New York, homosexual men are increasingly calling for the closing of the baths, and many are criticizing homosexuals who profit from their operation.

Both Governor Cuomo and Mayor Koch are reconsidering their positions that such places, licensed by the city’s Health Department, are useful forums for educating homosexuals about the sexual practices that spread acquired immune deficiency syndrome, which is usually fatal.

“Because the circumstances have changed, because political opinion makes us bad guys, that doesn’t mean I’m doing something morally incorrect,” said Mr. Mailman.

leaders, believed that since multiple unprotected sex acts took place in bathhouses, classic public health practice dictated that closing the bathhouses would help stop transmission. In 1984 the argument was settled in San Francisco when political and public health leaders agreed that the bathhouses should be closed. The following year Los Angeles and New York City also moved to close bathhouses.

Public education programs in the United States about AIDS were strongly split in content according to which group produced them. Those funded by the U.S. government emphasized “getting the facts” about AIDS. There was virtually no emphasis in government-funded educational campaigns on communicating specifically to the gay community or on discussing safe sex through the campaign’s posters. AIDS community action groups and other private-sector groups took the lead in producing stark, graphic messages that communicated the urgent need for condom use and clean needles.

One segment of American society that proved particularly difficult to reach with AIDS prevention messages was the African American community. Traditionally, the black church had been the most effective vehicle for communicating health messages within the African American community, but strong sentiments against homosexuality within the black church made safe gay sex extremely difficult to address. The African American community also had scant trust of health messages from the federal government because of the infamous Tuskegee *syphilis* study, in

which African American men in Alabama had been left untreated for the disease without their knowledge or consent in order for the effects of syphilis in untreated patients to be observed.

AIDS Doubters and AIDS Quackery. In 1987 Peter Duesberg (b. 1936), a distinguished molecular biologist, authority on retroviruses, and member of the U.S. National Academy of Sciences, published a paper asserting that HIV was merely a benign passenger

virus and not the cause of AIDS. Leading scientists refuted Duesburg's theory, but his arguments drew adherents from people who wished to believe that AIDS had no link to viral causation and could be cured by living a "healthy" lifestyle. Questioning the cause of AIDS also fueled the industry of unorthodox treatments for AIDS. From the earliest days of the epidemic, desperate patients had been willing to try almost anything advertised as a cure. Early in the epidemic, promoters of questionable cancer treatments expanded their claims to encompass AIDS because of its link to Kaposi's sarcoma. As the underlying immune deficiency in AIDS became common knowledge, remedies purporting to boost the immune system flourished. The growth of the World Wide Web in the late 1990s allowed the AIDS doubters to spread their message widely and opened the door to multiple **quack** therapies and urban legends relating to AIDS.

AIDS in the New Millennium. In 2001 the world marked 25 years since the earliest recognition of AIDS. By this date AIDS in America had been transformed from a disease identified almost exclusively with affluent homosexual men into a disease of marginalized groups—injecting drug abusers and poor minority populations. Between 2001 and 2004, 50 percent of HIV diagnoses were among African Americans and 20 percent were among Hispanics, even though those groups constituted only 12 percent and 14 percent of the U.S. population respectively. Men who had sex with other men still accounted for more than 70 percent of AIDS cases in the United States. This was also true in Canada and in Latin America as a whole. Among Caribbean island populations, however, AIDS now strikes men and women equally.

Americans have played a leading role in efforts to halt AIDS in the rest of the world. In poorer regions of the world, AIDS patients cannot afford the cost of antiviral drugs, even those whose prices have been greatly reduced. In 2007 the U.S. government committed \$30 billion over five years to fight AIDS in developing countries. Major philanthropic organizations, such as the Bill and Melinda Gates Foundation, have also invested heavily in research on ways to prevent AIDS as well as in helping those already infected.

For the United States, AIDS has become essentially a chronic disease. In 2005, the CDC reported just over 433,000 people living with AIDS in the United States and 17,000 deaths from AIDS during the year. Between 1993 and 2003, highly active antiretroviral therapy (HAART) produced an 80 percent drop in the death rate from AIDS. Since the 1986 release of Azidothymidine, or AZT, new AIDS drugs have been developed that target different points in the life cycle of HIV. In 1995 a new class of drugs called protease inhibitors was approved, and in 2007 integrase inhibitors were introduced. Even more antiviral drugs are in research and development. None of these drugs, however, can eliminate HIV from an infected person, and the disease requires drug treatment with toxic side effects for the rest of an infected person's life. Because of the rapid mutation of HIV, moreover, a conventional vaccine against AIDS has proved impossible to make, and it may take decades before novel approaches to the vaccine concept produce positive results.

The very success in managing AIDS in the United States has produced worry among public health officials that young people will not understand the serious side effects that accompany antiviral regimens and be lulled into thinking that AIDS is no longer a danger. Among affluent homosexual men—the initial group struck so hard by AIDS—some risky behaviors have reemerged. Many gay bathhouses in major cities, closed in the mid-1980s, reopened quickly with regulations restricting unsafe sexual practices in public areas. Sexual activity in the bathhouses' privately rented rooms was and still is

**The first thing
that should go on between
two consenting adults.**



The sexual revolution may be over,
but the casualties are still mounting.
Don't be counted among them. Use condoms.

**Milwaukee AIDS Project
273-AIDS**

“The sexual revolution may be over, but the casualties are still mounting. Don’t be counted among them. Use condoms.” Milwaukee AIDS Project (1980s). Courtesy of the National Library of Medicine.

unregulated, illustrating the ongoing tension between **personal liberty** and the community's right to coerce healthful behavior. Exacerbating the problem has been the widespread use of the drug methamphetamine, which in the twenty-first century has fueled a return to unsafe sex with multiple partners in bathhouses.

It has been a hard-won truth that AIDS in America is best prevented in the twenty-first century with traditional, twentieth-century public health techniques. Educational campaigns about how HIV is transmitted help individuals protect themselves by abstaining from sex or engaging in safe sex practices. Efforts to expand testing for HIV and reduce the stigma of a positive diagnosis likewise help individuals to know their personal status and protect their sexual partners. Before 2005 public health efforts to exchange clean needles for used ones to protect injecting drug users from AIDS had been illegal under most state drug laws, but volunteer programs were often tolerated by law enforcement. In that year, however, needle exchange won official support in California, and since then, other states and municipalities have endorsed this effort. *See also* AIDS in Africa; AIDS, Literature, and the Arts in the United States; Cinema and Epidemic Disease; Disease, Social Construction of; Drug Resistance in Microorganisms; Human Immunity and Resistance to Disease; Literature, Disease in Modern; Medical Ethics and Epidemic Disease; Popular Media and Epidemic Disease: Recent Trends; Poverty, Wealth, and Epidemic Disease; Public Health Agencies, U.S. Federal; Race, Ethnicity, and Epidemic Disease; Religion and Epidemic Disease; Scapegoats and Epidemic Disease; Sexual Revolution; Trade, Travel, and Epidemic Disease.

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VICTORIA A. HARDEN

AIDS, LITERATURE, AND THE ARTS IN THE UNITED STATES. AIDS has been variously called an “**epidemic of signification**” and the first postmodern epidemic. In the early years after its discovery, the syndrome was diagnostically defined only by its second-hand disease manifestations (its “**signifiers**”) rather than by the infectious agent itself.

(Only later was the viral cause identified, and a test for its antibodies developed.) Perhaps more than any other infectious epidemic, HIV/AIDS has resulted in an excess of public discourse attempting to define what it means, over and above its status as a public health issue.

Because the first observed vectors of transmission, namely intravenous (IV) drug use and homosexual sex, and the first populations in which it was observed, namely poor, IV drug users, and gay men, were socially stigmatized behaviors and socially stigmatized groups, AIDS has absorbed more than its share of metaphorical significance: God's wrath, a CIA experiment gone awry, a punishment for violating Nature, and so forth. The struggle to comprehend the epidemic, therefore, became a struggle to control its representations in public discourse, literature, and the arts. That gay men are disproportionately represented in the worlds of fine arts, performing arts, and literature meant that many culture workers in the 1980s and 1990s would undertake the task of remembering lives lost, encouraging survivors, and calling citizens to action on behalf of the infected. That the world of cultural production tends to be progressive in its politics meant that some artists became activists in opposition to America's swerve toward conservatism in the 1980s.

Literature. AIDS emerged in 1981 as a text, first in published reports in mainstream journalism, then in sensationalized accounts in tabloid media, then in Christian fundamentalist apocalyptically tinged accounts. In their quest to take control of the tendencies to demonize or to sentimentalize the infected, writers were among the first artists to contend with the epidemic.

Some of the earliest fiction attempting to represent AIDS came from gay writers publishing in marginal small presses rather than mainstream venues. Paul Reed's 1984 *Facing It: A Novel of A.I.D.S.* (arguably one of the first, if not the first, AIDS-themed novel) was published by Gay Sunshine Press, and Samuel R. Delany's 1985 "The Tale of Plagues and Carnivals; or, Some Informal Remarks toward the Modular Calculus, Part Five" appeared as an appendix to his science-fiction book, *Flight from Nevèrjôn*. Toby Johnson's futuristic and dystopian 1987 *Plague: A Novel about Healing* was published by the gay publisher Alyson Publications. Knights Press published several novels, including *The World Can Break Your Heart* (1984) by Daniel Curzon, *The Wrong Apple* (1988) by David Rees, *Genocide: The Anthology* (1989) by Tim Barrus, and *Gardy and Erin* (1989) by Jeff Black, among others.

By the late 1980s, more mainstream writers and publishing houses brought out AIDS-themed fiction. Christopher Bram's *In Memory of Angel Clare* (1989) recounted the lives of a circle of friends after losing another friend to AIDS. Sarah Schulman's unflinching *People in Trouble* (1990) and *Rat Bohemia* (1995) resisted sentimentality, explored political engagement, and represented the responses to AIDS of straight and queer women. Alice Hoffman's *At Risk* (1988) explored a middle-class child's infection with HIV (by a blood transfusion), her development of AIDS, and the social stigma associated with her diagnosis. James McCourt's *Time Remaining* (1993) was by turns brilliantly witty and poignantly elegiac.

Love lost and mortality are not unusual themes in poetry, and AIDS certainly provoked an outpouring of elegiac verse, collected in anthologies such as *Poets for Life: Seventy-Six Poets Respond to AIDS* (edited in 1989 by Michael Klein) and *Brother to Brother: New Writings by Black Gay Men* (edited in 1991 by Essex Hemphill). Some poets produced sustained lyric sequences thematically dealing with AIDS, including Robert Boucheron's *Epitaphs for the Plague Dead* (1985), Paul Monette's *Love Alone: 18 Elegies for*

Rog (1988), Thom Gunn's *The Man with Night Sweats* (1992), Walter Holland's *A Journal of the Plague Years* (1992), Mark Doty's *Atlantis* (1995), and Essex Hemphill's collection of prose and poetry *Ceremonies* (1992).

Performing Arts. The arts of stage and screen were profoundly affected by the AIDS epidemic, which was reflected in a new cultural phenomenon, the benefit performance to raise funds for AIDS service organizations, and in a variety of new artistic creations. The deaths from AIDS of ballet dancer Rudolf Nureyev, Broadway director Michael Bennett, musician Liberace, and actors Brad Davis and Rock Hudson, among others, gave AIDS a high public profile and allowed mainstream America to identify with the epidemic.

Dramatists engaged the epidemic in its first years. Larry Kramer's *The Normal Heart* (1985) chronicled early AIDS activism (eventually supplemented with his plays *Just Say No* [1989] and *The Destiny of Me* [1993]), whereas William Hoffman's *As Is* (1985) situated the epidemic within human relationships. Comic playwright Harvey Fierstein created a trilogy of one-acts titled *Safe Sex* (1987). Terrence McNally's *Love! Valour! Compassion!* (1994) was a humorous and poignant reflection on mortality and friendship. Perhaps the most ambitious stage treatment was Tony Kushner's 1991 *Angels in America: A Gay Fantasia on National Themes*, an epic drama in two parts over two performances totaling about seven hours (directed by Mike Nichols for HBO in 2003).

The 1980s and 1990s also saw the emergence of solo-performance art as a politically engaged agitprop medium designed to catalyze audiences to action in the face of growing political, religious, and economic conservatism. Usually in the form of monologues, frequently engaging the audience directly and physically, sometimes featuring a naked performer, solo-performance art was confrontational in its politics and sexuality, dismantling the notion of sex as a "private" (and therefore apolitical and invisible) matter. So successfully did performers like Tim Miller, Karen Finley, John Fleck, and Holly Hughes test the limits of what constitutes theatrical performance, that grants from the National Endowment for the Arts that they had been awarded were withdrawn after political pressure from the first Bush administration. A tamer version of this phenomenon was David Drake's *The Night Larry Kramer Kissed Me* (1993, made into a film in 2000), a memoir of his coming out and a fantasy of a world after AIDS.

Musical composers contributed to this creative outpouring. John Corigliano's Symphony No. 1 was precipitated by his seeing the traveling AIDS Memorial Quilt. Jazz composer and pianist Fred Hersch composed "Tango Bittersweet," pianist and composer Kevin Oldham, a "Concerto for Piano," composer Lee Gannon a "Triad-O-Rama" for wind quintet, and Calvin Hampton a set of variations on "Amazing Grace" (collected in a 1994 CD entitled *Memento Bittersweet*). Vocal performer Diamanda Galas created a series of searing vocal performance pieces, including *The Divine Punishment* and *Saint of the Pit* (1986, 1989), *Masque of the Red Death* (1988), *Plague Mass* (1990), and *Vena Cava* (1992).

The Broadway musical would seem an unlikely genre for a reflection on the AIDS epidemic, but two stand out. William Finn's *Falsettos* (1992) depicted gay men dealing with AIDS with the support of family and friends (and won Tony Awards for Best Book and Best Score). Jonathan Larson, an aspiring Broadway composer, achieved posthumous fame when his rock musical *Rent*, set in Manhattan's East Village and based on Puccini's opera *La Bohème*, opened in 1996 shortly after his death (from an undiagnosed congenital heart defect). The musical, which substitutes AIDS for the opera's tuberculosis, generated some

controversy after novelist Sarah Schulman pointed out its parallels to her novel *People in Trouble*, published six years before.

Major Hollywood filmmakers were slow to bring AIDS to the big screen. That role was ably performed by independent filmmakers such as Bill Sherwood's *Parting Glances* (1986), Craig Lucas's *Longtime Companion* (1990), Todd Haynes's *Poison* (1991), and Gregg Araki's *The Living End* (1992). Television surprisingly brought some of the earliest popular representations of people with AIDS, including Daniel Lipman and Ron Cowen's *An Early Frost* (NBC, 1985), playwright Harvey Fierstein's *Tidy Endings* (HBO, 1988) and Terrence McNally's *Andre's Mother* (PBS, 1990). *Tongues Untied* (1991), directed for PBS by black filmmaker Marlon Riggs, explored the lives of African American gay men and homophobia in black communities, creating a larger public controversy about funding for public television because of its frankness about sexuality. The Hollywood release *Philadelphia* (1993), starring one of America's most beloved and affable actors, Tom Hanks, as a lawyer with AIDS who is fired by his firm, finally brought a mainstream cinematic treatment, though in a nonthreatening and sexually chaste mode.

Visual Arts. Graphic and visual arts can either be among the most public (mechanically reproduced and circulated) or among the most cloistered (the sole copy existing in a private collection) of the arts. The arts scene during the 1980s witnessed an economic boom for some artists as new wealth sought out (and paid ever higher prices for) new art as an "investment" or status marker. Many of these artworks were the detached, ironic, and apolitical grandchildren of Andy Warhol.

However, the AIDS epidemic decimated the art world (including its creators, critics, and brokers) to the point that, beginning in 1989, December 1 of each year has been declared a Day Without Art in order to engage art communities in the struggle against AIDS. During the 1980s and 1990s, some politically engaged visual artists employed graphics, photography, collage, and installations in order to represent the lives of HIV-infected people and to advocate action to end the epidemic.

Art collectives like Gran Fury working with the AIDS Coalition to Unleash Power (ACT UP) created striking postmodern graphics (e.g., posters, signs, crack-and-peel stickers) for direct-action demonstrations. ACT UP also created at New York's Museum of Contemporary Art an installation entitled *Let the Record Show*, which drew parallels between the actively hostile or merely complacent religious and political authorities in power at the time with Nazi war criminals on trial at Nuremberg after World War II.

By late in the twentieth century, photography had emerged as an art form, not just a journalistic tool, which, when focused on AIDS, documented the lives of HIV-infected people and their caregivers, as well as the activists working on their behalf. Photographers like Nicholas Nixon, Gypsy Ray, Jane Rosett, Brian Weil, and Sal Lopes counteracted the prevailing sensationalism of many media images and the invisibility of the poor and ethnic or racial minorities living with AIDS.

Two photographers drew special notoriety for the frankness of their depictions of the body and their hostility to mainstream sensibilities. Robert Mapplethorpe, who died of HIV-related illness in 1989, produced a body of work that contrasted its cool formalism with its candid sexuality. A posthumous retrospective of his work was canceled by the Corcoran Gallery of Art in Washington, D.C., (prompting the arts community to boycott the museum) and when the director of Contemporary Arts Center of Cincinnati, Dennis Barrie, presented the exhibition, he was charged with a violation of obscenity laws (but later acquitted by a jury). An activist artist and a person with AIDS, David Wojnarowicz,

became embroiled in a larger controversy about public funding for the arts through the National Endowment for the Arts, involving conservative Republican Senator Jesse Helms and Christian fundamentalist minister Donald Wildmon of the American Family Association.

Equally libidinal but somehow tamer, more accessible, and less confrontational were the graphics of Keith Haring, who died of AIDS in 1990. A “guerilla” artist whose cartoon graffiti drawings appeared on subways and urban wallsapes before his work became commercialized, Haring contributed graphic designs to AIDS education publications and activist materials. His life and career were celebrated in a musical, *Radiant Baby*, in 2003.

A classic American folk art genre was revived in the AIDS epidemic: the quilt. The AIDS Memorial Quilt began as an effort simply to document the names of those who had died (the NAMES Project), but grew as a grassroots effort to provide a more personal memorial for those who had died by using an artifact of material culture that often comforts the ill or afflicted, a quilted blanket. Consisting of 3-foot by 6-foot panels (the approximate size of a funeral plot) now numbering over 40,000, with each panel stitched and embroidered by family or friends to represent the unique quality of an individual lost, the AIDS Memorial Quilt has been exhibited (in parts, because it is too large for one public space) throughout the world.

During the first two decades of the AIDS epidemic, literature and the arts were media to express grief and rage, to celebrate sexuality at a time when the erotic was represented as dangerous, and to engage those affected by AIDS in solidarity and productive action. *See also* AIDS in Africa; AIDS in the United States; Black Death: Literature and Art; Cinema and Epidemic Disease; Literature, Disease in Modern; Plague Literature and Art, Early Modern European; Popular Media and Epidemic Disease: Recent Trends; Poison Libels and Epidemic Disease; Religion and Epidemic Disease; Scapegoats and Epidemic Disease; Sexuality, Gender, and Epidemic Disease; Trade, Travel, and Epidemic Disease.

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THOMAS LAWRENCE LONG

AIR AND EPIDEMIC DISEASES. Historically, the conception that imbalances between the **human body** and the environment create illness frequently gave air a primary

role in both natural and transcendental explanations of communally experienced illness.

Early considerations of air and disease occur in several texts of the **Hippocratic Corpus** (e.g., *On the Nature of Man* 9, *Breaths* 6, *Regimen in Acute Diseases* 2, *Epidemics* 2.1 and 3, *Airs, Waters, Places*), and a comingling of natural and transcendental etiologies appears around the term *miasma* (“pollution”). Miasmas resulting in **epidemic** plagues could be brought on by “polluted” actions (such as in Sophocles’s [495–406 BCE] *Oedipus the King*) or by air rendered unhealthy by natural processes. Over time, prevailing medical theory held that plagues were caused by air fouled by wet organic materials decomposing and entering the air through heat (Diodorus Siculus [c. 90–30 BCE] 12.58.3; **Galen** *De febrium differentiis* 1.6). However, other related theories, such as a concentration of unhealthy atoms in the air (Lucretius [99–55 BCE] 6.1093–97), minute airborne creatures (Varro [116–27 BCE] *On Rural Farming* 1), or noxious materials brought up by earthquakes (Seneca [4 BCE–65 CE] *Naturales quaestiones* 6.27) also occur.

In general, it was broadly accepted well into the nineteenth century that miasmas resulted from decaying organic material and that they were the cause of epidemic diseases that we would now recognize as disparate (e.g., **cholera, smallpox, influenza**, and

THE CAUSE OF CHOLERA: NOT CONTAGION BUT MIASMA (1831)

It is chiefly for the purpose of quieting these unnecessary alarms, that this essay is published; in which it is intended to prove, (notwithstanding all the assertions to the contrary) that the mild Cholera of this country [England], is essentially the same disease, and proceeds from the same cause, as the malignant Indio-Russian Cholera; modified, however, by the state of the bodies of the individuals attacked. Besides this, the cause, symptoms, mode of prevention, and the plan of treatment, which has been successfully employed, is laid down.

If the disease had been viewed in the light afforded by the celebrated **Sydenham** [1624–1689], whose accurate observation of the operation of morbid causes upon the body have justly entitled him to the appellation of the English **Hippocrates**, many of the evils, which have resulted from the unqualified and groundless statements of the contagious nature of Cholera, would have been prevented. In the chapter on Epidemic Diseases he says, “There are various constitutions of years, which owe their origin neither to heat nor cold, dryness nor moisture, but which depend upon some secret and inexplicable action in the bowels of the earth, whence the air is contaminated with certain effluvia, which subject the body to particular diseases, so long as that constitution predominates.”

In this short sentence, we have a rational explanation of the origin of spasmodic Cholera, which has traveled from Asia, through Europe to England, not by contagion above ground, but by underground alterations and consequent emanations of certain effluvia from the earth, by which the atmosphere is contaminated.

From Isaac Pidduck, M.D., *The Identity of the Asiatic, Russian, and English Cholera: Its Cause, Symptoms, Prevention and Cure* (London, 1831), pp. 3–4.

diphtheria). As urban centers grew, thanks in part to **colonization** and the **Industrial Revolution**, miasmatic theory influenced advancements in Western public health that were aimed to curb epidemic outbreaks through better civil engineering and health reforms. These advancements often went hand-in-hand with convictions that people, especially the poor and the uncivilized, needed both moral and hygienic regulation and education.

From the Renaissance through the nineteenth century, however, competing theories of **transmission** and disease generation, influenced by developments in the natural sciences, challenged miasmatic theory. These theories contended that specific contaminants entered or contacted the body through the air or **water** and caused specific diseases to grow rather than to occur spontaneously from miasmatic air. One of the earliest was **Girolamo Fracastoro's** suggestion (1546) that seed-like particles caused infectious disease. However, these theories did not gain the upper hand until the nineteenth century through the work of pioneers such as **John Snow**, **Louis Pasteur**, Joseph Lister (1827–1912), **Robert Koch**, and Theodor Klebs (1834–1913). Some physicians and health reformers, such as Florence Nightingale (1820–1910), vigorously opposed the new theories. However, the rapidly spreading **influenza pandemic of 1889–1890** hastened worldwide acceptance of the new theories and turned attention toward air contamination by specific aerosolized agents as a cause of many epidemic illnesses. The subsequent identification of these various agents and their methods of transmission led to modern medical and public health approaches toward airborne illness and air pollution, as well as to weaponization of some airborne agents such as anthrax for **biological warfare** or **bioterrorism**. *See also* Astrology and Medicine; Avicenna (Ibn Sina); Contagion and Transmission; Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Disinfection and Fumigation; Environment, Ecology, and Epidemic Disease; Flight; Germ Theory of Disease; Greco-Roman Medical Theory and Practice; Islamic Disease Theory and Medicine; Pneumonic and Septicemic Plague; Sanitation Movement of the Nineteenth Century; Urbanization and Epidemic Disease.

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ERIC D. NELSON

ANIMAL DISEASES (ZOOSES) AND EPIDEMIC DISEASE. Animal **epidemics**, or epizootics, also affect humans. Epizootics mean less food for people, making them more susceptible to disease. Zoonotic diseases—those transmissible between humans and animals—usually begin with birds, reptiles, amphibians, or mammals, and end up in human populations (although the reverse occurs as well). Contemporary biologists Fuller Torrey and Robert Yolken estimate that microbes originating with nonhuman animals in the past and those currently transmissible to humans from nonhuman animals cause approximately three-quarters of all human infections. Humans and cattle both suffer from **tuberculosis**, **smallpox** and cowpox are closely

related, and human **measles** is a cousin to rinderpest in cattle and canine distemper. True zoonoses, those diseases currently transmissible between animals and humans, include **bubonic plague**, rabies, and anthrax. These infections have caused both devastating epidemics and less dramatic endemic diseases (such as tuberculosis and **dysentery**) that have caused even more deaths over time.

Transmission of zoonoses can occur in numerous ways that depend on genetic and ecological changes in populations of humans, animals, and microorganisms. Historical outbreaks of disease have pointed to the importance of understanding the ecology and evolution of zoonotic diseases. For example, in 2006 scientists determined that a mutated bird **virus** caused the **influenza pandemic of 1918–1919**, which killed between 20 and 100 million people. This was announced in the midst of an Asian outbreak of avian (bird) **influenza**. Some epidemiologists feared that the bird infection would jump to humans, creating a deadly **pandemic**, like that of 1918–1919. A long history of biological relationships between humans and animals has given the pathogens and their hosts plenty of opportunities to develop new ecological and evolutionary strategies. People, animals, and pathogens may trigger epidemics by finding a new species to infect, traveling on a ship or plane, or undergoing a genetic mutation, for example.

This article focuses on bubonic plague and influenza to demonstrate how ecological and evolutionary changes have helped cause epidemics (or, in a global context, pandemics). The same questions could be asked about any zoonotic disease. Bubonic plague depends on ecological interactions between wild reservoirs (Asian and North American rodents) and the movements of people along **trade** routes. The example of influenza draws attention to the importance of the biological mechanisms used by pathogens to adapt to new ecological circumstances. The influenza virus undergoes genetic alteration rapidly and easily jumps between species—sometimes initiating epidemics or pandemics. The two case studies that follow provide a model for understanding and writing about the ecology and evolution of zoonotic diseases.

The Ecology of Bubonic Plague. Bubonic plague is caused by *Yersinia pestis*, a **bacterium** that diverged evolutionarily from its nearest relatives only a few thousand years ago. This organism infects native rodents on the Asian steppes. It hitched a ride to Europe with rats, which first arrived in the Mediterranean basin on ships from central Asia around 500 CE. The **Plague of Justinian** of the sixth century followed, killing around 40 percent of the population of Constantinople and up to a quarter of the human population of the entire eastern Mediterranean. Smaller outbreaks occurred for the next 200 years or so, until bubonic plague disappeared in European populations. *Y. pestis*'s major European reservoir, the black rat (*Rattus rattus*), continued to spread and expand in numbers, however, and local wild populations of rodents also became infected. As human population densities and trading activities recovered over the years, the ecological conditions were right for plague to appear again.

In 1338, plague broke out among people living on the Asian steppes in what is now Kyrgyzstan; it spread along trade routes to India, China, and the Middle East where it killed an estimated 35 million in China alone. Ten years later, it arrived with rats on ships coming to the ports of Genoa, Messina, and Sicily. By this time, black rats had adapted very successfully to living in close contact with European people, and as plague spread among the rats, it spread to people also. Historians have estimated that between 1348 and 1352 up to one-third of Europe's entire population died of the **Black Death** and the chaos that accompanied the epidemic. Although rats had been suspected as a reservoir of

plague, the disease's causative organism was found much later, in the 1890s, by **Alexandre Yersin** and **Shibasaburo Kitasato**. *Y. pestis* was transmitted between animals and to humans by another animal: a vector, the flea.

The **third plague pandemic** originated in China in the 1860s and spread quickly. An estimated 12 million people died, mainly in India and China. This pandemic affected every continent on the globe except Antarctica. Infected rats carried plague from Hong Kong to Honolulu to San Francisco in 1900, where it hit Chinese neighborhoods near the docks hardest. *Y. pestis* had just been given its greatest ecological break in centuries—a vast land mass with new populations of animals and people to colonize. Rapidly infecting prairie dogs and ground squirrels in the North American West, the microbe has crossed the Rocky Mountains and is moving eastward. Although rare in people and domesticated animals in wealthier countries, plague still kills people in the developing world and in areas suffering from natural or human-made disasters.

Scientists now understand that *Y. pestis* has evolved to what researchers Sharon Collinge and Chris Ray call “spectacular generalism”: it occurs naturally in more than 200 species of mammals and over 260 species of fleas worldwide. This makes it easy for plague to spread from wild animals to domesticated animals, such as cats, and thence to humans who otherwise would have little direct exposure to wild rodents. *Y. pestis* has now established itself so firmly around the world that its eradication is all but impossible, and future outbreaks will occur.

As long as people and the wild reservoirs avoided each other, plague did not cause human pandemics. From its limited range in wild central Asian rodents, *Y. pestis* tagged along as rats spread along human trade routes, both over land and by sea. Rats adapted very successfully to cohabitation with populations of humans, especially in crowded cities. Once established in these rats, *Y. pestis* spread to people, thus ensuring positive conditions for its continued survival. In this framework, humans are only one species of many that provide a substrate for the microbe's evolutionary success; but for us, bubonic plague remains one of history's most devastating and terrifying zoonotic diseases.

The Evolution of Influenza. Influenza is a disease caused by a family of viruses (although this idea was not agreed upon by scientists until the 1930s). Influenza viruses have caused disease in humans for quite some time; major outbreaks have occurred approximately every 40 years since 1800. Influenza was responsible for the third most devastating pandemic in history (following the Justinian plague and the Black Death). In 1918–1919, 20 to 100 million people around the world died from influenza and its complications. Scientists and historians have estimated that about one-third of the world's population was infected and sickened by influenza. Influenza flourished in the chaos of World War I: in the trenches, bomb shelters and basements, railway cars, and encampments of people weakened by malnutrition. It also spread rapidly across the United States, a nation not as directly impacted by the war. The influenza pandemic of 1918–1919 remains an historical puzzle that involves not just human but also animal populations.

The disease seemed to “explode” simultaneously in Asia, Europe, and the United States, and it came in three waves that spanned over a year. The human pandemic coincided with outbreaks of similar respiratory diseases in pigs (swine) and horses. Both human and swine populations seemed immunologically naïve to the pandemic virus (a piece of information noted by witnesses at the time), which made it unlikely that the

virus had “incubated” in pigs before jumping to human populations. Within a few years of the 1918–1919 pandemic, moreover, influenza seemed to have become an ordinary (far less fatal) disease. After the horrors of 1918, as modern historian Alfred Crosby has argued, most people wished to forget about influenza (Crosby, 1989).

Following World War II, **World Health Organization** researchers surveyed animals and people around the world, looking for influenza. They took blood samples from human, swine, horse, and bird (avian) populations, compared them serologically, and banked them. This research began the process of understanding what had happened in 1918 because the researchers found virus strains in all of the human and animal populations. Scientists recognized that animal populations served as reservoirs and mixing vessels for human influenza. In the 1990s, geneticists began to apply newly available scientific tools to old questions about the influenza pandemic of 1918–1919. Where had the virus come from? Why had it emerged so quickly, only to disappear just as quickly?

In terms of mutation and ability to infect new species, influenza has evolved for speed. It exists on the edge of what geneticists call “error catastrophe”: it mutates so promiscuously and rapidly that its genome teeters on the brink of dysfunctionality. These potential problems are, however, outweighed by the advantages of being able to mutate and adapt to new hosts very quickly. These genetic characteristics help to explain how influenza (and other infections) can transcend species barriers so efficiently. Indeed, the strain of the virus that caused the 1918–1919 pandemic, “H1N1,” has been called “the mother of all pandemics.” H1N1 was the origin of all known strains circulating in populations of people and pigs circa 2000. Descendants of the 1918 virus are responsible for all recorded pandemics since that time; moreover, swine have served as the major reservoir for H1N1 strains (which have now recently reemerged in humans as the result of a laboratory accident).

Using preserved autopsy material from people who died of influenza in 1918, scientists have concluded that the deadly virus from that pandemic was an avian-like strain that had mutated dramatically. In contrast, it was determined that subsequent pandemics (with lower mortality) in 1957 and 1968 had been caused by the reassortment of genetic segments from wild bird viruses. Scientists believe that the 1918 virus appeared so rapidly and was so deadly because it had undergone dramatic mutations with which humans’ and pigs’ immune systems were unfamiliar. Although the virus seemed to have disappeared just as quickly as it came, it had only moved out of the human population; it continued to live and evolve in swine. In both pigs and people, herd immunity provided the most likely explanation for the virus’ decrease in virulence in the 1920s. In the early 2000s, an outbreak of H5N1 influenza in Asian birds caught the attention of scientists when about 200 people became infected, and several died. All of the infected people had had close contact with infected birds, but fears of the virus mutating so that it could be spread directly between people conjured up visions of the 1918–1919 pandemic. No historical data exist to support the idea of avian outbreaks preceding the 1918 pandemic. However, it has become clear that we must understand the circulation of viruses in human *and* animal populations, through time and across space, in order to predict and prepare for future outbreaks. *See also* Bubonic Plague and related articles; Human Immunity and Resistance to Disease; Influenza Pandemic, 1889–1890; Plague: End of the Second Pandemic; Plague in San Francisco, 1900–1908; Plague in China; Simond, Paul-Louis.

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SUSAN D. JONES

ANIMAL RESEARCH. Although animals were occasionally used for scientific experimentation at least since the days of ancient Greece, animal experimentation did not become significant until the **Scientific Revolution**, when discoveries such as the circulation of the blood clearly demonstrated that such experiments could lead to useful scientific knowledge. Even then, some raised objections to animal experimentation on both moral and scientific grounds.

With the emergence of physiology as a scientific discipline in the early nineteenth century, the use of animals in experimentation became much more widespread. As other biomedical sciences, such as pharmacology and bacteriology, were established later in the century, animal experimentation also became central to their focus. This increased use of animals in experimentation also led to the first organized efforts promoting animal welfare, such as the founding of societies for the protection of animals, in the nineteenth century. In England and America a vigorous anti-vivisection movement emerged. Although the term "vivisection" originally referred to dissection of living animals, by this time it had come to be applied to animal experimentation in general.

As animal experimentation led to the introduction of important medical advances around the turn of the twentieth century, such as the development of an antitoxin for the treatment of **diphtheria**, an infectious disease that especially affected children, the popularity of the anti-vivisection movement waned. Animals were also utilized in the production and testing of the antitoxin, as well as in the research leading to its discovery. Animal research was involved in the development of many other preventive and treatment methods for infectious disease, among other illnesses, such as the **polio** vaccine and **antibiotics**. Animals also became increasingly important in the twentieth century in the testing and standardization of the new **pharmaceuticals** and other therapies developed as a result of biomedical research.

The use of animals in the life sciences has undergone further expansion since the Second World War. Increases in funding for medical research, the number of chemicals in the marketplace, and the regulations governing drugs and other products have all contributed to the growing use of animals in research and testing. Under U.S. law, for example, new drugs for infectious and other diseases must be tested first in animals for efficacy and safety before they can be approved for clinical trials involving **human subjects**. Tens of millions of animals are used annually in the United States today for research, testing, and education.

The postwar period has also witnessed a revival of the animal protection movement, especially since the publication of ethicist Peter Singer's *Animal Liberation* in 1975. Animal rights activists and the scientific community have frequently clashed over the necessity and ethics of using animals in medical research. The efforts of the animal rights movement have helped to increase sensitivity about the treatment of animals and to enact animal welfare legislation, such as the Animal Welfare Act of 1966 and subsequent amendments. There has also been an increased emphasis on the development of alternatives to animals, for example, greater use of nonsensitive organisms (such as bacteria) and computer modeling, but it does not seem likely that the need for animals in research will be eliminated any time soon. Thus animal research is likely to remain an important tool of biomedical science and an area of controversy for the foreseeable future.

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JOHN PARASCANDOLA

ANTIBIOTICS. Antibiotics are the class of drugs used to treat infections caused by **bacteria**. When the term was coined in 1941, it referred specifically to substances produced by one microorganism that inhibit or kill another form of microorganism. More recently, the term has been generalized to include drugs synthesized in the laboratory or **pharmaceutical** factory.

Antibiotics work by inhibiting a variety of metabolic processes of bacteria. **Penicillin** and similar drugs destroy the cell walls of some bacteria. Other antibiotics inhibit the ability of bacteria to make DNA, RNA, or proteins essential for metabolism and replication. Many of the mechanisms that bacteria use to construct proteins are different from the processes that higher animals use, so it is possible for antibiotics to target specific bacteria without harming the patient.

The first uses of substances to fight infections are likely lost in prehistory. Many ancient peoples used honey as a wound dressing without recognizing that it possesses hydrogen peroxide and other antibacterial compounds and that its high sugar content makes bacterial growth impossible. They also plastered wounds with moldy bread, foreshadowing the eventual development of penicillin. These primitive efforts were effective in treating superficial wounds and skin infections, but were worthless in treating internal infections.

The ability to treat internal infections effectively began in the early twentieth century. Salts of mercury, arsenic, and other metals were used to treat syphilis, but were highly toxic. Later, organic aniline dyes led to the use of **sulfa drugs**, which were much safer antibacterial treatments. In 1928 penicillin, the first true antibiotic, was discovered, but its commercial production lagged until the Second World War. The use of sulfa drugs and penicillin on the battlefield dramatically decreased combat mortality and led to rapid growth of antibiotic production for the civilian population.

The initial enthusiasm for these new “miracle drugs” was followed by disappointment because relatively few types of bacteria were affected by them. Gram-positive bacteria, such as streptococcus and staphylococcus, have a cell wall and are susceptible to the effects of penicillin. Gram-negative bacteria lack a cell wall and include a host of disease-causing organisms that are unaffected by penicillin. The promise of treatment for infections caused by these organisms led to the rapid development of new antibiotics.

Streptomycin was the first major antibiotic to be developed after penicillin. It is a member of the aminoglycoside family, and its initial role was in the treatment of **tuberculosis**, but it also is effective against some Gram-negative bacteria. Streptomycin was derived from *Streptomyces*, a species of soil bacterium, by Ukrainian American biochemist Selman Waksman (1888–1973). He and others postulated that sites of high bacterial population would be likely to have a variety of bacteria that produce antibiotics as a matter of survival, decreasing the competition from other species in the same area. This hypothesis led to the productive pursuit of other antibiotics from soil and even sewage samples.

The development of the tetracycline family of antibiotics soon followed. This group of drugs is important because they were the first “broad spectrum” antibiotics, effective against a wide variety of both Gram-negative and Gram-positive bacteria. This ability of the tetracyclines to treat many types of infection was balanced by a disadvantage. Penicillin, streptomycin, and similar drugs are bactericidal—they kill bacteria outright. Tetracyclines and many other antibiotics are bacteristatic—they inhibit the ability of bacteria to reproduce and rely on the ability of the immune system to clear the infection by destroying the still-living bacteria.

The class of bactericidal antibiotics with the greatest number of drugs is the cephalosporins. The first of the cephalosporins were isolated from bacteria growing in a sewer in 1948. There are now well over 50 drugs in the cephalosporin class, and its members have widely varying properties. They have different patterns of absorption and penetration into different internal organs. Most important, the members of the group have great variation in the spectrum of bacteria that are susceptible to them. The number and variation of the cephalosporins demonstrate the ability to manipulate the molecular structure of antibiotics to alter their effects.

Once the ability to manipulate the structure, and therefore the function, of the cephalosporins had been harnessed, the ability to totally synthesize antibiotics without a biological source followed. This led to the development of the fluoroquinolones, the best known of which is ciprofloxacin. Cipro is a very broad-spectrum antibiotic that became an everyday word during the anthrax scares of 2001.

Another problem of antibiotic use is that bacteria have a tremendous ability to develop resistance to nearly any antibiotic. It was initially thought that this happened only after bacteria were exposed to a drug, but not for a long enough time to kill them all. It was believed that the survivors would then transmit their ability to resist the antibiotic to future generations of the bacteria. It is now apparent that even before some antibiotics are made commercially available, bacteria can develop a resistance to the drugs, possibly through exposure to the natural antibiotics produced by other bacteria in the natural environment.

There are a number of practices that increase the likelihood that bacteria in a host will develop resistance. One is failure to complete a full course of antibiotics, instead stopping before all the bacteria have been killed. Another is using an overly broad spectrum of

treatment, which kills both the disease-causing organism and the human host's normal "friendly" bacteria, thus allowing the overgrowth of more resistant species. Perhaps one of the greatest causes of resistance is the widespread use of broad-spectrum antibiotics as nutritional supplements in animal feed. This practice encourages the emergence of resistant forms that contaminate the meat and make their way into the food chain, thus infecting us.

Some "superbugs" appear to be able to develop resistance faster than new antibiotics can be developed. This pattern of rapid mutation of bacteria along with the decreasing rate of production of new antibiotics has led to concern that we may again enter an era of bacterial diseases that are untreatable by any safe drugs—that we may witness a chilling return to the fearsome pre-antibiotic era. *See also* Capitalism and Epidemic Disease; Drug Resistance in Microorganisms; Human Body; Human Immunity and Resistance to Disease.

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CHARLES V. BENDER

ANTONINE PLAGUE. *See* Plagues of the Roman Empire.

APOTHECARY/PHARMACIST. Medicines are among humanity's oldest tools, and the making of medicines is the central concern of the modern field of pharmacy. Despite pharmacy's prehistoric origins, a specialized occupation dedicated to the production and distribution of medicines—the pharmacist—did not arise until the Middle Ages. Before that time, healers of all sorts, including domestic healers and religious leaders, usually mixed together their own remedies and administered them to their patients.

The ancestors of today's pharmacists arose in the flowering of Islamic culture in Baghdad in the late eighth century CE. This new city quickly became a center of scholarship and of trade, including exotic spices and drugs. A specialized shopkeeper appeared, the *sayādilah*, who concentrated his business in the making and selling of medicines. In the decades that followed, governmental authorities initiated a system of licenses and inspections, and the idea of regulated medicine makers spread across the cities of the Arab world. During the eleventh century, the concept of specialized medicine sellers emerged in southern Europe where Islamic culture had its greatest influence. By the middle of the thirteenth century, public medicine shops were so common that Frederick II (1194–1250), as King of Sicily, issued edicts that called for the separation of medicine and pharmacy and the regulation of apothecary shops. As their shops spread through Europe, apothecaries became incorporated into the guild system that regulated trade and political life in the late medieval and Renaissance cities, usually joining spice merchants, grocers, or physicians. Not all guildsmen, however, were actively involved in the trade: the Italian poet Dante Alighieri (1265–1321), for example, became a member of the guild of apothecaries and physicians of Florence for political reasons.

Some European medicine dealers took on a version of the name “apothecary,” which was derived from the Latin *apotheca* or storehouse. These shopkeepers were identified directly with the goods they sold. In other parts of Europe, the specialist’s name was derived from the Greek *pharmakon* meaning medicine, the source of the modern term “pharmacist.” In this case, the occupational name was derived from the work done, as was the case with other trades such as smith or cooper.

Guilds and Pharmacopeias. A primary activity of apothecary and physician guilds was to promote the compiling and publication of pharmacopeias. These books of drug standards and medicine formulas served to guide apothecaries as they filled the prescriptions written by physicians. The guilds also set standards for the training of apprentices and the quality of medicines in shops. Eventually, apothecaries grew in power and prestige to the point at which they split off to form their own associations such as the Worshipful Society of Apothecaries of London (1617).

In the 1500s, changes swept through the fields of medicine and pharmacy. Followers of **Paracelsus** applied the emerging technologies of chemistry to the making of medicines, greatly expanding the drug armamentarium of physicians. Moreover, European explorers to the New World brought back other new plant drugs, such as cinchona bark and tobacco, which increased the stock of apothecary shops. Apothecaries became versed in chemistry and botany to serve their clientele. By the 1600s, French pharmacists like Nicaise LeFebvre (c. 1610–1669) and Nicolas Lemery (1645–1715) were writing the leading chemistry texts of the era. In the eighteenth and nineteenth centuries, pharmacists such as Carl Wilhelm Scheele (1742–1786), Antoine Baumé (1728–1804), Martin Klaproth (1743–1817), and Carl Freidrich Mohr (1806–1879) produced some of the greatest achievements in early modern chemistry. By combining their chemical expertise with their knowledge of plant drugs, pharmacists Friedrich Wilhelm Sertürner (1783–1841), Joseph Bienaimé Caventou (1795–1877), and Pierre Joseph Pelletier (1788–1842) isolated pure crystalline alkaloids including morphine and quinine in the early 1800s. These drugs revolutionized both medical practice and research by granting precision to the prescriptions of physicians and the experiments of scientists.

Modern Europe. Most apothecaries, of course, were not explorers or scientists. They were owners of small shops specializing in the making and selling of medicines. Their status in society, however, did benefit from the fame of their profession’s achievements and the highly regulated nature of their practice. In northern Europe, especially, governmental units tightly controlled pharmacy, limiting competition and setting up price schedules for medicines. Apothecaries operated as solid members of the middle class, and across most of Europe they had a status similar to physicians well into the twentieth century. Since the end of World War II, restrictive regulations on the number pharmacists and pharmacies have gradually disappeared across most of Europe. Pharmacists have maintained their standing as middle-class health professionals through the general adoption of college diplomas as a requirement for licensure.

Anglo-American Differences. In the Anglo-American context, however, the occupation of pharmacist developed differently. Beginning in the late seventeenth century, English apothecaries shifted more closely toward the role of general practitioners of medicine. Because university-trained physicians were rare and expensive, most ailing people consulted apothecaries, who charged only for the medicine they sold, not for advice. Moreover, the apothecaries had benefited from stories that they stayed behind their counters even during plague times, when

physicians abandoned London and other cities. As more and more apothecaries moved into medical practice, a new class of shopkeepers—the chemists and druggists—appeared to take over the routine making and selling of medicines. In sharp contrast with the Continent, government authorities in England did not choose to regulate pharmacy until well into the 1800s.

During this period of change and turmoil within the English health scene, the North American colonies were settled. Until towns and villages reached a critical size to support specialized shops like those of apothecaries, most medicines in the English colonies were sold in general stores or by wholesale druggists in the largest coastal ports, who serviced the needs of ships or plantations. According to *Kremers and Urdang's History of Pharmacy*, American community pharmacy arose from four distinct roots: the apothecary shop, the general store, the wholesale druggist, and the doctor's shop. The last type of establishment was run by a physician who diagnosed, prescribed, and dispensed all out of a small shop. The practices of medicine and pharmacy in the United States did not clearly begin to separate until the middle of the 1800s.

Two events of the early 1800s marked the beginnings of professional pharmacy in the young United States. In 1820, nine physicians gathered at the Capitol in Washington, D.C., and founded the *United States Pharmacopoeia*. This book of drug standards was meant to guide apothecaries and wholesalers as they prepared the basic ingredients that went into medicines. The book was needed because physicians had come to rely on druggists and apothecaries. The second event was the establishment of the Philadelphia College of Pharmacy in 1821. This local association of apothecaries organized to foster professional development through publications and a school for apprentices. During the middle third of the 1800s, other local societies sprung up following the Philadelphia example. In 1852, the American Pharmaceutical Association was formed and has fostered professional development to the present day.

In the late nineteenth century, large-scale manufacturing methods were applied to the making of prescription ingredients as well as proprietary remedies. In the face of industrialization, pharmacists organized state associations, which worked to pass state pharmacy laws that regulate practice. At the same time, Schools of Pharmacy also began to appear alongside medical schools at large state universities.

The early days of the twentieth century witnessed reforms that included the expansion of the pharmacy education system and the introduction of a requirement for pharmacy school diplomas (began in New York in 1910). By the 1930s, pharmacy school expanded to a uniform four-year Bachelor of Science degree requirement. Because most American pharmacists continued to practice in a drugstore setting, however, their professional status suffered. It was only in the post–World War II era, when the modern pharmaceutical industry began to mass-produce medicines effective against a wide spectrum of diseases, that the prestige of American pharmacists rose. By 1970 the proportion of prescriptions requiring compounding expertise dropped significantly. Pharmacists gained stature within the health-care system by providing drug information and counseling to their patients. In the early 1990s, American pharmacy embraced the practice model of “pharmaceutical care,” which called for pharmacists to assume responsibility for proper drug outcomes. In addition, pharmaceutical education began the shift to a single Doctor of Pharmacy (Pharm. D.) degree.

In the early years of the twenty-first century, the roles of pharmacists continue to evolve. Still in charge of the distribution of medicines, pharmacists seek more authority



Interior of pharmacy in 1800s. Pharmacist behind the counter is pouring mixture into a jar while the assistant, in the foreground, prepares mixture in a butter churn. A pestle and mortar and other containers are shown on the counter; apothecary jars can be seen on shelves in the background. Caption: "Please Sir I dont think Mister Foozle takes his Fissick regler No! Why?—Cos he's getting vell so precious fast." Courtesy of the National Library of Medicine.

over proper drug use and a larger role in matters pertaining to public health. See also Antibiotics; Bimaristan/Maristan; Capitalism and Epidemic Disease; Empiric; Folk Medicine; Islamic Disease Theory and Medicine; London, Great Plague of (1665–1666); Pest Houses and Lazarettos; Pharmaceutical Industry; Plague and Developments in Public Health, 1348–1600; Poison Libels and Epidemic Disease; Public Health Agencies in the West before 1900; Public Health in the Islamic World, 1000–1600; Quacks, Charlatans, and Their Remedies; Sulfa Drugs.

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GREGORY J. HIGBY

ARMSTRONG, RICHARD (1805–1860). Although not a medical practitioner, Richard Armstrong was deeply involved in fighting the **smallpox epidemic** that swept the Hawaiian Islands in 1853. A member of King Kamehameha III's (1813–1854) privy council, he led the **vaccination** program during the epidemic and afterward conducted a census to determine the disease's toll. In the aftermath of the disaster, he and another cabinet member, Dr. Gerritt Judd (1803–1873), were accused of having mishandled the government response to the epidemic. He defended his actions in public hearings and managed to retain his government position, whereas Judd, who had led the Royal Commissioners of Health, was forced to resign.

A teacher and Princeton Theological Seminary-trained minister, Armstrong and his family moved to Hawaii in 1832 to serve as missionaries. Armstrong served at several churches in the Hawaiian Islands before becoming Minister of Public Instruction in 1848, a position he would hold until his death in a riding accident in 1860.

The smallpox epidemic began in February, 1853, when the *Charles Mallory*, a merchant ship from San Francisco, appeared in Honolulu's harbor flying the yellow flag that signaled disease aboard. The single afflicted sailor, who eventually recovered, was isolated on a reef in the harbor while the rest of the crew was vaccinated and **quarantined** at Waikiki. This quick action seemed to have kept the **contagion** from spreading, but in May, more cases began to appear, probably unrelated to the *Mallory's* sailor. After the *Mallory* incident, Armstrong had been charged with directing an intensive vaccination program as part of a comprehensive plan developed by the Royal Commissioners of Health and had secured a supply of vaccine by the end of March.

The vaccination program was plagued with problems, including difficulty in securing good quality vaccine supply. Whereas most whites complied with government orders to be immunized, many native Hawaiians avoided the vaccinations, preferring the **folk medicine** of native healers called *kahuna*. Lacking sufficient medical personnel to handle the

workload, Armstrong trained laymen to give immunizations and vaccinated a number of people himself.

Rev. Armstrong drew upon his connections to the missionary community to spread smallpox information through churches. He set up vaccination stations at both Protestant and Catholic churches. He also persuaded the king to designate June 14 as a national day of prayer and fasting.

The epidemic peaked in October 1853 and had run its course by the middle of January 1854. The islands had a population of over 73,000 just prior to the epidemic, and official statistics generated by Armstrong's 1854 census set the toll of the epidemic at 6,405 cases of smallpox resulting in 2,485 deaths. These figures are generally agreed to be inaccurately low. Convinced that at least two-thirds of all cases went unreported, Armstrong himself contended that the actual death toll was over 6,000. This catastrophe prompted Hawaiian lawmakers in 1854 to make vaccination of natives and visitors compulsory. *See also* Measles Epidemic in Fiji (1875) and Eugenics; Smallpox in Canada and the United States since 1783; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Smallpox in European Non-American Colonies; Trade, Travel, and Epidemic Disease.

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TERESA LESLIE

ARTHROPODS. *See* Insects, Other Arthropods, and Epidemic Disease.

ASTROLOGY AND MEDICINE. From ancient Sumerians and Egyptians to modern Chinese who use traditional medicine, medical practitioners of many cultures have assumed and sought to account for the influence of planets and stars on the human body and on **epidemic** diseases. Islamic scholars significantly developed Greek astrology during the ninth and tenth centuries CE, creating its central place in Western medicine. **Physicians** relied on astrology to understand and treat epidemic disease into the eighteenth century. An ancient art, astrology differed from astronomy in its emphasis on the supposed effects of stars and planets on earthly life. Practitioners of both disciplines observed celestial bodies—their magnitude, motions, phases, and so forth. Astrologers, however, searched for causal relationships between earthly events and celestial motion. Though generally not astrologers themselves, physicians used astrology as a tool to understand the physical constitution and temper of their patients and to determine the best courses of treatment.

There were two varieties of astrology practiced in the premodern West: prognosticative (or “natural”) astrology, which physicians and the Catholic Church accepted, and unapproved judicial astrology, which used celestial events to foretell the future. Many **quacks** regularly practiced the latter, and cash-strapped professional astrologers sometimes attempted it as well. Prognosticative astrologers confidently utilized complex quantitative methods as they tried to interpret celestial phenomena they completely misunderstood. Medical students in medieval and early modern Europe learned this form of astrology to

AN ASTROLOGICAL EXPLANATION OF THE BLACK DEATH'S CELESTIAL ORIGINS IN 1345

Because Saturn was dominant, he brings cold (greater than the sun could counter) to each country under his rule, and because of the sign in which the conjunction occurred men will experience the onset of lingering illnesses such as tuberculosis, catarrh, paralysis, and gout; passions of the heart arising from unhappiness; and the deaths of those who have endured long weakness. And since the conjunction was in the air sign of Aquarius it signified great cold, heavy frosts, and thick clouds corrupting the air; and since this is a sign that represents the pouring out of water, the configuration signifies that rivers will burst their banks and the sea flood. And because of the persistently cold atmosphere bitter humors cannot be expelled from the sea as usual, and because of the persistent cold there will be few fish in the sea and those that are there will rot because of the cold, which traps vapors and humors in their bodies. For his part, Mars in that sign denotes strife among men, and sudden death that comes among all sorts of men, especially among children and adolescents, and illnesses entailing fevers and the spitting of blood, and also violent death and ulcers.

From astrologer Geoffrey de Meaux, astrological treatise in Bodleian Library, Oxford, MS Digby 176; translated by Rosemary Horrox in her *The Black Death* (New York: Manchester University Press, 1994), p. 172.

help them understand health and disease. Curricula included both cosmology and planetary astrodynamics, though many physicians learned how to chart horoscopes without understanding the underlying astronomical theory. The primary focus was on the correlation between astrological influences and disease and on the practical application of this understanding.

Astrologers used astronomers' observational data recorded in complex tables to track the positions of planets in the 12 divisions of the heavens, denoted by the familiar "signs" of the zodiac. They constructed a chart (geniture) to map effects of the thousands of planetary (and other celestial) movements on a specific individual. This did not predict particular events but presented many probable outcomes based on trends. The primary factors believed to influence an individual's "nature" shaped genitures vastly more complex than modern popular horoscopes. One zodiacal sign or "house" dominated a person, but the relative and changing positions of the five known planets, the moon,

and the sun also mattered. So did the relative positions of all of these bodies at the time of the individual's birth, the "aspects." Together these gave the astrologer a complete portrait of a client's natural "dispositions."

Physicians considered two kinds of astrological influence when diagnosing diseases. One was specific to an individual, as a result of the sum of celestial forces acting on him or her from conception beyond birth; this component described a person's predispositions, chronic conditions, or disabilities. The second was the celestial influence on the terrestrial environment: weather, waters, crops, and so forth. Physicians held certain astrological events or moments responsible for the rise and spread of diseases now known to be infectious; a "malign" planet like Saturn in the right position caused plague outbreaks by "putrefying" air. The outbreak of the **Black Death** in 1347, for instance, was interpreted as the result of the 1345 "Great Conjunction" of Jupiter and Saturn, which prominent astrologers considered the harbinger of most of that decade's mishaps, including serious economic problems. Later plagues were also attributed to conjunctions and sometimes to comets. Geographical locations influenced by malign celestial bodies were considered breeding grounds for pestilence. For treatment, physicians, following **humoral theory**, considered appropriate plant and mineral substances by correlating the astrological influence on the medicine and the disease or provided purgative or bloodletting treatments

only when astrologically appropriate. Medicinal astrology in the West disappeared with the successes of the **Scientific Revolution**. See also Chinese Disease Theory and Medicine; Islamic Disease Theory and Medicine; Medical Education in the West, 1100–1500; Medical Education in the West, 1500–1900; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500.

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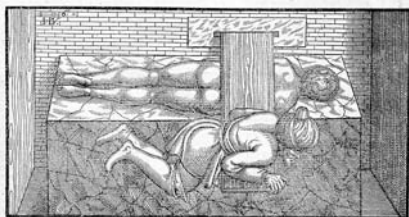
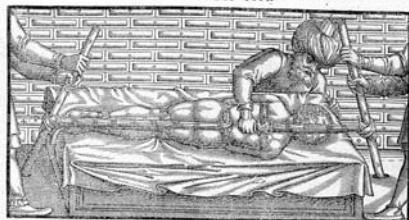
DENNIS GREGORY CARAMENICO

AVICENNA (ABU ALI AL-HUSAYN IBN ABDULLAH IBN SINA; 980–1037).

The medieval Persian philosopher and **physician**, known in the West as Avicenna, had an enormous influence on the interpretation and treatment of plague **epidemics** in the Middle East and in Europe. Born in Bukhara, southern Uzbekistan, he mastered all the Greek sciences by the age of 18. Physician and political administrator at an early age, he became the envy of many and fled from place to place, writing by night on horseback, his memory serving as reference. Avicenna finally settled in the capital, Isfahan, in central Iran, and after a protracted bout of colic, died and was buried in Hamadan, northwest of Isfahan.

Though his mother tongue was Persian, Avicenna wrote mainly in Arabic, not only on medicine and the sciences, but also on philosophy, music, and poetry. His most famous work, *al-Qanun fi al-tibb* (*The Canon of Medicine*) is a record of all the medical knowledge of his time, including translations of Greek writings that would otherwise have been lost, supplemented with his own observations. Clear and well ordered, *The Canon*, more accessible than **Hippocrates** or **Galen**, was translated into Latin in the twelfth century and remained an essential medical textbook until the nineteenth century. Avicenna recognized the presence of infectious diseases such as **leprosy**, scabies, **smallpox**, **measles**, and pestilential fevers (plague) and adopted, from the Greeks, the theory that epidemics are caused by pollution in the **air** (miasma). In Volume III of *The Canon*, in the chapter "Epidemics [Plague] and similar fevers," Avicenna wrote that impure air is like boggy, stagnant **water**; pollution is caused by smoky winds that cover the land with dust, by contact with swamps, by rotting carcasses, and by contaminated bodies. When air is polluted, his advice was to stay indoors. Plague epidemics, he wrote, thrive on hot, damp air, usually occurring at the end of summer and in the autumn. Avicenna described the symptoms of plague infection as the appearance of swellings (buboes) on armpits, groin, or behind the ears. Pestilence, he said, contaminates plants, the animals that feed on them, and the people who consume these animals. He saw an increase in the number of frogs, insects, and rats that surfaced as a sure sign of an impending epidemic, but only as a forewarning; he did not recognize the causal relationship between rats and plague.

LIBER IIIII



De^o 1^o [dislocation] aliofo. et q^uo iudicare esse canle. Cap. 116
 A Libofas quando dislocatur, tunc illud fctur fctur. Sed & magna fctur dislocatonis fctur per fen-
 nam itarum: quod p^{er} non expandi pedem, neg in loco dislocatonis neg a p^{ar}ti genis, immo
 est p^{ar}ti genis et laboriofus. Requiem auro illis et: quoniam cum uti aequare illud, oportet ut in-
 tro mittat medium digiti in anam utiqueq^{ue} opponatur loco, deinde preme cum eo ad iuperfora cum
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Illustrations showing dislocation and mas-
 sage. From *Liber canonis, de medicinis
 cordialibus, et cantica* [canon of medicine]
 by Avicenna, published by J. Hervagius,
 Basle in 1556. Courtesy Wellcome Library,
 London.

The uncertainty that dominated Islamic, as well as European, opinion about the cause of an epidemic made it very difficult for physicians to find a cure for plague. Treatment centered on ways to improve air quality or advice to flee to uncontaminated areas. Avicenna recommended bloodletting; applying Armenian clay to buboes; improving the air with aromatic fruits and herbs; cooling the patient's surroundings by spraying water and vinegar; fumigating with camphor, pomegranate peel, myrtle, and sandalwood; and, in line with previous Islamic and Greek recommendations, giving the patient a daily potion of aloes, saffron, and myrtle. See also Contagion Theory of Disease, Premodern; Greco-Roman Medical Theory and Practice; Islamic Disease Theory and Medicine; Rhazes.

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SELMA TIBI-HARB

AYURVEDIC DISEASE THEORY AND MEDICINE. Long before there were written languages, the peoples of the regions now called Pakistan and India, following patterns established further back than memory could reach, set broken bones, treated wounds, and tended the disease-stricken. Some of these practices included strong doses of religious belief in disease-causing demons and healing deities, others were based on astrological cults, and still others on the observations of **empirics**. Elements of some of these manifold traditions may remain in contemporary **folk medicine**, but only one major strain has survived, having been recorded first in Sanskrit during the fifth century BCE, about the time of the Greek **Hippocrates**, and over centuries after. These texts served medical students in schools that taught the “knowledge for longevity,” one translation of the Indian term Ayurvedic, an elite and learned tradition. Ayurvedic medicine remains actively studied and practiced today alongside Western medicine in India, and the Indian government even supports its teaching and practice. In the West, Ayurveda is often treated as a trendy “alternative” medicine.

Distinctively nonreligious, Ayurveda does share with Buddhism a concern for moderation or “the middle way” in all things, especially diet, mood, and morality. Practitioners believe that the human body consists of tissues, the three humor-like *dōsas* or *tridoṣa*, and wastes awaiting removal. To these are added the body’s seven “constituents”: chyle, blood, fat, flesh, bone, marrow, and (the highest) semen. The *tridoṣa*—wind, bile, and phlegm—are byproducts of food that move through the body’s tubes, and blockages in these cause many of the conditions labeled disease. Regulation of these through a regimen of **diet**, exercise, and bathing is the key to good health.

But the body is also acted on by the **environment**, which is what brings on **epidemics**, or *janapada-uddhvamsa*. When a single disease afflicts many in a given area, the cause clearly must be in the place: its **air**, **water**, vegetation, pests, and even earthquakes and ghosts. Time (seasons, conjunctions of events) also plays a role, and Ayurvedic texts reflect this concern with their inclusion of astrological material. The earliest surviving text, *Caraka’s Compendium* from northwest India, equates epidemic preconditions with “corruption” of the air, water, locale, and time. Essentially, each is unusual or abnormal in one or more distinctive, negative ways: the air is too humid or smoky, the water is sour or cloudy. These four corruptions are rooted in “bad judgments” made recently or in the past by the social leaders in the area, which resulted in bad acts or unrighteousness. In a kind of cascading effect, the unrighteousness grows, virtue is overwhelmed, the gods abandon the area, and the abnormalities of corruption set in. These affect the inhabitants in roughly the same fashion, and an epidemic arises, the specifics of the disease being dependent on the specifics of the corruption. Bad karma corrupts. The role in epidemic disease of **contagion**, or spread of disease by personal contact, is hinted at but never fully developed in Ayurvedic texts

In Caraka’s account, the appropriate medicines must be gathered before conditions deteriorate, or their potency will likewise drain away. Ayurvedic doctors used long lists of both animal and plant materials as medications, and Caraka’s text asserts boldly “when people are treated [prophylactically] with medicine they will not become sick.” The use of emetics, purgatives, enemas, sinus clearing, and later bloodletting, douches, sweating, massage, and other therapeutic procedures meant to affect the *tridoṣa* took their place as well, both as prophylaxes for and treatments of disease. Though highly traditional, Ayurvedic medicine changed and evolved over time: minerals appear in the pharmacopoeia around 1000 CE; **syphilis** (French/*phiranga* disease) appeared among treated diseases around 1500; and more effective means of diagnosis replaced less reliable ones over time. Though practiced in India by at least 1700, **inoculation** is never mentioned in Ayurvedic texts. See also *Astrology and Medicine*; *Chinese Disease Theory and Medicine*; Galen; *Greco-Roman Medical Theory and Practice*; *Humoral Theory*; *Islamic Disease Theory and Medicine*.

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JOSEPH P. BYRNE

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B

BABESIOSIS. While treating patients for the **bacteria** that cause **Lyme disease**, medical practitioners eventually realized that tick bites, such as painless bites from period-sized deer ticks, were “dirty” and carried a wide range of infections. One of the most important of these deer tick infections is the tiny parasitic infection caused by protozoa of the genus *Babesia*, which is named for Romanian biologist Victor Babes (1854–1926). This is an infection that affects the interior of red blood cells, with effects similar to **malaria**. Babesiosis and other conditions caused by *Babesia* are considered emergent. The two main reasons it has escaped detection in so many countries for so many decades are the lack of advanced testing to detect its presence and the fact that little attention has been given to this type of disease by the modern world medical community. The veterinary medicine community has done much more study and treatment of *Babesia* infection in **animals**—for example, cattle—than have **physicians** treating humans.

Babesia diseases are not rare. In one study, 36 percent of Mexican citizens tested were infected with the species *Babesia canis*. This infection is not supposed to be common in humans and is typically understood to be an infection that affects dogs. In another study, 3 to 8 percent of U.S. blood donors had *Babesia microti*. Researchers have found that *Babesia* is a common coinfection and is present in 66 percent of patients with Lyme. This coinfection causes the patient to commonly suffer from nearly 50 different symptoms, which include fever, waves of warmth, sweating, chills, and fatigue. *Babesia* can also cause red blood cells to become deformed inside tiny organ capillaries and cause dozens of debilitating symptoms. It may also possibly increase the probability of strokes and heart attacks as the result of blood clots.

Because of the tiny size of the *Babesia* protozoa, testing for this infection is challenging. For example, bloodstains of infected people can require hours of manual searching with a **microscope** at high, 1000x magnification. This tedious searching is rarely

performed. The severe diagnostic limitations of blood smear testing are similar to those experienced in the process of malaria testing. Under the microscope, malaria appears very similar to *Babesia* when present within the red blood cell. In one Baylor Texas Medical Center study of 59 patients with clear, clinical malaria, 80 percent were given the wrong initial diagnosis based on blood, and some patients died as a result.

Babesia Signs and Symptoms. Babesiosis can cause many different signs and symptoms, including a period of high fever or persistent low fever, listlessness, chills, sweats, headaches, excessive sleep, fatigue, and muscle or joint aches. *Babesia*, *Bartonella*, *Mycoplasma*, and mold spore surface mycotoxin exposure should always be considered in patients who do not respond well to indicated Lyme treatment. The research is universally clear that *Babesia* with Lyme is much more disabling for patients, and the treatment requires more aggressive and diverse options.

Treatment. Most *Babesia* research suggests the best treatment for adult patients is Mepron (atovaquone) 750 mg at least twice a day combined with Zithromax (azithromycin) 250 mg twice daily. The research on all treatments is very limited, and each treatment is usually based on as few as one to nine studies, most of which were not performed at an advanced academic level. Much of the current research represents only small groups of patients or animals receiving clinical care utilizing various treatment options. Further, most of the treatments suggested are applications of malaria research because malaria has some similarities with *Babesia*.

Another treatment option for *Babesia* involves the use of Artemisia plant derivatives. This approach is taken from Chinese medicine and is now recommended as a leading treatment against malaria according to the **World Health Organization (WHO)** and the United Nations Children's Fund (UNICEF). For example, many drugs are derived from the Artemisia plant; some are potentially damaging to hearing and are toxic to the brain, whereas others are well tolerated. Some Artemisia advertisements falsely call this herb "Wormwood," because it is popularly called "Sweet" or "Annual Wormwood," but it does not have Wormwood's toxic chemicals. Effective forms of Artemisia preparations kill *Babesia* by methods that include free radical formation, so multiple antioxidant supplements are recommended to catch free radicals and help the red blood cells regain their smooth surface. These also help to prevent Artemisia medications or nutrients from causing free radical damage to other organs.

Babesia is an emerging pathogen, which means in part that new species are being discovered, and medical science is far from mastering the infections it causes. See also *Bartonella* Diseases.

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JAMES SCHALLER

BACTERIUM/BACTERIA. Bacteria are small, free-living, single-cell organisms without a true nucleus and bounded by a rigid cell wall composed of protein and carbohydrate components. These organisms reproduce asexually by binary fission (splitting). As a group they are among the most numerous and diverse organisms in the world. Individual bacteria, however, are only visible with the aid of the **microscope**. Bacteria are distinguished from other single-cell organisms such as yeasts, molds, and **protozoa** by the lack of an organized nucleus as well as by more subtle biochemical properties.

The study of the unseen world of these organisms was first revealed through the use of the microscope, invented in the early decades of the 1600s. These early microscopes were simply single lenses of high curvature, such as small spherical glass beads of very short focal length. The best of these “simple” microscopes had a magnification of about 200x.

The acknowledged pioneer in both microscope construction and careful observation was the Delft cloth merchant **Anthony van Leeuwenhoek**. Leeuwenhoek produced a series of landmark communications to the Royal Society of London which extended from 1673 until his death in 1723. Leeuwenhoek described what appeared to be little animals (“animalcules”) in many seemingly “pure” substances, from melted snow and vinegar to extracts of spices from the Far East. These are the first reports on the organisms we now take to be the subject of the field of microbiology. Not only did Leeuwenhoek note that these little animals had regular structures, which he arranged in a simple classification scheme, but he also reported that some were motile (able to move themselves) and that they seemed to increase in number, that is, to grow and multiply over time.

Although many objects that Leeuwenhoek described are now recognized as amoeba, paramoecia, diatoms, and small multicellular organisms such as rotifers, some of the smallest objects appear to have been true bacteria. Leeuwenhoek’s classification scheme is the distant precursor of that in use today. He described four types of these tiny organisms based on shape and size: round cocci, rod-shaped bacteria (two sizes), and helical spirillia.

In 1773 Otto Friedrich Müller (1730–1784) published a treatise on “infusoria,” the name for the collection of organisms that were found in various teas and other water extracts of plant and animal materials. Müller, using the improved microscopes of the eighteenth century, including the “compound” microscope with multiple lenses, recognized two main groups of infusoria, *Monas* and *Vibrio*, which contain bacterial forms.

Müller’s scheme was used in the late eighteenth century and was extended in 1838 with the famous study by Carl Gustave von Ehrenberg (1795–1876), who published *Die Infusionstierchen als vollkommene Organismen*, a large folio atlas with extensive hand-colored, engraved plates. Ehrenberg, like his predecessors, did not make a distinction between protozoa and bacteria. They were all classified as Infusoria, and all were believed to have tiny stomachs and other parts analogous to those of larger animals. His classification scheme was detailed, complex, and extensive. Of relevant interest are his descriptions of the family Vibrionia, which was comprised of five genera: *Bacterium*, *Vibrio*, *Spirochaeta*, *Spirillum*, and *Spirodiscus*. In spite of Ehrenberg’s detailed descriptions, we cannot unequivocally identify many of his organisms with current microbial classifications.

Throughout the nineteenth century, the classification of microorganisms evolved and developed, but all attempts were limited by the fact that they were superficially descriptive, not physiologic, morphologic but without the aid of chemical stains, and mixtures rather than homogeneous samples of the organisms.

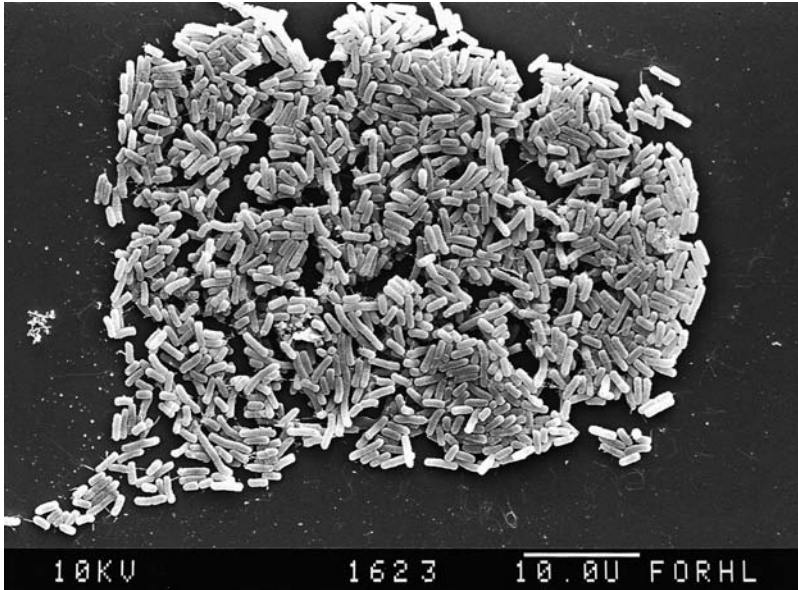
As soon as bacterial culture became routine, following the work of the nineteenth-century bacteriologists, it was noted that growth requirements and culture conditions were properties that were useful in characterizing the various bacterial types. These physiological studies paralleled the study of metabolism in both plants and animals and showed that bacteria were similar in many ways to higher forms of life.

Although bacteria share basic metabolic pathways with all other organisms, they are in general much more adaptable and exhibit a great diversity of special physiological and metabolic processes. As free-living, single-cell organisms, functional and biochemical specialization that is a hallmark of multicellular organisms is not usually available to them as a survival strategy.

The relationship of bacteria to disease, fermentation, and putrefaction was elucidated toward the end of the nineteenth century initially through the work of **Louis Pasteur**, **Robert Koch**, and their colleagues. So-called **germ theories of disease** provided an explanation for the specificity of various diseases while also explaining mechanisms of **contagion**, pathogenesis as a result of bacterial toxins, and subsequently, **immunity** to infectious diseases.

Bacteria living in diverse environments have many special structures, chemicals, and metabolic pathways to exploit their particular ecological niches. Thus, the membrane lipids of bacteria living at low temperature differ significantly from those of bacteria adapted to warm temperatures. The differing lipid compositions allow maintenance of membrane fluidity at different temperatures. The differing lipid compositions allow maintenance of membrane fluidity at different temperatures. The adaptive utilization of a wide variety of carbon compounds for energy, the presence or absence of the requirement for oxygen for energy production, and the production of secondary metabolites that are toxic to environmental competitors are all examples of this biological diversity. This diversity of bacterial metabolism has been exploited for many useful purposes, including such age-old processes as production of vinegar by *Acetobacter* and such recent discoveries as **antibiotic** production from *Streptomyces*.

Many bacteria have evolved special, mutually beneficial relationships with other organisms. The bacteria that inhabit the intestines of animals are supported by the food that the animal eats, but at the same time, the bacteria produce certain essential nutrients as byproducts, which are absorbed by the animal host. One such example is the vitamin, biotin. The intestinal bacteria *Escherichia coli* produce all the biotin needed by humans. In the case of certain animals that subsist on a diet of grass, such as cattle, special bacteria in their stomachs can digest cellulose to produce sugars which are absorbed by the cattle as their main source of nutrition. These animals, called ruminants, are absolutely dependent on being colonized by these cellulose-digesting bacteria. A similar situation exists in some plants (legumes) which harbor bacteria in small root nodules. These bacteria are able to absorb atmospheric nitrogen and convert it (by a process called nitrogen fixation) into ammonia and related compounds, the most important of which are the amino acids. These amino acids are then provided to the plant for protein synthesis and growth. The process of nitrogen fixation is crucial to the existence of life on earth. An extreme case of this type of mutual benefit is represented by the subcellular organelles called mitochondria which exist in most eucaryotic cells. There is strong evidence that mitochondria evolved from bacteria which long ago invaded the cytoplasm of some cells, became a useful source of oxidative energy production for the cell, and along the way lost the ability to live independently.



Scanning Electron Micrograph (SEM) of *Escherichia coli*. Courtesy of David Gregory and Debbie Marshall, Wellcome Library, London.

One type of growth process distinguishes bacteria from many higher organisms: the ability, when placed in unfavorable environments, to develop into a dormant state known as a spore form. Spores are living cells which are metabolically quiescent, surrounded by a durable wall, and relatively dehydrated in comparison with normal cells. Under normal growth conditions, spores germinate to produce normal vegetatively growing bacteria again. The spore forms of bacteria are highly resistant to drying, to temperature (they are not killed by boiling water temperature, but require high pressure steam above 120°C to be killed), and to ultraviolet light. Sporulation is a survival strategy that is common to bacteria that live in diverse environments and is less common in bacteria that inhabit more constant ecological niches such as the mammalian intestine, for example.

The widespread presence of bacteria and their adaptability to many ecological niches provide them with the ability to move about in nature with speed and efficiency. Humans perceive such survival strategies as contagion and the basis for **epidemic** disease. Bacteria can often be spread by simple physical contact, which transfers a few organisms to a new location. Often, however, **water** or **air** currents serve to carry bacteria to new environments. Some bacteria have evolved to be carried by other organisms (called vectors) such as insects or other animals. One important example is the transmission of human plague bacteria by the bite of the rat flea.

Although bacteria do not have a membrane-bounded organelle, the nucleus in which the genetic apparatus of the cell resides, their genetic organization is similar to that of all other cellular life. Genes are encoded in DNA, and the genetic code of bacteria is

identical to that of higher organisms (with a few interesting variations in the evolutionarily ancient Archea). Most bacteria reproduce by binary fission so they form clonal populations, all descended from a founder organism. However, some bacteria have evolved mechanisms for mating and genetic exchange as a way to increase genetic diversity and, presumably, evolutionary fitness. So-called bacterial sex has been a very useful tool for analysis of genetic mechanisms at the molecular level.

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WILLIAM C. SUMMERS

BARTONELLA DISEASES. *Bartonella* is the cause of one of the most serious emerging bacterial infections in the world. It has the potential to infect tens of millions of people because it is found throughout the entire world, with the exception of the polar ice caps, and can easily infect patients in cities, suburbs, or rural areas. Further, in contrast to many vector-borne infections, *Bartonella* can be spread by many vectors and by many means: flea bites, flea feces, dust mites, cats, and dogs can carry this infection in their paws and saliva, and can infect a person by a scratch, lick, or playful bite.

Bartonella is so common that laboratory findings show that 40 percent of California cats have contact with the illness. Since one-third of all homes in the United States have a cat, this means that many of the 70 million cats in the United States can playfully bite, lick, or scratch a human and infect him or her. But it is very probable that the 40 percent figure seriously understates the case. Researchers have discovered that blood samples with *Bartonella* infection sent to labs have routinely been falsely declared negative, meaning that labs routinely miss the presence of the pathogen in both humans and animals. A new blood cell stain by Dr. Stephen Fry and new genus-level DNA testing (PCR testing) both hold hope for better diagnosis in the future.

Amazingly, however, *Bartonella* has still other agents to spread its infection: lice, ticks, and certain flies. Finally, examination of fetus pregnancy tissue shows that *Bartonella* clearly infects the placenta, and infected baby mice are born smaller than normal.

Bartonella typically hides in the human and animal body, literally infecting red blood cells and the cells lining the blood vessels, and it can suppress the immune system and remain undetected. If other **bacteria** were floating in blood or lining the red blood cell endothelial cells, they would likely cause death within hours or days; yet *Bartonella* escapes detection.

It was formerly thought that most types of *Bartonella* were harmless to cats and humans, but emerging research has found that close examination under the **microscope** shows tissue damage to cats from *Bartonella*. In the same manner **Lyme disease** was initially seen as merely an arthritis disease and **Babesia** as a pathogen that simply caused fevers, fatigue, and sweats. With each passing year it becomes clearer that both of these infections have hundreds of symptoms. *Bartonella* is similar in the number of new strains being found and the increasing evidence for diverse human body damage.

Bartonella was initially discovered and named after Alberto L. Barton (1874–1950), a Peruvian **physician**. In 1909 he published an article on elements found in the red blood cells of patients with dangerous Oroya fever. In this article he identified the blood parasite (*Bartonella bacilliformis*) that is the causative agent of Oroya fever and verruga peruana. The organism is now placed in the genus *Bartonella*, which was named after him in 1915. It was first considered a **virus**, and then a bacterium having only three species. Now it is known to have approximately 10 species, including a newly discovered species that infects humans, *Bartonella rochalimae*. Most experts expect to find additional species. In 2005 French researchers found *Bartonella* DNA in the tooth pulp of French soldiers buried in 1813 in Vilnius, Lithuania, indicating that Napoleon's troops suffered from *Bartonella* diseases as well as typhus and others well known to historians.

As research on the effects of *Bartonella* has proceeded, it has become clear that it causes over 200 signs and symptoms in humans. These include numbness or loss of sensation; dizziness; headaches; oxygen deprivation; abscesses; gingivitis; muscle spasms and/or weakness; joint pain; liver disease; intestinal disorders; and kidney, bladder, and genital disorders. Also common are fatigue, sleep and memory problems, and drowsiness. Because it is a red blood cell infection and blood enters all tissues, the illnesses *Bartonella* causes in humans can involve any organ. For years this infection was naively felt to be only as serious as a cold, with a few transient enlarged lymph nodes, skin tag-like papules, and maybe an occasional small painless rash. Now, however, we know that a percentage of patients die from heart rhythm damage caused by *Bartonella* fat spots made in the heart. Others experience weakening blood vessel walls that can lead to a stroke. Still others with *Bartonella* struggle with agitated depression, bipolar disorder, panic disorder, addiction, or aggressive rage, all of which makes them prone to suicide. The psychiatric treatment of a patient with *Bartonella* is highly specialized, and most family physicians and psychiatrists do not know how to treat a patient suffering from *Bartonella*-induced psychiatric disorders.

Yet despite advances in understanding and agreement on the seriousness of *Bartonella* infection, lab testing and health-care worker training in the diagnosis of this infection are poor, and so the vast majority of infected and ill patients go undiagnosed, misdiagnosed, and untreated.

Treatment. Currently, no standard of medical care exists for *Bartonella*. Many treatments tested in the laboratory do not seem to work in live animals or humans. Research shows that routinely prescribed **antibiotics** fail in individuals ill with *Bartonella*, particularly if only given for a few weeks, and that even after the blood is cleared some infection remains in the walls of the blood vessels, and repeat pulsed treatment is needed for a cure. This is the probable cause for so many “relapses” in past studies—short treatment and a lack of appreciation that the antibiotic was not killing the *Bartonella* hiding in the blood vessel walls. However, longer-term treatment with breaks, followed by restarted pulsed treatment, is not yet routine. Because no treatment is universally agreed upon at this time, and no book in English exists on advanced clinical *Bartonella* medicine, no standard has currently clearly been shown to be effective in the eyes of the broad medical community. As traditional medicine looks for new effective antibiotics, researchers have found that some modern Chinese medicine antibiotic herbal treatments are effective; however, they are under-prescribed, and patients still require pulsed treatment once their blood has been initially cleared of infection.

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JAMES SCHALLER

BEHRING, EMIL VON (1854–1917). Emil von Behring is one of the founders of the science of **immunology**. Prior to his work, the prevailing concept was that the body's ability to fight infection could be attributed to the cellular response, the ability of phagocytes and other cells to engulf and destroy **bacteria**. He was one of the first proponents of the humoral aspects of immunology that led to using antitoxins and antibodies to fight infection.

Von Behring was born in East Prussia on March 15, 1854. While in high school he developed an interest in medicine and later attended Friedrich Wilhelm University in Berlin where he received his medical degree in 1878. His early medical career occurred during a time of great progress in medicine's ability to deal with infectious diseases. **Louis Pasteur** developed **germ theory**, **Robert Koch** refined the ability to grow and identify bacteria, **Paul Ehrlich** introduced the use of specific chemical agents to treat infections, and Elie Metchnikoff (1845–1916) formulated the concepts of the cellular immune response.

During his work as a military physician, von Behring recognized the importance of infected wounds as a cause of deaths. In the 1860s, British surgeon Joseph Lister (1827–1912) instituted the use of carbolic acid sprays during surgery as a method of preventing contamination of surgical incisions and subsequent infection. Following on this idea, von Behring attempted using the antiseptic iodine compound iodoform internally as a means of fighting the effects of infection by neutralizing toxins produced by bacteria, but the side effects of the iodoform were themselves too severe to allow its use. Nonetheless, he persisted in his attempts to reduce the effects of infections not by killing the bacteria causing the infection, but by destroying the toxins produced by the bacteria.

Diphtheria was an ideal disease for von Behring to study. Many of the deaths from diphtheria are not the result of the local infection itself, but rather the effects of toxins produced by the bacteria. Von Behring and his associates, primarily **Shibasaburo Kitasato**, first confirmed that bacteria-free filtrates contained toxins that, when injected into animals, caused the systemic signs of these diseases. When very minute doses of the toxins were injected, an adequate amount did not exist to cause disease. However, repeated minute doses did protect the animals from ill effects of subsequent larger doses. They postulated that the animals had developed an ability to neutralize the toxins with an antitoxin that the animals themselves had produced. They next injected the serum of an animal that had the ability to neutralize the toxin into animals that were infected. Those infected animals developed no signs of disease, thus demonstrating that the ability to neutralize the toxin could be passed on with injection of the antitoxin. In 1891 von

Behring administered an injection of antitoxin obtained from a sheep into a girl dying of diphtheria, saving her life and establishing the value of antitoxin therapy.

Emil von Behring received the first Nobel Prize in Physiology or Medicine in 1901 in recognition of his work on the antitoxin serum therapy of diphtheria. He died of pneumonia in 1917. *See also* Animal Research; Disinfection and Fumigation; Human Immunity and Resistance to Disease.

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CHARLES V. BENDER

BIBLICAL PLAGUES. The scriptures of ancient **religions** contain many accounts of pestilence, often reported in catastrophic language. This is not surprising because these episodes were often dramatic events that swept through populations, killing many and frequently occurring at times of social disorder, population displacement, or **environmental** adversity. It must therefore have always seemed probable that these scourges were a form of divine punishment for moral or devotional failure. The ancient apocalypticism, which characterized the thinking of early Christianity, readily interpreted the social disaster and institutional collapse associated with these pestilential events as a battle that had been duly lost against the Power of the Lord. A similar subtext of divine displeasure underlies the ancient accounts of pestilence in the Sumerian epic of Gilgamesh, in the Indian Mahabharata, and in Oedpius's Greek city-state of Thebes.

There are many overt references to epidemic outbreaks of infectious disease in the Hebrew Scriptures, also known as the Old Testament of the Christian Bible. There were the plagues of Egypt during Israel's bondage in that powerful land, occurring late in the Middle Kingdom. One plague entailed "sores that break into pustules on man and beast." Another plague, more notorious, killed the first-born Egyptian children on the night of the original Jewish Passover: "and there was a great cry in Egypt, for there was not a house where there was not one dead." The Book of Deuteronomy records that after the Israelites escaped from Egypt, braving the parted waters of the Red Sea, Moses received subsequent divine instruction on Mount Sinai to exact a ransom to God from each of the newly liberated Israelites in order "to avert plague."

During the two immediate pre-Christian millennia, as city-states and civilizations came increasingly into commercial and military contact, infectious agents were often exchanged. The initial contact of a virgin population with a novel microbe would have often caused violent **epidemics**. For example, in Deuteronomy it is recorded that the Hittites suffered in great anguish from the 20 years of pestilence that followed their capture, importation, and enslavement of Egyptians as prisoners-of-war. The enslaved Egyptians would almost certainly have inadvertently carried with them a range of infectious agents from the microbial repertoire of their more ancient civilization (to which the Egyptians would have developed some low-level immune resistance). Once loosed among the less cosmopolitan and immunologically defenseless Hittites, however, these alien microbes wreaked havoc, despite the anguished and wailing pleadings of the prostrated Hittite priests.

THE BIBLICAL PLAGUES OF THE APOCALYPSE

And the seven angels came out of the temple, having the seven plagues, clothed in pure and white linen, and having their breasts girded with golden girdles. And one of the four beasts gave unto the seven angels seven golden vials full of the wrath of God, who liveth for ever and ever. And the temple was filled with smoke from the glory of God, and from his power; and no man was able to enter into the temple, till the seven plagues of the seven angels were fulfilled.

And I heard a great voice out of the temple saying to the seven angels, Go your ways, and pour out the vials of the wrath of God upon the earth. And the first went, and poured out his vial upon the earth; and there fell a noisome and grievous sore upon the men which had the mark of the beast, and upon them which worshipped his image. And the second angel poured out his vial upon the sea; and it became as the blood of a dead man: and every living soul died in the sea. And the third angel poured out his vial upon the rivers and fountains of waters; and they became blood. And the angel said: For they have shed the blood of saints and prophets, and thou hast given them blood to drink; for they are worthy.

And the fourth angel poured out his vial upon the sun; and power was given unto him to scorch men with fire. And men were scorched with great heat, and blasphemed the name of God, which hath power over these plagues: and they repented not to give him glory.

And the fifth angel poured out his vial upon the seat of the beast; and his kingdom was full of darkness; and they gnawed their tongues for pain, and blasphemed the God of heaven because of their pains and their sores, and repented not of their deeds.

And the sixth angel poured out his vial upon the great river Euphrates; and the water thereof was dried up, that the way of the kings of the east might be prepared. And I saw three unclean spirits like frogs come out of the mouth of the dragon, and out of the mouth of the beast, and out of the mouth of the false prophet. For they are the spirits of devils, working miracles, which go forth unto the kings of the earth and of the whole world, to gather them to the battle of that great day of God Almighty. And he gathered them together into a place called in the Hebrew tongue Armageddon.

And the seventh angel poured out his vial into the air; and there came a great voice out of the temple of heaven, from the throne, saying, It is done. And there were voices, and thunders, and lightnings; and there was a great earthquake, such as was not since men were upon the earth, so mighty an earthquake, and so great.

From Revelations 15:6–16:18 (KJV)

The Hebrew First Book of Samuel recounts how, in the seventh century BCE, the Lord smote the neighboring Philistines for their seizure of the Israelites' Ark of the Covenant. The text records that "after they [the Philistines] had carried it about, the hand of the Lord was against the city with a very great destruction. And He smote the men of the city, both small and great, and they had emerods in their secret parts." Over 5,000 men were smitten "with a great slaughter." Historians have long been tantalized by these embarrassingly located emerods. The word refers to tumors—so were these emerods swollen lymph nodes in the groin, the telltale swellings of the **bubonic plague**? Even more

tantalizing, indeed remarkable, the Bible records that the penitent Philistines offered up “golden mice.” Was this an inspired allusion—and, if so, an extraordinarily prescient one—to the rodents whose infected fleas spread the bubonic plague **bacterium**?

In Leviticus, the Hebrew priests are made the judges of ritual uncleanness, including “**leprosy**,” and are instructed to banish the impure from the bounds of the camp. The term “leper,” translated by medieval Europe’s scholars from the original Hebrew, was taken to refer to the specific condition then recognized as leprosy. Most probably, the word was actually generic, referring to conditions of gross and menacing disfigurement of face and limbs, and deemed in biblical times to be the mark of divine rejection or displeasure. For this reason, or because of folk wisdom about the possibility of some type of **contagion**, those afflicted were often required to identify themselves by ringing a hand-bell. A description of lepromatous leprosy—the most severe, systemic, form—appears in Hindu Sanskrit texts from around 600 BCE. Although there is no corroboration from skeletal remains in the Indian subcontinent, the writings seem to indicate that the disease was familiar within that part of the world.

The vicissitudes of pestilence were not confined to the Biblical Lands. By around 2,500 years ago, agrarian-based civilizations had begun to form in many fertile regions around the world. Each region duly acquired its own distinctive new infections, and local exchanges of these diseases between populations then occurred, sometimes with devastating consequences. Over time, however, coevolutionary pressures tended to render these endemic infections less virulent—a change that benefited both parties, in terms of survival probabilities. Various ancient texts, including the Sumerian *Epic of Gilgamesh* from 4,000 years ago, the ancient court texts from Egypt and China, and the Hebrew Scriptures, indicate that by the second millennium BCE epidemic outbreaks of these pestilences were no longer dire enough to enfeeble the civilized societies in the Middle East and constrain their imperial ambitions. This apparent virulence-lessening evolution of infectious agents in order to enhance accommodation with their human hosts was, however, less evident elsewhere. In the less consolidated and often later-developing civilizations of the Yellow River (China) and the Ganges Valley (India), and in the Aegean-Mediterranean coastal region, the ecological balance between microbes and humans was less settled.

Later, there came from the early Christian era the extraordinary text of the biblical Book of Revelation. The purported author, St. John (who had been exiled by the Romans to the Greek island of Patmos), gives a lurid account of pestilential diseases as a fearsome instrument of God. He describes the Four Horsemen of the Apocalypse, the fourth (pestilence, riding on a white horse) being the harbinger of near-certain death. These four horsemen are instructive in reminding us that, around two millennia ago in the eastern Mediterranean region, warfare, enslavement, famine, and pestilence were the four main recurring scourges of human happiness, health, and survival. *See also* Diagnosis of Historical Diseases; Leprosy in the Premodern World; Plagues of the Roman Republic; Religion and Epidemic Disease.

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ANTHONY MCMICHAEL

BIMARISTAN/MARISTAN. *Bimaristan* is the Arabic form of the Persian word designating the hospital in the Arabo-Islamic tradition. The question of the origin of hospitals in the Arabo-Islamic world has been long debated. The *bimaristan* is most probably a continuation of the hospital in the Byzantine world (*xenodocheion*), the origin of which has probably to be sought in Egyptian Christian monasticism rather than in fourth-century Christian charitable foundations in Asia Minor, as some historians believe. The fifteenth-century historian Al-Maqrizi asserted that Caliph Al-Walid established the first *bimaristan* in Damascus in 707. Hospitals clearly flourished in Baghdad from the early tenth century and spread across the Islamic world. The exception is Al-Andalus (Spain), where hospitals seem to have been built only from the very end of the fourteenth century. They were generally endowed with a *waqf*, a grant of productive agricultural land with the peasants tied to it, though some were directly funded by the state.

Bimaristan were large architectural structures with many wards for the patients. Some wards were devoted to such specialties as gynecology (but not obstetrics), psychiatry, and surgery. *Bimaristan* also included several peripheral units such as a kitchen(s), pharmacy, school, library, shops, and even in some cases an entire caravanserai. Some scholars believe that many had **leproseria** located adjacent to them, as at Dimnah Hospital, in al-Qayrawan, established around 830. **Physicians** with different specialties, working in collaboration with different corps of assistants and nurses, visited the patients daily, performed surgical interventions, and prescribed appropriate medications. Hospitals provided the populace with a wide range of services not strictly limited to the treatment and cure of illness. These included some forms of public hygiene and prevention of diseases, as well as other social functions such as a retirement place for the elderly. They were directed by a chief physician and managed by a civil administrator. Among the most important *bimaristan* were the 'Audi hospital in Baghdad, the hospital in Rayy, and the Mansuri hospital in Cairo. Over time, hospitals became important scientific and teaching institutions, as physicians did not limit their activity to the care of the sick but also conducted theoretical investigations, the results of which they communicated to audiences of students. Some of the historic hospitals of the Islamic world remained active well into the nineteenth century.

It is difficult to assess the role that the *bimaristan* might have actually played in the management of **epidemics** in the Islamic world because of the etiology attributed to epidemics in Muslim theology and **Islamic disease theory and medicine**. Since physicians in the Islamic world subscribed to both **miasma theory** and **humoral theory**, prevention relied on such methods as **fumigating** by burning perfumes and odoriferous substances,

practicing a quiet lifestyle, and embracing a **diet** consisting of such foods as raw onions, lentils, pomegranates, grapes, vinegar, and lemon juice. As for the treatment, it consisted first of bleeding the patients in order to eliminate the supposed excess of corrupted humor out of the blood and body. Caregivers also administered topical remedies of differing natures according to the disease. Although bimaristan certainly helped in educating the population by promoting supposedly preventive methods and dispensing such treatments, they probably did not have a specific impact on the prevention, diffusion, and eradication of epidemics. *See also* Apothecary/Pharmacist; Astrology and Medicine; Avicenna (Ibn Sina); Black Death (1347–1352); Hospitals in the West to 1900; Plague in the Islamic World, 1360–1500; Plague in the Islamic World, 1500–1850; Public Health in the Islamic World, 1000–1600.

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ALAIN TOUWAIDE

BIOLOGICAL WARFARE. Warfare and disease have always gone together, and in all wars prior to World War II (1939–1945), deaths from disease surpassed deaths from combat, for both soldiers and civilians. It is no wonder, then, that there have been attempts to harness disease as a weapon. The term for such a practice is biological warfare (BW): the use by countries of microbes or toxins as a weapon to cause disease. This is distinct from **bioterrorism** or biocriminality, which is the use of disease as a weapon by individuals or groups.

Biological Warfare before the Twentieth Century. Diseases are complex phenomena, and controlling them sufficiently for use as weapons was not truly possible in a rational fashion until the twentieth century, after the microbial causes of infectious diseases had begun to be understood. Nevertheless, there were sporadic cases of biological warfare in prescientific times. Several incidents of the use of plant toxins as weapons are recorded in ancient times. And in Europe in the fourteenth century, there were several alleged instances of attempts to transmit disease into besieged cities by hurling biological material over the walls. In one such report, at the beginning of the **Black Death**, Mongol armies besieging the Crimean city of Kaffa in 1346 hurled corpses of their plague dead, apparently starting a plague **epidemic** within the city.

Probably more common was the use of disease as a weapon by European settlers in the New World. Several deliberate attempts to transmit **smallpox** to Native Americans have been recorded, usually by giving them contaminated material from a smallpox victim. However, only one has been documented beyond any reasonable doubt: a 1763 incident at Fort Pitt (now the site of Pittsburgh, PA), in which civilian and military leaders of the Fort gave besieging Indians two blankets and two handkerchiefs from smallpox patients. No results were recorded. There were probably additional such incidents that went unrecorded. But even accounting for these, the practice appears to have been rare. However, given the ravages of smallpox on indigenous peoples in the New World, it is likely that some of these attempts caused outbreaks and possibly many deaths.

There have also been suggestions that the British might have used smallpox as a weapon during the American Revolution, although the evidence is scanty. In both the siege of Boston in 1775 and the siege of Quebec in 1775–1776 there were suspicions that civilians with smallpox were sent out of the cities to infect Continental Army troops. Similar actions may have been taken in the South, using escaped slaves infected with smallpox. The British planned to return them to their owners, as many slave-holders were supporters of the revolution. Whether the plan was executed is not known.

World War I (1914–1918). By the time of World War I, infectious diseases were beginning to be understood, and the scientific basis for using them as weapons was being laid. One of the belligerents, Germany, established a systematic program of secret agents in neutral countries that were trading partners of France and Britain—mainly in the United States (neutral until 1917) and Argentina, with smaller programs in Spain, Norway, and Romania. These secret agents tried to infect animals, mainly horses and mules being shipped to the Allies, by pouring cultures of the causative agents of glanders or anthrax in the animals' feed or by jabbing them with contaminated needles. It is unclear whether this program had any success in infecting animals—it appears likely that it did not, but the reasons are unclear. It is notable that the German government explicitly ruled out attack on humans with biological weapons: that was considered to be immoral.

After the war, the nations of the world negotiated a treaty banning both biological warfare and chemical warfare (chemical weapons such as mustard gas had been extensively used in the war). Called the Geneva Protocol of 1925, it has become one of the pillars of the international arms control regime.

World War II (1939–1945). Despite the Geneva Protocol, Japan made extensive use of crude biological weapons during World War II, against the Chinese. **Bubonic plague** was transmitted by dropping infected fleas from airplanes, or by releasing infected rats in cities. Intestinal diseases like **typhoid fever** and **cholera** were spread by infecting wells and food left behind during a Japanese retreat. The results are unclear, but it is estimated that these events left hundreds of thousands of Chinese dead. Another 10,000 are thought to have been killed during Japanese experimentation on prisoners.

Although the atrocities of Japanese biological warfare became known after the war, and most of the officers in charge were captured by U.S. forces, none was tried for war crimes. They were all given immunity in exchange for their cooperation with U.S. military. This deal was probably motivated largely by fear that the information would fall into Soviet hands (because the Soviet Union was a co-prosecutor in the Tokyo War Crimes Tribunal). However, a desire to see the results of human experiments and of actual use of biological weapons may also have played a role, as the U.S. biological warfare program

could not use **human subjects**, and the United States had never actually used the weapons.

Although Japan was the only country to use biological weapons during World War II, several were attempting to develop them. The British developed and stockpiled a low-tech weapon—cattle biscuits laced with anthrax spores—to be used against German livestock as retaliation if Germany used unconventional weapons. These were never used and were destroyed after the war.

A number of countries, including the United States, the United Kingdom, and the Soviet Union, also had programs to develop traditional military munitions—bombs, artillery shells, mortar rounds, and so forth—to deliver live biological agents. Although much progress was made, no country had a militarily useful weapon by the end of the war. Quite notably, Germany did not have a biological weapons program of any significance; Hitler was adamantly opposed to them, for unknown reasons. France had a biological weapons program before the war, but it was ended by France's defeat by the Germans. It was restarted, however, after the war ended.

The Cold War Era. Most countries' BW programs petered out in the 1950s or 1960s, leaving the United States and USSR as the only nations with major programs. The United States developed a number of pathogens (for both humans and animals) as weapons and made stockpiles of these in bombs, shells, and spray tanks. The Soviet Union appears to have lagged far behind the United States in its capabilities and probably had no usable weapons in this time period.

Although the U.S. military had developed biological weapons for battlefield use, it recognized that their utility was quite limited: they could be easily protected against with a respirator, their effects would be delayed by one to several days, they would be very sensitive to the weather conditions, and their effects would be unpredictable. However, they offered great potential to attack civilians covertly. A single plane, equipped with a spray device and several tens of kilograms of a concentrated preparation of a biological agent, could blanket hundreds of square kilometers, causing very large numbers of deaths.

Nevertheless, in 1969 Richard Nixon (1913–1994) announced that the United States would unilaterally destroy its biological weapons and would in the future only develop defensive capabilities. This followed the advice of an expert panel that considered the weapons essentially useless, as the United States had alternatives to biological weapons, most importantly nuclear weapons. It also recognized that possessing biological weapons sent a message to the world that these were useful weapons, and encouraged other nations to follow suit, whereas disarming suggested the weapons had limited utility.

This disavowal prepared the way for a second major treaty limiting biological weapons: the Biological Weapons Convention (BWC) of 1975. This treaty banned the development, production, and stockpiling of biological weapons, plugging the gaps in the Geneva Protocol (which only banned their use).

Despite the treaty, the Soviet Union secretly maintained, and even expanded, its program. It was not until 1992 that Russia (which had inherited most of the Soviet Union's weapons programs) admitted that it had been violating the BWC and decreed an end to the bioweapons program. After its weak start in the 1950s and 1960s, this program had matured in the 1970s and 1980s with major successes in developing plague, anthrax, and smallpox, among others, as weapons. Soviet developers designed them to be delivered on intercontinental ballistic missiles, as second-strike weapons to follow an initial nuclear attack.

The Contemporary World. Other countries are also known to have violated the BWC since it came into force. South Africa's minority white government had a modest program to develop biological and chemical agents for nonbattlefield use, such as assassination and special forces use. This was voluntarily ended when the black majority government came to power in 1994.

Iraq under Saddam Hussein (1937–2003), too, had a program, and actually developed several agents to the point of accumulating modest stockpiles of (militarily insignificant) filled munitions. Iraq devoted a great deal of effort to preventing UN inspection teams (UNSCOM, and its successor UNMOVIC) from learning of the program, but eventually the basic outlines became clear. UNSCOM was then able to destroy the production facilities. After the second Iraq war, the U.S.'s Iraq Survey Group confirmed that the biological weapons program had been effectively terminated, although Iraq appears to have been maintaining the ability to restart the program quickly after UN inspectors left the country.

Several other UN countries are suspected by Western intelligence agencies of trying to develop biological weapons, but the available evidence is quite weak, and it remains to be seen if any of these suspicions are true.

In addition to suspicions that some countries may be trying to develop biological weapons, there have been periodic accusations that some countries have actually used them. The most prominent of the allegations includes charges that the United States used them against China and North Korea during the Korean War; that the United States used them repeatedly against Cuba; that the Burmese (Myanmar) government used them against insurgent indigenous tribes; and that the Rhodesian government used them against blacks during the Zimbabwean war of independence. Some of these allegations are almost certainly false (evidence suggests that the United States did not use biological agents in Korea or Cuba), and the others are generally thought to be unlikely.

For the moment, the total ban on biological weapons, one of the major triumphs of arms control in the twentieth century, seems to be robust, and it is unlikely that the world will see biological weapons used in warfare. Use by terrorists is another matter, and there is concern that this could be a serious problem in the near future. *See also* Bioterrorism; Poison Libels and Epidemic Disease; Smallpox and the American Revolution; Smallpox in Colonial North America; War, the Military, and Epidemic Disease.

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MARK WHEELIS

BIOTERRORISM. Bioterrorism is (a) the use, or the threat of use, of biological agents as weapons, (b) by individuals or groups (but not by nations), (c) for political, ideological, or religious motives. By biological agent we usually mean any microorganism that causes diseases in plants, animals, or humans, or any toxic compound produced by a living organism (termed toxins). This is not an official definition; in fact there is no generally agreed upon definition of terrorism, much less of bioterrorism. But this definition distinguishes bioterrorism from two other closely related activities: biological warfare and biocriminality. Biological warfare is the use of biological agents as weapons by nations; biocriminality is the use of such agents for personal motives, such as financial gain or revenge.

The 2001 U.S. Anthrax Letter Attacks. Bioterrorism has a rather short history, and there have been very few actual attempts. Most prominent, at least for Americans, is the 2001 anthrax letter attacks. In this incident, letters containing spores of the causative agent of anthrax, *Bacillus anthracis*, were sent to several U.S. media outlets (print and TV) and to two U.S. senators. A total of five letters were sent, infecting 22 people, 11 with the pulmonary form of the disease, and 11 with the cutaneous form. Five of the victims with pulmonary anthrax died.

Ironically, it appears that the perpetrator did not intend to kill anyone. All of the envelopes contained warnings that they contained anthrax spores and advised taking **antibiotics** (which would prevent the disease). Most victims were postal workers exposed unintentionally when spores leaked out of the envelopes during sorting or recipients who did not take the warning seriously and discarded the letters and contents without notifying authorities or taking protective steps. Dozens or hundreds of deaths probably would have resulted if the perpetrator had had a serious intent to harm.

At least two of the letters contained high-purity spores, and this led investigators to conclude that the perpetrator was an insider in the U.S. military-scientific community with experience in preparing anthrax spores (the U.S. has, for many years, produced anthrax spores for defensive testing). This conclusion has since been softened, and the FBI now appears to think that a wider range of people might have had the expertise necessary to carry out the crime. Nevertheless, most investigators and scientists believe that the perpetrator must have been a Ph.D.-level microbiologist, with experience in working with dangerous microbes, and possibly with access to classified biodefense information.

In another irony, this case may not even be an example of bioterrorism. Because we do not know the motive, we cannot be sure whether this was an incident of bioterrorism or biocriminality.

Although the anthrax letters were not intended to cause casualties, there have been two attacks that were intended to do so: a 1984 bioterrorist attack in The Dalles, Oregon, by the Rajneesh sect, and attempted bioterrorist attacks in Japan by the Aum Shinrikyo sect from 1990 to 1995.

The 1984 Rajneesh Attacks. In 1981 an East Indian sect, including many American, Western European, and Australian members, relocated from India to the Big Muddy ranch in rural Oregon south of the county seat, The Dalles, on the Columbia River. The sect's guru was the Bhagwan ("enlightened one") Shree Rajneesh (1931–1990). They

incorporated a town (named Rajneeshpuram) on the ranch and built accommodations for several thousand people. However, by 1984 things were going poorly; many lawsuits had been brought against the group, its incorporation of Rajneeshpuram as a town was being challenged, and the outlook for the group's remaining in Oregon was bleak. The Rajneesh responded with a plan to take over the county government by electing their members to office in the election scheduled for November 1984.

The number of sect members is unclear, but was probably around 2,000, whereas there were about 15,000 registered voters. The Rajneesh intended to import thousands of homeless people from urban areas all over the country to overcome the numerical disadvantage. In anticipation that even with the influx of homeless people the election might be very close, a few senior sect leaders (including the nurse who ran the sect's infirmary, who provided the technical expertise) hatched a plot to make townspeople sick on election day. Their strategy was to pour suspension of the bacterium *Salmonella enteritica* (obtained by the nurse) on foods in salad bars in restaurants in The Dalles. To test the method, they attacked two restaurants around September 8 and many more (10 to 20) around September 20. The result was a major outbreak of salmonellosis (diarrhea, vomiting, fever). The **Centers for Disease Control and Prevention** (CDC) eventually identified 751 cases, 45 of whom were hospitalized. However, salmonellosis is typically under-diagnosed by as much as an order of magnitude, so it is virtually certain that there were at least several thousand cases. The successful trial was not followed by an election-day attack, however, as recruiting of the homeless fell far short of its goals, and it was clear that the Rajneesh had no hope of winning the election.

Interestingly, this outbreak was never suspected to be a bioterrorist attack, despite having a number of suspicious features that should have alerted public health personnel, and despite widespread public suspicion that the Rajneesh were involved. This was before there were serious concerns about bioterrorism (which began in the early 1990s); a similar outbreak today would certainly be recognized as a deliberate attack.

The attack was recognized as bioterrorism about a year later, when an independent police investigation of the sect turned up evidence that the Rajneesh were responsible for the outbreak. Two of the instigators of the attack were tried and convicted of first- and second-degree assault and product tampering, as well as unrelated crimes, and were sentenced to 20 years imprisonment. However, both were released after two and a half years and deported.

The 1990–1995 Aum Shinrikyo Attacks. The only other major attempt at bioterrorism was also perpetrated by a religious sect, this one the Japanese group known as Aum Shinrikyo. It was led by Shoko Asahara (b. 1955), who had developed a large following after a magazine published a photo showing him apparently levitating. At its peak, the sect had more than 15,000 members in Japan, and many thousands more abroad. Many members were young professionals, with good incomes, so the sect was also very wealthy.

To further its goals, Aum plotted to take over the government by running candidates for the Diet (Japan's parliament). When none of their candidates won, the cult's leadership decided to use violence and instituted an ambitious, \$20 million program to acquire a wide variety of weapons, from assault rifles to attack helicopters, as well as nonconventional weapons like chemical and biological weapons. Their biological attacks on Japanese cities spanned the years from 1990 to 1995. Most were attempts to disseminate botulinum toxin in an aerosol, using sprayers mounted in vehicles or in briefcases. Botulinum toxin

is a protein that causes the disease botulism; it is one of the most toxic substances known. However, Aum seems not to have succeeded in producing it, and the material they disseminated appears not to have contained any toxin.

Aum also tried to disseminate anthrax spores but again failed. The group's most ambitious attack, in the summer of 1993, was from the roof of one of its buildings in Tokyo and involved spraying thousands of liters of *Bacillus anthracis* culture into the air over several days. The failure to cause any cases of disease was the result of several factors: the group had an avirulent strain of *B. anthracis* (one used as a veterinary vaccine); its dissemination device produced large droplets, rather than the tiny ones needed to cause pulmonary disease; and the concentration of spores in the cultures was very low.

Because these attempts were uniformly unsuccessful in causing disease, they were not detected by the authorities. However, Aum had more success with chemical weapons, and its attack on the Tokyo subway with sarin led to rapid police action. Aum's leaders were arrested and tried for various crimes. About a dozen senior leaders, including Asahara, have been convicted of murder (for the sarin attacks) and sentenced to death.

Hoaxes. Although actual bioterrorist attacks have been extremely infrequent, hoaxes have been very common, particularly in the United States, which has seen well over a thousand. Hoaxes commonly involve an envelope containing a white powder (talcum powder, baking soda, or some other innocuous material) and a letter claiming that the powder is anthrax spores or some other hazardous biological material. Each one of these hoaxes has to be taken seriously by authorities, who need to counsel potentially exposed people, test the powder, and open a criminal investigation. The cumulative costs of responding have probably been more than \$100 million in the United States alone.

In most cases the perpetrators have not been caught, and many of the incidents may be criminal rather than terrorist in nature. Some are clearly terrorist acts, however; for instance, motivated by religious and ideological fervor, many hoaxers target abortion clinics in an effort to harass and intimidate them. This is clearly bioterrorism.

The record of serious bioterrorist attempts to cause mass casualties is clearly very sparse, suggesting that the threat of bioterrorism may not be as serious as many have estimated. For 15 years senior American policy makers have been making very public claims that America's greatest vulnerability is to bioterrorism; nevertheless, no international terrorist group has yet taken up biological arms. Although there are periodic reports that Al Qaeda has some interest in chemical and biological weapons, there is no evidence that such interest has gone beyond some very rudimentary exploratory steps. The success of the perpetrator of the U.S. anthrax letter attacks in making highly purified anthrax spore preparations serves as a caution, however. If the expertise of the anthrax letter attacker were combined with the desire of organizations such as Al Qaeda to cause mass casualties, the result could be very serious. Furthermore, the failure of the FBI to arrest and convict the perpetrator may lead terrorists to believe that this kind of attack is safer than traditional ones, and that by escaping detection they may be able to mount multiple attacks.

Thus, the threat of bioterrorism needs to be taken seriously, and the danger is probably increasing steadily as time goes by. Yet even in the United States funds are not unlimited, and bioterrorism prevention and response funding should be viewed in the context of other priorities, such as the death toll from natural infectious diseases. For instance, ordinary influenza causes approximately 35,000 deaths per year in the United States, almost all of them preventable by immunization; this dwarfs anything that a terrorist attack could reasonably be expected to cause. This does not mean that bioterrorism

funding should be diverted to flu **vaccination** programs, but it does suggest the need for a mechanism to balance competing needs in public health. See also *Biological Warfare*; *Bubonic Plague*; *Smallpox*.

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MARK WHEELIS

BLACK DEATH (1347–1352). The Black Death is the term most often applied to the initial outbreak of **bubonic plague** that began the second **pandemic** of plague. This outbreak, which spread across Europe, the Levant, and North Africa between 1347 and 1352, brought bubonic plague into Europe from the Asiatic steppes where it had long been endemic. Following this **epidemic**, Europeans experienced recurrent outbreaks of plague over the next four centuries. As a result of the many effects of the plague on society and culture, many historians consider this half-decade a turning point in European history.

Although the term "Black Death" came into common use only in the nineteenth century, it has remained a popular descriptive term for this epidemic. Many accounts of the Black Death offer an explanation for the term based on physical symptoms, but it actually comes from a misunderstanding or mistranslation of the Latin *atra mors*, which can mean either "terrible death" or "black death." Those living through this epidemic did not give it a specific name, but used general terms including pest, pestilence, plague, and mortality.

The Black Death was one of the most significant events of the late medieval world and spawned numerous changes, most visibly in the drastic reduction of population in those areas affected. Estimates of the overall mortality from the Black Death are difficult to obtain, as none of these areas kept accurate or consistent census or burial records. Historians working with a variety of local studies, however, continue efforts to approximate overall mortality. Those estimates currently range between 45 and 60 percent across the affected areas.

Historical Record. The historical record of the Black Death is extensive, as there are numerous first-hand accounts of the epidemic from Europe, North Africa, and the Near East. Best known are the accounts of Italian chroniclers, such as Gabriele de' Mussis (c. 1280–?) who described the transfer of disease from besieging Mongol troops to besieged residents of the Black Sea port of Caffa (Kaffa; modern Feodosiya) via dead bodies catapulted over the city's walls. Another Italian writer, Giovanni Boccaccio

(1313–1375), included a vivid description of the plague in the introduction to his collection of short stories *The Decameron*, the frame story of which is set during the pestilence in Florence in 1348. These and many other accounts and descriptions have been translated and are increasingly accessible, often in abridged form, in studies on the Black Death.

In addition to individual chronicles detailing events, evidence of the reaction to and impact of the Black Death may be found across all areas of society that generated any type of records. These include municipal, ecclesiastical, medical, and scientific authorities. Scholars have made use of diverse records such as city council meeting minutes, municipal statutes, sermons, tax rolls, court records, medical and scientific treatises, and personal letters to uncover information about the Black Death.

Nature of the Disease. That some disease swept through Europe in the mid-fourteenth century, causing death rates unlike anything previously experienced, is clear. What is less clear is the exact cause of those deaths. Although bubonic plague is generally assumed to be the infectious agent, it is important to note that a number of scholars have raised questions about whether plague—in its three forms of bubonic, **pneumonic**, and **septicemic**—truly fits the symptoms, spread, seasonality, and mortality rates described by chroniclers in the early modern era. Few satisfactory alternatives have been proposed, however, and in the absence of conclusive evidence otherwise, most historians continue to attribute the Black Death to bubonic plague. In addition, recent work in paleomicrobiology has confirmed the existence of DNA from *Yersinia pestis* (the causative bacteria of bubonic plague) in tooth samples from plague-era graves in France, lending credence to the argument for the existence of plague there. Nonetheless, the Black Death remains a case study in the difficulties of **diagnosis of historical disease** and **historical epidemiology**.

Accounts and descriptions of the Black Death exist in such numbers that only a general summary of the symptoms given in them is possible. All of the accounts describe a horrible and painful disease that struck suddenly and killed rapidly. It was the rapid course of the disease that most contemporaries commented on, recording accounts of acquaintances healthy in the morning but dead by nightfall. Descriptions of symptoms most often include some sort of swellings (also referred to as tumors, boils, or apostemes) in the groin or armpit, which were exquisitely painful and the contents of which (when lanced open) were foul smelling. Others describe pustules, blisters, or black spots, the coughing or spitting of blood, and a high fever followed by great thirst and delirium or prostration. Because the disease spread quickly among family members or households, many blamed the contaminated breath of the sick for spreading the disease.

Origins and Spread. Bubonic plague, endemic to certain mammal populations but not to humans, has natural reservoirs scattered across the Asian steppes region. The epidemic of 1347–1352 likely began from one of these, spreading as a result of Mongol traders opening new trade routes. Chroniclers describe outbreaks of disease among the Mongols or “Tatars” in the early 1340s. By 1346 outbreaks had occurred in the region between the Caspian and Black Seas. According to contemporary accounts, Genoese traders helped spread the pestilence outward after visiting the city of Caffa, a Genoese colony located on the Black Sea. While there, traders became trapped by a Mongol siege of the city. Plague broke out among the Mongols, who responded by catapulting the bodies of the dead over the city walls. Some ships managed to leave Caffa in the fall of 1347, passing through Constantinople (Istanbul) and stopping briefly in Messina

(Sicily) before returning to Genoa. Although the movements of these **trade** ships may well have helped the outward spread of the Black Death, evidence from the Near East and Africa show that it was quickly spreading in several directions by the late 1340s. In 1347 it appeared in Constantinople, Greece, Venice, and most of the Mediterranean islands (Crete, Sicily, Sardinia, Mallorca) as well as Alexandria in Egypt. Once in the Mediterranean, the epidemic spread both northward across Western Europe and westward across North Africa in 1348. In Europe it spread across Spain, southern France, and most of Italy in 1348, then passed to Germany, England, and Norway in 1349. Continuing northeastward, plague infected Eastern Europe and the Low Countries in the next year, and then finally arrived in Russia in 1351–1352.

Religious Responses. By far, the strongest reaction in Christian lands was a religious interpretation of the plague as a punishment from God. This belief, held across all levels of society, led to conflicting responses. As Boccaccio eloquently describes, some, believing there was little that mankind could do in the face of such a scourge, abandoned morality in favor of pleasures. Others turned to extreme piety and prayer in an effort to appease an angry God. In parts of Europe, the **flagellant** movement (named for the *flagellum* or whip) flourished for a time. These groups of **pilgrims** moved about from town to town holding displays of public piety in which they offered bodily penance in the form of whippings as a supplement to traditional prayers. The movement initially gained many converts and strong popular approval, but within a year had lost official support and was forbidden by Pope Clement VI (1291–1352) in October 1349. Less drastically, communities across Europe organized a variety of public processions, pilgrimages to shrines, and other forms of communal piety. Responding in part to a surge in pilgrimages to sacred sites in Europe, including Canterbury and Santiago de Compostela, the papacy declared 1350 a jubilee year, offering plenary indulgences (remission from the obligation to carry out penance for confessed sins) to all those who visited the principle churches of Rome that year.

Alongside prayers to the Virgin Mary, Mother of Mercy, came prayers to St. Sebastian, a third-century martyr who became increasingly associated with plague. Sebastian, a member of the imperial guard under Roman Emperor Diocletian (r. 284–305), was sentenced to death for his Christian beliefs. Shot with arrows and left for dead, he was found while still alive and nursed back to health. His subsequent execution by bludgeoning made him a true martyr, but his survival of the arrows created the association with plague. Fourteenth-century thinkers often described the sudden onset of the disease as akin to being shot by an arrow (and the communal onset as a sort of rain of arrows from heaven). Thus, Sebastian's success in surviving *his* (real) arrows made him an empathetic patron saint who would likewise work to protect people from *their* (metaphorical) arrows.

A tragic religious response to the Black Death, encouraged in part by the anti-semitism preached by the flagellants, was the persecution and massacre of Jews. As the epidemic spread and the death toll mounted, many searched for **scapegoats** to blame for the disease. Accusations were leveled against various groups of outsiders, most notably Jews who came under suspicion of deliberately spreading disease. Despite the efforts of many civil and ecclesiastical authorities (including the papacy) to protect Jewish residents, thousands were rounded up and executed in Spain, in southern France, and across central Europe.

Social Response. One of the most striking features of accounts of the Black Death is the overwhelming fear expressed by most authors. Accounts of the epidemic are rife with stories of **flight** and abandonment, though whether these stories are objective

records of fact or simply literary expressions is unclear. But regardless of how commonly “brothers abandoned brothers . . . fathers and mothers refused to nurse and assist their own children” as Boccaccio describes, it is clear from the records of this epidemic that there was a notable shift in society. The most common prescription of the era, reproduced into a variety of languages, was to “flee far, fast, and for a long time,” and flight (from cities to countryside, from one town to another) was a common reaction during this and later epidemics. The observed patterns of illness led to popular beliefs that it spread from person to person, which would have been the case with pneumonic plague. Whereas medical theories held on to the miasmatic concept of disease (caused by “corruption” in the air), the popular belief in **contagion** led to a noticeable fear not just of disease, or even just of the sick themselves, but also of the potentially sick. Public venues such as markets, churches, or public squares were increasingly avoided, and care for the sick often fell to either the very pious—those willing to place themselves in danger—or the very poor, who may have sought to profit however they could. Burials, which could no longer be carried out individually as a result of the excessive number of **corpses** accumulating, were likewise left in the hands of the charitable or the desperate. The accumulation of bodies faster than they could be buried led to a variety of psychological reactions—guilt, fear, anger, sorrow—none of which is directly measurable but all of which are indirectly evident in the sources.

Medical Response. Although medical theory lagged behind popular conceptions in formulating a theory of contagion, medical personnel developed a variety of theories on how plague spread and how it could be prevented. In some areas, especially Italy, efforts were made to understand better the disease by conducting autopsies on victims. These principally discovered problems in the lungs, which helped reinforce the **humoral theory** of corrupted air causing disease. The disease was viewed as being so virulent that it was believed to be spread by the very breath of the infected (which it may have been, in the case of pneumonic plague). Prescriptions for prevention of plague included the burning of aromatic herbs (often carried out in public squares) to cleanse the air as well as the regulation of **diet** to maintain humoral balance. Other plague treatises advocated keeping one’s mouth covered with a handkerchief or the use of a posy of sweet-smelling herbs while in public. One author

AN IRISH FRANCISCAN FRIAR DESCRIBES THE HORRORS OF THE BLACK DEATH (1349)

Since the beginning of the world it has been unheard of for so many people to die of pestilence, famine or any other infirmity in such a short time. Earthquakes, which extended for many miles, threw down cities, towns and castles and swallowed them up. Plague stripped villages, cities, castles, and towns of their inhabitants so thoroughly that there was scarcely anyone left alive in them. This pestilence was so contagious that those who touched the dead or the sick were immediately infected themselves and died, so that the penitent and confessor were carried together to the grave. Because of their fear and horror men could hardly bring themselves to perform the pious and charitable acts of visiting the sick and burying the dead. Many died of boils, abscesses and pustules that erupted on the legs and in the armpits. Others died in frenzy, brought on by an affliction of the head, or vomiting blood . . . Among the Franciscans at Drogheda 25 brothers died before Christmas, and 23 died at Dublin . . . At Kilkenny the pestilence was strong during Lent, and eight Dominicans died between Christmas and 6 March. It was very rare for just one to die in a house; usually husband, wife, children and servants went the same way, the way of death.

From John Clynn, OFM, in *Annalium Hibernae Chronicon* (edited by R. Butler); translated by Rosemary Horrox in her *The Black Death* (New York: Manchester University Press, 1994), p. 84.

advocated ensuring a patient's eyes had been covered before entering the room, believing that the disease could be passed along via direct eye contact.

A notable disparity existed in reactions to plague between Christian and Muslim populations, both within Spain and in the Middle East. Though plague took a high toll on both groups, and though both believed plague to be sent from God, their reactions were distinct. Whereas Christians blamed human sin as the cause of God's anger and punishment, Muslims viewed plague as a disaster to be endured, one which offered a martyr's death to its victims. Muslim submission to the will of God meant a strong focus on prayer rather than the flight and self-preservation seen among Christians, though observers noted many cases of Muslim flight. There was no scapegoating or placing of blame among Muslims, and likewise little tolerance for theories of contagion, which challenged God's supreme power over all events. Ibn al-Khatib, a Spanish Muslim medical writer in Spanish Granada, offered a treatise in which he argued for the contagious nature of plague, an argument that likely led to his subsequent persecution for heresy and his ultimate exile.

Historical Effects. The Black Death is acknowledged as a momentous event in European history, one that affected all aspects of society. Alongside the more obvious demographic and economic effects, scholars have also argued for indirect psychological effects, manifested in art, intellectual development, and social changes. Part of the difficulty in assessing these changes, however, is the fact that the Black Death was just the first (though the most widespread and the most lethal) epidemic of many during the second pandemic that would continue to haunt Europe until its gradual disappearance in the eighteenth and nineteenth centuries.

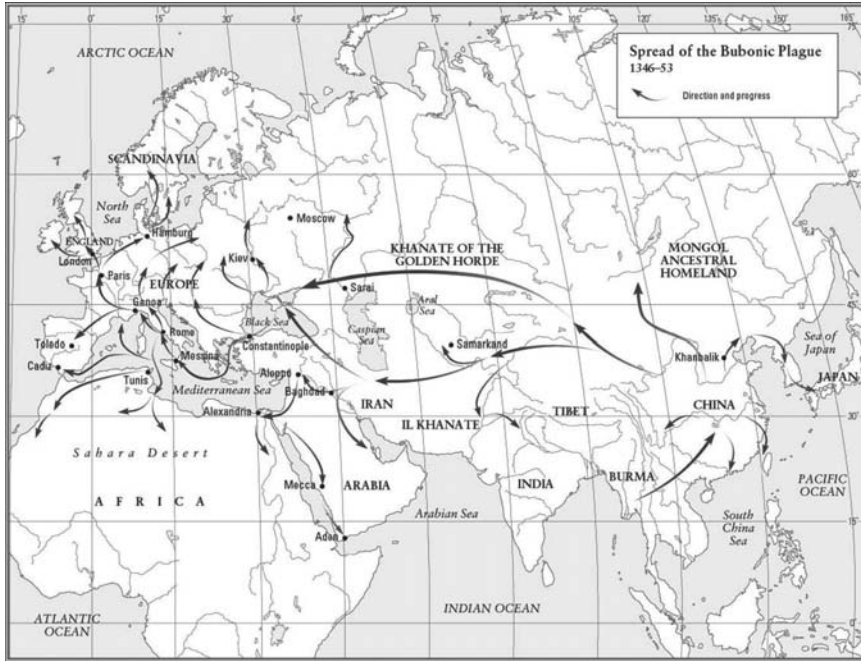
The overall mortality of the Black Death has fascinated historians for generations, but reliable figures remain elusive. Accurate census numbers from the era prior to the Black Death simply do not exist, nor do reliable death or burial records for more than scattered territories. Thus, calculating the overall impact on Europe as a whole is extremely difficult, if not impossible. Nevertheless, estimates have steadily risen in recent generations from roughly a third of Europe to nearly two-thirds. It is considered safe to assume at least half of Europe died in the Black Death, and possibly more than half. These deaths occurred in all levels of society, from the very poorest to royalty, including King Alfonso XI of Castile (1312–1350) who fell sick and died in 1350 while besieging Gibraltar. Those who tended to the sick suffered the highest losses, including **physicians, surgeons**, clergy, and notaries (who recorded last wills). These losses had their own ripple effects, as medical and clerical positions stood empty or were filled with less qualified (or less dedicated) applicants. Throughout Europe the drastic population decline had repercussions on several generations that, coupled with recurrent epidemics, meant that population levels did not recover in most regions until the late fifteenth century.

One significant result of Black Death was an overall shift in rural population away from marginal agricultural lands and onto more fertile ones. The evidence of a large number of deserted villages in Europe, once taken to be a result of massive mortality, is now recognized as resulting from both deaths and relocation as survivors moved in search of better economic opportunities.

Economic Impacts. The most obvious economic impact of the Black Death was a rise in the standard of living for survivors. For both free and enserfed farmers, the loss of so much population meant that lands stood open awaiting workers. This provided greater opportunities for them to gain mobility and to negotiate favorable terms of employment. For landowners, finding and retaining workers now meant paying higher wages or offering



Eighteenth-century street scene showing several people attending to plague victims. Etching by Huttin. Courtesy of the National Library of Medicine.



Map of the spread of the Black Death across Asia, the Middle East, Europe, and Africa.

better terms of living. Across many trades, wages and prices rose dramatically in the immediate aftermath of the Black Death, as there were simply fewer skilled workers to provide goods and services.

As early as 1349 authorities across Europe (at both the local and national levels) began to respond to these economic shifts by regulating wages, prices, and the mobility of workers. Wages were held to pre-plague levels and attempts were made to prevent secret agreements offering bribes or bonuses. These statutes led to further political and economic tensions as workers sought to capitalize on gains while employers sought to rescind them.

Cultural Changes. Alongside the written records that reflect people's experiences with the Black Death are artistic depictions. A wealth of art, created both in direct response to the Black Death and in response to subsequent epidemics in later generations, reflects themes of death and the transitory nature of life, wealth, and power. Images increasingly showed "King Death," personified as a skeleton, stalking or attacking victims, often now armed with a scythe. The *Danse Macabre* ("The Dance of Death") became a common theme, illustrating how quickly and easily death could interrupt life and "dance" the unsuspecting victim into the grave. In addition, new cults devoted to plague saints Sebastian and Roch (Roche) sprang up, and both are depicted with greater frequency after the Black Death.

The intellectual impact of the Black Death is the hardest to quantify, but there is evidence that the massive population loss created new intellectual space for upcoming generations to fill. The loss of intellectual continuity, which allowed older ideas and

traditions to slip slightly seems to have provided opportunities for new approaches, such as the increased use of the vernacular in a variety of writings, and for new ideas, such as the Renaissance humanists' new interest in reviving ancient models. Though there is no consensus on the issue, many scholars have argued that the Renaissance, which emerged on the heels of the Black Death, owes its birth to the intellectual upheavals and questions raised by the epidemic and its successive waves. Although historians do not agree on the extent to which the Black Death represented a "turning point" in history, it clearly had long-lasting repercussions and must be taken into account as a contributing factor for long-term social, economic, and intellectual shifts. *See also* Astrology and Medicine; Black Death and Late Medieval Christianity; Black Death, Economic and Demographic Effects of; Black Death, Flagellants, and Jews; Black Death: Literature and Art; Black Death: Modern Medical Debate; Environment, Ecology, and Epidemic Disease; Islamic Disease Theory and Medicine; Medical Education in the West, 1100–1500; Plague and Developments in Public Health, 1348–1600; Plague in Medieval Europe, 1360–1500; Plague in China; Plague in the Islamic World, 1360–1500; Plague of Justinian, First Pandemic; Public Health in the Islamic World, 1000–1600; Quarantine; Religion and Epidemic Disease.

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KRISTY WILSON BOWERS

BLACK DEATH AND LATE MEDIEVAL CHRISTIANITY. When the **Black Death** swept across Asia, North Africa, and Europe in the mid-fourteenth century, it killed between one-third and one-half of the population. In Christian areas, the Church mobilized immediately, as it had with natural disasters in centuries past. In doing so it

drew from two distinct but related sources: the Bible and Catholic tradition. The Bible made it clear that plagues, regardless of the type, were a sign of God's judgment. In sermons, priests counseled against sin and encouraged penitent behavior by reciting the stories of Noah, Sodom and Gomorrah, and Nineveh. The story of Nineveh illustrates the clearest parallel to a plague visitation and the power of faith, as it tells of a king willing to join his people in a public penance that ultimately appeases God and spares the nation from obliteration. Specific forms of penance included fast days, communal prayer, processions, pilgrimage, monetary offerings, and devotion to saints. Equally important were public displays of thanksgiving, with church communities joining together to praise and thank God when deaths declined. These rituals were standard for all natural disasters, lending a degree of the ordinary to that which was otherwise unimaginable.

The devotion to saints at this time took on a unique form, with the recognition of saints who were considered particularly potent against the plague. Many prayed to the Virgin Mary, mother of Jesus, and artists depicted her as shielding her clients (devotees), and sometimes entire towns, from an angry God. The late third-century Saint Sebastian is the most recognizable of the plague saints, with his naked, arrow-strewn body clad only in a loincloth. In late medieval paintings and statues, his arrows are metaphorical "arrows of the pestilence," and the story of his recovery from these wounds stands as an account of escape from the plague. St. Michael the Archangel also figures in the late medieval Christian plague-time paintings that once adorned churches and covered processional placards. As the Christian tradition tells of Michael driving a dragon-like Satan from Heaven, so did late medieval Christians consider him able to drive away the Black Death. The only plague-specific saint of international repute was the purported fourteenth-century Saint Roche (known in various countries as San Rocco, Saint Rock, and San Roque). Few of the details of his biography are verifiable, but by the early fifteenth century, believers knew him as a healer of plague victims who had become ill and recovered from the disease. One can identify him in paintings by his dog, his pilgrim's staff, and his unusual gesture: he points under his tunic to suggest that he has a bubo on his upper thigh.

In spite of these church-sponsored efforts, it was clear that the Black Death was a more menacing threat than other scourges. It could kill an entire household within a matter of days and often reduced town populations by a quarter in a single season—all while its victims suffered enormous pain. Naturally, those who witnessed the horrors feared that they were living in the end times, as told in the book of Revelation. Late medieval writers embraced apocalyptic thinking, imagining that the end result of God's plague-time wrath might be a nation of animals only, with the entire human population extinguished.

Some of the faithful became more zealous in their determination to avert damnation. Among this small portion of the faithful were the **flagellants**, a group known more for their oddity than for the number of their followers. The flagellant movement did not last, as its adherents' extreme behavior and directives threatened church authority. Other zealous Christians used the plague as an opportunity to clear their cities of Jews. They spread rumors that the Jews worldwide had joined together to poison wells, staging a medieval terrorist attack. Still others saw the conversion or murder of Jews as essential to the cleansing of the world in anticipation of the coming of Christ at the apocalypse. In 1349 citizens of several European cities attacked Jewish communities in spite of Pope Clement's (1291–1352) efforts to prevent such killing. These activities were short-lived, however, as people soon saw that the Black Death appeared to kill entirely at random, making it

impossible to identify a particular community of people, let alone a specific water source, as its origin. More troubling was that the disease killed saints as well as sinners and the very young as well as the very old. Late medieval Christians expressed again and again their difficulty in thinking about the infants, virgins, monks, and nuns struck down by plague. Surely, they reasoned, these people were not all sinners. This led some to conclude that God chose to end the lives of such devout individuals because he was sparing them from life in a corrupt world.

Many late medieval Christians sought urgently for answers and finally found the church ineffective. It is not surprising that some began to turn to other sources of spiritual and physical aid. Scholars debate the degree to which the Black Death was the primary cause of the anti-clerical movement in Europe, but all agree that it contributed to it. With bodies in pain, social structures in disarray, and the church unable to provide safety—even for its most devout or innocent members—late medieval Christian communities struggled to manage plague-time chaos on all levels and to make sense of their lives in the aftermath. *See also* Biblical Plagues; Black Death, Economic and Demographic Effects of; Black Death, Flagellants, and Jews; Black Death: Literature and Art; Bubonic Plague; Pilgrimage and Epidemic Disease; Plague in Medieval Europe, 1360–1500; Plague Memorials; Plague of Justinian, First Pandemic; Poison Libels and Epidemic Disease; Religion and Epidemic Disease; Scapegoats and Epidemic Disease.

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REBECCA TOTARO

BLACK DEATH, ECONOMIC AND DEMOGRAPHIC EFFECTS OF. The **Black Death** pandemic of 1347 to 1352 had devastating results for the population of Europe, and it led to many dramatic changes within European societies and economies. Though scholars disagree over matters of degree, the general trends are broadly accepted: one-third to one-half of Europeans died; a good deal of wealth and property changed hands through inheritance; most of those who died in major cities were replaced rather quickly by migration from the countryside; wages dropped and prices rose; and both local and national laws sought to dampen what authorities saw as negative effects of the population disaster.

One problem with establishing exact figures for medieval population loss is that there are few reliable demographic statistics. One of the best-documented regions is England. A poll tax was collected in 1377, which was essentially a census of English citizens in order to establish and collect a head tax. A previous census had been taken in 1086, and this census allows historians to estimate the toll that the plague took on at least the English population. Another source for population figures is church burial records, but these were neither universally maintained nor accurate throughout Europe, nor have they survived in large numbers. Even so, most historians agree that the population of Europe fell by at least one-third in the initial outbreaks of 1347–1352; perhaps as many as 70 to 80 percent of some regions

(particularly cities and towns in Italy and England) were lost in that and subsequent outbreaks in the late fourteenth century. Contemporary poets and chroniclers, some of whom did not survive the plague, describe losses of 90 percent of their towns' populations, although many of these accounts may be exaggerations. Italy may have had the highest losses, because of high population density and because it was the first region in Europe to be hit; Eastern Europe, the most sparsely populated and the last to be struck, may have had the lowest.

Some populations were devastated more thoroughly than others. Populations of cities, which were densely packed and thus more susceptible to contagion, seem to have had higher mortality rates than rural areas, but even this was not consistent: villagers, too, died in appalling numbers. Clergy had higher mortality rates than lay people because they had more contact with plague victims when they delivered last rites and other sacraments. Because priests had such a high mortality rate, the Church was particularly devastated. New priests were quickly ordained in the decades following 1347; as a result, most were not fully trained and entered their new profession unprepared. This led to a gradual decrease in respect for clergy.

The plague seemed to strike the young most of all, especially during later outbreaks, an impression noted by many contemporaries. Those who survived the initial outbreak were apparently more likely to survive subsequent outbreaks and grow older (though exposure to plague is not known to confer immunity). This meant that the demographic state of Europe was drastically altered by the Black Death; by the early 1400s, many towns had more elderly than young; adults in their twenties and thirties were rather few in number. The sheer number of people who died meant that the economics of Europe also changed. Craftsmen and skilled laborers died of plague, and, in order to replace them, craft guilds began to recruit and approve underage members. Guilds, like society as a whole, had to replace deceased members and train new ones quickly. Plague losses also meant that guilds, and towns in general, were willing to accept strangers and people from outside the guild and town boundaries, which they had been reluctant to do before the Black Death. The plague increased the mobility of labor in Europe. In fact, some older theories held that the plague was a correction to overpopulation—prior to the Black Death, Europe's population had exceeded its resources, and it therefore suffered the resulting **Malthusian** check—a position no longer tenable.

Fewer students enrolled at universities; Oxford, the University of Paris, and Bologna all had reduced numbers for decades after the Black Death, perhaps because there was simply no superfluous population not needed for labor. There was also a reduction in the charitable economy of Europe, on which schools (including universities), hospitals, and churches depended. New universities were created; they were smaller, local institutions that did not require travel by the main roads, which were increasingly dangerous. This, too, was a result of the plague: an increase in violence and lack of order as a result of desperation and loss of civil stability.

The Black Death may have also diversified the economic culture of Europe, although there is some dispute among historians regarding exactly what changes occurred. Prices for basic commodities, especially grains and foodstuffs, immediately rose after the plague. This was partially the result of the reduction in labor; fewer people were available to work fields or mills for grinding grain. The decline in the supply of labor allowed for the surviving laborers to charge higher prices for their service or goods, at least immediately after the first outbreak. Wages also went up, whereas rents and other demands by those who hired laborers often went down. Rising inflation of prices and wages, together with lower

rents, very quickly led rulers and governments to attempt to limit prices and wages. These laws, such as the Statute of Labourers in England in 1351, were only partially successful; commodities prices went down, wages were forced artificially low (set by law at pre-plague levels), but the laws also stirred up civil discontent which eventually led to rebellions, such as the Peasants' Revolt in 1381. *See also* Black Death and Late Medieval Christianity; Black Death, Flagellants, and Jews; Black Death: Literature and Art; Plague in Medieval Europe, 1360–1500; Plague in the Islamic World, 1360–1500.

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CANDACE GREGORY-ABBOTT

BLACK DEATH, FLAGELLANTS, AND JEWS. The first outbreak of the **Black Death** across Europe and the Mediterranean world in 1347–1352 disrupted the social world of European Christians, creating chaos and widespread fear across the continent. Whereas some blamed Jews for creating and spreading plague, others concluded that the plague was in fact an instance of divine judgment for their sins and those of their communities. Among the cultural legacies of the plague were the emergence of specific forms of lay religious organizations and the increased persecution of Jews, frequently by members of these organizations and by itinerant preachers.

The enormous casualties caused by the plague led many to conclude that divine judgment had fallen upon Europe for its sins, and some such individuals believed that the end of the world was upon them. Church doctrine taught that self-punishment and renunciation of pleasure could assuage the wrath of God, which was made manifest in the plague. In Germany, many laymen organized themselves into wandering bands of flagellants who practiced extreme asceticism: punishing their bodies as penance for sin by flogging themselves with multi-tailed whips called *flagella*. These organizations of penitents sought to cool God's anger and stave off further punishment, or at least to prepare themselves for the return of Christ, by renouncing worldly goods and punishing their bodies. Flagellation had been practiced for centuries as a form of extreme asceticism, but it had been largely confined to reformist orders of monks whipping themselves in their monasteries. The first known disciplinary confraternity (pious lay brotherhood) began around 1260 in central Italy. During the fervor caused by the plague, however, the number of flagellants spiked sharply as many confraternities adopted the practice, particularly in German states and the Low Countries.

The flagellants were groups of men from the general population who traveled in fairly large groups, singing penitential hymns, venerating a holy relic, and beating

POPE CLEMENT VI CONDEMNS THE PERSECUTION OF JEWS DURING THE BLACK DEATH (1348)

Recently, however, it has been brought to our attention by public fame—or, more accurately, infamy—that numerous Christians are blaming the plague with which God, provoked by their sins, has afflicted the Christian people, on poisonings carried out by the Jews at the instigation of the devil, and that out of their own hot-headedness they have impiously slain many Jews, making no exception for age or sex; and that Jews have been falsely accused of such outrageous behavior so that they could be legitimately put on trial before appropriate judges—which has done nothing to cool the rage of the Christians but has rather inflamed them even more. While such behavior goes unopposed it looks as though their error is approved.

Were the Jews, by any chance, to be guilty or cognizant of such enormities a sufficient punishment could scarcely be conceived; yet we should be forced to accept the force of the argument that it cannot be true that the Jews, by such a heinous crime, are the cause or occasion of the plague, because throughout many parts of the world the same plague, by the hidden judgment of God, has afflicted and afflicts the Jews themselves and many other races who have never lived alongside them.

We order you by apostolic writing that each of you, upon whom this charge has been laid, should straightly command those subject to you, both clerical and lay, when they are assembled in worship at mass, not to dare (on their own authority or out of hot-headedness) to capture, strike, wound or kill any Jews or expel them from their service on these grounds; and you should demand obedience under pain of excommunication.

Papal order to the Catholic clergy of September 26, 1348; from *The Apostolic See and the Jews*, vol. 1, *Documents: 492–1404*, edited by S. Simonsohn (Toronto: Pontifical Institute of Medieval Studies, 1988), Doc. #373.

themselves bloody. When they arrived near a city and set up camp, they read a letter detailing a message from Christ or an angelic messenger validating their ascetic practices and exhorted everyone to repentance. Much of their preaching stirred audiences to prepare for the imminent apocalypse. Major condemnations of the flagellants began in 1349 with that of Pope Clement VI (r. 1342–1352) and other bishops and lay leaders who distrusted the self-led and very charismatic groups. Flagellant influence diminished by the late 1300s, as the church increased its censure of their more heretical teachings, and continued into the next century when large numbers were burned at the stake as heretics. Penitential confraternities based in parishes, operating in secret, and directed by clergy practiced flagellation past the sixteenth century. They were less associated with apocalyptic concerns and more with the everyday life of repentance and renunciation.

Many European Christians in the fourteenth century, and some modern scholars, believed that Jews suffered less from the plague than the Christian population, though this view has come under much academic scrutiny of late. Jewish ghettos often had **water** supplies apart from the Christians and drank from their own wells. This raised concerns among many Christians who believed the plague was a waterborne poison planted by Jews (**poison libel**).

These accusations caused sporadic but brutal attacks on Jewish individuals and communities. Itinerant preachers—particularly Franciscan friars—along with flagellants, and sometimes local clergy, preached against Jews on many occasions. Frequently, they claimed that the presence of unbelieving Jews in Christian communities was the cause (or at least, one cause) of God's judgment in the form of the plague. Older anti-Semitic accusations, such as the blood libel (the claim that Jews murdered Christian children on Passover) persisted, but most of the furor directed against Jews stemmed from the poison libel. On the shores of Lake Geneva many Jews were harassed, and some were killed

because of these accusations. In February 1349, angry townspeople attacked the Jewish community in Strasbourg despite the efforts of local authorities; uncontrollable mobs burned to death many Jews in Alsace and exiled many more. In Avignon, however, the Jewish community was sheltered by papal command; Pope Clement VI, along with civil authorities from the Alps to the Elbe, condemned the disorder and random violence that pogroms caused. Even so, over the following year throughout the Rhineland, Jews were frequently drowned or burned. The poison libel moved northeast through Germany before reaching certain parts of Poland and the Baltic States. Violence against Jews by civil authorities was rarer, often involving the prosecution and execution of one or a few Jews for well poisoning. Some evidence suggests that communities targeted Jews who acted as moneylenders, to kill their creditors and escape paying their debts. Though incidents occurred in many regions throughout Europe, mob violence against Jews often clustered in specific regions, such as the Rhine valley.

The persecution of Jews triggered by the Black Death led to expulsions of Jews from some communities and the enlargement of Italian ghettos as many Jews fled to Venice and Rome. The worst of the persecutions subsided by 1350, thanks at least in part to an assertion of political authority. Traveling groups of mendicants commanded respect for a long time afterward, often provoking public hostility against Jews, sometimes bullying the public into persecution of them. The plague had cleaved Jews away from some communities that had previously not quarreled with them. In consequence, the high medieval tolerance of Jews diminished even more quickly than it had before the plague.

The flagellants and various forms of violence against Jews were symptoms of the fear and chaos caused by plague outbreaks. Attempts by civil and ecclesiastical authorities to quell both problems culminated in Pope Clement VI's joint condemnation of the flagellants and the violence against Jews. These efforts were not very successful. Although the itinerant flagellant movement did fade away, persecutions of Jews associated with plague outbreaks continued into the sixteenth century. *See also* Bubonic Plague; Plague in Medieval Europe, 1360–1500; Religion and Epidemic Disease; Scapegoats and Epidemic Disease.

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DENNIS GREGORY CARAMENICO

BLACK DEATH: LITERATURE AND ART. Devastation of the scale wrought by the **Black Death** produced wide-ranging cultural changes and reactions. Some of these caused pre-plague literary and artistic genres to focus on the plague and prompted the development of new plague-specific themes. The year 1347 marks the initial outbreak of the plague, which makes it the focus of the first literary reactions to the Black Death, and

1562 was the year in which the Flemish artist Pieter Brueghel the Elder (c. 1525–1569) painted his horrifying plague masterpiece, *The Triumph of Death*. These years bracket this article. The seeds of Brueghel's terrifying artistic vision, however, were planted in "popular" literature produced when the plague first appeared in 1347.

Italian poet Giovanni Boccaccio's (c. 1313–1375) introduction to the *Decameron* (c. 1351) is a famous example of "popular" plague literature. In 1348, Boccaccio informs his readers, the streets of once-beautiful Florence were covered with plague victims' corpses. All who were able either fled the city for a safer refuge in the country or locked themselves in their homes to escape the plague. Boccaccio mentions that the plague struck the Near East with a ferocity equal to that with which it hit western Europe. The *Report on the Pestilence* (1348), by Boccaccio's Syrian Muslim contemporary Abu Hafs Umar ibn al-Wardi (d. 1349), is written as a prayer to Allah, but it shares with Boccaccio's *Decameron* a keen eye for detail which allows the reader to understand just how terrible the plague was wherever it struck. Poetry by Boccaccio's friend Francesco Petrarca (1304–1374) (especially *Ad te ipsum*) painfully and intimately details the devastation caused by the plague. In England, poet Geoffrey Chaucer's (1343–1400) bawdy *Canterbury Tales* (c. 1387–1400), based largely upon Boccaccio's *Decameron*, contains important references to the Black Death.

The medical *consilia*, or physicians' advice pamphlets, existed before the era of plague, but the advent of Black Death prompted *consilia* authors to focus almost solely on the plague. The first and most often copied was that by the medical faculty at the University of Paris. These "plague tracts" contain an interesting blend of classical allusions, Christian and Muslim traditions, common sense strategies, and outrageous recipes to cure and avoid the Black Death. For example, plague tracts advise readers to close all of the doors and windows of one's home and then burn noxious herbs in an attempt to keep out "corrupted air." Thus, if one could avoid "bad air," and those stricken with the plague, one might be able to survive an outbreak.

Nearly everywhere the plague struck, local plague-tract genres developed. Fourteenth-century Spanish physicians such as Alfonso de Cordoba, and French and Moorish doctors such as Pierre de Damouzy and Abi Gafar Ahmed ibn Ali ibn Khatimah, contributed to the plague-tract genre. Each sought to provide remedies and treatments for the Black Death in his locale.

The obsession with plague found in some "popular" and most medical literature is mirrored in the emerging genres of "plague art," but the development of plague art is more hotly debated. Following the lead of scholar Millard Meiss (1904–1975), some art historians argue that Italian art appeared to "revert" to medieval themes of death and judgment because the plague radically changed the Italian and European artistic consciousness. Undoubtedly, the plague affected European art by killing nearly an entire generation of artists and their private and civic patrons, but the post-plague "reversion" to medieval themes was also the result of the influence of the Church. As the greatest patron of the arts, the Church had long used a fairly uniform iconography of the Last Judgment and Death to prompt repentance. With the advent of the Black Death in 1347, pre-plague themes such as the *Danse Macabre* quickly transitioned into symbols of the Black Death. With its writhing skeletons dancing arm-in-arm with soon-to-be-dead men, women, and children, the "Dance of Death" came to represent the need for repentance in the face of death by plague. In time, the *Danse Macabre* genre was joined by other "plague art" themes.



The plague of Florence in 1348, as described in Boccaccio's *Decameron*. Etching by L. Sabatelli after himself. Courtesy of Wellcome Library, London.

The *King Death* genre is an example of this type. It is “plague art” in the truest sense, developed in the post-1347 Black Death era. Paintings of *King Death* often depict a grinning skeleton—the Black Death personified—wearing a golden crown, mocking and torturing the living. *King Death* served as an effective reminder to the living that all would one day be subjects of his corpse-realm. Still other types of plague art depicted Death as an angel or demon, or even as God hurling plague-tainted arrows at unsuspecting mortals. Saints like Mary, Sebastian, and Roche (Rocco) became popular heavenly intercessors on behalf of mankind, as witnessed by hundreds of paintings and sculptures. Through plague art, the Church urged its adherents, faced with certain and perhaps untimely death, to repent before they too succumbed to God's wrath, the plague. However, repentance did not guarantee physical protection from the Black Death, and funeral paintings of plague victims show this. Early examples depict full funeral processions with priests presiding over individual funerals, whereas only slightly later scenes show bodies, priest and layperson alike, in makeshift coffins, being dumped unceremoniously into mass graves.

By 1562, the year in which Pieter Brueghel painted his masterpiece, *The Triumph of Death*, religious influence had waned and the promise of redemption had come to seem hollow. As skeletons romped over a wasteland strewn with corpses, living human beings failed to fend off random sword slashes, bony hands, and hangmen's gallows. Brueghel's vision of life is bleak, but it certainly serves to remind the viewer, following the earlier *Danse Macabre* and *King Death* traditions, that death “comes to us all.” See also Black Death and Late Medieval Christianity; Black Death, Economic and Demographic Effects of; Plague in Medieval Europe, 1360–1500; Plague Literature and Art, Early Modern; Plague Memorials.

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WILLIAM LANDON

BLACK DEATH: MODERN MEDICAL DEBATE. Since the early twentieth century, the historical **Black Death** has been identified as the flea- and rat-borne bacterial **bubonic plague**. Specialists from several different academic fields, however, began challenging this diagnosis of the Black Death in the latter years of the century. These revisionists argue that the features of the Black Death that resemble modern bubonic plague are misleading and that the medieval environment and the behavior of the pestilence suggest a different disease altogether.

Bubonic plague is a disease of rodents, and the black rat (*Rattus rattus*) is deemed the most likely culprit of medieval epidemics, passing on the *Yersinia pestis* bacteria to humans through their fleas, who abandon the dead and dying rats. It is assumed, therefore, that the medieval world had the abundance of black rats needed to sustain the epidemics of the second pandemic (1347–1770) and that they were dying in droves immediately preceding human outbreaks. Historical sources from the fourteenth century, however, make little or no mention of the black rat's presence during times of plague. This issue has been thoroughly explored by several authorities, notably contemporary British medical historian J. F. D. Shrewsbury, who has concluded that because of the absence of evidence of rats in medieval Britain and the cold climatic conditions of northern Europe that suit neither rats nor their fleas, their populations must have been insignificant. He reasoned, therefore, that the Black Death, if it had been bubonic plague, could not have been particularly severe and that other diseases like **typhus** were acting in concert. More recently, British zoologist Graham Twigg took a similar tack, noting the lack of literary and archaeological evidence for the medieval black rat and suggesting anthrax as the cause of the Black Death. He emphasized historical descriptions of the disease spreading by touch or by contact with victims' possessions, the existence of rash-like symptoms, and the deaths of diseased animals. He also proposed the late medieval textile industry as a possible means of dissemination because human anthrax cases are commonly associated with contaminated animal products.

Proponents of bubonic plague respond that anthrax has never caused widespread **epidemics** and that medieval populations did not record the activity of rats or other vermin at any time. Others argue that the disease was not dependent upon the presence of sufficient rat populations or a climate hospitable for their fleas because bubonic plague could have been spreading from person to person via the human flea *Pulex irritans* or by

the contagious variant **pneumonic plague**. Although several historical sources do mention that the disease manifested in different forms, including a more deadly type of lung infection that suggests pneumonic plague, these counter-theories remain questionable because the human flea is generally considered an unreliable vector and because pneumonic plague cases rarely occur outside a substantial bubonic epidemic.

The strongest evidence supporting the identification of Black Death as bubonic plague is the long list of references to the symptomatic buboes (lymphatic swellings). As contemporary historian Samuel Cohn argues, however, these references constitute only a minute percentage of the historical descriptions of the Black Death; myriad other symptoms also occurred. In addition, the bubo is not specific to bubonic plague; it also appears with numerous other infectious diseases.

Whereas the medieval pestilence took only five years to travel to almost every corner of Europe and the Middle East, modern bubonic plague took as long as forty years to spread outside of China during the **third pandemic** of the nineteenth century. This suggests the Black Death had a means of transmission much faster than the period needed for bubonic plague to spread among rat populations before being passed to humans. This is supported by numerous historical descriptions of the Black Death that attest to its almost instantaneous contagion. Additionally, whereas deaths caused by modern bubonic plague number around 13 million since the inception of the third pandemic a century ago, conservative estimates of the mortality inflicted by the Black Death suggest as much as 40 to 50 percent of the total population of Europe and the Middle East over five years. Problems of identification also stem from the nature of the historical data. For example, the extent of the mortality caused by the disease is still questioned because the population size of medieval Europe and the Middle East is unknown.

Revisionists such as British scientists Susan Scott and Christopher Duncan (d. 2005) have studied available mortality data (including wills, testaments, and burial records) from early modern plagues and suggest that the behavior of the Black Death more closely resembles that of a **virus**. They propose a hemorrhagic disease, similar to **Ebola**, as the possible cause.

Despite apparent differences between medieval and modern plague, bubonic plague is still commonly accepted as the cause of both. Recently, medieval skeletal remains of suspected pestilence victims from French burial grounds have tested positive for plague bacteria (*Y. pestis*) DNA. While this evidence has not been corroborated with data from other plague burial grounds, it seems to confirm the presence of the disease during the late medieval period. Medieval bubonic plague may have been a more virulent strain than the modern version, and the pathogen may have mutated into a more benign form, which would explain the apparent differences in speed, contagion, and mortality. The Black Death could possibly have been caused by marmot (a type of ground squirrel and common carrier of *Y. pestis*) plague—the only form of rodent plague known to be directly contagious—spreading to humans. See also *Diagnosis of Historical Diseases; Historical Epidemiology; Insects, Other Arthropods, and Epidemic Disease; Plague: End of the Second Pandemic; Plague in Medieval Europe, 1360–1500*.

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KARL BIRKELBACH

BUBONIC PLAGUE. Bubonic plague and its variants have killed millions of people in three devastating **pandemics**—including the **Black Death**—and countless regional **epidemics**, causing major social upheavals. The very word “plague” retains the power to terrorize people. Plague has inspired writers such as Giovanni Boccaccio (1313–1375; *The Decameron*), Daniel Defoe (c. 1660–1731; *A Journal of the Plague Year*), and Albert Camus (1913–1960; *La Peste*). Although **antibiotics** and public health measures have limited major epidemics, the threat of **bioterrorism** has brought plague back into the news.

Yersinia pestis is a rod-shaped **bacterium** classified as Gram-negative because it does not take up the purple dye of the classic Gram stain. With Wright, Giemsa, and other special stains, dye clumps at the poles, giving a “safety-pin” appearance. Working independently in Hong Kong, **Shibasaburo Kitasato**, a Japanese microbiologist who had worked with **Robert Koch** in Germany, and **Alexandre Yersin**, a Swiss microbiologist from the Pasteur Institute, identified the bacterium responsible for bubonic plague in 1894. Originally named *Pasturella pestis*, for **Louis Pasteur**, the bacterium was renamed in 1971 in honor of Yersin.

Infection with *Y. pestis* causes three symptom complexes, with incubation periods ranging from one to six days. Classic bubonic plague is characterized by swollen, intensely painful lymph glands or buboes (Latin for “groin swelling”) in the groin, axilla, or neck, accompanied by fever, chills, and headache. The infection may spread quickly into the bloodstream; release of inflammatory toxins leads to circulatory collapse, organ failure, and death within days. Clotting defects cause purpura (bleeding into the skin), while blockage of small blood vessels leads to gangrene. Bacteria may also spread secondarily through the bloodstream into the lungs causing shortness of breath and bloody sputum. Untreated bubonic plague has a 50 percent mortality rate. It remains unclear whether survival of bubonic plague confers any lasting immunity. In primary **septicemic plague**, the bacteria invade the bloodstream directly at the site of the flea’s injection of the bacteria. Primary **pneumonic plague** is transmitted from patient to patient through respiratory droplets.

Antibiotics must be started as soon as the disease is suspected based on the patient’s history of exposure, results of physical examination, and evidence of plague bacilli in the blood, sputum, or fluid from buboes. Confirmatory testing by special staining techniques, growth of *Y. pestis* in cultures, or detection of plague antibodies in the blood takes several days. Efforts are under way to develop a rapid bedside screening test. The antibiotic streptomycin proved effective in the early 1950s. Today, less toxic drugs of the streptomycin class, such as gentamicin, are preferred. Tetracyclines and other classes of antibiotics are acceptable alternatives. People in close contact with infected patients or **animals**, as well

as exposed laboratory personnel, are protected by prophylactic antibiotics. With prompt treatment, bubonic plague mortality is less than 10 percent.

Plague is a zoonosis, a disease transmissible from animals to humans. In 1898 experiments conducted in India and Pakistan by **Paul-Louis Simond** of the Pasteur Institute pointed to the rat flea *Xenopsylla cheopis* as a plague vector. Despite initial skepticism, further experimentation by other researchers led to general acceptance of the flea vector by about 1906. During plague epidemics, the black rat, *Rattus rattus*, is infected through the bite of the rat flea. The digestive tract of the flea becomes clogged with rat blood and bacteria. As the rat dies of plague, its fleas seek a new host. After an infected flea punctures human skin, its blocked digestive tract regurgitates thousands of plague bacilli under the skin. The bacteria enter the lymphatic channels or the bloodstream, causing bubonic or septicemic plague.

In the long intervals between epidemics, infected fleas retreat to wild rodents (sylvatic plague) which serve as reservoirs for *Y. pestis*. This enzootic cycle maintains the bacterium in nature until conditions are favorable for new epizootic and epidemic cycles. But black rats are not the only mammals that can support plague-carrying fleas: species of squirrels, prairie dogs, chipmunks, marmots, gerbils, and rats, as well as larger animals such as coyotes, rabbits, and even cats and dogs can also do so.

Historically, infected rats and their fleas traveled easily in **trade** caravans and ships' holds, and in **war** time accompanied moving armies and refugee populations. Domestic rats thrived in thatched roofs, granaries, and human refuse. Infected fleas survived for weeks in sacks of grain or woolen cloth.

The first recorded pandemic was the Plague of Justinian in the sixth century. The Black Death of the fourteenth century killed between one-quarter and one-half of Europe's population and similarly affected the Islamic world. In the 1890s pandemic, rapid steamship travel spread the plague from Chinese ports to much of the Pacific Rim, including Hawaii and the western coast of the United States.

Social Responses to Bubonic Plague. In the Middle Ages and well into the modern era, plague was seen as divine punishment for sinfulness. At various times, plague was blamed on contaminated food or water, foul **air**, witchcraft, unfavorable alignment of the planets, or climatic conditions. Minorities such as Jews were **scapegoated** for causing the plague and were exiled, persecuted, and murdered. Personal responses ranged from public displays of self-flagellation to fatalistic hedonism. Assigning blame for plague continued into modern times. During the third pandemic, heavy-handed interventions by the British colonial administration in the 1890s led some Indian citizens to suspect that the imperialists themselves were spreading plague. In San Francisco, the arrival of plague from Honolulu in 1900 created public panic. Because most of the early victims were Chinese immigrants, a harsh **quarantine** and other restrictions were quickly and irrationally imposed on all residents of Chinatown.

Early public health efforts to control plague included forced isolation of the sick and their families in locked and shuttered homes, appointment of plague **physicians**, establishment of health magistracies, enforcement of naval and land quarantines, erection of **cordons sanitaires**, fumigation and **disinfection** measures, and forced removal to dreaded plague hospitals or **pest houses**. **Flight** from affected areas was a universal response.

The experience of **plague in San Francisco** between 1900 and 1907 reflected new developments in bacteriology, **epidemiology**, and public health. Plague, a bacterial disease that flourished in crowded, unsanitary neighborhoods, fit in well with the sanitarian belief that cleaning up filth and proper management of sewage could limit epidemics. Initial **sanitation** measures included fumigation with sulfur dioxide gas, disinfection with chloride of

lime, and the burning of household refuse in the Chinese district. Residents of Chinatown understandably resisted efforts at forced **vaccination** with the plague vaccine developed in India in 1897 by Russian/Swiss microbiologist **Waldemar Haffkine**. The San Francisco epidemic caused 113 deaths over several years. Plague returned to San Francisco in 1907 during the sanitation crisis precipitated by the earthquake of 1906. The role of the rat flea was well accepted by that time, and health officials focused their efforts on destroying rats and their habitats.

Plague in Recent Times. Between 1987 and 1998, the **World Health Organization** registered 26,000 plague cases with an overall mortality of 8 percent. Major epidemics were reported in Vietnam in the 1960s and 1970s, with limited outbreaks in the 1990s in India, Madagascar, Myanmar, and Peru. The Vietnam epidemic was linked to **environmental** and population disruptions as a result of war, underlining the close relationship between epidemic diseases and social factors.

Today, most plague cases in developed countries are sporadic rather than epidemic. In the rural western United States, infected rodents such as squirrels and prairie dogs transmit plague to rabbits and domestic animals. Ten to fifteen human plague cases are diagnosed annually in New Mexico and other western states. In the United States, all confirmed cases are reportable to the national **Centers for Disease Control and Prevention (CDC)**. To protect those living in endemic areas, the CDC recommends rodent and flea control as well as public education about rodent habitats, insect repellents, safe handling of suspect animals, and indications for prompt medical attention. A vaccine offering limited protection was used in American military personnel in Vietnam and others at high risk, but was recently withdrawn. Research continues toward developing an effective plague vaccine.

Plague is a **bioterrorism** threat. During World War II, a Japanese **biological warfare** unit airdropped plague-infected fleas over China causing deadly local epidemics. Today, classic flea-borne bubonic plague is much less of a bioterrorism threat than aerosolized pneumonic plague. The United States and the Soviet Union conducted research on weaponized aerosolized pneumonic plague during the Cold War. Pneumonic plague is classified by the CDC as a Category A bioterrorism threat. The feared scenario is the introduction of aerosolized plague bacteria into a population. Although the bacilli would die within hours on exposure to sunlight, target populations infected with pneumonic plague would spread the rapidly fatal disease from person to person. Initially, doctors would logically suspect ordinary bacterial pneumonia rather than pneumonic plague, delaying mobilization of emergency public health resources. *See also* Black Death and related articles; Bubonic Plague in the United States; Historical Epidemiology; Insects, Other Arthropods, and Epidemic Disease; London, Great Plague of (1665–1666); Plague: End of the Second Pandemic; Plague in Britain (1500–1647); Plague in China; Plague in East Asia: Third Pandemic; Plague in Europe (1500–1770s); Plague in India and Oceania: Third Pandemic; Plague in Medieval Europe, 1360–1500; Plague in the Islamic World, 1360–1500; Plague in the Islamic World, 1500–1850; Plague of Justinian, First Pandemic; Public Health Agencies, U.S. Federal.

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SANDRA W. MOSS

BUBONIC PLAGUE IN THE UNITED STATES. Although the plague caused by the **bacterium** *Yersinia pestis*, and normally spread by rodent fleas within rodent populations, may have entered Latin America during the first century of contact with Europe, there were no signs of plague in the United States or Canada until the **third plague pandemic** at the end of the nineteenth century. It arrived at U.S. ports with shipborne rats and, predictably, sparked small **epidemics** along the West Coast. After a quarter of a century, researchers noted that the disease had established itself widely among local rodent populations in 14 western states. Human encroachment on this wide reservoir has accounted for most American plague cases since 1925.

Research into the *Y. pestis* genome has demonstrated that all plague found in the United States is of the Orientalis biovar and was introduced in the 1890s. This process began in San Francisco in June 1899, with the arrival of the Japanese freighter *Nippon Maru*, which contained stowaways and plague-infected rats. This was about four years into the third pandemic, which saw the dissemination of plague by steamship from East and Southeast Asia. It was also subsequent to the discoveries of the bacterial cause of plague, and its flea and rodent vectors. San Francisco's first victim was a Chinese man living in the squalor of Chinatown; he died on March 6, 1900. Officials erected a **cordon sanitaire** around the neighborhood's 12 blocks, while its Asian-American inhabitants did their best to hide further plague fatalities, and the press mocked public health efforts. On May 19 the presence of **bubonic plague** was officially admitted, and a wave of racist anti-Asian discrimination resulted. State and civic officials clashed, federal researchers investigated, and some called for the eradication of Chinatown itself. On April 8, 1901, the cleanup of Chinatown began, as **disinfectants** and fumigants flowed and some 14,000 rooms were cleansed. In the end, there were 121 reported cases in the city and 5 elsewhere, with 122 fatalities: a very high mortality rate of 97 percent.

Plague scares also struck New York City and Washington State's Puget Sound region in 1899 and 1900. The British ship *J. W. Taylor* had departed plague-struck Brazil and had lost its steward to plague, but docked in New York's harbor and underwent **quarantine**

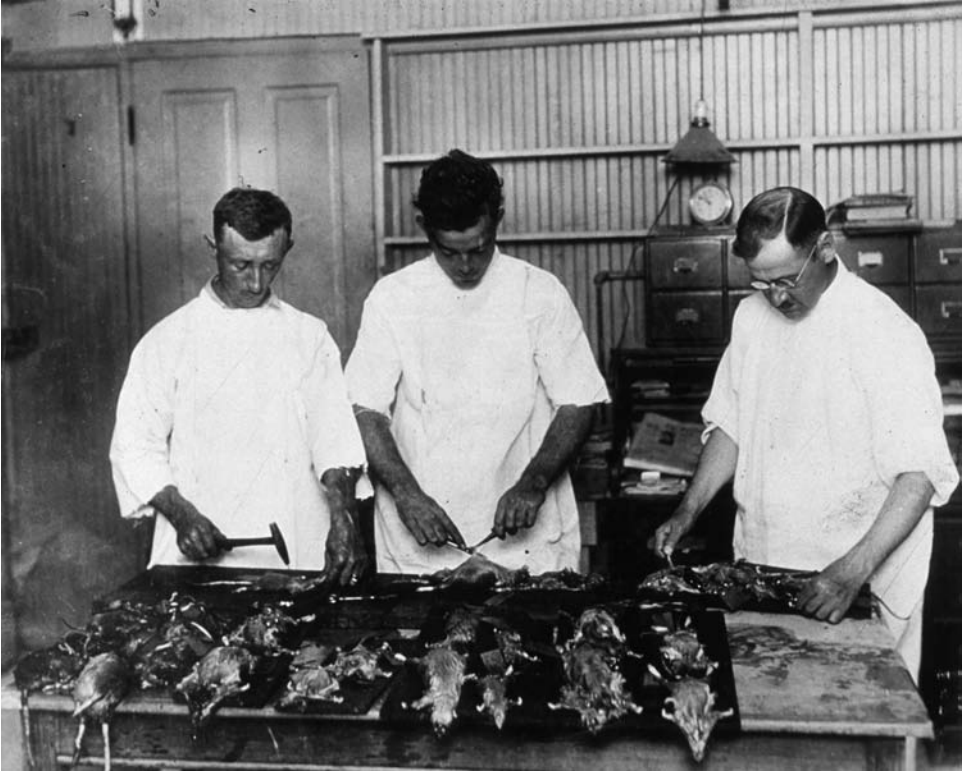
without incident. The Japanese *Nanyo Maru* was halted and quarantined at Port Townsend, Washington, as three on board had died of plague. In the fall of 1900 Seattle suffered three deaths of suspected plague, though only one was confirmed. Watchfulness and luck served American ports well.

The San Francisco Earthquake of April 18, 1906, reduced much of the city to rubble and set the scene for a second Bay Area epidemic. Infected and virgin populations of rats mixed, and stores of food aid lay carelessly about in the refugee-camp conditions about the Bay. On May 26 the first plague death was confirmed, but cases picked up only a year later, reaching epidemic levels in August 1907. By late in the year investigators found that 1.4 percent of captured rats had plague—a very high percentage—and reported cases rose to 190, with 96 fatalities. In February 1908 civic response was mobilized as incoming ships were fumigated and a plague hospital established. Incidence dropped, and by March 1909 the epidemic—America's worst—had ended. Of 205 known cases, 103 died. Second-year medical student Charles B. Hare took a sample of the bacteria back to his laboratory in Ann Arbor, Michigan, and accidentally contracted a case of **pneumonic plague** from a self-rolled, contaminated cigarette: the first American lab-acquired case of plague. He sustained heart damage but recovered, dying at age 50.

In 1908 the first domestic rodent with plague, a squirrel, was trapped in California. This set off a decade-long campaign during which 700,000 California squirrels were destroyed. Meanwhile plague had struck Cuba, and America's Gulf Coast began surveillance for plague. Investigators found plague-infected rats around New Orleans's docks beginning in 1912, and in June 1914 a man died of what could have been plague. This was quickly followed by 30 cases, with 10 deaths. Businesses, the press, and civic officials cooperated, and rat-trappers received a bonus for diseased rats. The diligence paid off and only a single case appeared in 1915, and another in 1916.

America's worst outbreak of pneumonic plague developed among Mexican nationals living in a Los Angeles neighborhood in 1924. In October 30 cases occurred among members of a family and boarders at their home. By month's end 11 were dead and 16 were dying. On November 2 civic authorities placed a cordon around the neighborhood, severely limiting contacts. Though more cases developed, the spread was contained. By its end, the epidemic had produced 33 cases of pneumonic plague, with 31 fatalities, and 8 cases of bubonic plague with 5 deaths.

Over the next quarter-century only 27 cases of plague were reported in the United States, with 14 fatalities. Sylvatic, or wild, rodents far from the West Coast became the most common vectors, whereas deaths from rat-borne fleabites became virtually unknown. A typical case was an Oregon sheepherder who contracted plague from a squirrel that lived with squirrels among whom plague was enzootic. Such geographically isolated cases were hard to treat, but they greatly reduced the likelihood of plague epidemics. Although the period saw the implantation of plague further and further eastward, it also saw the development of **Haffkine's** vaccine, **sulfa drugs** and later **antibiotics**, and effective **pesticides**. By the latter part of the 1950s, four Southwestern states—Arizona, Colorado, New Mexico, and Utah—accounted for most cases of plague in the United States, and until 1965 only two or three cases erupted during most years. An intertribal gathering of Navajo Indians at Gallup, New Mexico, became the focal point of a plague outbreak vectored by infected prairie dogs. Eight—possibly ten—cases occurred, but only one fatality was suffered, testimony to swift action on the part of public health officials.



Examination in New Orleans of rats suspected of carrying bubonic plague in 1914. Courtesy of the National Library of Medicine.

From the mid-1960s the number of observed epizootics among wild rodents increased, as did the number of human cases. Growth in tourist traffic and **urbanization** in the Southwest would seem to account for much of this activity, as humans more frequently encroached on increasingly extensive plague reservoirs. From 1970 to 1991 there were 295 indigenous cases of plague in the United States, with 82 percent occurring in Arizona, Colorado, and New Mexico. Ground squirrels and, increasingly, domestic cats were the typical vectors. Fatality rates were 17 percent for men and 11 percent for women. Greater public awareness—including that among EMTs and primary care **physicians**—and stepped up public health surveillance may account for the decline in cases: from 1990 to 2005 only 107 cases were reported, of which 18 were primary septicemic and 5 primary pneumonic; 78.5 percent were primary bubonic plague. Despite years of human activity, a recent study shows that almost 15 percent of the so-called “four corners” region of the Southwest remains an area of “high risk” for plague infection. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Kitasato, Shibasaburo; Plague in East Asia: Third Pandemic; Plague in San Francisco, 1900–1908; Plague in the Contemporary World; Public Health Agencies, U.S. Federal; Race, Ethnicity, and Epidemic Disease; Simond, Paul-Louis; Trade, Travel, and Epidemic Disease; Yersin, Alexandre.

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JOSEPH P. BYRNE

BUBONIC PLAGUE, SECOND PANDEMIC. See Black Death and related articles and Plague-related articles.

C

CAPITALISM AND EPIDEMIC DISEASE. Capitalism is an economic system in which *the means of production*—or the tools, land, materials, and ideas used to create products and services—are generally privately owned and operated for profit by individuals or groups that form a corporation. In theory, individuals and corporations work (investing, producing goods, trading, etc.) in a free market, meaning that all parties mutually agree to prices and terms of exchange with minimal coercion or laws regulating supply or pricing. In application, though, capitalism is often regulated by society, either through public processes or laws. Capitalism and **epidemic** diseases have a complex relationship, each affecting and influencing the other in a number of ways.

Epidemics Can Impede Capitalism. People are the backbone of capitalist economies, as producers, innovators, and consumers. Epidemics impede the ability of capitalist economies to function and grow by negatively affecting people. First, epidemics decrease productivity by making people unable to work. For example, in parts of Africa where **malaria** is endemic, parents often miss weeks of work each year in order to care for suffering children. In addition, malaria may hurt the cognitive development of children and prevent them from attending school, often making them less able to work in the future.

Second, human capital, or the labor, skills, knowledge, and connections people use to carry the economy forward, is decreased when adults are sickened or die from epidemics. In Botswana, for example, life expectancy has fallen from 64 years of age in 1990 to 35 years of age in 2004, primarily as a result of the high number of deaths due to **AIDS**. The actual number of adults alive and well enough to work and start businesses has fallen dramatically. Their human capital is also lost to the economy and to future generations of entrepreneurs. In such a society, there is also an increased dependency burden, or a higher proportion of elderly, children, and sick individuals for whom adults must care, which results in decreased amounts of time and energy that can be devoted to economic

activities. Similarly, a family may spend most or all of its disposable income on medicine or medical care. This decreased purchasing power slows consumer spending and the economy as a whole.

Stewardship of Resources. Capitalism impacts the trajectory of epidemics through stewardship of key resources. For example, **water** is the most common vector for epidemic diseases such as **cholera** and **schistosomiasis**. A capitalist monopoly over water provision in South Africa in 2003 raised prices to cover the cost of new pipes. Poor families that could not pay their water bill had their service shut off and turned to unsanitary rivers and gutters for drinking water. This resulted in a deadly cholera outbreak affecting thousands. The public cost of treating these scores of sick reached into the millions of dollars by the time the epidemic was controlled.

Medical Care and Capitalism. Access to adequate medical care includes access to health-care practitioners and infrastructure such as nearby hospitals and clinics with diagnostic technology. Modern capitalist states recognize the importance of wide access to at least basic emergency care for the public good. Monitoring, isolation, and treatment of infectious diseases have been in public hands for over a century, supported by taxes on private enterprises and with the products of profit-motivated pharmaceutical firms. Historically, capitalist societies, often influenced by Judeo-Christian moral and ethical codes, have made the greatest strides in human health and longevity; have provided the widest range in health-care options; and, given the profit motive, have shared these globally. Capitalism's economic surplus has been plowed back into basic and technical education, as well as into both basic and applied research that continues to benefit the world population.

Access to health-care practitioners in low-income countries is compromised by a worldwide "brain drain" driven in part by the global capitalist economy. Thousands of health practitioners from poor countries immigrate to developed countries each year in part because of vastly higher salaries and job security. In some African countries, for example, over 90 percent of medical school graduates lack incentives to remain and go on to practice medicine in the United States or Europe. Another factor is that low income countries often lack the infrastructure necessary for **physicians** and **nurses** to put their skills to use fully and care for patients. Many of these countries suffer from political and economic systems that misallocate resources toward self-aggrandizing individuals or elites, or toward bloody factional wars.

Investment in infrastructure, such as hospitals, diagnostic equipment, ambulances, laboratories, and so on, is also influenced by capitalism. Low-income areas that have the greatest burden of epidemic disease do not represent a profitable investment of capital because the potential consumer base simply cannot afford the product and because local instability makes the risks of investment too high. Unlike many other goods and services, however, inability to afford health-care has the serious consequences of sickness, disability, or death. Some countries have attempted to overcome the problem of access by using various combinations of taxes and public and private insurance systems to pool health-care risks and costs so that care is more affordable and accessible. Unfortunately, even these systems have significant gaps in reach or quality, and in many parts of the world they simply do not exist. Capitalism and its benefits will thrive where there are clearly recognized property rights and the rule of law.

Development and Access to Treatments. Capitalism often impacts epidemics by directing how treatments for these diseases are developed and accessed. In a capitalist econ-

omy, the central function of any company is to make a profit in the free market. **Pharmaceutical** companies research and produce treatments for diseases. Eighty percent of drugs are purchased by people in North America, Europe, and Japan—wealthy, developed areas which together account for only 19 percent of the world's population. Following this market demand, pharmaceutical companies have generally focused their efforts on developing and marketing drugs for the diseases that are most common in these countries, such as cancer and ischemic heart disease. Indeed, such advances may help people all over the world suffering from such diseases. However, common epidemic diseases in poorer, tropical regions, such as malaria, **Chagas's disease**, and leishmaniasis, have spawned little research and therefore have few, or in some cases no, treatment options. In fact, a mere 16 of 1,393 new drugs or medicines registered in the United States and Europe between 1975 and 1999 were for the treatment of diseases from which people in developing countries typically suffer.

Developing a new drug involves enormous financial investments in researchers, labs, materials, along with large-scale human studies to test safety and efficacy. These investments carry financial risk. Experiments may repeatedly fail to yield a successful drug, or a competitor may develop a better or more popular product. Companies are willing to make a risky investment because they are confident that if there is a positive result, the profits will belong solely to them. This is because international organizations such as the World Trade Organization and national government agencies such as the U.S. Patent Office protect intellectual property (such as scientific discoveries) with patents. If a company has a patent on a new drug in the United States, for example, it has the rights to all manufacture, use, and sales of that drug for 20 years. During this period the company may set any price it chooses, which sometimes prevents access to the drug for the largest number of people who would benefit. In addition, though it significantly increases development costs, pharmaceutical companies also advertise drugs widely to increase consumer demand that may allow for a higher selling price.

Although capitalist enterprises produce many life-saving drugs, by no means does capitalism ensure that these drugs reach everyone. Access to treatment and care continues to be a persistent problem in areas with the highest burden of epidemic disease. This is particularly salient in the case of drugs that control **HIV**. Pharmaceutical companies, with the help of publicly funded universities, have transformed HIV from a death sentence to a survivable disease for those able to access Highly Active Antiretroviral Treatment (HAART). However, the price of a HAART regimen (also known as a “drug cocktail”) even at a special discount from one major pharmaceutical company for the 30 poorest countries in the world, or “Low Development Index” countries, is still over \$1200 per person per year. In these countries 50 to 90 percent of the population lives on less than \$2 per day, or a total of \$600 per year. Some companies have illegally broken patents to create cheaper, generic “copycat” HAART drugs that have significantly increased access—but, some argue, they have endangered intellectual property rights. Around the world fewer than one in four of the 35 million people living with HIV who require HAART drugs receive them. The consequence for many poor people suffering from epidemic disease is that, because they are not viable consumers, their lives are simply outside the capitalist market altogether. By being priced out of the market, their diseases have also been priced out of effective prevention and treatment. *See also* AIDS in Africa; Colonialism and Epidemic Disease; Cordon Sanitaire; Diet, Nutrition, and Epidemic Disease; Geopolitics, International Relations, and Epidemic Disease; Industrialization and Epidemic Disease; Industrial Revolution; International Health Agencies and Conventions; Malaria in

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LINDSAY BROOCKMAN AND DANIEL PALAZUELOS

CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. See Public Health Agencies, U.S. Federal.

CERVICAL CANCER. See Human Papilloma Virus and Cervical Cancer.

CHADWICK, EDWIN (1800–1890). Edwin Chadwick, the architect of the public **sanitation movement**, was born in Longsight, near Manchester, on January 24, 1800. His mother died when he was young, and his father remarried, moving the family to London. Chadwick studied law at Middle Temple in 1832 and supported himself through journalism; both occupations brought him into contact with the ravages of **poverty** in the slums, courts, fever dens, prisons, and workhouses of London. He also worked as an assistant to political philosopher Jeremy Bentham (1748–1832) from 1830 to 1832.

The **cholera epidemic** of 1831–1832 prompted a governmental inquiry, and Chadwick, who disagreed with the report, conducted an investigation into the relationship between disease and sanitation. He presented his findings in *The Sanitary Conditions of the Labouring Population of Great Britain* (1842), demonstrating the necessity of public health reform. The report, which became the leading text on sanitation in the nineteenth century, concluded that disease and life expectancy were directly related to social conditions, calculating that the average lifespan of the working class was one-third that of the gentry and professional classes. Chadwick's report raised awareness of the need for action to improve living conditions to curtail premature death and disease amongst the poor. A healthy population would work longer and harder thus requiring less relief. Remedial suggestions included a constant supply of fresh, clean water; water closets in every residence; ventilation; and a system of transporting sewage to outlying farms that would be an inexpensive source of fertilizer.

Chadwick was responsible for the formation of the first Board of Health in 1848, which established central and local governing bodies to oversee regulation. Opposition to public health reform came from **water** companies and landlords who had vested interests in preserving the current system. Chadwick's unpopular views culminated in his forced resignation in 1854 to ensure the advances he achieved would be maintained. He wrote numerous reports and pamphlets, and he continued to campaign for legislative reform in the areas of tropical hygiene, poor law, drainage and sewage systems, army sanitation, burials in urban areas, public space, child labor, water supply, education, transportation, and sanitation.

Chadwick presided over the Sanitary Institute and the Association of Sanitary Inspectors in 1878, and he was a corresponding member of the Societies of Medicine and Hygiene in Belgium, France, and Italy. His insistence on the relationship between poverty and disease and the importance of state regulation of sanitation made him a pioneer in the history of public health reform. Chadwick was knighted in 1889 by Queen Victoria. *See also* Cholera: First through Third Pandemics, 1816–1861; Environment, Ecology, and Epidemic Disease; Epidemiology, History of; Industrialization and Epidemic Disease; Public Health Agencies in Britain since 1800; Public Health Agencies in the West before 1900; Snow, John; Urbanization and Epidemic Disease; Virchow, Rudolf.

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HEIDI M. RIMKE

CHAGAS'S DISEASE. *See* Sleeping Sickness.

CHILDHOOD. *See* Children and Childhood Epidemic Diseases.

CHILDREN AND CHILDHOOD EPIDEMIC DISEASES. Until the 1930s, health perils were a hallmark of childhood in every area of the world. In the United States alone in 1900, 13 percent of children died before their first birthday and 18.5 percent died before their fifth birthday. Children in western Europe fared no better; the infant mortality rate in Britain was 15 percent in 1906. The medical and lay communities in both Europe and the United States viewed these deaths fatalistically, contending that children were weak by nature and thus unusually vulnerable to illness. Not until the late nineteenth century did public health officials begin to view the high rate of childhood morbidity and mortality as preventable.

The publication in 1906 of *Infant Mortality: A Social Problem* by Sir George Newman (1870–1948), a British **physician** and pioneer in public and child health, ensured that the infant mortality rate—the number of deaths before age one in a particular population per 1,000 live births—would become the international measure of societal welfare. Newman argued that because babies were wholly dependent on others for care, infant mortality represented the state of everyone's wellbeing. This use of infant mortality as a communal gauge ensured that alleviating illness and death among children would become the focus of significant interest and investment in all societies.

Special attention to diseases affecting children was, and remains, necessary. Children have always been more susceptible to certain diseases than adults, by virtue of their lack of immunological experience, their anatomy, and their vulnerability in inhospitable **environments**. The traditional childhood diseases—which include **measles**, mumps, rubella (German measles), varicella (chicken pox), and **diphtheria**—confer lifelong **immunity** and thus, once experienced, cannot be contracted as an adult. Prior to the mid-1960s, when inoculating infants and children against these diseases became routine in most

countries, the traditional childhood illnesses were so endemic (and occasionally **epidemic**) that most people had contracted them before age 15.

Of the infectious diseases now prevented by **vaccination**, diphtheria and pertussis (**whooping cough**) were the most deadly, each killing many hundreds of children annually in every large American and European city. In 1890 in New York City alone, diphtheria caused almost 2,000 deaths, mostly of children under the age of five; in some areas of the world between 45 and 55 percent of children who contracted diphtheria died of the disease. In England and Wales as recently as 1937, diphtheria was second only to pneumonia as a cause of death in childhood, killing 32 per 100,000 children under the age of 15. Campaigns to inoculate children against diphtheria were highly successful; by 1930 in New York City hundreds of thousands of children had been immunized.

Measles was also a serious illness because of its occasional tendency to cause deadly complications, including pneumonia and **encephalitis**. Rubella, although not dangerous to the sufferer, caused fetal defects in 25 percent or more pregnancies when contracted by a mother in the first trimester of pregnancy. Defects could include deafness, cataracts, microcephaly, mental retardation, congenital heart defects, miscarriage, and stillbirth. The worst recorded rubella epidemic in the United States occurred in 1965, resulting in 11,250 miscarriages and stillbirths, 2,100 newborn deaths, 11,600 cases of infant deafness, 3,580 cases of infant blindness, and 1,800 cases of infant mental retardation.

Another infectious disease disproportionately affecting children was **poliomyelitis**, an intestinal **virus** that had caused only a mild, inconsequential illness for most of human history. Between 1840 and the 1950s, however, polio became epidemic worldwide with the worst outbreaks of the twentieth century occurring in North America and Western Europe. Most victims were children under 15. During the epidemic, about 1 percent of polio cases attacked sufferers' central nervous systems and destroyed nerve cells, causing temporary paralysis or, in more severe cases, permanent paralysis or death. To this day, scientists do not know why polio affects mostly children, especially boys, and why the illness is most virulent in the summer. Outbreaks of polio still occur among nonimmunized groups, particularly in Nigeria, India, Pakistan, and Afghanistan.

Today, immunizations have largely eliminated the endemic and epidemic childhood diseases of yesteryear. Public health systems around the world strive to vaccinate as many children as possible to confer "herd immunity"—that is, because not all immunizations are wholly effective in every child, the higher the population's vaccination rate, the more everyone, even the un- and under-vaccinated, is protected. When public health systems break down—which does happen in areas affected by **war**, civil unrest, political turmoil, famine, drought, or poverty—and a significant percentage of children go unvaccinated, traditional childhood illnesses often return with devastating results. After the breakup of the Soviet Union in the early 1990s, for example, a once well-established childhood vaccination program faltered, and a diphtheria epidemic ensued; more than 140,000 cases resulted in more than 4,000 deaths. Epidemics such as measles have also returned to some communities in the United States. As an increasing number of American parents balk at getting their children immunized for fear that some immunizations cause autism (a suspicion not supported by studies to date), herd immunity wanes, and children, as well as some adults, are once again susceptible to the life-threatening diseases of yesteryear.

As lethal as the traditional childhood illnesses have been historically, they were by no means the biggest killers of children. Because of children's anatomy and their occasional exposure to toxic environments, the most deadly disease affecting children has always been diarrhea. Compared to adults, small children have meager water reserves. Faced with

even a mild case of diarrhea, children dehydrate quickly. Infant diarrhea became epidemic in Europe and the United States as rapidly burgeoning cities became sanitation nightmares in the nineteenth century. Before the advent of sewers to separate human waste from drinking water and the passage of laws governing the production and distribution of cows' milk, children in urban areas died of diarrhea by the thousands each summer when milk and other food spoiled quickly. More than half the infants who died in late-nineteenth-century United States and Europe died of diarrhea. Today, diarrhea continues to be the main cause of death among children in developing countries where the recommendations for the prevention of the illness remain the same as they were more than 100 years ago: breastfeed, and if breastfeeding is not possible, provide infants with clean water and milk, keep food fresh, use latrines, and wash hands often.

Infant deaths from diarrhea began to ebb in the twentieth century only after urban reformers, public health departments, physicians, and urban newspapers joined forces to lobby for the passage of laws to ensure pure milk for children. The milk crusades, which lasted in some American cities for up to three decades or more (from roughly the 1890s through much of the 1920s), were highly visible and served to edify the public about the primary cause of infant death. In an era before refrigeration, pasteurization, and pure food laws, milk was shipped in 8-gallon uncovered vats and traveled for up to 72 hours in railroad cars before reaching the urban consumer. Milk spoilage was only one cause of infant diarrhea—the vat system of milk distribution also facilitated the adulteration of milk. To increase profits, shippers and merchants often added myriad substances to the content of vats—plaster, for example, to make skimmed milk look rich with cream, and powdered chalk to whiten milk dirtied by the open vat system. Consumers contributed to the disaster. Understandably wary about the milk they purchased, they often dipped their fingers into vats for sampling before ladling milk into vessels. In this way, diphtheria, scarlet fever, **tuberculosis**, and infant diarrhea all became milkborne diseases.

The seasonal incidence of deadly diarrhea among babies disappeared in most areas of the United States by the 1930s, thanks to reformers' successful efforts to improve the production, shipping, and sales practices of the dairy industry. Chicago was typical in that deaths from diarrhea went from 53.7 percent of all infant deaths in 1897, to 40.9 percent in 1905 (after milk vats were sealed by law), 39.4 percent in 1912 (after cows' milk had to be shipped and sold in individual, sealed bottles), 35.9 percent in 1918 (after cows' milk had to be pasteurized), 16.9 percent in 1924 (after milk had to be kept cold during shipping), and 11.1 percent in 1930 (after cows' milk had to be tested for bovine tuberculosis). As was typical throughout most of the United States and Western Europe, by 1939 in Chicago only 1.4 percent of the babies who died, died of diarrhea. As the general urban environment improved, the infant mortality rate in urban areas went from roughly 18 percent in 1897, to 12 percent in 1912, 8 percent in 1924, and 3 percent in 1939. This dramatic lowering of the infant death rate long before the availability of antibiotics and routine childhood immunizations is a prime example of how improvements in the environment contributed far more than medical treatment to declines in mortality.

After diarrhea, respiratory ailments were the second most significant cause of death among children. Those most at risk for infection were children younger than two and those already weakened by another health problem. This latter factor ensured that the youngest children were highly susceptible to respiratory disease—by the early twentieth century, urban health departments admitted that for decades many of the infants listed as dying from pneumonia or bronchitis likely died from opportunistic respiratory infections facilitated by a weakened condition as a result of diarrhea.

Sexually transmitted infections among adults also affected children. In the pre-**antibiotic** era, mothers with **syphilis** passed the disease to their children in utero. Children with congenital syphilis were predisposed to **meningitis**, severe mental retardation, and hydrocephalus and often died in infancy. **Gonorrhea** could be passed from mother to baby in the birth canal, affecting an infant's eyes and resulting in permanent blindness. In the nineteenth-century United States, gonorrhea was the most common cause of blindness among children, prompting physicians to often remark that this was a classic case of the "sins of the father" being visited on the children.

Change in daily habits occasionally triggered other diseases in children. Rickets, which causes softening of the bones and severely stunted growth in infants and children, was epidemic in late-nineteenth-century European and American cities. The disease is caused by insufficient calciferol, a hormone that helps balance calcium in the body. Sunlight triggers the body's manufacture of calciferol, also known as Vitamin D (despite not being a vitamin). In the nineteenth century, changes in human living patterns and behaviors prompted the illness: tenements had no windows, soft coal polluted cities and blocked sunlight, and unpaved urban roadways were so full of mud and muck that mothers kept their children indoors for fear they would drown in the deep puddles dotting city streets. In the 1930s, the addition of calciferol to infant formula and cows' milk (hailed as "Vitamin D fortified milk") eliminated rickets in Europe and America but unfortunately perpetuated the notion that rickets is a disease of dietary deficiency rather than of sunshine deficiency. Today the disease has appeared once again, mainly in breastfed infants, because concern about skin cancer has prompted mothers to cover infants from head to toe and slather sunscreen on any exposed skin. The growth in the number of working mothers has also contributed to the problem; many daycare providers tend to keep children indoors during daylight hours.

Today the leading cause of death among infants in the developed world is no longer diarrhea or any infectious disease but congenital abnormalities, premature birth, and Sudden Infant Death Syndrome. Among older children, the leading causes of death are unintentional injury, homicide, and suicide. In the developing world, however, as in the United States and Western Europe in the nineteenth and early twentieth centuries, diarrhea remains the leading cause of childhood death. That entirely preventable illnesses such as infant diarrhea and traditional childhood diseases are still ongoing threats in some areas of the world signifies that the root cause of infant and child mortality remains: some parents are still denied access to the resources they need to properly care for their children. *See also* Heredity and Epidemic Disease.

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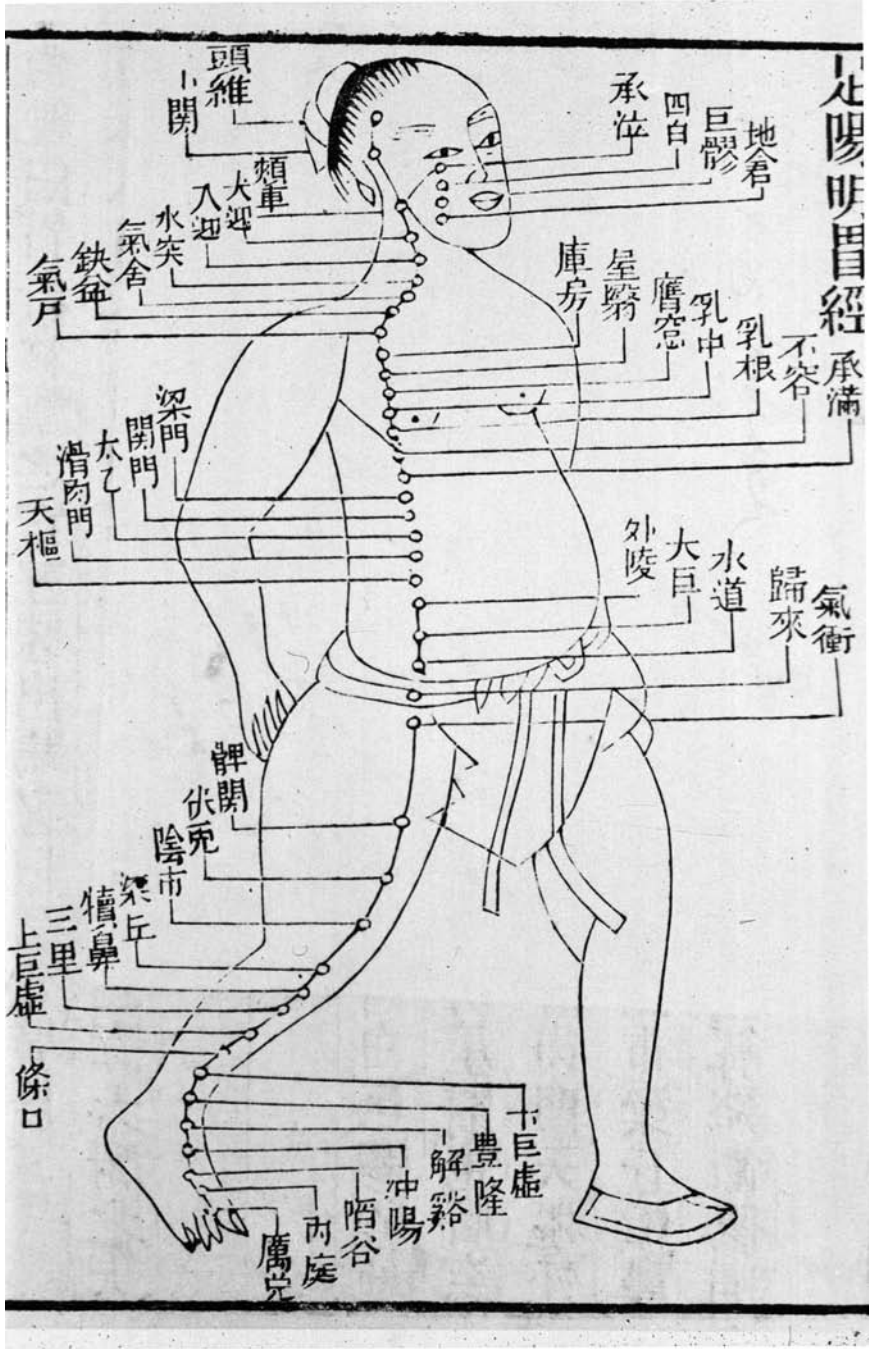
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JACQUELINE H. WOLF

CHINESE DISEASE THEORY AND MEDICINE. Archeological evidence for scientific and technological knowledge in China extends back at least to the **Neolithic** period (c. 6000 BCE), and written material is available from as early as the Shang period (c. 1700–1025 BCE). Early artifacts, dating from the Shang, include divinations written in the precursor to modern Chinese script on flat bones and turtle shells (“oracle bones”), as well as technically advanced bronze castings. The Zhou dynasty (1122–256 BCE) was characterized by the development of the dominant philosophical schools of traditional Chinese thought: Daoism, Confucianism, Moism, and Legalism. By the Han dynasty (206 BCE–220 CE) comprehensive cosmological views of the universe had been developed by the Daoists. These were based on a few universal principles: *yin* and *yang* complementarity, the relations and correspondences of *wu xing* (the five phases of the universe: wood, fire, earth, metal, and water), and the notions of *qi* (pronounced “chee”—vital force, or “matter–energy”) and *li* (natural order or organizing principle). Traditional Chinese understanding of illness, disease, and healing is framed in terms of this worldview.

Two of the most important texts in Chinese medicine are *Huang di nei jing* and *Ben cao gang mu* (“The Yellow Emperor’s Classic of Internal Medicine” and “The Great Pharmacopoeia”). These texts are still used as the bases for Chinese Traditional Medicine. The *Huang di nei jing* is a multi-authored text compiled between the second century BCE and the second century CE, in which a dialog between the mythical Yellow Emperor and one of his chief ministers explores many aspects of medicine: the concept of the body and its function; the detection, causes, and treatment of illness; and the way remedies act. The *Ben cao gang mu*, the life’s work of Li Shizhen (1518–1593), is a compendium of medication (in the broad sense) that gives the historical background for the drugs, much botanical information, and the indications for the uses of the materials. The literary tradition of such treatises on drugs (*Ben cao*) gives a good idea of Chinese understanding of those areas now identified as botany, geology, and mineralogy, as well as pharmacology and physiology.

Chinese medical theory views the body as a microcosm of the cosmos, and its concepts are particularly rich in political metaphors. The body and its functions are likened to the government, with the need for storage depots, transportation routes, officials high and low, and regulations. Thus, the vital energy of the body, *qi*, must be regulated in its flow by the organs, with analogies to government officials; there are depots and storage sites for *qi*. Disease is often viewed in terms of the faulty regulation of *qi* flow, either too much or too little, and treatments are designed to help the internal regulators to do their jobs. This political conception of bodily function is joined to a system of regular correspondences that relate organs, symptoms, points on the body surface, and therapeutic approaches. This system of correspondences is universal and is not just part of medical thought. For example, the *yin-yang* and *wu xing* theories provide ways to think about the heart’s correspondence to fire, and hence, because fire is overcome by water, the role of diuretics in treating heart disease is explained and rationalized. Not all such correspondences, however, are so clearly congruent to Western views. Therapeutic approaches to influence and regulate *qi* flow can involve insertion of needles (acupuncture), pressure, or heat (moxibustion) applied at specific places related to *qi* channels.



Full-length figure with acupuncture points and meridian in Chinese characters for stomach and foot disorders, 1875. Courtesy of the National Library of Medicine.

Another concept that is crucial in Chinese medical thinking is the distinction between internal and external aspects of the body and its relation to illness. Some illnesses arise from internal imbalances, for example in *qi* distribution. Other illnesses arise from external influences such as wind, dampness, or demons. A precise correlation between these Chinese concepts and Western categories, however, is not entirely successful. For example, to a Westerner the Chinese concept of the “triple burner” might seem to refer to some anatomical structure, but it actually refers to internal bodily functions, and is really much closer to the Western concept of “metabolism.”

Because basic Chinese cosmological thinking allows both for action at a distance and for local variations, Chinese medicine searches for “patterns of disharmony” that are specific for a given patient. Thus, **astrological** as well as social and geographical factors influence both diagnosis and therapy. **Epidemic** diseases are often characterized as being the result of “External Pernicious Influences.” Weather, external dampness, diet, exercise, sexual activity (or the lack of it) all have both internal and external aspects and are used to explain and avoid epidemic diseases or pestilences.

The available Western literature on science and medicine (both of which are Western analytical categories, not Chinese) in China is of two types: scholarly work and popularized works on exoticism. Western readers have been fascinated with tales of the exotic East at least since the days of Marco Polo in the late thirteenth century. Even today, there is a large market for uncritical accounts and explanations of the “mysteries of the East.” Much of this is published under the rubric of health advice or “Eastern Religion.” The serious student of the history of science and medicine in East Asia should evaluate this literature with the same level of criticism as any other scholarly work, that is, based on its documentation and argumentation. *See also* Ayurvedic Disease Theory and Medicine; Folk Medicine; Greco-Roman Medical Theory and Practice; Humoral Theory; Islamic Disease Theory and Medicine; Physician; Plague in China; Religion and Epidemic Disease; Severe Acute Respiratory Syndrome (SARS).

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WILLIAM C. SUMMERS

CHLAMYDIA. *See* Gonorrhoea.

CHOLERA. Cholera is an acute diarrheal disease caused by the **bacterium** *Vibrio cholerae*—short, curved, anaerobic, motile, Gram-negative rods. Spread by food and **water** supplies contaminated with the fecal discharges of cholera sufferers, cholera's violent symptoms tend to run a rapid course; once ingested, the incubation period for cholera can be as

CHOLERA'S MANY ALIASES

Originally, the term *Cholera-morbus* came from the time of **humoral theory** and denoted an illness or combination of gastric symptoms. It derives from the Greek word *chole*, which means bile, and the Latin *morbus*, meaning illness. In 1832 J. Kennedy noted other designations: epidemic cholera, spasmodic cholera, cholera asphyxia, and malignant cholera. French authors called it the *maladie noire* (black illness), *maladie bleue* (blue illness), *trousse-galant* (popular name), as well as the more clinical *cholérée*, *cholerragie*, and *cholarée lymphatique* (lymphatic cholera). Arabic and Hindi share the name *hyza*; Iranians call it *tokhmu*. In Sanskrit cholera is *dissochtau*, and in Mahāratta it is *fural*. The Japanese use an adverb that indicates brutality, *korori*, and in Chinese the characters for tiger and wolf are used to compose the word, a reference to the aggressiveness of the illness.

Donato Gómez-Díaz

short as 12 hours or as long as 72. Although clearly an ancient disease that resided in South Asia for hundreds of years before becoming pandemic in 1816, cholera is considered the quintessential **epidemic** disease of the nineteenth century. The disease killed with such vivacity that it probably helped provide the major impetus for modern developments in public health such as clean water, hygiene, and sanitation. Cholera is still a formidable public health problem around the world, as there is currently a seventh world pandemic that began in the early 1960s. Cholera continues to thrive where systems of public health fail to provide basic sanitation and an adequate source of clean, unpolluted water.

The exact origins of cholera are unclear. **Historical epidemiologists** are uncertain of the pre-1816 history of cholera, but most agree that the disease was endemic to India for hundreds of years. Ancient Indian texts describe a disease that is most likely cholera. Cholera gets its name from the Greek words for “bile” (the brown fluid secreted by the liver) and “to flow.” Before the nineteenth century, cholera was used to describe any severe vomiting and diarrhea. Epidemic cholera did not begin to extend pandemically until 1816, reaching England in 1831 and North America in 1832. It was only in the nineteenth century that the deadly and specific epidemic disease caused by *Vibrio cholerae* began to be called cholera. To avoid confusion, many medical authors added the prefixes “Asiatic” or “Indian.” Others simply called it “cholera morbus,” with specific reference to social fears generated by the **Black Death** (see sidebar).

Knowledge about cholera outbreaks after 1816 is far more substantial. Commonly used dates for the seven pandemics are as follows: the first pandemic lasted from 1816 to 1825; the second from 1827 to 1838; the third from 1839 to 1861; the fourth from 1862 to 1879; the fifth from 1881 to 1896; the sixth from 1899 to 1947; and the seventh from 1961 to the present. What makes cholera particularly elusive are the abilities of the bacterium to adapt to changing **environmental** conditions and of the host to develop resistance to otherwise effective **drugs**. Although only three strains of cholera are recognized to be epidemic, over 200 serogroups exist. The three known epidemic strains are *V. cholerae* O1 of the classical biotype, *V. cholerae* O1 of the El Tor biotype, and *V. cholerae* O139. All cholera strains are divided between the O1 group antigen (*V. cholerae* O1) and the non-O1 group (*V. cholerae*). Although laboratory evidence has confirmed that the fifth and sixth pandemics were caused by *V. cholerae* O1 of the classical biotype, the strains that caused the first four pandemics are unknown. Presumably, if the illnesses labeled **cholera before the pandemics** were indeed the disease currently recognized, a variety of strains and virulence levels existed. The El Tor biotype first emerged during the seventh pandemic in

Indonesia in 1961, creating a wave of fear around the globe. Although the O1 strains were thought to be the exclusive cause of epidemic cholera, the O139 serogroup emerged in southeastern India in 1992 as the first non-O1 *V. cholerae* strain to cause an epidemic outbreak.

The clinical and epidemiological features of *V. cholerae* O139 are identical to *V. cholerae* O1 of the classical biotype and *V. cholerae* O1 of the El Tor biotype. However, **immunity** to the O1 group is not protective against the new O139 strain. Horizontal gene transfer is probably responsible for the two newest strains of cholera. The genetic makeup and virulence levels of *V. cholerae* O139 are nearly the same as those of the O1 El Tor strains, which appear similar to the classical O1 stains as well. The appearance of the O139 strain led many public health authorities to believe it replaced the El Tor biotype. However, by 1994 the El Tor strain was responsible for a series of outbreaks in Bangladesh and currently resides endemic in most regions of Southeast Asia. As of 2007, in some areas of the world the O1 *V. cholerae* remains dominant, and in others the O139 periodically reemerges.

Cholera enters the body via the fecal-oral route of **transmission**—the cholera bacillus is passed on in the excreta of sufferers and enters new hosts through the mouth and digestive system. After a 24- to 48-hour incubation period, the bacterium synthesizes an exotoxin that triggers the massive secretion of water and electrolytes into the small intestine. Acute diarrhea, spasmodic vomiting, and severe cramps mark the onset of symptoms, and fever is usually absent. The clinical manifestations are a result of the amount of water and electrolytes lost: after losing 3 to 5 percent of normal body weight, thirst develops. After 5 to 8 percent loss, the victim suffers bodily weakness and postural hypotension, the face turns a blue-gray color, and the extremities become cold and darkened. After 10 percent weight loss, the pulse becomes weak, the eyes sunken, the skin wrinkled, and coma and somnolence are present. Although in the early stages of the disease the stools of cholera patients may contain fecal matter, the stools quickly become white and opalescent, the characteristic “rice-water” stools of cholera (termed because of the resemblance to water to which rice has been added). If not treated properly, profuse diarrhea and vomiting eventually lead to the near complete depletion of body fluids, dehydration, and death—a quarter of the body’s fluids and vital body salts may be lost within a few hours. Feces from persons acutely infected with cholera are the main source of explosive epidemics. In a single day, a single cholera patient may produce up to 20 liters of stool containing as many as 10,000,000 vibrios per milliliter.

Cholera treatment is simple and inexpensive. Oral rehydration therapy (ORT), which constitutes the rapid replacement of fluids and electrolytes, is the most common and effective treatment. **World Health Organization** statistics show that the mortality rate for appropriately treated disease is usually less than 1 percent. Alternative treatment options include cereal-based formulations, intravenous fluid replacement for the initial management of severely dehydrated persons, and **antibiotic** treatments (usually tetracycline or doxycycline). Several types of cholera **vaccines** are under clinical trial.

Like other waterborne disease such as **dysentery** and **typhoid**, cholera is spread along the various pathways leading to the human digestive tract. Case-controlled investigations of cholera transmission since the nineteenth century have identified a wide range of water and food vehicles. Water clearly plays the most important role in spreading cholera. When urban water supplies have become contaminated with sewage that harbors the excreta of cholera victims, the most severe and widespread epidemics

have ensued. Even immobilized persons can infect large numbers if basic **personal hygiene** and public sanitation are not followed. Other routes can be just as fatal. Uncooked fruits and vegetables, soiled linens, and unwashed hands have all frequently contributed to the spread of the disease. Recent research has also shown that cholera can live for extended periods in aquatic environments, adhering to crustaceans, zooplankton, and phytoplankton. This research also indicates shellfish as potential carriers of cholera and helps explain the ecology of the disease, its seasonal occurrence, and its endemic tendencies.

As a result of a combination of massive **urbanization, industrialization,** and an underdeveloped public health infrastructure, cholera ran rampant in Western countries for most of the nineteenth century. However, not everyone who ingests cholera contracts the disease, and many people probably ingested the disease without harm, as high concentrations of stomach acid often kill the organism before it is able to reach the small intestine. Only recently has the host-parasite relationship and full epidemiological picture of cholera become clear. Recent epidemiological and experimental studies have revealed that levels of gastric acidity and ABO blood group status are two leading factors that predispose individuals to cholera. People with relatively low levels of gastric acidity and type O blood are at the greatest risk.

Historically cholera has played an important role in the history of diseases that have affected civilization generally and public health specifically. When cholera struck the western world in the nineteenth century, lay and medical opinion alike disagreed on its defining features. Society looked at cholera with relentless fear; the debilitating symptoms of a disease that could strike and kill within a number of hours led to social unrest and summoned fears about plague. Although mortality rates from cholera at times approached those of the medieval plague epidemics, the morbidity rates were much lower. Cholera's morbidity trends were even lower than those of nineteenth-century **tuberculosis**, a much more dangerous disease that was feared much less than cholera.

Until the end of the nineteenth century, most of the western world believed in the miasmatic theory that cholera was transmitted through the **air**. Having roots in the **Hippocratic** medical tradition and having been refined throughout the medieval and early modern periods, this theory held that epidemics were transmitted through the putrefaction of the air by rotting **corpses** or animal or vegetable material. Victorians also ascribed moral and religious value to cholera; the disease was a punishment from God or a consequence of the neglect of natural laws. Indeed, the correlation among cholera, morality, and **poverty** persisted throughout the nineteenth century, reinforced by social reformers and religious zealots.

Recent research has expanded the understanding of cholera. The most important findings have been the emergence of the previously unrecognized strain, *V. cholerae* serotype 0139. Other research has shown that the El Tor biotype appears to be more resistant to adverse environmental factors and better adapted to foodborne transmission than the classical biotype. Cholera remains a global threat. Although it no longer poses a threat to countries with proper hygienic practices and basic sanitation, it poses a serious threat where access to safe drinking water and adequate sanitation are not guaranteed. See also Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1863–1947; Cholera: Seventh Pandemic, 1961–Present; Disease, Social Construction of; Epidemiology, History of; Germ Theory of Disease; Historical Epidemiology; Koch, Robert; Public Health Agencies in the West before

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JACOB STEERE-WILLIAMS

CHOLERA BEFORE THE PANDEMICS. Many early sources record the presence of **cholera** before the nineteenth century. It was described in China in the first century CE, and later in the seventh century by Wong and Wu Lien Teh. Both **Hippocrates** and **Galen** described an illness resembling cholera, and various European authors considered it one of the gravest **epidemic** diseases in ancient history.

India is without doubt cholera's place of origin, with an endemic pocket on the delta of the Ganges River. There, Hindu **pilgrimages** and festivities attracted large crowds that were exposed to cholera, creating a noticeably high correlation between cholera and holy days. In Bengal, Oola Beebee, the goddess of cholera, was worshipped, and a temple in her honor has stood in Calcutta since the end of the nineteenth century. Some Indian descriptions date as far back as 2,500 years ago, and fifth-century CE Sanskrit scriptures detail the spread of an illness with cholera-like symptoms. The disease periodically overextended its natural limits, probably being carried by ships.

After the arrival of the Portuguese in India in 1498, various Europeans documented the presence of cholera. Gaspar Correa (1496–c. 1563), a Portuguese historian in Goa, wrote of a new sickness that he called “moryxi” in his book *Legendary India* (1543). He described vomiting and cramps that could kill a man by the end of the day. Other names for this condition evolved, such as the French term *mort de chien* (a dog's death). In the spring of 1503, 20,000 men in the army of the Sovereign of Calcutta came down suddenly with a disease that struck the belly very painfully, so that many died in less than eight hours.

In 1563 another Portuguese doctor in Goa, García da Orta (1501–1568), published *Conversations on Simples and Drugs and Medical Materials from India*, a volume that contained the first modern description of cholera. In 1585 a French observer noted that the epidemic fired up once again. In 1629 a physician of the Dutch East India Trade Company

reported in his *On Medicine of the Indies* that the General Governor of Batavia (present-day Jakarta, Indonesia) died of an acute dehydrating diarrheal illness. Goa was once again invaded by an outbreak in 1683.

The English and French colonial presence in India was marked by numerous cholera epidemics. Around 1760 the Scotsman James Lind (1716–1794) described a condition called “mordechin,” and a Frenchman wrote of an epidemic that occurred from 1768 to 1771, taking the lives of 60,000 people (it is probable that this extended into Burma and Malaysia in 1770). Cholera appeared in Calcutta in 1781–1782, and the following year in the holy city of Hardwar, at which time 20,000 pilgrims died in eight days. At the same time, the Maratha armies, fighting for Tipu Sahib (1750–1799), Sultan of Mysore, were also afflicted. In 1787 another observation of the illness was described by an English physician, “Dr. Paisley,” and in 1796 a Catholic friar recorded yet another. Sixty-four additional references to major cholera outbreaks in India date from 1503 to 1817, but the limitations in transportation probably contained the spread of the disease. *See also* Cholera: First through Third Pandemics, 1816–1861; Colonialism and Epidemic Disease; Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Environment, Ecology, and Epidemic Disease; Trade, Travel, and Epidemic Disease; Water and Epidemic Diseases.

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DONATO GÓMEZ-DÍAZ

CHOLERA: FIRST THROUGH THIRD PANDEMICS, 1816–1861. Cholera was one of the most feared illnesses of the nineteenth century. The great **pandemics** started in India, and their spread coincides with the increase of **trade** and communication and with the **Industrial Revolution**. The first pandemic essentially had an Asiatic expanse, whereas the second and third reached Europe and the greater part of the Americas. The effects of cholera cast doubt on the power of science because theoretical approaches had little to offer against its unstoppable transmission. A bitter controversy arose between those who believed it was contracted by direct human contact (**contagion**) and those who believed it was produced by environmental factors. In England, this dichotomy erupted into the political debate in which Conservatives (Contagionists) disputed Liberals (Anticontagionists) on not only matters of public health but of free trade as well. Lastly, to solve the sanitary problem that private ventures had failed to accomplish, governments strengthened public health in a bid to control transmission factors by means of public hygiene.

Sources on **cholera before the pandemics** are fragmented. Most are descriptions of historians, travelers, and **physicians**, who since ancient times recorded instances in which symptoms indicated the presence of cholera. There are also accounts from the arrival of the Portuguese in India and the subsequent incursions in the colonial period by the Dutch, French, and English, and even references in Italian literature, that contain information about contagious epidemics that resemble cholera. After the first cholera pandemic (1816–1825), efforts were made to study and compile information, first by means of diverse English military-medical reports, and later through the use of Indian literature. The extension of cholera into Europe during the second (1827–1838) and third

pandemics (1839–1861) left many accounts and studies that described its catastrophic course, as well as medical literature about prophylactic measures that governments adopted. In contrast, there was less information about what had happened in the Far East and Africa.

Nature of Disease Involved. Cholera is an acute illness caused by the bacterium *Vibrio cholerae*. In its most fatal form, after an average incubation period of two to three days—and in some cases five hours to five days—the illness propagates, resulting in painful symptoms and a high likelihood of death. Acute nausea provokes violent vomiting and diarrhea; stools turn into a whitish liquid described as “rice water,” until fragments of the intestines are passed. Afterwards, victims endure ferocious cramping and an insatiable thirst, followed by a state of prostration. Dehydrated and close to death, a patient shows the classic physiognomy of cholera: a sunken and withered face with wrinkled and cyanic lips.

Although other microorganisms can have similar clinical manifestations, the term cholera is reserved exclusively for the toxigenic species of *V. cholerae* O1 (two strains: Classical and El Tor) and O139, regardless of the intensity of symptoms shown. The bacterium of cholera is transmitted by the oral-fecal path, primarily by water contaminated by fecal sediment and sometimes by the ingestion of contaminated food. For the prevention of cholera it is necessary that a community be outfitted with an adequate supply of clean, drinkable water and an effective sewage elimination system.

Two main positions emerged with respect to the nature of the cholera found in the outbreak of 1817. One interprets it as a form that existed since ancient times but with a newly aggressive transmission. The second agrees that the illness existed in forms of “cholera morbus” or “sporadic cholera” before the nineteenth century, but posits that the cholera of 1817 had new characteristics. With respect to the first position, Europe had suffered epidemics that doctors of the time described as resembling cholera. For example, a Flemish physician described in 1643 what he called *flux de ventre* (abdominal flow). The English doctor **Thomas Sydenham** documented the clinical manifestations and treatment of an epidemic of cholera in London in 1669. Nicolas Philibert Adelon (1782–1862), a specialist who edited a nineteenth-century French medical encyclopedia (1822), continued to use the traditional definition of cholera current since **Galen**. In his *Plagues and Peoples* (1984), William McNeill (b. 1917) claims that the only change was that in 1817 the illness stretched its usual boundaries and flourished in new and nonhabitual territories completely lacking resistance and accustomed reactions to its presence.

Many English physicians who tried to understand the first pandemic were aware of cholera’s existence and asserted that the epidemic of 1817 had its own characteristics. In 1829 James Annesley (d. 1853) also maintained that he did not find prior references in Indian medical literature that coincided with the cholera suffered in 1817 and concluded that there existed two different types of cholera. One called “cholera morbus,” which was typical in Europe, and the Indian “cholera sporadic.” He also observed that neither form, as previously experienced, had manifested all of the characteristics of the new, pandemic form.

There was not a consensus among Indian physicians who wrote about what the causes were or how cholera was transmitted. Following traditional medical principles, it was believed that cholera was related to meteorological factors such as torrential rain or a fall in temperature, or to **air**-related factors such as poisonous and pestilent emissions from decomposing vegetal and human waste in dwellings. Europe initially adopted the same set

of theories when it found itself in the same situation. Eventually, an effort was made to systematize a single theory involving various causes: the nervous, which attributed the disorder to infective illnesses of a cerebrospinal type; the humoral, which attributed changes in the blood from airborne causes to the illness; and the gastroenteric, which claimed it as gastroenteritis accompanied by other factors, the causes of which were essentially unknown.

Mortality. Although cholera has been called the most significant epidemic in the nineteenth century, from a demographical viewpoint it can be seen as having had limited repercussions for multiple reasons. First, the most severe outbreaks lasted five or six years. Second, the percentage of the total population affected was quite low. In France the percentage of the population affected between 1832 and 1854 was 0.4 percent, which is far less than the 2 or 3 million victims of the plague from 1600 to 1870. There were widespread locations with significant mortality from cholera—the Cité quarter of Paris in 1832 had a 10 percent mortality rate, and Ariège in 1854 had a rate of 20 percent—but the outbreaks in these areas did not have a significant effect on the population. In other locations, like India, the situation was much more grave when cholera broke out in 1818 and affected 7.5 percent of its population; from 1817 to 1865, 15 million people perished.

The mortality rate varied. In the beginning of an epidemic the mortality rate was quite high, varying from 50 to 60 percent; later, the number of milder cases rose, and the mortality rate fell to between 25 percent and 30 percent. In 1876 the Spanish author Sánchez Merino set the rate of mortality between 36 and 40 percent, which was calculated to be 3 to 5 percent of the population. Hamburg, Germany, was battered by successive cholera epidemics. In 1832, 1.13 percent of the city's population perished, in 1848 1.06 percent, and in 1859 0.65 percent.

The pandemics also had a social and urban geography. Belgium's working class was especially hard hit in urban and industrial centers. In France during the 1832 epidemic, the poorest died in a ratio of 1.5 to 1 in comparison to upper classes, though the situation did improve over the course of the century. The epidemic was particularly fatal for the young and elderly compared to adults: French children and seniors were four times more likely to die than were adults.

Origins and Spread: The First Pandemic (1817–1825). Though the Greeks and Romans may have suffered from cholera, it was endemic in parts of Asia and the Indian Ocean. European merchants and colonists first described contact with it in India at the end of the fifteenth century. Eighteenth-century **colonialism** in India brought England and France into close and lasting contact with South Asia and its cholera reservoirs. The Asian cholera epidemic of 1816–1821, however, is considered the first of the pandemics. Earlier accounts refer to the existence of some cases of cholera in Eastern India in 1814 and in August 1817 in Jessora, a village close to Calcutta, where 10,000 perished in a few months. Afterward, English soldiers stationed at Fort William in Calcutta fell victim. It rapidly spread; 5,000 soldiers died in a few weeks, devastating the army of General Francis Rawdon-Hastings (1754–1826). In a few months, 25,000 were treated for cholera in Calcutta, and 4,000 died; the following year, epidemic cholera propagated throughout India.

Advances in commercial exchange and navigation contributed to cholera's dispersion. Trade and maritime traffic brought the sickness northward. It hit China first, through the western port of Canton in 1820, and between 1822 and 1824 it sprawled through the

Yangtze Valley. Korea lost 10,000 to 100,000 in 1821. It entered Japan through Nagasaki in 1822 and was confined to the west. Cholera struck Sri Lanka in 1818, the Philippines in 1820, and Borneo in 1821; Java suffered 100,000 victims in 1820. Land routes brought it to western Afghanistan, to Shiraz in Persia (1821), to Basra (15,000 died in three weeks), and to Baghdad by way of the Tigris and Euphrates river valley. At the limits of the Mediterranean, it reached Syria in November 1822. The march proceeded to Anatolia and the port of Astrakhan in Russia where an exceptionally harsh winter (1823–1824) impeded its transmission beyond the Caspian Sea. It arrived at Africa's eastern coast and was carried by British troops stationed to help the Sultan of Oman in 1821. In the Persian Gulf, the slave trade directed it along the coast to Zanzibar. It also reached Egypt in 1823.

The Second Pandemic (1826–1838). Scholars dispute the date of origin of the second pandemic. Some assign the years 1826 to 1838 and others 1829 to 1851. Beginning with the earliest accounts, it originated in the northeastern province of Bengal in India with diverse outbreaks in the Ganges delta in 1826. This sets it apart from the typical points of origin. From Lahore in the northeast, cholera followed along the caravan routes to Kabul and Balkh in Afghanistan and crossed into Russian territory at Bukhara in 1827. It reached Chiva in 1827 and was carried by Kirgis hordes to Chkalov (Russia) in the southern Ural Mountains in 1829; Tehran (Iran) was suffering by the end of 1829. Moscow was stricken in August of 1830, and before the end of 1831 the epidemic had spread to other main cities and towns of Russia. In 1831, Cossack troops were ordered to Poland, and they brought the disease with them. Hungary was affected in June of 1831 (100,000 deaths), and the spread extended to Germany (Berlin in August and Hamburg in October of 1831). In 1831 it reached Finland and Sweden, and Vienna was affected the same year. In October of 1831, England, Wales, and Scotland were stricken (31,474 victims) despite **quarantines** for people and freight. London and Glasgow were particularly punished. Before March of 1832, cholera was detected in Ireland, leaving 25,000 dead. Panic pushed governments to take measures against the disaster.

France was hit in 1832, killing 102,000 people. That same year, Irish immigrants brought cholera to Canada and the United States. Quebec, Philadelphia, and New York (3,000 victims in July and August) were simultaneously affected. It reached New Orleans in October, and in the course of three weeks, 4,340 residents were left dead. Passing through small cities and towns, the West was not spared cholera's spread. In the United States, the pandemic lasted from 1832 to 1849 and killed 150,000 people.

In February 1833, Havana, Cuba was left with 9,000 dead. The rate of mortality was almost 60 dead for every 1,000 inhabitants. In the rural areas, the total number of victims was three times that in the capital. Mexico followed with 15,000 dead in August. By 1837, it reached Nicaragua and Guatemala, and as a final lashing, it hit Colombia in 1850.

In the spring of 1831, **pilgrims** traveling through Mesopotamia and the Arabian Peninsula brought cholera to Mecca during the annual *hajj*. In three weeks, almost 3,000 pilgrims perished returning to their homes—a situation that would repeat itself throughout the nineteenth century. Another branch of the epidemic passed toward Syria and Palestine, while a third headed to Cairo (July, 1831) affecting the Nile delta. Muslim pilgrims brought cholera to Tunisia in 1831, and in the following years Ethiopia, Somalia, Zanzibar, Algeria, and Sudan were all stricken.

LIVING CONDITIONS IN ENGLAND AT THE TIME OF THE SECOND CHOLERA PANDEMIC, AS REPORTED IN EDWIN CHADWICK'S REPORT ON THE SANITARY CONDITION OF THE LABORING POPULATION OF GREAT BRITAIN (1842)

Mr. Robert Atkinson, Gateshead, states that: It is impossible to give a proper representation of the wretched state of many of the inhabitants of the indigent class, situated in the confined streets called Pipewellgate and Killgate, which are kept in a most filthy state, and to a stranger would appear inimical to the existence of human beings, where each small, ill-ventilated apartment of the house contained a family in number from seven to nine, and seldom more than two beds for the whole. The want of convenient offices in the neighborhood is attended with many very unpleasant circumstances, as it induces the lazy inmates to make use of chamber utensils [chamber pots], which are suffered to remain in the most offensive state for several days and are then emptied out of the windows. The writer had occasion a short time ago to visit a person ill of the cholera; his lodgings were in a room of a miserable house situated in the very filthiest part of Pipewellgate, divided into six apartments, and occupied by different families to the number of 26 persons in all. The room contained three wretched beds with two persons sleeping in each; it measured twelve feet in length and seven in breadth, and its greatest height would not admit of a person standing erect; it received light from a small window, the sash of which was fixed. Two of the number lay ill of the cholera, and the rest appeared afraid of the admission of pure air, having carefully closed up the broken panes with plugs of old linen.

From Edwin Chadwick's *Report on the Sanitary Condition of the Laboring Population of Great Britain*, reprint edition by M. W. Flinn (Edinburgh: University of Edinburgh, 1965).

Portugal fell victim in 1833, when an English ship of Polish volunteers arrived to fight for the liberal cause in the Portuguese civil war. In light of this event, Spain applied a rigid system of quarantines but was infected in August of 1833 and 1834, suffering 100,000 victims. By means of Catalonia it entered France and over the next two years passed through southern France and much of Italy, leaving 236,473 victims from 1834 to 1837. In 1837, it killed close to 3,000 people on the island of Malta.

It spread over China from 1826 to 1835, entering Malaysia and Singapore in 1826, and Japan in 1831.

The Third Pandemic (1845–1859).

The third pandemic occurred during the years 1845 to 1859, although some authors list it from 1839 to 1861. In 1845 cholera broke out again in Bengal with a bidirectional projection towards Arabia in 1846 (Aden and Djeddah), arriving in Mecca in November, Mesopotamia (Baghdad, September 1846) and at the coast of the Black Sea (Tibilissi, July 1847). From there it propagated towards Turkey, hitting Istanbul in autumn 1847 and principalities of the Danube and Central Europe in 1848. In the spring of 1848, it was found in Norway, Finland, and the north of Germany; it then reached Berlin, and later Holland. From Rot-

terdam the illness passed through Belgium and Ireland in 1848. A ship from Hamburg, a port that suffered 5,400 victims, brought the disease to England in 1848–1849 (62,000 dead), to which it returned in 1854. In 1849 it appeared in Austria, Switzerland, and France (110,000 victims). From there it passed to Algeria. Austrian troops brought it to northern Italy (24,000 victims) in 1848–1849.

In the beginning of the 1850s, the pandemic resurged with new strength. In 1852 it invaded regions that had escaped its wrath, for example, the south of Germany. During the years 1854–1855, France and Italy were left with 146,000 and 248,514 dead, respectively. The Crimean War permitted cholera's arrival at major Mediterranean ports like Ancona and Naples in Italy. The mobilization of English, French, and Italian troops towards the Black Sea brought cholera to Bulgaria, Greece, and Turkey. In Spain, the

spread of the epidemic in 1855 was one of the most lethal of the nineteenth century. It extended from the Mediterranean coast to the interior (236,744 victims; 1.5 percent of the population). From there it arrived again in Morocco and Algeria.

In December 1848, cholera appeared in the port cities of the United States and affected 5,000 New York residents. From the ports it spread rapidly along the rivers, canals, railroad lines, and stagecoach routes, bringing it to far-reaching areas. The main outbreak was in 1848 and 1849 and was followed by a series of sporadic outbreaks over the next six years. New Orleans, for example lost 5,000 people from 1850 to 1855. It went up the Mississippi, toward California, and toward southeastern Mexico, where it claimed 200,000 victims. In 1854 and 1855 it entered Venezuela; Brazil also suffered in 1855.

From Bengal, cholera arrived at Singapore in 1852, and from there it spread to China and Japan in 1854, the Philippines in 1858, and Korea in 1859. It ravaged Egypt from 1853 to 1858 and advanced towards Sudan and Eritrea. In 1859 Zanzibar, Mozambique, and Madagascar were affected.

Factors in Cholera's Spread. Cholera's origin was in Bengal where it endemically appeared every year. Water was the fundamental vehicle of transmission, as a result of the persistent pollution of the Ganges's water, the abandonment of large ancient hydraulic works, the custom of leaving cadavers in the river, the general lack of hygienic conditions, and the domestic use of water reservoirs that were exposed to the air and contaminated with excrement and urine. Even these factors, however, do not explain the expanse it reached in the nineteenth century. Military expeditions and English attempts to extend colonial influence in India were fundamental during the first pandemic of 1817. The routes taken by the British East India Company's army were similar to those along which cholera spread. Troop movements also permitted the extension of cholera throughout the world. For example, when British troops participated in the war in Burma (1823) cholera appeared; when Russian troops marched toward Poland (1831), cholera infected their path until their arrival in Warsaw; Polish troops arriving to fight in the Portuguese civil war introduced the illness; General J. R. Rodil (1789–1853) advanced through Spain spreading cholera; and troops dispatched to fight in the Crimean War spread the disease toward Eastern Europe. But military campaigns are only part of the story. It is undeniable that cholera is an indicator of hygienic sanitation of a population. In this sense, the English conquest affected Indian society because it disrupted ancient systems of living, changing social solidarity and making survival more difficult.

Another argument for cholera's rapid and wide dispersion was the creation of new markets. Cholera was a great example of the diffusion of an illness along international trade routes, especially those connected with British imperial activity. The rise of British naval commerce in Bombay after 1815, which converted the city into the hub of many important maritime routes, allowed the advance of cholera toward the Persian Gulf and the Mediterranean, Caspian, and Baltic Seas. When ships from cholera-affected ports reached their destinations, cholera quickly spread. This is what occurred in the Mediterranean in 1854, with the arrival of ships at Messina for the invasion of Sicily and the ships moored in the port of Piraeus that infected Greece, which, after stopping in Gallipolis left cholera to be spread to the Dardenelles, Istanbul, and Varna. British control in the ports of Calcutta and Madras produced similar

results in China, Taiwan, the Philippines, Tonkin, Vietnam, Java, Sumatra, Thailand, and Myanmar. As the means of transportation grew faster, the speed of disease propagation directly corresponded.

Cholera's spread was also facilitated by migration and temporary displacements like pilgrimages to Mecca and Medina, which allowed pilgrims to afflict places along their journey home.

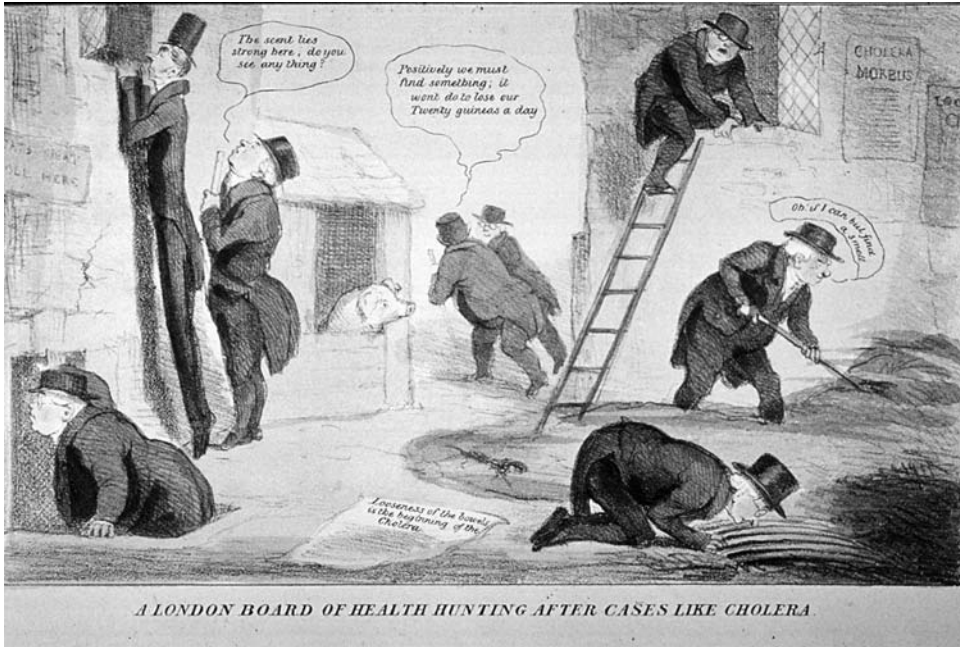
Reactions. During the nineteenth century, cholera was more than just an illness. It was also a social and political question because the diffusion of germs and subversive ideas went hand in hand. The epidemic revealed as much social animosity as it caused political confrontation.

After cholera arrived in England in October of 1831, a famous riot took place at the Swan Street Hospital in Manchester. Several thousands of people freed cholera patients believed to be the targets of homicidal doctors. This situation was repeated in other places in Europe. In the United States, in 1832 initial medical reports in New York City were ignored because of fear of the social and economic problems they would cause (although sanitary measures were adopted later). The sickness affected the poor above all, and **poverty** was popularly associated with vice. Hence, the idea emerged that cholera attacked those who were immoral. For this reason, religious leaders from the entire country appealed for prayer and fasting in hopes of a divine intervention. This approach was repeated in the epidemics of 1849 and 1854, although by then Americans were associating cholera with the poverty of Irish immigrants spurred by the **Irish potato famine**. What many overlooked was that these people were not affected by cholera because they were immigrants but because of they lived in deficient conditions. Finally, however, many resorted to the age-old response to epidemic disease: **flight**.

Historical Effects. From the beginning of the eighteenth century, the number of doctors defending a contagion model for the spread of cholera increased. From this emerged the clash between supporters of this theory (contagionists) and the defenders of another, the anticontagionists, who believed its spread was airborne and was the result of environmental causes. Contagionists believed in the transmission of the illness through human-to-human contact or animal-to-human contact (as **Girolamo Frascatoro** had described in 1546 with his idea of invisible seeds). They believed that isolation, quarantines, and **cordons sanitaires** were adequate measures to avoid its spread. On the contrary, the anticontagionists held that the illness was propagated by respiratory emissions of the patient into environmental agents like air and water, from which others contracted it. They therefore opposed quarantines and proposed public sanitation and hygiene as an alternative.

When the affliction reached Europe in 1831, doctors tried to identify the manners of propagation and specify the nature and treatment they should adopt for cholera. They also advocated for public adoption of the measures dictated by their opinions on the nature of the disease. This led to constant conflict between contagionists like William Budd (1811–1880) and **John Snow** (at least initially) and anticontagionists like **Edwin Chadwick**, Southwood Smith (1786–1861), and **Rudolf Virchow**, though the opinion of the second group prevailed for much of the century.

Medical and political positions were allied. Wealthy merchants who worried about delivering their merchandise and governments in post-revolutionary Europe that sought to avoid alarming the population, allowed anticontagionism to triumph momentarily. Quarantine and all measures that impeded the liberty of exchange were abolished until the agent of transmission was identified.



Officials from the London Board of Health “sniff” out the causes of cholera. Courtesy of the National Library of Medicine.

Though investigators like Budd, Snow, and Filippo Pacini (1812–1883) suspected the existence of a specific germ that caused the disease, it was not until 1883 that Robert Koch isolated and cultivated *V. cholerae*. In 1854, the Florentine Pacini discovered that various infected intestines contained a type of bacteria that he considered the cause of the epidemic. However, because he published his conclusions in a journal with only limited circulation, the significance of his discovery remained hidden.

The English physician John Snow already suspected during the epidemic in London of 1834 that cholera was transmitted essentially by water, but he lacked conclusive evidence. When cholera broke out again in 1848, he started an investigation that he published the following year. He explained his belief that poor sanitation and unclean water were tied to the epidemic. The Industrial Revolution increased the amount of urban housing and had terribly deteriorated the sanitary conditions of large cities. In 1854 he was able to demonstrate a common denominator between deaths from cholera in London, with his famous study of the Broad Street well. The discovery of the relationship between contaminated water and cholera created a model for explaining the transmission of the disease. It also demonstrated the necessity of public intervention with regard to general sanitation.

Determination of the factors affecting the contraction and spread of cholera during the nineteenth century began to be an obsession for Europeans and Americans because they were important elements for the investigation and solution of more general public



A woman extravagantly equipped to deal with the cholera epidemic of 1832; satirizing the abundance of dubious advice on how to combat cholera. The animal's sign reads "Only no fear." German etching, c. 1832. Courtesy of Wellcome Library, London.

health problems. The consequences were significant because they consolidated the convictions of the sanitationists, who gained increasing influence over governments. They carried out the fight against the unhealthiness of cities with regular collection of refuse, the enclosure of open sewers, water filtration, and the progressive reform of housing conditions. These measures were accompanied by campaigns that strengthened a growing sense of the importance of **personal hygiene** in the battle against disease. The early cholera epidemics constituted a spur for practical conduct that was channeled through every nation and on an international level. For example, in England, after the outbreak of 1848, the General Board of Health was created, and in the United States, the quarantine officially established in ports in 1878 was a direct result of the 1873 epidemic. Action alone was not effective unless it was met by collaboration from other countries, and therefore a series of international conferences was convened. In 1851 the sanitary authorities of 14 European nations gathered to hold the world's first Sanitary Conference, a predecessor of the **World Health Organization**. See also Cholera before the Pandemics; Cholera: Fourth through Sixth Pandemics,

1862–1947; Cholera: Seventh Pandemic, 1961–Present; International Health Agencies and Conventions; Public Health Agencies in Britain since 1800.

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DONATO GÓMEZ-DÍAZ

CHOLERA: FOURTH THROUGH SIXTH PANDEMICS, 1862–1947. Modern usage reserves **cholera** as a term to describe the acute diarrheal disease caused by *Vibrio cholerae*, the comma-shaped **bacterium** first recognized by the Italian scientist Filippo Pacini (1812–1883) in Florence in 1854, and discovered by **Robert Koch** to be the cholera’s causative agent during January 1884 in Calcutta, India. Contemporary Europeans after 1816 labeled what for them was a new disease “Asiatic cholera,” though a variety had probably been endemic from ancient times in the Ganges Delta. Before 1920 it was still a lethal disease, although in the most industrialized countries it later became a nuisance no longer to be feared. From the time of the fifth **pandemic** (1881–1896), improved sanitation in Europe and the Americas began to diminish cholera’s global impact, a trend that continued until the sixth pandemic (1899–1947) began to wane in the 1920s. The last major international cholera emergency of the sixth pandemic occurred in Egypt in 1947.

Documentary evidence for the fourth through sixth pandemics in the West is rich. For the fourth pandemic (1862–1879), cholera’s terrible trajectory in West Africa has left almost no documentary trace. But East Africa, Zanzibar, and the Indian Ocean are well served by means of the remarkable, horrific eye-witness account (1876) left by James Christie (fl. 1865–1873), who was then physician to the Sultan of Zanzibar.

With no effective treatment for classic cholera, nineteenth-century case fatality rates (CFRs) of 50 percent and mortality of over 100 per 1,000 population were common. Human susceptibility to this spectacular disease varied widely. People with blood types other than O and those with high levels of acidity in the digestive tract were less vulnerable and often asymptomatic, but their opposites were subject to alarming sickness. Immunity rarely persisted longer than a year or two.

Cholera’s cause is the ingestion of an infectious dose of a serogroup of the *V. cholerae* bacterium present in **water** or food that has been contaminated either by fecal matter from an infected person or from free-standing bacteria present in plankton or seafood living in infected brackish water. The bacteria then multiply and attach themselves to the lining of the human bowel, producing an enterotoxin poison that interferes with the absorption of water, salts, and other electrolytes into the large intestine. In 20 percent of cases, a severe illness results, manifested by profuse watery diarrhea and repeated vomiting, leading to rapid loss of body fluids and salts. Feces and vomit easily infect water, soil, or food and result in a highly contagious stage. Severe dehydration, circulatory collapse, and death can result in a matter of hours without treatment.

The worst of diarrheal infections, cholera remains a fearful disease, deeply embedded in the collective memory of many societies globally. The serotype probably responsible for the first six cholera pandemics was *V. cholerae* O1, called “classical.” A new strain, *V. cholerae*

O1 El Tor, less virulent but producing more asymptomatic infections, was responsible for the seventh cholera pandemic, which began in Sulawesi, Indonesia, in 1961.

For most of the nineteenth century, medical remedies for cholera remained as varied, and often downright harmful, as they were ineffective. Instead of replenishing fluids and electrolytes, misguided treatments often involved accelerated loss through purging, and the administration of alcohol, morphine, and other undesirable practices. Since the 1960s, fortunately, the development of improved rehydration techniques has reduced CFRs well below 20 percent, and often even below 1 percent. Even before, beginning with the fifth pandemic in 1881, cholera had begun to retreat from the most industrialized societies. This retreat, moreover, became a virtual disappearance as a result of improvements in standards of living that included welfare state reforms in housing, public health, and nutrition.

Origins and Spread. The first pandemic (1817–1825), after spreading havoc in India during 1817, had reached throughout Asia soon after. Europe and the Americas were spared, and the impact on the regions of the Middle East and Africa was probably milder than subsequent visitations. Diffusion took place by land and sea, and was closely linked to **trade** and **warfare**. The second (1827–1838) and third (1839–1861) pandemics followed a similar path, crossed over to the Americas, and were far more devastating.

Innovations in transportation like the railway and faster ocean navigation assisted cholera's spread after 1862, as did numerous annual **pilgrimages** and fairs related to the Hindu and Muslim faiths. Once the Suez Canal opened in 1869, Muslim pilgrims could board a passenger vessel taking them through the Canal and to the southeastern corner of the Mediterranean at Alexandria in a week.

In what retrospectively became the start of the fourth pandemic in 1862, cholera once again left the Ganges Delta, heading this time for Indonesia. By 1864 cholera had again exploded on the world scene in what was one of its most devastating decades until it burned itself out by 1873. With the exception of China and Japan from 1877 through 1879, the world was once again free of cholera. The worst pilgrimage outbreak ever in Mecca during 1865 marked the fourth pandemic when 15,000 of the estimated 90,000 pilgrims died. Also severe was cholera's association with the Hindu pilgrimage to Hardwar, India, two years later, when half of the quarter of a million visitors succumbed. Another feature was that cholera reached Europe not through Russia and overland, but by water via the Mediterranean into southern France and Italy.

The fourth pandemic probably killed more people than any other, and the years between 1865 and 1867 were exceptionally devastating in all corners of the globe. East Asia, the Middle East, and Europe reeled from successive blows, and the pandemic was Africa's worst of the nineteenth century. Cholera not only revisited sites in North and East Africa, but also made its maiden voyage to West Africa. The African invasions came from a variety of sources. Ships carried cholera from Bombay via Aden to Eritrea and Somalia, and then caravans transported the pathogen into the Ethiopian highlands from the port of Massawa on the Red Sea coast. In Ethiopia, cholera was indirectly responsible for a large shift in the distribution of the population.

From 1865 through to 1871, cholera worked its way down the East African coast by a variety of means. Overland, it reached the Great Lakes of Africa through Masai country in Kenya, and then moved south to Tanzania and the bustling city and island of Zanzibar,

devastating that great market city with an estimated 70,000 deaths in 1869–1870. Indian Ocean sailing vessels engaged in coastal trade also carried cholera down through the Swahili ports to its southern limits just short of Delagoa Bay at Quelimane. Cholera also journeyed southeast to the Indian Ocean islands of Mauritius, the Seychelles, the Comoros, Nossi-be, and the Malagasy port of Majunga.

Beginning in 1865, cholera traveled across North Africa all the way west to Morocco, spreading from both Mecca and southern Europe. Tunisia's 1867 outbreak began with smugglers returning from Sicily. That same year, cholera traveled from France to Algeria and killed 80,000.

In November 1868, cholera spread from Algeria to Senegal (whether overland or by sea is not clear). In this, its first call ever to West Africa, cholera wreaked havoc in the small French colonial capital of Saint-Louis, and then reached inland to the Upper Senegal Valley. There, its arrival coincided with the rise of an Islamic messianic movement called *madiyanké*. Its leader pointed to the deaths of Fulbe tribal notables as punishment for collaborating with the French infidels. From the Senegal Valley, cholera traveled south through village after village among the Wolof states, reached Malinke country in the Upper Gambia River Valley in 1869, and penetrated south on the Atlantic coast as far as Portuguese Guinea.

In western and northern Europe, cholera casualties were lower, but by no means insignificant. In the dreadful year 1866, Sweden, Britain, Holland, and Belgium lost tens of thousands each. Even though it had not been the first visited, Russia eventually recorded significant deaths during the fourth pandemic. In the Mediterranean, Italy became infected through its eastern port of Ancona, France through Marseilles, and Spain through Valencia and Murcia. From these launching points, cholera easily made its way into the continent, facilitated by the significant movement of troops involved in a series of conflicts in the 1860s. Austria's war with Prussia in 1866 led to widespread outbreaks and deaths.

High death rates were also noted in the Americas. In the aftermath of the American Civil War (1861–1865), while large numbers of soldiers were still in military camps such as the one in Newport, Kentucky, cholera invaded the United States in May of 1866 through the ports of New York and New Orleans. That year, an estimated 50,000 persons died from cholera from the East Coast and the Gulf of Mexico as far west as Texas and New Mexico. Though it was not perceived at the time, these would be cholera's final visits to North America. Meanwhile, Canada and Mexico were almost entirely spared from cholera during the fourth pandemic.

Death tolls in the Caribbean, on the other hand, were high. Cholera made its way to Guadeloupe from Marseilles in 1865–1866, claiming 12,000 victims among a population of only 150,000. In South America, war abetted *V. cholerae*'s spread. Paraguayan troops engaged in a conflict against combined forces from Argentina and Brazil were overwhelmed by an outbreak in April of 1866. The war's victors also suffered epidemics, as did Uruguay and Peru.

The fifth pandemic was far less widespread globally. Especially in the North Atlantic world, many countries, applying hard-won lessons of sanitarianism concerning prevention through improved water systems, had seen the last of classic cholera during either the third or the fourth pandemic. Yet where cholera did strike after 1881, it continued to do so with great intensity, indicating that treatment had not improved at all.

Cholera launched its fifth escape from its endemic home in the Ganges Delta in 1881. In East Asia, unlike Europe and the Americas, the fifth pandemic was the worst on record. In Japan, where epidemiology was emerging as a discipline and where registrations of cholera infections were now being accurately tallied, seven separate outbreaks between 1881 and 1895 produced 340,000 cases. Anxious to respond with Western sanitary tools, the Meiji government addressed urban drinking water and sewage in legislation between 1878 and 1890. Numbers are not available for Japan's neighbors, but most endured multiple outbreaks between 1881 and 1895. China had six; Indonesia and Korea had five each; the Philippines had two; and Sri Lanka, Thailand, and Malaysia might have considered themselves fortunate to have suffered one visitation each.

The fifth pandemic arrived in Mecca from India's Punjab in 1881 and struck again the following year. Once again, the toll was terrible, estimated at over 30,000 dead among 200,000 pilgrims. From there, the infection quickly spread to Egypt, which experienced two waves. Over 16,000 Egyptians died during the second wave in 1895–1896, the last visitation of the disease until after the Second World War. Foreigners were not immune. In 1895, before the British garrison could withdraw from Cairo to Suez, it suffered through a nightmarish 139 deaths among its 183 cases. Only then did the British dramatically improve the water supply for troops in Cairo and Alexandria.

This second wave disseminating directly or indirectly from the Mecca pilgrimage meant almost certainly that pilgrims would again carry cholera back to North Africa. The pathogen appeared across North Africa spreading to Morocco in the early 1890s. From Morocco, cholera was able to make its way by caravan across the Sahara and into the Senegal Valley of West Africa in 1893–1894. The fifth pandemic also touched the Horn of Africa in this same period when it followed a terrible famine in the Ethiopian highlands and Eritrea. Known in Amharic as *ye nefas beshita*, “the disease of the wind,” cholera added its misery to what was already a devastating rinderpest epizootic which was then killing most of the draft animals in Ethiopia.

By 1884 the Mediterranean ports of Toulon, Marseilles, Palermo, and Genoa were infected. In 1885 there were serious epidemics throughout Spain. Italy tried a **quarantine**, but a major outbreak at Naples claimed over 5,000, and the disease remained widespread for the next two years. In central Europe the fifth pandemic brought cholera only to Germany. Hamburg in 1892 suffered 7,582 deaths among 19,891 cases in an infamous epidemic that was directly traced to the city's poor water supply. Sporadic cholera struck another 250 German communities.

The cholera scene in Russia remained grim in the 1890s, and its victims possibly included the illustrious composer Peter Ilyich Tchaikovsky (1840–1893). Entering from Afghanistan and Persia, cholera reached Moscow and St. Petersburg, and moved on to the empire's western borders. Only in Russia did a phenomenon of earlier pandemics persist—peasant revolts against authority. Cholera in 1892 followed a famine the previous year and brought with it a familiar trail of riot, murder, and angry attacks on government and medical officials. Tsarists were still rigidly enforcing quarantine, isolation, and **disinfection** on the shoulders of an impoverished peasantry, and the medical profession had little success in educating peasants about the value of preventive measures.

Rare as well as mild outbreaks were the norm in the Americas during the fifth pandemic. The closest North America came to disaster was when eight badly infected

ships arrived in the port of New York in 1892, but careful inspection and control resulted in only ten cases in the city. In the far south of the Americas, between 1893 and 1895, mild outbreaks occurred in Brazil, Uruguay, and Argentina.

The sixth pandemic began in 1899, after a hiatus of three years, and continued to be benign in the West and more sporadic elsewhere than earlier visitations. Arguably fewer people were dying from cholera, and effective rehydration treatments were just beginning to be developed.

In Europe the new pandemic proceeded from east to west following a pattern identical to previous visitations. Most Europeans never saw the dreaded disease; only Italy and Russia were exceptions. In Italy, a cholera disaster coincided with efforts at political consolidation in the new Republic. Both the epidemics of 1884 and 1910–1911 were implicated in such national issues as the “Southern Question,” mass emigration, organized crime, and urban renewal. Cholera in Russia was more continuous. Turmoil, revolution, and civil war abetted cholera enormously during the years from 1902 to 1925. The cities of St. Petersburg, Jekaterinoslav, Kiev, and Orenburg all suffered terribly during the civil wars. Outside of South Asia, no region suffered greater losses from cholera than the vast Russian Empire. Its recorded total of 5,537,358 cases and 2,140,558 deaths, undoubtedly under-reported, included cholera outbreaks in no less than 58 of the 103 years between 1823 and 1926. Nevertheless, as the Red Army consolidated political power after the Bolshevik Revolution in 1917, cholera began to wane. The last bad year was 1922.

War was also cholera’s handmaiden in central and southeastern Europe. Beginning with the Balkan Wars of 1912–1913 and continuing through the First World War and its aftermath, Romania, Serbia, Bulgaria, and Turkey all had to cope with the unwelcome presence of *V. cholerae*.

Triumphs there clearly were. Newly sanitized Japan mastered control of the disease, and North Africa, the Indian Ocean, Sub-Saharan Africa, most of Europe, and the Americas were virtually cholera-free during the sixth pandemic. The Second World War did not cause much cholera anxiety, despite the dramatic increase in air travel. The Egyptian cholera outbreak of 1947 may have been an exception as it did have a link to aviation. Cholera’s sudden appearance in Egypt during September 1947 caught cholera experts everywhere by surprise. Its origins are obscure, but returning pilgrims were not involved this time. Some authorities suspected air travelers from India to Egyptian airfields run by the British. Among the first cholera victims were laborers working at the airfields near El Korein. The town of 15,000 on the eastern fringe of the Nile Delta and close to the Suez Canal was also the site of an annual fair, when thousands of date merchants gathered from all over Egypt and beyond. Also billeted there in 1947 were the 6,000 workmen from the British airfield. The panicked departure of laborers, together with merchants, helped spread cholera throughout Egypt before any local controls could be enforced.

Others who suffered terribly, this time at the beginning of the sixth pandemic, were the people living in the Philippines archipelago of over 7,000 scattered islands. Although no stranger to cholera, this locale suffered its worst cholera experience between 1902 and 1904 when it lost as many as 200,000 of its population of 7.6 million to the dreaded disease. The outbreak struck just as a three-year insurrection against American annexation was ending. The Philippine-American War took 800,000 additional Filipino lives and

played a key role in exacerbating the impact of cholera. It is difficult to draw a line between the American war to subdue the Philippines and efforts to “conquer” cholera.

After the 1920s, with a few exceptions, cholera again retreated to its home waters in the Ganges Delta. Many medical historians in fact date the end of the sixth pandemic to the year 1923.

Reactions. In Eastern Europe and Russia, so deeply embedded did cholera become in collective memory that the very term *kholera*, or *kholeria*, became a synonym for disaster in the Russian, Polish, and Yiddish languages. What was remarkable was that, as the rest of Europe steadily moved away from irrational and panic-inspired responses, in Russia little change occurred. The government reforms in all spheres, including public health and cholera control, remained sporadic and uninspired.

The final watershed for cholera in Europe was the devastating cholera outbreak that struck the major German port of Hamburg in 1892. This sad story demonstrated the risks involved in postponing the improvement of water services. Ironically, Hamburg had been a pioneer in sanitation, and was one of the first cities in Europe to introduce a centralized water supply and a sewage system in 1842. By the 1880s, however, Hamburg and Munich were the only holdouts against contagionist and bacteriological approaches in Germany. An old free city and self-governing in the new Second German Reich, Hamburg continued to draw its drinking water from the Elbe without treatment. Adjacent Altona, part of the Prussian State, had by 1892 introduced a modern water filtration plant. Altona was entirely spared during the 1892 epidemic, whereas Hamburg suffered roughly 7,500 deaths among over 19,000 cases in slightly over six weeks. After this dramatic confirmation of **germ theory**, Hamburg city fathers could no longer thwart public health reforms.

The tragedy at Hamburg also helped reinforce the American public health movement, which was already moving forward at full speed. As Hamburg was enduring its disaster, public health officials used their testing and quarantine powers to identify the first carriers arriving in New York that summer from Europe. A handful escaped but were tracked down by an army of health department staff and volunteers. Health workers also filled toilets and privies with disinfectants. As a result, only 10 people died of cholera in New York in 1892.

In Italy, a cholera disaster early in the sixth pandemic evoked popular emotions only seen in Europe almost a century earlier. The summer of 1910 saw cholera riots, attacks on physicians, mass panic and flights from cities, a return of religiosity and superstition, and sometimes furious rage directed against gypsies, who were the favorite **scapegoats** for the medical disaster.

Historical Effects. As the fourth pandemic raged, the growth of scientific knowledge about cholera proved disappointing. A British physician, **John Snow**, in a remarkable epidemiological undertaking, used London’s cholera epidemic of 1853 to argue that contaminated drinking water was the cause of this dread disease. But Snow’s reasoning was not anchored in scientific proof, and scoffers at his waterborne theory remained long in the majority. Advances in technology, whether for shipping or warfare, seemed only to have benefited cholera’s diffusion. Rapid sea transport led to major cholera outbreaks aboard ships and in quarantine stations at points of entry in the new world like New York, New Orleans, or Halifax, Nova Scotia. Faster travel only made the consequences of the Muslim pilgrimage worse. Meanwhile wars in Europe and the Americas continued to serve as cholera’s allies.

Efforts to contain and control cholera were, however, not hopeless. Sanitarian successes in the United States were impressive, and smaller initiatives in Europe, India, China, and Japan were bearing fruit. In the Western enclave of Shanghai, China, cholera was much reduced through precautions such as the boiling of water. In 1870 the wealthy expatriate community there also invested in a 10-year campaign for a pure water supply. In Japan under the Meiji Restoration, the government by 1879 had modernized sanitary surveillance and created an improved water supply according to the Western model.

Scientific understanding finally began to advance with a breakthrough achieved by Robert Koch and his German research team in Egypt and India in 1883–1884. However, although the team succeeded in isolating the cholera bacillus, many in the scientific community remained unconvinced by Koch's research. Koch's opponents were able to neutralize his arguments, but they could not for long refute them. His identification of the bacillus was a major advance because it made possible the use of the laboratory to test for the disease even among asymptomatic carriers. He was also a strong advocate of state intervention in public health, and a believer in quarantine, isolation, disinfection, and the policing of the water supply.

Treatment and therapy based on the new epidemiology of cholera mushroomed in the 1880s and 1890s, even if success was elusive. Vaccine therapy, owing much to the enthusiasm for immunization generated by **Louis Pasteur**, began in Spain during a major cholera outbreak in 1885 when a Catalan physician named Jaime Ferrán y Clúa (1851–1929) became the first to apply Pasteurian principles when he inoculated over 40,000 Spaniards. A French commission of investigation impugned Ferrán's vaccine and methods. Although shortcomings certainly existed, theirs was an excessively harsh judgement on a pioneering medical microbiologist working in the very early days of **immunology**.

Experiments did not stop in Spain. Most successful of these early microbiologists was **Waldemar Haffkine**, a Jewish Ukrainian Pasteurian. From 1890 he began working at the Pasteur Institute in Paris on a live anticholera vaccine that required two doses. Between 1893 and 1896 in India, he was the first to conduct genuine field trials, mainly among laborers on tea estates, British troops, children in boarding schools and orphanages, and inmates of nine civil jails.

Haffkine's results were also mixed. His vaccine produced immunity against acquiring cholera but was of no therapeutic value if the disease had already been acquired. One serious problem was his difficulty in producing the vaccine in large quantities and standardizing it. The problem which haunted vaccine therapy then and now was that it could not eradicate cholera by producing the herd immunity effect, achieved when a threshold of 80 percent immunity makes the disease unable to persist.

In Europe, studies of the effectiveness of cholera inoculations during conflict in the Balkans and among First World War armies found that **vaccination** was not statistically significant either in preventing cholera or in shortening the length of time that recuperating patients remained carriers. New studies in Calcutta by 1928, however, came out more strongly in favor of cholera vaccination. By the late 1940s, international health experts recommended vaccination, especially in times of pilgrimage, war, or social breakdown, when regular sanitary measures could not be used.

Mass vaccination during the first half of the twentieth century became a popular, easily grasped, and visible indication that health authorities were doing something. Yet this very popularity became a danger insofar as it instilled a false sense of security. Vaccination

could neither eradicate cholera nor provide herd immunity, and it was less effective than the provision of safe water in controlling the disease.

Improved international surveillance and cooperation did slowly evolve during the sixth pandemic. The good offices of International Office of Public Hygiene (IOPH) under the League of Nations, and of the **World Health Organization** (WHO) through the United Nations after its creation in 1948, were the chief agencies of this improved approach. Two control elements were safety of the water supply and surveillance of potential carriers. The first was associated with chlorination, a standard procedure where more permanent guarantees of safe water could not be met. The second, sometimes problematic, involved stool examination of suspected carriers, a procedure that only developed with the advance of a scientific means of carrying out the laboratory work. Yet even as early as 1926, the scientific consensus of the cholera subcommittee of the IOPH in Geneva declared this procedure to be of dubious value. Later, the WHO agreed. In its 1951 revision of International Sanitary Regulations, it dropped stringent rules for stool examination.

Without doubt, potentially the most important breakthrough in treatment of cholera patients was the advance in rehydration therapy during the sixth pandemic. Sir Leonard Rogers (1868–1962) of the Indian Medical Service pioneered in the administration of a hypertonic saline supplement with alkali and potassium combined with purified water. In some instances, this new technique reduced mortality by one-quarter to one-third. Rogers lent his services to the city of Palermo during the Italian cholera emergency of 1910 and was able to reduce CFRs to below 20 percent, something of a miracle compared with alarming rates in Naples and other Italian cities of the day. Later recognition that glucose added to salts helped stricken patients keep down orally administered solutions was yet another milestone.

Nevertheless, potential cholera victims would have to wait half a century until rehydration became a widespread therapy. Only with the development of simple orally administered rehydration solutions to replace more technically complicated intravenous procedures during the seventh cholera pandemic after 1968 did CFRs fall to 1 percent and below, making cholera no longer a fatal disease, provided treatment was timely.

Cholera continued as a serious endemic disease in colonial India, but it seemed no longer to be spreading internationally as the twentieth century progressed. A congratulatory note sounded internationally as the sixth pandemic faded almost from sight by mid-century, and some even declared that new knowledge of the etiology of disease and effective controls meant that the sixth cholera pandemic would be the world's last. Few in the WHO or in research institutions envisioned how a changing global ecology would permit a modified cholera pathogen to establish a free-standing and permanent niche in marine habitats not just in the Ganges Delta but in brackish water environments on several continents, and launch the seventh pandemic in 1961, one that shows little sign of abating at the present time. *See also* Cholera before the Pandemics; Cholera: First through Third Pandemics, 1816–1861; Cholera: Seventh Pandemic, 1961–Present.

Further Reading

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**Cholera
Morbus**

is about as sure to
come as Summer is.
It comes suddenly and
without warning —
is **Dangerous** and often
Fatal.

ARE YOU PREPARED
for its coming?

If any of your family are
attacked **PROMPT** action
only may save life. For
46 YEARS ONE medicine has
ALWAYS cured
**CHOLERA, CHOLERA MORBUS,
DIARRHOEA, DYSENTERY** and
all **SUMMER COMPLAINTS**
CHILDREN can take it with
perfect safety.

This medicine is
Perry Davis'
Pain Killer.

To be on the safe side get
some **NOW** and have it on hand.
For sale by all Druggists.

PERRY DAVIS & SON, PRINCE PROVIDENCE, R. I.

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MYRON ECHENBERG

CHOLERA: SEVENTH PANDEMIC, 1961–PRESENT. The seventh pandemic has coincided with the phenomenon of globalization, with which it is intimately linked. **Cholera epidemics** have become for some a litmus test of whether a national state possesses a modernized public health system. Alternative explanations would suggest that when cholera has been absent from one place for a century but present elsewhere, international connections to its etiology, not unsanitary practices in the region, constitute a more profitable area of investigation. Second, a wider historical perspective reveals how the economic restructuring of the 1980s weakened populations and helped make the outbreak in Peru and elsewhere so severe.

The seventh cholera pandemic was different from the first six in several respects. Its agent was a new variant of the cholera pathogen *Vibrio cholerae* O1 El Tor. El Tor held lower virulence for humans, enabling less severely ill patients to be more mobile and, therefore, to have the capacity to infect others over a longer period of time. Moving more slowly than cholera pandemics of the nineteenth century, the seventh pandemic had the greatest geographic span and made use of the fastest new technology (air travel), yet lasted longer than any earlier pandemics. At present, it shows no signs of abating.

The mildness and diminishing impact of the sixth cholera pandemic (1899–1947) had led many to believe that they had seen the last of this terrible scourge. Suddenly, in January of 1961, *V. cholerae* O1 El Tor began to spread from its starting point around Makassar on the large island of Sulawesi, Indonesia.

El Tor moved slowly, first through southern Chinese and Southeast Asian locales, and then to India in 1964. Over the rest of the decade, it followed a familiar nineteenth-century route to western Asia. By 1966 it was present on the borders of the Asian republics of the Soviet Union. The first global phase began in earnest in 1970 when cholera El Tor reached everywhere in the Middle East, struck the Soviet Black Sea ports of Odessa and Kerch, and hit West Africa hard. At this stage, the new wave of cholera spared the Americas and most of Europe, though it infected such old haunts of southern Europe as Lisbon, Barcelona, and Naples, allegedly carried from North Africa by seasonal workers and tourists. In the early 1990s, Russia, Romania, and a few other former Soviet bloc countries saw cholera's return.

A mild appearance of cholera at the Islamic holy site of Mecca, Saudi Arabia, in 1974 aroused concern from health authorities with historical memories of how **pilgrims** had

involuntarily helped spread the disease in the nineteenth century. Fortunately, only a few cases were diagnosed among the 1 million Mecca pilgrims, and the disease did not spread from there. Sporadic but serious outbreaks occurred in the Kathmandu valley of Nepal. **War** zones like the Kabul region of Afghanistan also produced cholera flare-ups, but on nothing like the African scale.

The Americas, beginning with Peru in 1991, experienced a public health shock from which they are only now recovering: the first appearance of cholera in almost a hundred years. This time, the disease spread widely in South and Central America, and was present for a decade in Peru. Health officials everywhere were aghast at the force of cholera's impact on the Americas. A watershed in the seventh pandemic, the year 1991 was by far the worst since the nineteenth century, with 595,000 cases worldwide, over half of which were reported by Peru, although that country suffered a remarkably low 4,002 deaths and a CFR (case fatality rate) of only 1 percent. Peru and other locations in the Americas continued to face perils from cholera after 1991. Though rates fell, Peru continued to record cholera cases each year, which some researchers have attributed to local effects of the strong El Niño weather phenomenon. Devastation caused by Hurricane Mitch (1998) and other manifestations of extreme weather destroyed basic services and infrastructure in Central America as well.

Cholera's spread through the Americas by discontinuous leaps and sudden introductions from the far south in Argentina as far north as central Mexico encouraged rumors and fears about potential carriers. Culprits included migrant shrimp farm workers voyaging from Peru to Ecuador, itinerant preachers moving from El Salvador to Honduras, and drug smugglers flying with cocaine shipments from Amazon jungle bases to airstrips in Mexico.

Although Venezuela did not suffer huge losses to cholera overall, the differential impact of the disease on a concentrated region and ethnic group held many lessons. Cholera struck in the Orinoco Delta, in the remote State of Delta Amacuro, far to the east of the national capital of Caracas. Worst hit were the native peoples called the Warao living along the Mariusa River, a tributary of the Orinoco. After suffering terribly in 1992, the Warao faced second and third visitations of cholera in 1996 and 1997. The Venezuelan government deliberately downplayed cholera, underreporting cases and deaths by as much as a factor of 10.

For Africa, the seventh pandemic proved to be especially devastating. Unlike the localized, if severe, experiences with cholera that the continent witnessed in 1868 and 1893, this time almost every African state reported cholera to the **World Health Organization** (WHO). Even worse, free-standing cholera developed in the coastal lagoons and large river valleys of West Africa, in Lake Chad, on the coast and in the oases of Somalia, in the Great Lakes of East and Central Africa, and throughout Mozambique. Newly created reservoirs permitted the entrenchment of endemic cholera, which usually attacked affected regions at the start of the rainy season and died away at its end.

Africa's continuing struggle with cholera came in two waves. A dramatic beginning occurred in August 1970 when a group of Guinean students returned to the capital of Conakry from the Soviet Union, carrying this unwelcome visitor with them in what was possibly the first time cholera had used air transport to gain a significant new foothold. From Guinea, cholera spread like wildfire along the West African coast as far as Nigeria and north to the Niger Valley and Lake Chad. Its eastward journey continued to the Horn of Africa, and then down the East African coast to southern Africa.

After waning in the 1980s, the seventh pandemic surged in 1991. It struck 21 African states and continues to be a menace today. Political instability and state collapse in Central Africa were features of the postcolonial era, and cholera certainly profited. In 1994 war and terrible violence in Rwanda triggered a huge mass migration to the refugee center of Goma, in the Democratic Republic of the Congo (then called Zaire), where cholera exploded.

Southern Africa has also encountered serious cholera epidemics and has become an endemic focus since the 1970s. Official reporting of cholera along with much else changed as South Africa went over to majority rule by 1994. Nature, however, was not kind to the new South Africa. In 2000, endemic cholera from Mozambique spread to the state of Kwazulu-Natal. In 2001, South Africa reported the alarming figure of 106,151 cases, which was roughly 58 percent of the global total. Also reporting regional cholera were Swaziland, Zambia, and Malawi.

Although cholera exacted a terrible price in the nineteenth century, the Indian Ocean area and the neighboring East African coast has not been a hotbed for modern cholera. Off the coast of Tanzania, the Comoros Islands endured a major outbreak beginning in January 1998, its first experience with cholera in 20 years. Two years later, the large island of Madagascar, cholera-free for decades, suffered an outbreak in three provinces that would spread throughout the island the following year.

Latin American and African reactions to the seventh cholera pandemic were closely monitored by the WHO and by international cholera experts. Despite facing terrible morbidity, Peruvian health authorities responded quickly and efficiently to the pandemic and were able to keep CFRs remarkably low. Crucial elements in their success were the advance preparations: experience and confidence in oral rehydration therapy, an epidemic field investigation service for diarrhea, and laboratory resources to identify the cholera organism early in the outbreak. They were simultaneously criticized, however, for their reluctance to reinvest in **water** and sewage systems and for their continuing public health emphasis on curative rather than preventative programs.

The Venezuelan experience confirms that cholera stigmatization in Latin America was instrumental in further marginalizing the poorest inhabitants of society. One favorite explanation focused on culture and food preparation, just as had been the case in Peru with *ceviche*, marinated fish and seafood. Crabs were a diet mainstay not only of the Warao but of everybody in the Orinoco Delta, but it became a powerful belief that the Warao often ate them raw and that this was how cholera contamination began. The story was entirely mythical, as the Warao boiled crabs, a preparation that killed the bacteria. This invented discourse was widespread in the press and was even shared by professional health workers.

Although no one would deny that standards of public sanitation had been breached in many parts of the Americas, what was so striking was how many scientists avoided the central point: that the cholera pandemic of the Americas spread by means of drinking water contaminated with feces, not because of “cultural” practices, and that the poor could not afford to turn to more reliable but costly sources of potable water. The experiences of Peru, Venezuela, and so many other countries during the seventh pandemic demonstrated clearly that cholera is an excellent mirror of inequalities.

At the time, blaming of victims in Africa was also common. The issue was frequently both quantity and quality of water. So too was the singling out of African cultural practices, including allegedly unsanitary behavior of people at funerals, nomadic lifestyles,

and the use of waterways for travel and **trade**. Clearly, Africa absorbed terrible death tolls not seen since the days of classical cholera in the nineteenth century. In the Lake Chad region, some villages lost as many as half to three-quarters of their populations. But blaming culture for these terrible outcomes did not explain how behavior made African people any more exposed than those in other parts of the globe.

A more fruitful area of explanation turned on natural factors, such as **environment**. Severe droughts drove hungry migrants to concentrate around fewer sources of water and food, which could quickly become contaminated. Conversely, unusually heavy rains could cause makeshift latrines to pollute water sources, and in cities, crumbling sanitary infrastructure to collapse. Such was the case during 2004 and 2005, which saw large increases in cholera cases in Senegal, for example.

Coinciding with natural phenomena has been the decline or collapse of African civil societies. As in the past, cholera profited from political instability. In the 1990s, war refugees from Liberia and Sierra Leone, who were often subjected to especially unsanitary living conditions, raised cholera rates there and in neighboring countries.

Occasionally, cholera's explosion had more to do with misguided government policy. In 2000, as the South African state was in transition under majority rule, local government authority in KwaZuluNatal, under pressure from the World Bank to reduce spending as part of their so-called "structural adjustment policy," or SAP, ceased providing free water to local residents. The very poor people living in the squatter settlement on the fringes of the town of Empangeni were forced to use local rivers for drinking water and sanitation, and a nasty cholera outbreak spread rapidly. *See also* Cholera before the Pandemics; Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1862–1947; Colonialism and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Race, Ethnicity, and Epidemic Disease; Scapegoats and Epidemic Disease.

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MYRON ECHENBERG

CINEMA AND EPIDEMIC DISEASE. During the first decades of the 1900s, disease and messages about its meaning to society began to find their way onto the big screen with the growing popularization of film as a medium of mass entertainment and information. Diseases and epidemics, real and fictional, have long served as both backgrounds and important elements of plot in feature dramas and thrillers and have provided metaphors

for societal ills and fears. Filmmakers have also produced a large number of movies of an educational or informative nature, whether documentaries, newsreels, or discussions of personal hygiene and disease.

As a tool of preventive health, films have been used to disseminate information and warnings about disease outbreaks to the general public and to specific groups (e.g., school children, military inductees). From the early decades of the twentieth century, in the years before television, it was common for movie theaters to screen such productions along with newsflashes and official messages. These films were also presented in outdoor locations, particularly in more sparsely populated rural communities. During the First World War (1914–1918) the International **Red Cross** Society produced and screened preventive health films, such as those on epidemic prevention in **war** zones, and after the war the **Rockefeller Foundation** followed with movies on hookworm disease, which for many were their first exposure to the new medium.

Filmmakers quickly tapped the entertainment potential of adding disease and disaster to feature films, however, relegating educational movies to classrooms and military induction centers. Although disease had long had a place in fiction, the portrayals on film reflected deeper sociocultural anxieties arising from the vicissitudes of the era, ranging from **industrialization** and **urbanization** and the globalized conflicts of the First (1914–1918) and Second (1939–1945) World Wars to the even deadlier threats of the early Cold War (1945–1989) era.

In general, the thematic trends of popular cinema on epidemics can be categorized into those belonging to the first half of the twentieth century and those produced after 1945. Early in the century, audiences would have been familiar—and perhaps even have identified—with diseases like **tuberculosis** (*The Red Cross Seal*, 1910; *White Terror*, 1915) and **syphilis** (*Dr. Ehrlich's Magic Bullet*, 1940) that accompanied increasingly polluted workplaces and residences and changing social norms. In films of this era, hope for success over epidemics lay in the revolutionary advances of **germ theory** and biomedical sciences. Researchers such as **Louis Pasteur**, **Paul Ehrlich**, and **Robert Koch** were hailed and depicted as modern saviors of humanity (*Arrowsmith*, 1931; *The Story of Louis Pasteur*, 1935; *Citadel*, 1939).

Diseases and epidemic outbreaks in cinema took on more apocalyptic dimensions after 1945. New fears were spawned not just by the threat of weapons of mass destruction, but also by apprehensions over increasingly fluid borders brought about by innovations in transportation and communications as well as accelerating patterns of **trade** and migration. According to the cinematic world, governments and corporations have been responsible for generating epidemics by flirting with evil from highly dangerous but grandiose and promising experiments that they failed to control and contain (*Virus*, 1980; *Pandora's Box*, 1996; *Resident Evil*, 2002). Hence, epidemics on screen have resulted from accidental leaks in major biomedical projects, contagions released deliberately by sophisticated bioterrorists (*12 Monkeys*, 1995; *Winds of Terror*, 2003), or unidentified foreign germs imported unwittingly from exotic lands through primates, planes, and people themselves (*Outbreak*, 1995; *Fatal Contact*, 2006). Unlike the depictions of more limited and personalized scales of suffering from epidemics of the first half of the twentieth century, more recent depictions of the destruction from diseases have become increasingly rapid, overwhelming, and spectacular. Cinematic germs have the tendency to lay waste to entire cities, countries, and even civilizations. The microbe is visualized through and embodied

SELECTED THEATRICAL FILMS DEALING WITH EPIDEMIC DISEASE

- The Andromeda Strain* (Robert Wise, 1971)
Arrowsmith (John Ford, 1931)
Awakenings (Penny Marshall, 1990)
Cabin Fever (Roth Elis, 2002)
Cassandra Crossing (George Kosmatos, 1976)
The Citadel (King Vidor, 1939)
City of SARS (Steve Cheng, 2003)
Code Name Trixie (George Romero, 1973)
Contagious (Joe Napolitano, 1997)
The Crazies (George Romero, 1973)
D.R.E.A.M Team (Dean Hamilton, 1999)
Dawn of the Dead (George Romero, 1978)
Day of the Dead (George Romero, 1985)
Daybreak (Stephen Tolkin, 1993)
Deadly Outbreak (Rick Avery, 1995)
Dr. Bull (John Ford, 1933)
Dr. Ehrlich's Magic Bullet
 (William Dieterle, 1940)
80,000 Suspects (Val Guest, 1963)
Epidemic (Las Von Trier, 1987)
Fatal Error (Armand Mastoianni, 1999)
Gypsy Fury (Jacques Christian, 1949)
Hei Tai Yang 731 (Tun Fei, 1988)
I Am Legend (Francis Lawrence, 2007)
Infection (Ochial Masayuki, 2004)
Intimate Agony (Paul Wendkos, 1983)
Isle of the Dead (Dwain Esper and
 Mark Robson, 1945)
Jericho Fever (Sandor Stern, 1993)
The Killer that Stalks New York
 (Earl McEvoy, 1950)
Last Man on Earth (Sidney Salkow, 1964)
Longtime Companion (Norman René, 1990)
The Missing are Deadly (Don McDougall, 1975)
Mission Impossible II (Brian De Palma, 2000)
Morte a Venezia (Luchino Visconti, 1971)
Mosquito Man (Tibor Takacs, 2005)
The Navigator: A Mediaeval Odyssey
 (Vincent Ward, 1988)
Night of the Living Dead (George Romero, 1968)
Nineteen Eighteen (Ken Harrison, 1985)
Nosferatu: Phantom der Nacht (Werner
 Herzog, 1979)
The Omega Man
 (Richard Fleischer, 1971)
Operation Delta Force
 (Sam Firstenberg, 1997)
Outbreak (Wolfgang Petersen, 1995)
The Painted Veil (John Curran, 2006)
Pandora's Clock (Eric Laneuville, 1996)
Panic in the Streets (Elia Kazan, 1950)
The Periwig Maker
 (Steffen Schäffler, 1999)
La Peste/The Plague
 (Louis Puenzo, 1992)
Die Pest in Florenz (Fritz Lang, 1918)
Philadelphia (Jonathan Demme, 1993)
Plague (Ed Hunt, 1978)
Plague Fighters (Ric Bienstock, 1996)
Quiet Killer (Sheldon Larry, 1992)
Rats (James Felter, 2006)
Resident Evil (John Anderson, 2002)
The Satan Bug (John Sturges, 1965)
The Seventh Seal
 (Ingmar Bergman, 1957)
Sister Kenny (Dudley Nichols, 1946)
The Stand (Mick Garris, 1994)
The Story of Louis Pasteur (William
 Dieterle, 1935)
Trollsyn (Ola Solum, 1994)
12 Monkeys (Terry Gilliam, 1995)
28 Days Later (Danny Boyle, 2003)
28 Weeks Later (Juan Carlos Fresnadillo,
 2007)
Virus (Kingi Fukasaku, 1980)
Virus (Armand Mastroianni, 1995)
Voyage of Terror
 (Brian Trenchar-Smith, 1998)
Winds of Terror (Robert Mandel, 2001)
Yellow Fever/La Fièvre Jaune
 (Glen Pitre, 1978)
Yibola Bing Du (Herman Yau, 1996)

in infected, mutated, and hostile human bodies (*28 Days Later*, 2003; *Mosquito Man*, 2005), animal hosts, and delicate test tubes, as well as in the minds of scheming conspirators. Just as importantly, the saviors in films on epidemics are not prominent historical personalities in medicine but usually a motley crew of accidental heroes frantically racing against time to avert doomsday either by finding the vaccine or containing the spread of the virus. The staging of such desperate acts to overcome these unprecedented public health emergencies have become what Carl Elliot describes as “public health thrills” for the consumer market.

Since their deployment almost a century ago in public health films, cinematic portrayals of epidemic disease have shifted from providing history lessons to generating high-tech entertainment. Feature films’ production costs far outstrip those of official notices and other means of disseminating public service information on the transmission of diseases, yet they may well serve to educate viewers about epidemic threats and official responses. Cinema now provides for audiences the virtual experiences of unfolding dramas of public health emergencies on biblical scales from the comfort of their seats. See also *AIDS, Literature, and the Arts in the United States*; *Capitalism and Epidemic Disease*; *Popular Media and Epidemic Disease: Recent Trends*; *Scapagoats and Epidemic Disease*.

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COLONIALISM AND EPIDEMIC DISEASE. Colonialism may be defined as a relationship in which one population's government assumes political and economic control and authority over another population, usually with the intention of subjugating that population and carrying out resource and revenue extraction. Colonialism is thus an unequal relationship in which the colonized are subject to considerable forms of exploitation and in which colonizing groups justify their activities with the belief that they benefit colonized groups, which are in turn seen as culturally distinct or different, and often inferior. These underlying beliefs take a variety of forms. In the case of Spanish colonists, for example, they believed they were serving a just and benevolent mission in the Americas because they sought to carry out the evangelization of native populations. Alternatively, more modern forms of colonialism in the nineteenth and twentieth centuries depended on the idea that colonists engaged in a "civilizing mission" in the colonies at great personal cost and sacrifice. Like earlier Spanish versions, such convictions were founded on the unfortunate belief that non-European populations were culturally and racially inferior and thus needed the tutelage of Europeans. Racism and the denigration of cultural difference formed the cornerstones of the colonial project, and colonists justified their work with the argument that colonialism would serve the best interests of conquered groups.

Colonialism, however, often involved more than just political domination and contact between different groups. In many cases it also involved the unintended exchange of diseases, much to the detriment of colonized populations. **Epidemic** diseases, in particular, played a prominent role in shaping the experience of colonization and the transformation of colonial societies in different parts of the world. They also led colonial states to undertake various endeavors to understand and prevent disease.

Disease in Latin America. Devastation as a result of colonialism and disease was particularly notable in Latin America, where contact with Spanish and Portuguese explorers beginning in the late fifteenth century devastated populations. Combined with labor exploitation and the violence of conquest and early colonial settlements, disease wiped out nearly the entire indigenous populations of the Caribbean islands settled by Spain between 1492 and 1519. On some Caribbean islands fewer than 100 indigenous people remained by the time Spanish colonists' attention shifted to the exploration and conquest of Mexico in 1519.

More generally, historians estimate that in much of the Americas, upwards of 90 percent of the indigenous population died in a massive demographic collapse after the Spanish Conquest. The collapse was largely the result of disease, and most of the population drop took place within decades of Spanish invasion. This process of depopulation was more dramatic in some regions than others, but after the first decades it transformed into a slow process of population decline punctuated by epidemics. Population loss was also more extreme in particular kinds of **environments** and climates. Diseases such as **smallpox** and **measles** flourished in warm, low altitude, tropical climates. They were relatively less destructive in dry, highland areas such as the Andes and Central Mexico, where a larger portion of indigenous populations survived.

The initial demographic collapse was so severe in Latin America's coastal lowland regions that it fuelled the initial extension of the **slave** trade to the Americas. African slaves provided labor for colonists in areas where diseases had wiped out the supply of indigenous labor, enabling the rise of plantation agriculture and fuelling the ascendancy of a rural landed elite. Colonists, however, frequently expressed concern about diseases

they wrongly associated with Africans and the slave trade. For example, in the capital of colonial Peru, Lima, residents believed African slaves had brought **leprosy** to the colony, even though evidence now suggests Hansen's disease had existed in the Americas prior to colonization.

During much of the Spanish colonial period **physicians** and other colonists thus neglected their own roles as trans-Atlantic disease carriers, incorrectly blaming African populations for a variety of epidemic diseases. These beliefs among colonists about diseased African populations were, of course, unfounded. We know that African populations suffered high rates of illness during the colonial period and were susceptible to epidemics, but this susceptibility was the result of several factors including the brutal conditions of the slave trade, the poor provision of food by masters, and the harsh conditions of work and daily life. There is no evidence to suggest that Africans brought any more diseases to the Americas than the Spanish did.

As with slavery, labor conditions and malnutrition among indigenous populations in colonial Spanish America increased the overall susceptibility of such populations to both epidemic and endemic diseases. Rates of respiratory infections such as **tuberculosis** were very high among indigenous groups forced to work in mines such as Bolivia's infamous silver mines of Potosí. The mining of mercury and the use of mercury to process silver also caused high rates of disease and other conditions related to mercury poisoning. Epidemic diseases such as measles were not uncommon among miners either, and life expectancy tended to be very low. For much of the colonial period authorities expressed concern about such rates of disease, yet they also saw indigenous people as crucial for providing the labor to produce silver, which generated lucrative revenue for the colony. These conflicting interests would gradually lead colonists to implement disease prevention measures in the eighteenth century.

Disease in Later Colonial Societies. Problems with diseases and epidemics were not by any means exclusive to the Spanish Empire or to early modern forms of colonialism. Rather, similar cases can be found in the British, French, and Dutch colonies of South Asia, Southeast Asia, and Africa during the nineteenth and twentieth centuries. Even in areas where colonization did not expose populations to virgin-soil epidemics, the changes in life brought on by colonization often exposed colonized people to new disease problems.

Writing about colonial Africa, the historian Megan Vaughan suggests that colonialism furthered the transmission of epidemic diseases by increasing the mobility and migration of populations, leading migrants to cities in southern Africa. Such groups would return to their communities with "the new diseases of **industrialization**, including tuberculosis and venereally transmitted **syphilis**, and facilitating the spread of other diseases." Colonialism also led to the introduction of epidemic diseases like measles that were new to many African societies and led to high mortality rates, while the broader process of conquest and colonization disrupted the rituals, practices, and beliefs indigenous people had traditionally followed in treating disease. More generally, in the modern period, forced migration, new labor requirements in extractive industries such as mining, and the requirement that subjects live in close residential quarters in cities furthered disease transmission in many colonies. Such changes often created venues in which disease could spread more easily, and they also required levels of exertion and potential hunger that weakened subjects' **immune systems**.

Problems with disease were also especially severe in colonial India. The historian David Arnold estimates that **cholera** alone led to the deaths of 15 million people in

British India between 1817 and 1865, and a further 23 million between 1865 and 1947, the year in which Britain relinquished colonial rule. Cholera constituted a source of tremendous administrative concern in the nineteenth century because it was difficult to control, it ravaged indigenous populations, it spread in epidemic form among colonial soldiers living in crowded barracks, and it threatened to spread among the colony's British settlers. Other diseases wreaked havoc on European colonies in Southeast Asia and Australia, where populations often had little or no previous exposure to certain diseases.

Understanding and Explaining Epidemic Disease. In many parts of the world, understanding and correctly diagnosing epidemic disease and other diseases constituted a problem for both the colonized and the colonizers. For colonizers, diseases generated all sorts of concerns about the viability of living for extended periods in foreign environments different from their own. The historian Warwick Anderson has documented these anxieties and fears of disease among colonial authorities and settlers in both the U.S. Philippines and British Australia in the nineteenth and early twentieth centuries. He shows that colonial officials and settlers theorized about the effects of tropical or harsh climates on their bodies. In some cases colonists even imagined that they suffered from unfamiliar diseases in the colonies, reasoning that this was the result of an incompatibility between their bodies and such climates and environments. They claimed settlers suffered from diseases that natives tended not to experience, although they sometimes also saw natives as potential sources of epidemic and endemic diseases that could spread among colonizers. In some cases colonists even imagined diseases and created conditions that we now know did not exist. In doing so, they imagined native bodies as adapted to environmental conditions, whereas their own bodies were seen as delicate and vulnerable.

For colonists seeking to explain epidemics, a central concern was thus the question of how disease varied or differed between the metropolis and the colonies. In the Spanish colonial period, a variety of theories abounded suggesting that environment and climate made the New World fundamentally different from the Old World. New World populations were thus also different from Old World populations and were subject to a variety of diseases, some of them in epidemic form. In British colonial Australia settlers grappled with the idea that the warm, dry environments of much of the territory would give rise to health problems different from those found in damp and muggy Britain. Likewise, Jennifer Seltz has shown that as the United States colonized and expanded into the West, settlers saw the environments of Texas, the Puget Sound region, and the San Francisco Bay Area as presenting distinct problems of disease and poor health. In all these cases it is worth noting that colonial attempts to understand disease predated the rise of **germ theory**, which posited that **bacteria** and **viruses** served as the sources or causes of most disease. Given the absence of a clear set of beliefs about germs, colonists employed a wide range of strategies to talk about and explain disease.

Colonists also saw the regions they had colonized as ideal locations for the investigation and study of disease. Making assumptions about the differences of nature and culture in regions such as Africa, they attempted to use their power to understand the unique workings of disease and its prevention in such settings. In the case of British colonial Africa, the historian Megan Vaughan argues that the British saw the continent as a wild and uncontrolled environment, and "the observations of early colonial medical men contributed to this larger European perception of Africa as a continent waiting to be tamed." In addition, anxious colonial administrators in Africa feared that indigenous populations served as reservoirs of diseases that could spread into settler communities.

Preventing Epidemics. Colonial officials generally believed disease prevention was vital to carrying out colonial rule and resource extraction successfully in many parts of the world. This was because they tended to link the health of indigenous subjects to labor output and revenue production. By increasing population size in the colonies through disease prevention, officials thought they would increase overall productivity. To do this required transforming the environment in the colonies, controlling the movement of populations, and modifying popular customs to hinder disease transmission. Attempts to refashion colonies to achieve these goals extended as far back as the colonial period in Spanish America. They continued well into the twentieth century in British colonial Africa and South Asia.

In Spanish America, eighteenth-century officials worried for decades that the diminishing size of indigenous populations would lead to fewer workers to serve in the mines. In this way, they saw disease as a direct hindrance to colonial productivity and the success of the colonial enterprise. Engaging **Malthusian** notions of demography, which focused on calculating the population size and carrying capacity of different societies and environments, these colonists believed they could maximize population growth by preventing the diseases that had increased infant mortality and reduced life expectancy. As a result, in the late eighteenth and early nineteenth centuries, in particular, representatives of the Spanish crown and settlers in the colonies themselves took unprecedented measures to prevent epidemic diseases from wreaking havoc on their populations.

The most dramatic example of these measures was the transfer of the newly discovered smallpox vaccine from Spain to Latin America in 1803. Given the particular difficulties of keeping vaccine fluid alive outside of the bodies of humans or cows for extended periods, authorities opted to use orphans to transport the vaccine across the Atlantic. Loading orphans onto a ship under the care of a Spanish doctor, Francisco Xavier Balmis, authorities planned to transfer the fluid from orphan to orphan over the course of the journey. They did this because the vaccine took about a week to produce an immunological response and create pustules on patients' arms. By draining pus from these pustules each week and injecting it as a vaccine into the arms of other orphans, they would maintain the vaccine's potency until they reached land.

Known as the Balmis Expedition, this campaign to bring the smallpox vaccine across the Atlantic to the Spanish colonies was perhaps the most ambitious attempt of its kind to prevent disease in the colonial world by the early nineteenth century. Divided into two groups in the Caribbean, the expedition traveled through Mexico, Central America, and South America, forming local vaccine brigades and training local doctors and healers in the procedure along the way. The group in Mexico would eventually acquire new orphans and set sail from the colony's west coast, cross the Pacific Ocean, and deliver the vaccine to the Spanish Philippines and China. The other branch of the expedition reached Peru and eventually Bolivia. In Peru the expedition formed a series of vaccine brigades and juntas, and local doctors quickly took control of their administration. Encouraged by the possibility of eliminating smallpox epidemics, local doctors even made calculations to estimate how quickly the vaccine would accelerate population growth in the colony's capital, Lima.

As with the Spanish, British colonists also made smallpox control and prevention central to their colonial project. In many parts of the British Empire, however, colonial efforts at mediating disease led to conflict with indigenous peoples because the latter held very different views of the workings of disease and the relationship between medicine and broader beliefs. For example, in colonial India British smallpox **vaccination** efforts largely failed for

several reasons. First, people were generally reluctant to receive the vaccine, which appeared to offer very little immunity and had been difficult to store. Second, Hindus considered the transfer of vaccine fluid from arm to arm a form of pollution, and they often objected on religious grounds to the use of calf lymph for cultivating the smallpox fluid. Furthermore, smallpox had long formed a complex part of Hindu religious beliefs before colonization, and in the nineteenth century it continued to possess clear spiritual overtones. It was directly linked to a Hindu deity named Sitala, who was seen not only as the source of smallpox, but also as a means to gain protection from the disease through worship. Because the vaccine contradicted these beliefs and was associated with both foreign rule and the intrusion of secular medicine, it became suspect in popular thought.

Given that colonies were places in which societies with widely divergent concepts of religion, cosmology, and the body all converged and mixed, the interpretation and treatment of diseases such as smallpox became a hotly contested act. Moreover, many cultures that were colonized by European societies possessed rich medical traditions of their own, creating situations in which different kinds of healers competed over who should have authority to speak about disease. Writing about India, David Arnold has documented the various ways in which epidemic diseases such as cholera generated conflict and acquired new meanings for both British settlers and Indian natives. For the British, cholera was a troublesome disease that was difficult to treat and thus “not only challenged attempts to establish the superiority of Western medicine but also emphasized the physical frailty and political vulnerability of colonial rule.” The British saw cholera’s spread as linked to Hindu rites and **pilgrimages**. The importance of these rituals and the abundance of cultural and religious interpretations of the disease frustrated their efforts to introduce sanitary measures and anticholera serum. Ultimately, for the British the inability to control cholera and the destructive, terrifying nature of the disease cast doubt on the ability of colonizers to reorganize, sanitize, establish order, administer, and exert political control over India. On the other hand, for indigenous people the unabated spread of cholera led them to question British rule and the authority of Western secular medicine. In many regions they held “a widely shared belief that the British were in some way responsible, whether through direct violation of Hindu taboos or indirectly through the disruptive effects of their military intervention on the Hindu cosmos.” In this way, disease could form a very real hindrance to the establishment and forging of colonial rule.

Finally, since the colonizing European countries adhered to one or another branch of the Christian religion, with its imperative to “spread the Gospel,” colonization—especially by majority Catholic countries and by others from the nineteenth century—was rarely unaccompanied by missionaries, who often possessed medical skills. Whether among Jesuit priests or nursing nuns, pious Protestant families or evangelical physicians, care for the soul and care for the body were symbiotic processes. The equation of Western medicine with Western Christianity by Hindus, Muslims, animists, or shamanists resulted in complex reactions, ranging from rejection of both to acceptance of both. Whether in New Spain or nineteenth-century British Africa, religion, medicine, and colonial political authority often formed a trinity that simultaneously aided and subjected, freed and enslaved native colonial populations. Control of effective healing and imposition of religion helped stabilize political authority, benevolent political authority and the Gospel message helped spread Western medicine, and Christian missions relied on both just colonial government and a monopoly on sophisticated medicine. These patterns played key roles in shaping the postcolonial health-care systems, especially in Sub-Saharan Africa.

See also Diet, Nutrition, and Epidemic Disease; Disease in the Pre-Columbian Americas; Disease, Social Construction of; Historical Epidemiology; Hospitals since 1900; Latin America, Colonial: Demographic Effects of Imported Diseases; Leprosy, Societal Reactions to; Malaria in Africa; Measles Epidemic in Fiji (1875) and Eugenics; Measles in the Colonial Americas; Non-Governmental Organizations (NGOs) and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Religion and Epidemic Disease; Sanitation Movement of the Nineteenth Century; Scapegoats and Epidemic Disease; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Smallpox in European Non-American Colonies; Trade, Travel, and Epidemic Disease; Typhus and Poverty in the Modern World; War, the Military, and Epidemic Disease; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in North America to 1810.

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ADAM WARREN

CONJUNCTIVITIS. Conjunctivitis is an inflammation of the conjunctiva and is the most common eye disease in the world. The conjunctiva is the thin, transparent mucus membrane that covers the posterior surface of the eyelids and the anterior surface of the eye (cornea or sclera). One of the most common symptoms of conjunctivitis is inflammation that causes a pinkish-red coloration (hyperemia), and because of this coloration conjunctivitis is frequently referred to as "pink eye."

Most nonmedical people tend to think of conjunctivitis as one disease, but it is actually a group of diseases with many causes and even more manifestations. The major categories are conjunctivitis caused by infectious agents, immunological (allergic) conjunctivitis, conjunctivitis caused by autoimmune disease and/or chemical irritation, and conjunctivitis of unknown cause. The category of conjunctivitis covered in this article includes those

manifestations caused by infectious agents such as **viruses**, **bacteria**, rickettsia, chlamydia, and parasites, because these are the causes of conjunctivitis **epidemics**.

Viral Conjunctivitis. Viral conjunctivitis is the most common inflammation of the eye. Most children have at least one episode during their childhood years. Conjunctivitis is not limited to children, but the spread of the virus from child to child is especially common because of the natural tendency of children to touch each other while playing. Viral infections are frequently responsible for epidemics of conjunctivitis within families and military units, and among people in schools, offices, and factories. In addition to direct contact, the virus can be spread by contaminated materials (fomites) and microscopic particles.

Adenoviral (viruses that usually invade the upper respiratory tract) conjunctivitis is the most common form of viral conjunctivitis. So far there have been 19 different subdivisions (serotypes) of adenovirus identified as causative agents for adenoviral conjunctivitis. Once a patient (who is not immunodeficient, as an **AIDS** patient is) has conjunctivitis caused by one serotype, that person develops immunity to that serotype but remains susceptible to the other 18.

Pharyngoconjunctival fever is a triad of pharyngitis, fever, and conjunctivitis caused by an adenovirus. The conjunctivitis is usually identified with a watery discharge, redness, and swelling (edema) of the conjunctiva and frequently involves swelling of the eyelids. It is most commonly seen in children less than 10 years of age. There are at least three different serotypes of adenovirus that have been identified as etiological agents. This condition usually resolves spontaneously in two weeks.

Epidemic keratoconjunctivitis is a more severe form of conjunctivitis; there are at least three serotypes of adenoviruses identified as causative agents. It is called keratoconjunctivitis because it affects both the conjunctiva and the transparent anterior portion of the sclera (cornea). This form usually lasts 14 to 21 days with some symptoms lingering for months. There is a watery discharge and swelling of the conjunctiva (chemosis), hyperemia, and swelling of the lymph glands in front of the ear (preauricular adenopathy). Treatment of the symptoms is the only care currently available.

A well-documented incidence of epidemic keratoconjunctivitis was reported in Germany in 2004. The epidemic broke out among people serving in the German Armed Forces. Eventually it spread over 197 barracks and affected 6,378 soldiers. The civilian population outside of the barracks was also affected. The infection spread to the young adult male population first, followed by the young adult female population, and finally to children. Transmission was from person to person, and a clear and consistent strategy for dealing with the disease had to be adopted. If the soldiers were restricted to the barracks, there would be an increased risk to the other soldiers, but sending them home would increase the risk of spreading the infection to the civilian population. Thirteen barracks were completely closed down and twenty-eight were partially closed. Control measures were implemented, including **disinfection** of rooms and an isolation period of 21 days for soldiers with conjunctivitis.

Acute hemorrhagic conjunctivitis was first identified in 1969, around the time of the first lunar landing, and is therefore sometimes referred to as the "Apollo disease." This disease is associated with two strains of the coxsackievirus. The conjunctivitis is painful, is of rapid onset, and features chemosis and bleeding under the conjunctiva (subconjunctival hemorrhage). The conjunctivitis clears in four to six days, but the hemorrhages may

last longer. This disease tends to erupt into epidemics involving up to half of the population of a city or region. There is only symptomatic treatment available.

There are several other forms of conjunctivitis-causing viruses. Each by itself is considered rare, but when combined they form a significant cause of conjunctivitis. A partial list of these viruses includes the viruses that cause fever blisters (Herpes simplex), chicken pox (varicella), shingles (Herpes zoster), **smallpox** (variola), German measles (rubella), **measles** (rubeola) and flu (**influenza**).

Chlamydial Conjunctivitis. Conjunctivitis caused by chlamydial infections can take multiple forms. The most severe form is trachoma. Trachoma is endemic in many developing countries and is the most common cause of preventable blindness in the world. It was first described in the Egyptian “Ebers Papyrus” written some 3,600 years ago. It is most often found in areas of **poverty**, overcrowding, and poor public sanitation. Trachoma is usually the result of multiple untreated or under-treated episodes of chlamydial conjunctivitis, rather than a single infection. There are 400 million persons worldwide affected by trachoma, making it the most common of all chronic diseases. It usually affects both eyes. The advanced stage of trachoma is known as trichiasis—the inward turning of the eyelashes that causes corneal scratching (abrasions) and eventual blindness. The victim develops extreme pain; sunlight, dust, and smoke all irritate the eyes. The disease is three times more likely to affect women than men. In some cultures, when married female victims are not able to perform their traditional domestic duties they are rejected by their husbands. Transmission is by direct contact, through fomites, and via insect vectors such as flies.

Chlamydial trachomatis conjunctivitis of the newborn (sometimes referred to as infant inclusion conjunctivitis) is frequently caused by *Chlamydia* from the mother’s cervix that infects the eyes of the newborn. The word “inclusion” was used because microscopic cyst-like structures (inclusions) were found in specimens of this disease in the early 1900s. It took almost 60 years before the *Chlamydia* organisms were isolated from these inclusions. The serotypes responsible for newborn conjunctivitis are usually the same as those responsible for adult inclusion conjunctivitis.

Adult inclusion conjunctivitis usually occurs in sexually active young adults and affects both eyes. Transmission of the *Chlamydia trachomatis* organism is commonly caused by oral-genital sexual practices or hand-to-eye contact. There have been reported outbreaks of indirect transmission in inadequately chlorinated swimming pools. The chlamydial agent is usually found in the urethra of the male and cervix of the female.

Bacterial Conjunctivitis. Because most western physicians tend to treat all conjunctivitis with **antibiotics** and seldom culture the material that seeps from the eye, the actual incidence of bacterial conjunctivitis is unknown. Many bacteria have the ability to cause conjunctivitis; the most common are *Streptococcus pneumoniae*; *Corynebacterium diphtheriae*; enteric Gram-negative rods; and *Haemophilus*, *Moraxella*, and *Neisseria* species. Most cases start unilaterally but soon spread to the other eye.

Hyperacute bacterial conjunctivitis is marked by copious yellow pus (purulent exudate). Any severely purulent exudate should be cultured and treated immediately with antibiotics because it may indicate an early stage of meningococcal conjunctivitis in children. Delay could result in septicemia and/or severe injury to the eye. The most common organisms for hyperacute conjunctivitis are *Neisseria gonorrhoeae*, *kochii*, and *meningitides*.

Acute bacterial conjunctivitis, sometimes called catarrhal (inflammation of mucus membrane with increased mucus) conjunctivitis, frequently occurs in epidemic form. In temperate climates, the most common etiological organism is *Streptococcus pneumoniae*, but in warmer climates it is usually caused by *Haemophilus aegyptius*. Chronic bacterial conjunctivitis is caused by acute or subacute conjunctivitis that was untreated or inadequately treated.

Ophthalmia neonatorum is a general term used to describe conjunctivitis of the newborn from multiple causes such as gonorrhea and chlamydia infections from the mother's vagina. All newborn infants should receive preventive treatment (prophylaxis) against this form of conjunctivitis. Silver nitrate eye drops have traditionally been used and are very effective against gonococci conjunctivitis, but they are not effective against *Chlamydia trachomatis* infections, which are more common in the United States. In recent years, treatment with tetracycline or erythromycin eye ointments has replaced treatment with silver nitrate. Povidone-iodine eye drops are used in many areas of the world.

Parasitic Conjunctivitis. In underdeveloped areas of the world, parasitic diseases Leishmaniasis and Microsporidiosis cause parasitic conjunctivitis. The tsetse fly, famous for causing **sleeping sickness**, can cause conjunctivitis. Previously uncommon **protozoa** have recently been found in the conjunctiva of patients with **AIDS**.

Infectious conjunctivitis runs the gamut from "simple pink eye" (uncomplicated viral and/or bacterial conjunctivitis), which can be irritating but self-limiting, to trichiasis, a painful, debilitating blindness leading to rejection by society. Many forms of conjunctivitis have no effective treatment or are traditionally over-treated in western society, whereas millions of people in underdeveloped societies lose their eyesight for lack of simple, effective, and inexpensive treatments. *See also* Children and Childhood Epidemic Disease; Contagion and Transmission; Meningitis; Personal Hygiene and Epidemic Disease; Poverty, Wealth, and Epidemic Disease.

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THOMAS QUINN

CONSUMPTION. *See* Tuberculosis.

CONTAGION AND TRANSMISSION. The *Dictionary of Epidemiology* defines "contagion" as "the transmission of infection by direct contact, droplet spread, or contaminated fomites." Strictly speaking, rabies is a contagious disease, but by convention we usually do not refer to human rabies as such because it is uncommonly transmitted from human to human. "Transmission" refers to the specific means by which infectious agents cause infection. Contagion is thus a particular type of infectious disease transmission. Unfortunately these terms are often used loosely.

Because “transmission” implies either two hosts or an **environmental** source and a host, the host/source that transmits and the host that acquires infection, and because the means of transmission may be different from the means of acquisition (e.g., so-called fecal-oral spread) it is helpful to speak of “transmission/acquisition,” or at least to keep the concept in mind. Some epidemiologists separate mechanisms of transmission into direct and indirect, based not only upon how the infection is transmitted, but also on how it is acquired (e.g., **inoculation** of cytomegalovirus during passage through the birth canal [direct transmission], or acquisition of **yellow fever** from the bite of an *Aedes aegypti* mosquito [indirect transmission]). Confusingly, transmission of diseases through large “droplet nuclei” that may arise from coughing or sneezing has been categorized as direct transmission, whereas acquisition of infectious agents from small aerosolized particles has been categorized as indirect transmission without regard to source. Moreover, respiratory agents such as “common cold” **viruses** that can be spread by droplet nuclei (direct transmission) can also be spread via contaminated fomites (indirect transmission). Many infectious agents can be transmitted by both direct and indirect means.

In general, when a human infection is acquired from another human by touching, kissing, sexual relations, passage through the birth canal, transplacentally (across the placenta), or via inhalation of infectious particles emitted from another person in close proximity (usually less than 1 to 2 meters)—all examples of direct transmission—we refer to the disease as being contagious. As noted, this provisionally sets aside as a special case animal to human spread, which by convention we usually do not refer to as contagious. Nevertheless, diseases such as rabies are said to be contagious when transmission occurs from animal to animal. When a human infection is acquired from an insect or environmental source (i.e., when the infectious agent is being maintained or is amplified in that source) we speak of noncontagious (indirect) spread. Noncontagious spread is usually broken down into vehicle-borne (e.g., **waterborne**, foodborne, fomite-mediated) and vector-borne, with the latter category referring to either mechanical or biological transmission by ticks, mosquitoes, sandflies, or other **insects**. (Biologic transmission refers to the support of replication and usually amplification of the infectious agent.)

Examples of contagious diseases include those acquired by direct inoculation (e.g., **syphilis** and other sexually transmitted diseases), by droplet acquisition (e.g., **influenza**, **measles**, **pneumonic plague**), and transplacentally (e.g., rubella). Examples of noncontagious infectious diseases include vector-borne diseases (e.g., yellow fever, **malaria**, **Lyme disease**, and flea-borne **bubonic plague**), vehicle-borne diseases (e.g., waterborne **cholera**, fomite-borne acute hemorrhagic **conjunctivitis**, foodborne salmonellosis), and airborne infection (e.g., coccidiomycosis, New World **hantaviruses**).

Development of Concepts of Contagion in the Twentieth Century. The discovery of the microbial causes of many diseases in the last quarter of the nineteenth century, stimulated by Casimir Davaine (1812–1882) and **Robert Koch’s** anthrax “co-discovery” (i.e., identification of the organism, characterization of its life cycle, and experimental determination of the natural history of infections) led to rapid advances. During this period there was a series of microbiological triumphs (e.g., establishment of the etiologies of **tuberculosis**, plague, and cholera) that led to epidemiologic understanding of infectious diseases’ transmission and acquisition. By the early 1900s, when the vector-borne etiologies of malaria, yellow fever, and **dengue** had been established, and when “filter-passing” infectious agents (particularly viruses) had been

identified, the framework was largely complete, and our understanding of the principles and mechanisms of infectious disease transmission were recognizably similar to those of the very early twenty-first century. With this knowledge came new public health control measures and clinical therapies, including vaccines (e.g., rabies, 1885), passive immunotherapies (e.g., **diphtheria** antitoxin, 1890), and environmental control (e.g., controls for yellow fever).

Yet it was not a time of complacency. A variety of methods and standards had to be worked out. For example, immunologic research led to serologic (blood) tests of **immunity** to infectious agents, and these tests led to the realization that **bacteria** and viruses were incredibly diverse antigenically. Such diversity had profound implications for treatment and prevention. Treatment of life-threatening pneumococcal disease with immune serums was complicated by the fact that different immune serums had different abilities to treat disease caused by different pneumococcal capsular polysaccharide types. In the first two decades of the twentieth century, four different polysaccharide types were identified, with a fifth category (pneumococcus Type IV) representing a number of different organisms that would have to be (and eventually were) distinguished from each other.

Among other important concepts established in this era was the realization that the presence of an infectious disease did not exactly correspond to the potential for contagion. Humans and animals could transmit a number of infectious diseases before they themselves became ill (i.e., during incubation), as well as after they had gotten better. Moreover, people could become carriers of some organisms, potentially transmitting disease directly or by shedding into the environment, continually or intermittently, over long periods of time.

Related to this was a better understanding of environmental introduction and persistence of infectious organisms such as *Vibrio cholerae* in drinking water. Indeed it was during this era that scientists came to understand why it had taken so long to understand and accept contagionism. Looking for general principles that would apply to all of the important epidemic diseases (e.g., cholera, **typhoid**, and plague), they had not appreciated the complexity of the problem. The same diseases could be transmitted directly from person to person but at the same time transmitted indirectly and at a distance between persons who had had no contact (e.g., via contaminated water [cholera, typhoid] or insects [plague]). Anthrax, an extreme example, was transmitted to humans by three distinct mechanisms to cause three distinct diseases (cutaneous, gastrointestinal, and pulmonary anthrax).

Taken as a whole, this new understanding of contagion and disease transmission/acquisition created many challenges for public health. That healthy people could transmit deadly diseases to others, for example, created a difficult new role for public health, as illustrated by the case of “Typhoid **Mary**” **Mallon**, whose involuntary incarceration by public health officials created a highly charged controversy that reverberates today in cases of **AIDS**, **XDR tuberculosis**, and other transmissible diseases.

Also of note was the development in the early twentieth century of the concept of microbial coinfection. Studies of immigrants housed at Ellis Island in New York, for example, revealed that crowding predicted not only attack rates from specific infectious diseases, but also mortality rates. Subsequent research demonstrated the interaction of different diseases in producing mortality: for example the mortality from measles was much higher in children who also had diphtheria. This phenomenon was shown most dramatically in

1917 during the epidemics of measles in U.S. Army training camps. In a number of camps the high death rates of healthy young men from measles were directly attributable to previously asymptomatic carriage of streptococci. A year later, during the **influenza pandemic of 1918–1919**, the identical phenomenon was found and exhaustively studied, leading to the almost universal conclusion that most deaths during the influenza pandemic were associated with, and probably caused by, severe secondary bacterial pneumonias (largely pneumococcal and streptococcal, with a smaller number of outbreaks associated with staphylococci, *Bacillus* [*Haemophilus*] *influenzae*, or other pathogens). Concepts of transmission and contagion as they related to actual disease risk had thus become bewilderingly complex; preventing diseases required not only public health knowledge but also immunologic and microbiologic efforts backed up by considerable experimental **animal research**.

Contemporary Concepts and Usages. During the last century, a solid understanding of disease transmission allowed identification and characterization of a number of new and newly recognized diseases. For example, the infectious nature and the several modes of transmission of AIDS (e.g., sexual, needle-borne) made it clear that AIDS was caused by an infectious agent several years before Human Immunodeficiency Virus (HIV) was identified. The 2003 SARS outbreak featured an epidemiologic picture so clear in indicating respiratory and/or close-contact transmission of an infectious agent that the epidemic was quickly stopped by familiar public health measures even before the causative virus was identified. Many similar examples can be given.

Contagion itself, and many other aspects of infectious disease transmission, have become common knowledge to almost everyone, including children, who after a certain age readily accept the wisdom of parental proscriptions against eating something that has fallen on the floor or kissing an aunt with a cold, and in favor of washing their hands after using the bathroom.

In his famous 1943 book, C. E. A. Winslow asked why it had taken so long to establish contagion as a mechanism for disease acquisition. There are probably a number of answers, not the least compelling of which is that events often look clearer in hindsight. Other factors probably include inability to imagine subclinical infection, transmission that occurs either before disease onset or after disease resolution, and the fact that a number of infectious agents can be transmitted by multiple means (e.g., cholera by contaminated water and by contaminated bed linens; **smallpox** by exhaled droplets and by contaminated clothes; plague by flea bites and by exhaled droplets; anthrax by inhaled spores, by ingested meats, and by direct skin inoculation).

From the organism's point of view, survival ultimately depends on access to animal or human hosts, and there may be many different roads and byways to get there. Direct person-to-person contagion via a single mechanism of transmission/acquisition (e.g., measles, influenza) may at first seem ideal, but it can be problematic if the organism in question kills or incapacitates its host, encounters uncrowded populations, or can be defeated by mechanical means (e.g., face masks). Organisms that cause human disease generally exist in complex microbial ecosystems in which survival may depend on flexibility and on ability to adapt to new hosts, to survive environmental differences of temperature and humidity, and to infect by more than one route. Each major infectious disease—plagues, pestilences, and inconsequential diseases alike—represents a complicated interaction between the host, microbial agent, and environment, in which the mode of transmission is but one facet of the negotiated picture. *See also* Immunology.

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DAVID M. MORENS

CONTAGION THEORY OF DISEASE, PREMODERN. Long before the emergence of modern bacteriology, the idea of **contagion** (from “contact”) was generally recognized by many human societies. Where groups accepted the idea that illness could be transmitted by “contact,” there developed a certain wisdom that shaped practices for protecting the health of the community against the dangers of diseases. But premodern concepts of contagion, and the customs they underpinned, showed a great deal of variation. In ancient Mesopotamia, for instance, taboos against touching the sick were based on a religio-magical belief that evil spirits possessing the ill could be transferred to a new victim by touch, whereas Indian medicine held that merely looking at a person might constitute contact enough for transferal. Although the transmissibility of **epidemic** diseases like the plague and the danger of remaining in a disease-stricken area were accepted, contagion played a minor role in India’s **Ayurvedic** epidemic disease theory and medicine. A survey of traditions illustrates the variety of possible beliefs and practices of contagion.

Ancient Hebrew medicine recognized the transmissibility of certain diseases, which led to the adoption of regulations regarding personal and public cleanliness; for instance, those who suffered from **leprosy** were considered unclean, and their clothing was burned.

Traditional **Chinese disease theory and medicine** revealed a degree of awareness about contagion. During the **smallpox** outbreaks in premodern China, it was observed that close contact with the sick caused infection. The Qing imperial family built shelters of isolation to prevent contagion. Medical texts recommended staying away from the sick bed, the corpse, and the coffin; avoiding noxious odors; and covering the nostrils and ears to prevent the penetration of poisonous vapors into the body.

Greco-Roman medical theories and practices also display an understanding of contagion. In his account of the **Plague of Athens**, Thucydides (c. 460–395 BCE) mentions the transmission of disease from one person to another. **Galen** warned against the dangers of having contact with the sick. Despite awareness of contagion, however, epidemic diseases were usually blamed on corruption of the **air** and **miasma**, or on exhalations rising from putrefying ditches, city garbage, human **corpses**, and rotting animals. Postulated by **Hippocrates** and further developed by Galen, this theory was combined with the **humoral theory** to explain the occurrence of epidemics. Belief in the association between **air and epidemic disease** was firmly established, holding that when air lost its normal composition, its substance and qualities putrefied, and it consequently posed a risk of disease to all who inhaled it.

Islamic disease theory and medicine embraced a vaguely defined awareness of contagion, both through direct person-to-person contact and through **heredity**, though Muhammad (570–632) explicitly denied its role in disease transmission. **Avicenna** observed that visible contact was not necessary for transmission in all cases: someone who

ENGLISH NURSE FLORENCE NIGHTINGALE AGAINST CONTAGION THEORY (1859)

The idea of “contagion,” as explaining the spread of disease, appears to have been adopted at a time when, from the neglect of sanitary arrangements, epidemics attacked whole masses of people, and when men had ceased to consider that nature had any laws for her guidance. Beginning with the poets and historians, the word finally made its way into medical nomenclature, where it has remained ever since, affording to certain classes of minds, chiefly in the southern and less educated parts of Europe, a satisfactory explanation for pestilence and an adequate excuse for non-exertion to prevent its recurrence.

And now, what does “contagion” mean? It implies the communication of disease from person to person by *contact*. It presupposes the pre-existence of certain germs like the sporules of fungi, which can be bottled up and conveyed any distance attached to clothing, to merchandise, especially to woolen stuffs, for which it is supposed to have an especial affection, and to feathers, which of all articles it especially loves—so much so that, according to quarantine laws, a live goose may be safely introduced from a plague country; but if it happens to be eaten on the voyage, its feathers cannot be admitted without danger to the entire community. There is no end to the absurdities connected with this doctrine. Suffice it to say, that in the ordinary sense of the word, there is no proof, such as would be admitted in any scientific inquiry, that there is any such thing as “contagion.”

From her “Notes on Hospitals,” quoted in *Medicine and Western Civilization*, edited by David J. Rothman, et al. (New Brunswick, NJ: Rutgers University Press, 1995) pp. 362–363.

stared at a victim of **conjunctivitis** might catch the ailment. Islamic medical writers adopted and developed Galenic ideas of disease transmission rooted in the idea of miasma. Leprosy, elephantiasis, scabs, **consumption**, smallpox, **measles**, and various forms of plague were cited as transmissible diseases in Islamic medical literature.

After the Crusades (begun in 1096), Europe came to be devastated by leprosy, **typhus**, smallpox, and especially **bubonic plague**. Starting from the mid-fourteenth century, several waves of plague struck Europe, killing at least a quarter of the population during the initial outbreak called the **Black Death** (1347–1352). The idea that plague was transmitted through contact was widespread. But it was also believed that talking to or looking at the sick or the dead, or encountering their clothing or dwellings, could confer the disease. This prompted the establishment of public health boards or health magistracies and the implementation of precautions such as the **cordons sanitaires** and practices of **disinfection**. **Quarantine** measures were adopted in several Mediterranean port cities, requiring that all arriving ships and immigrants wait 30 or 40 days before entering a city. Starting from the fifteenth century, **pest houses** were

constructed to isolate those who suffered from the plague. These were clearly meant to isolate sick individuals from the healthy public.

During the sixteenth century, **diphtheria**, **measles**, and, especially, **syphilis** and **gonorrhoea** became common in Europe. The first major epidemic of syphilis broke out among the sailors of Columbus returning from the New World, and then spread to Europe. It was understood that syphilis was transmitted through contact. **Girolamo Fracastoro**, a **physician** from Verona, speculated about the nature of contagion and suggested that syphilis spread through sexual contact. In 1546 he wrote a treatise (*De Contagione*) in which he explained disease transmission by invisible “seeds” of disease, which he called *seminaria*. He suggested that *seminaria* were transferred to the air from the sick, where they would multiply and move to another person. According to Fracastoro, there were three different types of contagion. The first occurred only through direct contact (e.g., scabies, tuberculosis). The second occurred through indirect contact with fomites deposited on intermediary objects used by the sick. The third occurred at a distance (e.g., pestilential

fevers, tuberculosis, smallpox). Although the ideas of contagion through contact with the ill and contagion through contact with clothing or wood touched by the sick were hardly new, Fracastoro was among the first to advance an account of indirect contagion in terms of a substance deposited on intermediary objects.

Until the microbiological and microscopic revolution of the nineteenth century, ideas along Fracastoro's lines were widely accepted. In fact, up until the mid-seventeenth century, disease was broadly considered to result from a set of causes drawn from a systematic hierarchy, and these causes could be combined in various ways. At the top of the hierarchy of causes there was God, without whom neither epidemics nor cures would be possible. After God, cosmic influences of the stars and astronomic events were accepted as causes of disease. God, stars, and planets all exercised indirect influences through a more direct agent: the air, a substance that, once corrupted, could damage the vital powers of the living when breathed. At the bottom of the hierarchy were people, who, either through natural dispositions or through lifestyles, were capable of falling prey to a disease.

Around the mid-sixteenth century, when Fracastoro wrote his work on contagion, a lively discussion was going on in learned medical circles regarding the nature of contagion, its mechanisms, its degree in different diseases, and its relationship to putrefaction. Although Fracastoro used the concept of seeds innovatively to explain contagion, the concept itself was nothing new to his contemporaries, as such ideas were available through the printed versions of ancient and medieval works. In fact, in ancient Greco-Roman medical writings, seeds of diseases were believed to remain as residuals in the body of the sick, even after the symptoms disappeared, and they could be reactivated as a result of a wrong regimen of diet and exercise.

Within a generation Fracastorian principles began to circulate among the learned, partly in the context of the plague of Venice in 1555–1557. Although most plague treatises written immediately after the Black Death said nothing about contact or contagion, a majority of later authors discussed plague in the terms set by Fracastoro. His views and terminology were quickly integrated into mainstream knowledge about epidemics, especially regarding the plague, measles, and typhus. What would become a modern theory of contagion became possible with the invention of the **microscope** and its use, initially by **Antony van Leeuwenhoek**, to investigate what are now called microbes. However, it was only to be two centuries later that a relationship between microbes and diseases would be accurately established. The **germ theory of disease**, proposing that small organisms were responsible for causing infectious diseases, acquired general acceptance with the pioneering research of **Louis Pasteur** and **Robert Koch**. Soon afterwards, the **bacteria** causing **tuberculosis**, **cholera**, **plague** and many other diseases were discovered. See also *Astrology and Medicine*; *Leprosy, Societal Reactions to*; *Magic and Healing*; *Mallon, Mary*; *Personal Hygiene and Epidemic Disease*; *Religion and Epidemic Disease*; *Scientific Revolution and Epidemic Disease*; *Syphilis in Sixteenth-Century Europe*.

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NÜKHET VARLIK

CORDON SANITAIRE. *Cordon sanitaire*, a French phrase meaning "protective line," is a barrier designed to prevent the spread of a disease by severely restricting the movement of people and goods between areas affected by disease and those where the disease is not present. The cordon may be intended to contain an outbreak of disease within its boundaries or to keep an epidemic out of the enclosed area. The earliest known *cordons sanitaires* were established during the late fifteenth century as Italian city-states tried a variety of methods, including **quarantine**, to battle the **bubonic plague**. *Cordons sanitaires* became a common tool to combat not only plague, but also **sleeping sickness, cholera, typhus, influenza, yellow fever**, and a host of other **epidemic** diseases.

For hundreds of years, the theory behind the sanitary cordon was that infected people and objects that had been in contact with them could spread the targeted disease. In most cases, the disease in question, such as bubonic plague, was not actually being spread by contagious individuals, but cordons were often nonetheless effective because they inadvertently blocked the passage of the actual vectors of disease, such as rat fleas.

Once the etiology of such epidemic diseases as plague, yellow fever, and cholera was understood, cordons became far less common, replaced by less burdensome, more cost-effective disease management tools. They did not disappear entirely, however, because they could be effective against diseases such as influenza that were actually spread by human contact. In other instances, cordons were modified to be more useful in the prevention of epidemic disease. For example, after World War I (1914–1918), an Allied sanitary cordon on Poland's eastern border was designed to thwart the spread of lice-borne typhus, which was then raging in the new Soviet Union. Travelers were not allowed to pass through the cordon without being bathed and deloused and having their clothing sterilized. The delousing was an effective component in the campaign against typhus, as it attacked the actual carrier of the disease.

European Cordons Sanitaires. Perhaps the best-known *cordon sanitaire* is the voluntary isolation of the English village of Eyam during a seventeenth-century epidemic. Late in 1665,

during the **Great Plague in London**, plague struck the village, supposedly brought in from the capital by fleas hitchhiking on a shipment of cloth delivered to the village tailor, who was the first to die. When casualties started to rise in the spring of 1666, the villagers, at the urging of their young minister, Reverend William Mompesson (d. 1709), and his predecessor, Rev. Thomas Stanley (d. 1670), made the noble decision to isolate themselves in hopes of preventing the spread of plague to other communities in the Derbyshire area. A few wealthier residents left or sent family members away before the village closed itself off, but approximately 350 shut themselves in. A perimeter of stones was laid out surrounding the village and no one passed the boundary in either direction until November, when the pestilence had run its course. Neighboring communities provided food for Eyam, leaving supplies in designated locations along the boundary cordon and receiving payment in coins “disinfected” by running water or vinegar. Mompesson’s wife Catherine died during the epidemic, but he survived to raise their children, who had been sent from the village prior to the imposition of the cordon. Only one in four residents survived, but the plague did not spread to the rest of the district.

Historically, such self-imposed cordons were exceptional; usually a *cordon sanitaire* was imposed by a government authority that used military forces to enforce the boundary restrictions. Because of their burdensome nature, sanitary cordons were usually temporary affairs, targeting a particular outbreak of disease. In the mid-1700s, however, the Habsburg rulers of Austria set up the first permanent military *cordon sanitaire* along its long frontier with the Ottoman Empire. By 1770 soldiers were stationed in sentry posts located no more than a musket-shot apart for a thousand-mile stretch, with larger forts situated at strategic locations. People and goods could only cross into Austrian territory at designated checkpoints with quarantine stations. Cotton and wool were held in storehouses for weeks, with peasants paid to sleep on the bales and monitored to see if they showed signs of disease. Other goods, including letters, underwent **fumigation** with burning sulphur before passing through the checkpoint. Travelers were quarantined for 21 days under ordinary circumstances and up to 48 days when there was confirmation of plague being active in Ottoman territory. The cordon was maintained until 1871, despite decades of complaint that the travel restrictions were an economic burden with little medical justification. There were no major outbreaks of plague in Austrian territory after the *cordon sanitaire* was established, whereas the Ottoman Empire continued to suffer frequent epidemics of plague until the mid-nineteenth century.

Europeans used *cordons sanitaires* as part of their strategy to fight other epidemic diseases besides plague. For example, the French response to an outbreak of yellow fever in Spain in the 1820s was to set up a cordon in the Pyrenees Mountains, manned by 30,000 troops, to prevent the disease from sweeping north. Travelers could only cross the barricade at three approved quarantine sites. During the 1830 cholera outbreak in Russia, Moscow was surrounded by a military cordon, most roads leading to the city were literally dug up to hinder travel, and all entrances to the city save four were sealed. Moscow and other cities found cholera immune to the barrier approach, strengthening a growing sense that the psychological and economic hardships presented by a sanitary cordon outweighed the health benefits.

Colonial Cordons Sanitaires. When Europeans began to establish colonies around the globe, they applied familiar tactics such as quarantine and establishment of *cordon sanitaires* against the epidemic diseases they encountered, even though there was considerable

debate over the relative efficacy of the contagionist and sanitarian approaches to public health. In colonial Asia and Africa, there were accusations that *cordon sanitaire* was imposed as a means of social control of native people, rather than as a truly effective medical tool. For example, the cordon utilized in an attempt to control sleeping sickness in the Belgian Congo in the early 1900s played havoc with native African social and economic life, whereas Europeans living in the region were largely unaffected by its strictures. In China, the French and other European powers established colonial enclaves surrounded by *cordons sanitaires* designed to protect themselves against diseases endemic in the native population. The British seemed to rely heavily on cordons and quarantines in both Egypt and India to combat such diseases as plague and cholera, until the measures proved overly disruptive of their economic interests.

American Cordons Sanitaires. Bubonic plague struck the American territory of Hawaii in 1899, triggering a *cordon sanitaire* around Honolulu's Chinatown district, where the disease first appeared. The Hawaiian National Guard was tasked with maintaining a cordon around a 35-acre area that housed 10,000 Chinese, Japanese, and native Hawaiian residents, a quarter of Honolulu's population. Commerce in the city was in turmoil, as immigrants could not reach their jobs. Food shortages soon developed within the quarantined area because residents were unable to fish or get to their farms. Asians working as live-in servants were not allowed to visit relatives or friends in the Chinatown district and were further required to take a daily public shower at a "disinfection station," a humiliation that illustrates the racial prejudice that underlay many of the quarantine regulations.

When cleansing the homes of plague victims with carbolic and sulfuric acid proved ineffective, unsurprisingly, in halting the spread of the disease, the Honolulu Fire Department began the controlled burning of buildings. On January 20, 1900, a fire set in a building where a plague victim had died got out of control and most of Chinatown was destroyed. As Asians rushed to escape the fire, they were at first turned back by the National Guard and white vigilantes maintaining the cordon. Finally, one exit from the district was opened, allowing terrified residents to evacuate the fire zone. Eight thousand people left homeless spent the next several months living in churches or warehouses as white city officials decided whether to rebuild their community or to turn the land over for commercial development. Many bitterly insisted that the government had deliberately allowed the fire to spread, a conviction only strengthened when one local newspaper printed an editorial celebrating the fire for wiping out the plague while simultaneously clearing off valuable real estate.

As the third plague pandemic reached the shores of the western United States, Asians were again singled out for special treatment. On March 6, 1900, a Chinese immigrant was found dead of bubonic plague in a hotel in San Francisco's thriving Chinatown. Members of the city's Board of Health moved with surprising swiftness; the very next day, March 7, they established a *cordon sanitaire* around the 12-block Chinatown district. Police officers manning the cordon allowed whites living or working within the quarantined area to leave while forcing more than 10,000 Asians to remain inside its boundaries. Negative press and vocal complaints by Chinese business leaders convinced city officials to drop the cordon after only two days. However, it was reinstated in May when more cases of plague began to appear among Chinese workers.

Between March 1900 and July 1901, there were 39 confirmed cases of death from bubonic plague in San Francisco, with 35 of the deceased being Chinese. Although health



AT THE GATES.

Our safety depends upon official vigilance.

"At the Gates: Our safety depends upon official vigilance." The specters of cholera, yellow fever, and smallpox recoil in fear as their way through the Port of New York is blocked by a barrier reading "quarantine" and an angel whose shield reads "cleanliness." New York, Harper and Brothers, September 5, 1885. Courtesy of the National Library of Medicine.

officials argued that the blockade was necessary to prevent outbreaks of the disease from spreading beyond Chinatown, race, rather than residency, seemed to be the determining factor regarding whether someone was subject to quarantine, as white Chinatown residents were free to travel outside the cordon. Asians living within the cordon were particularly alarmed when the Board of Health announced it had purchased land on an island in San Francisco Bay and was considering a plan to relocate Chinese and Japanese residents there and to raze Chinatown in the interest of public health. Leaders of the Chinese community went to court in June, complaining about the selective enforcement and suggesting that city officials had not made adequate arrangements to provide food and other essentials to those inside the *cordon sanitaire*. Judge William Morrow (1843–1929) ruled in their favor, ordering an end to the discriminatory cordon and to any plans to evacuate or demolish Chinatown. No major outbreak of plague subsequently developed in the city, although there continued to be deaths from the disease, particularly in the Chinese community.

In 1882, in response to a virulent outbreak of yellow fever in Brownsville, Texas, and northern Mexico, a *cordon sanitaire* was established 180 miles north of the city, terminating at the Rio Grande to the west and the Gulf of Mexico to the east. People traveling north had to remain quarantined at the cordon for 10 days before they were certified disease-free and could proceed. Similar cordons were used elsewhere in the United States to combat the spread of yellow fever, such as in Jacksonville, Florida, in 1888 and Brunswick, Georgia, in 1893. During the **influenza pandemic of 1918–1919**, sanitary cordons were part of the quarantine measures employed by many American communities, including Fairbanks, Alaska; Princeton University; and tiny Gunnison, Colorado (population 1,329).

Whether sanitary cordons will play a role in future pandemics is a matter of controversy. The ease of modern travel increases the speed at which carriers can unwittingly transmit disease before an effective cordon could be established, and maintaining a *cordon sanitaire* around a large modern city for any length of time would be a complex logistical nightmare. However, although both the **World Health Organization (WHO)** and the U.S. Department of Health and Human Services advise against the use of cordons except in unique circumstances, many local and national emergency preparedness plans for communicable diseases still contain provisions for *cordons sanitaires*. See also *Capitalism and Epidemic Disease*; *Cholera: First through Third Pandemics, 1816–1861*; *Colonialism and Epidemic Disease*; *Contagion Theory of Disease, Premodern*; *Disease, Social Construction of*; *International Health Agencies and Conventions*; *Medical Ethics and Epidemic Disease*; *Napoleonic Wars*; *Personal Liberties and Epidemic Disease*; *Plague and Developments in Public Health, 1348–1600*; *Plague in San Francisco, 1900–1908*; *Race, Ethnicity, and Epidemic Disease*; *Severe Acute Respiratory Syndrome (SARS)*; *Trade, Travel, and Epidemic Disease*; *War, the Military, and Epidemic Disease*.

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TERESA LESLIE

CORPSES AND EPIDEMIC DISEASE. During and in the wake of an outbreak of epidemic disease, dealing with excessive numbers of human corpses can prove problematic. As the numbers of the dead increase, the task of burying or otherwise disposing of bodies can overwhelm those who survive. Traditional funeral customs may become impossible or be deemed dangerous to follow. Corpses left unburied or hastily dealt with can become a threat to public sanitation. Likewise, diseased human and animal corpses can be a vector for the further spread of disease. Under epidemic conditions, corpses must be managed carefully in order to prevent conditions from worsening. For physicians, they have also proven to be important sources of information about specific diseases.

During the **Black Death** and subsequent outbreaks of **bubonic plague** in Europe, the number of corpses overwhelmed urban areas in particular. In Tudor and Stuart London, the task of determining whether a person had died of the plague fell to “searchers,” usually older women, dependent upon pensions, who were paid a small amount by their parish to inspect the bodies of those who died. If the searcher determined that a person had indeed died of plague, authorities would **quarantine** the rest of the victim’s family, locking them in their home, which often meant that they would also contract the disease and die.

Historically, the capacity of corpses to spread epidemic disease—real or imagined—was exploited for purposes of **biological warfare**. Among the most infamous stories of such activity was an account reported by Gabriele de Mussis (fl. c. 1345), whose work *Historia de Morbo* is the principal contemporary source on the arrival of plague in Europe. De Mussis claimed that the plague entered Europe through the city of Kaffa in 1346 (now Feodosia in the Ukraine), when the Mongol army attacking the city was struck by **plague**. Although they were losing the siege, the Mongols allegedly used catapults to fling the corpses of those who had succumbed to plague into the city. De Mussis reported that the **air** and **water** in Kaffa became infected, and the townspeople succumbed to the plague. According to some plague historians, it is more likely that the town’s population was infected when rats carrying the plague entered the city and triggered an epizootic, causing the rat fleas to move on to human hosts and infect them. However, without doubt, the plague-corpse missiles caused substantial terror and concern among Kaffa’s populace and may have carried plague-ridden fleas.

Burial practices during major plague outbreaks also shifted radically. In preparation for the arrival of plague in the late 1340s, Sir Walter Manny (c. 1310–1372) and Ralph Stratford (c. 1300–1354), bishop of London, each purchased fields outside of the city of London in which tens of thousands of corpses were buried. Mass graves became the norm in later outbreaks of the plague as well. English novelist Daniel Defoe (c. 1660–1731) reported that during the **Great Plague of London** (1665–1666), just one of the enormous pits dug by the buriers or “bearers” of the dead measured 40 feet by 18, and was 18 feet deep. Defoe wrote that more than 1,100 bodies were thrown into it. Plague outbreaks such as the Great Plague disrupted customary mourning rituals or interrupted them altogether. During the 1665 outbreak, the orders issued by the city magistrates included stipulations that no one was to accompany a corpse to the churchyard and that an infected corpse could not lie in the church itself. No sermon was to be delivered, and the bodies were to be buried only between sunset and sunrise.

Other epidemic diseases have caused similar disruptions to burial practices. Ebola, an extremely lethal strain of **hemorrhagic fever**, is known to be active for several days after its host has died. The U.S. **Centers for Disease Control and Prevention** recommend that



“The Plague in the City of Marseille in 1720.” Depiction of a waterfront scene with victims, dead and dying, and the removal of infected corpses. Original painting by J. B. De Troy. Courtesy of the National Library of Medicine.

burial practices be radically altered in cases of Ebola virus. Recommended practices include spraying the body with bleach and burying it in a hole at least 2 meters deep. Researchers have determined that although Ebola might not be readily transmitted during certain funeral rituals, sharing a meal with fellow mourners at funerals creates a strong risk factor for acquiring the disease.

Certain other cultural practices have aided the spread of epidemic disease. Some epidemic diseases are spread through the practice of eating corpses. Among the Fore tribe in Papua New Guinea, the disease *kuru*, related to “mad cow disease” or bovine spongiform encephalopathy (BSE) is known to have spread through the practice of eating the dead. Because women among the Fore have traditionally eaten the brain tissue of the dead, they have suffered from a higher rate of the disease than men. There are also indirect ways to consume human remains. Some researchers argue that BSE entered Britain with the importation of animal bone and tissue from India for use as cattle feed. Human remains, believed by some researchers to include tissue from sufferers of vCJD or Creutzfeldt-Jakob disease, the human variant of BSE, was thought to be mixed with the animal tissue. Human remains commonly wash up on the shores of the major river systems in India. Although burial practices there tend to involve cremation, many families are too poor to afford enough wood to burn the entire bodies of their loved ones and must settle for partial cremation. Bone collectors who work along the river shoreline then gather the human remains along with those of dead animals. Bones exported from India are ground up and included as a major ingredient in commercial cattle feed. The disease agent (an infectious

protein called a *prion*) spreads throughout the nerve tissue of the cattle, concentrating in the brain and spinal cord. Humans who consume beef infected with BSE are at risk for developing the disease themselves, especially if they consume the brain and spinal cord (often used in ground beef).

Corpses of epidemic disease victims have also provided Western doctors with important insights into effects of the disease on the body, and later of the pathogens themselves. During the Black Death, Pope Clement (r. 1342–1352) understood this and encouraged otherwise rare autopsies of plague victims. During later plague outbreaks, physicians and surgeons conducting risky dissections of victims contracted the disease. **Alexandre Yersin's** breakthrough insights into the bubonic plague pathogen followed his successful struggle to obtain corpses from British authorities in Hong Kong. *See also* Hospitals and Medical Education in Britain and the U.S.; Hospitals since 1900; Medical Education in the West, 1100–1500; Medical Education in the West, 1500–1900; Plague and Developments in Public Health, 1348–1600; Public Health in the Islamic World, 1000–1600; Religion and Epidemic Disease; Urbanization and Epidemic Disease; War, the Military, and Epidemic Disease.

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MELISSA SMITH

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DEMOGRAPHIC DATA COLLECTION AND ANALYSIS, HISTORY OF. The study of infectious disease is largely the study of demography, of patterns of human settlement and population characteristics that promote or inhibit the propagation and subsequent spread of this or that disease agent. It was in the collection of demographic data on disease incidence in populations that causes of disease were first studied and the social characteristics of disease events revealed.

A very early example of the systematic accumulation of national population data in Europe is the famous *Domesday Book* commissioned by William the Conqueror (1028–1087) in 1086 to assess patterns of land ownership for taxation purposes. It was so named because it was said to be as comprehensive as the definitive records that would be used to call all to account on Judgment Day: “there was no single hide nor a yard of land, nor indeed one ox nor one cow nor one pig which was left out.”

From the fourteenth to the eighteenth century, most European birth and death records were kept at the parish level and were at best haphazard, though record keeping tended to improve over time. By the eighteenth century, several trends were transforming both the relationship of the state to its population and the relationship between the state and the then-evolving science of disease studies. Mercantilism and the early **Industrial Revolution** prompted vast population shifts from the countryside to the city. Rapid **urbanization** resulted in population centers of previously unimaginable sizes. The densely packed cities that resulted became centers of **epidemic** disease propagation as well as commerce, reservoirs whose effect increased as the cities grew. The result was seen as an economic threat to the extent disease limited the available labor pool. As a result, the health of citizens became a subject of economic and political interest.

At the same time, English chemist Robert Boyle’s (1627–1691) program for establishing matters of fact through the social construction of assent created the context in which science, including medical science, would seek to understand disease. This new concept

of science demanded new systems of analysis in which social and medical data were to be analyzed mathematically.

In the 1600s William Petty (1623–1687), a London **physician** and economist interested in the health of populations, coined the phrase “political arithmetic” to describe “the art of reasoning by figures upon things related to government,” and especially population health as a critical barometer of the health of the state. His friend John Graunt (1620–1674) demonstrated patterns of regularity in mortality based on a study of London’s “Bills of Mortality.” These were systematic, parish-based weekly tabulations of mortality and causes of death that began in the mid-sixteenth century and were meant to signal the onset of plague. When the numbers rose beyond an expected norm, civic and royal authorities enacted public health precautions. Published from the early seventeenth century, they also informed the public when to flee the capital and when it was safe to return. The Dutch mathematician Christian Huygens (1629–1695) took up the problem of creating a table of life expectation and, in 1693, Oxford astronomer Edmund Halley (1656–1742) published an analysis of age-at-death statistics compiled in Breslau, a German town known for its record keeping, that marked the beginnings of actuarial science.

With increasingly precise public records of births and deaths came a series of practical applications that in retrospect are the beginnings of medical demography. In 1760, Daniel Bernoulli (1700–1782) analyzed **smallpox** mortality in a manner demonstrating the increased lifespan that resulted from inoculation. In the next century, the French mathematician Adolphe Quetelet (1796–1874) collected the statistical applications of his contemporaries and predecessors to create a systematic structure that could be applied to biological and social phenomena.

The ability to analyze datasets numerically was married to improved record keeping by the state. In France, a *méthode numérique* developed with increasingly accurate public records to permit an unprecedented description of disease events within national and regional populations. In England economists and moralists like Jeremy Bentham (1748–1832) argued for both the collection of health-related data and a numerical approach to its analysis. These arguments became the life’s work of Bentham’s former secretary, the barrister **Edwin Chadwick**, perhaps the single most significant figure in the public health movement in England in the first half of the nineteenth century.

In the 1830s a series of legislative changes in England began the transformation of the traditional, local system of reportage to one based on a national system of registration districts and registration sub-districts whose registrars would be responsible for the collection of demographic and health-related data. Chadwick championed these changes, along with a modern census of all British households. **William Farr** was hired by the General Record Office in 1839 and was deeply involved with England’s first comprehensive, modern national census in 1841.

Chadwick used the resulting data in his landmark 1842 *Report* on the sanitary condition of the laboring population of Great Britain, which demonstrated the relationship between health and social circumstance in the evolving metropolitan city. Beginning with Chadwick’s, a series of seminal studies relied on nationally collected data to analyze the nature of disease and its effect on populations. In 1852, for example, during the second **cholera pandemic**, William Farr used national population data and data on cholera mortality collected by London registrars, to argue the nature and origin of cholera. In this, he was the first to demonstrate a clear relationship between regional water supplies and epidemic cholera at the metropolitan scale.

The data was sufficient to advance local studies of disease incidence as well. This data was critical, for example, to **John Snow's** famous 1855 study of an 1854 cholera outbreak in his neighborhood of St. James, Westminster, in London. Thus by the mid-nineteenth century, demographic data had become a principle medium for both studies of disease causation, and more generally, the health of populations at a range of scales. *See also* Cholera: First through Third Pandemics, 1816–1861; Plague and Developments in Public Health, 1348–1600; Sanitation Movement of the Nineteenth Century.

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TOM KOCH

DENGUE FEVER. *See* Hemorrhagic Fevers; Hemorrhagic Fevers in Modern Africa.

DIAGNOSIS AND DIAGNOSTIC TOOLS. Health care practitioners work every day like detectives with many diagnostic tools to help treat a patient's illness. The process begins when a patient presents to a clinic with a symptom or problem. By asking him questions, performing a physical exam, and running diagnostic tests, the health care practitioner will be able to construct a list of possible diagnoses, called the differential diagnosis. Depending on what is found through the diagnostic tests, a single disease process from the list may prove to be most probable. The diagnosis can sometimes be made immediately, but often a trial treatment will be necessary to decide whether the diagnosis was correct or a new diagnosis needs to be sought.

Sensitivity and Specificity. No diagnostic test is perfect. The usefulness of a given test is described in two ways: how sensitive it is and how specific it is. A sensitive test will detect a positive result in someone who has the disease. Therefore, if a very sensitive test is negative, then the disease is very likely absent. A specific test reliably detects those cases in which the disease is not present, so if the test is positive, the disease becomes more likely. A sensitive test helps to “rule out” a disease (put it lower on the list of possible diseases), whereas a specific test helps to “rule in” a disease (move it higher on the list). Each test has its own sensitivity and specificity, depending on the inherent qualities of the test itself. Another concept called pretest probability refers to the likelihood that the patient has the disease—given other known factors—before the test is even ordered. It helps to put the sensitivity and specificity of a test in context. Each factor helps determine the probability that a diagnosis is correct.

The Clinical History. Any element of a person's past history, family history, or daily life may be considered a risk factor for a potential diagnosis. Smoking, for example, is a risk factor for lung cancer, whereas traveling in the Amazon is a risk factor for contracting

exotic tropical diseases. Asking a patient to explain the story surrounding her illness, along with any mitigating factors relating to her symptoms, is central to understanding these risk factors. Similarly, an effort should be made to list and understand the patient's past medical history, including the history of diseases she has had, chronic disease she still suffers from, **vaccinations** she has received, and the history of diseases that have affected her family members. Elements of a good social history include where she lives and works; whether she is sexually active and with whom; and whether she smokes, drinks alcohol, or uses illegal drugs. Many health care practitioners believe that the vast majority of diagnoses can be made from a good history alone. In certain situations, such as during a **cholera epidemic**, in which many people are gravely affected at once, the clinical scenario and the patient's symptoms are often the only elements needed to make the diagnosis and get the patient the treatment she needs in time to save her life.

Physical Exam. For centuries, the physical exam was the only diagnostic tool that doctors had, so new and descriptive terms were invented to describe their observations: bowel sounds were called "borborygmus"; unusual sounds in the lungs were called "crackles"; sounds in the heart were called "murmurs, rubs, or gallops." New tools were developed to aid in gathering this information, such as the stethoscope, reflex hammer, and tongue depressor. Sometimes tests pioneered by a certain doctor would take on the doctor's name; for example, the multicolored spots on the inside of the mouth of a patient infected with **measles** are called "Koplik spots." The physical exam thus can be seen as a series of hands-on tests that, like laboratory tests, provide data that is only as useful as the test's sensitivity, specificity, and pretest probability. It provides important clues to what disease process is occurring, and sometimes the diagnosis can be made with these tests alone. Many of the viral exanthemas, such as measles, mumps, or rubella, can be diagnosed alone by the skin's appearance and the clinical story of how the rash developed.

Laboratory Tests. A wide variety of tests can be performed on various body samples to aid in making a diagnosis. The following describes the most useful test categories in epidemic diseases.

Body Fluid Tests. Urine, stool, cerebrospinal, abdominal, lung-pleural, joint, amniotic, and vaginal fluid can all be collected from the body and studied. The analysis of these fluids is central to the diagnosis of many epidemic diseases. For example, the chemical composition of the fluid can be quantified, leading to important clues regarding what disease process may be affecting it. Similarly, it can be observed under a **microscope** to qualify what types of blood cells predominate, or what types of pathogens are infecting it.

Chemistry Tests. Countless chemical compounds, such as electrolytes, vitamins, lipids, and drug and hormone levels, can be tested for in most body fluids. In the metabolic panel, for example, multiple key electrolytes in the serum of the blood are quantified. How each falls within or varies from the normal range will help paint a picture of how the body's metabolic functions are operating. Similarly, the presence of various proteins called enzymes in the bloodstream implies that damaged cells in the body have lost their structural integrity and are leaking their contents into the blood. These tests are particularly useful when looking for liver, muscle, or heart damage. Epidemic diseases are usually not diagnosed with chemistries alone, but the damage that they do to the body is. For example, liver function tests may be greatly elevated when someone is infected with viral **hepatitis**. Finding the cause of the damage and treating the patient accordingly is critical to his survival.

Immunodiagnostic Tests. Another group of proteins called antibodies, generated by the body's immune system to fight off infections, can also be tested for in the blood. If a specific antibody is present, then there is proof that the person was once infected or may still be infected. Immunodiagnostic tests study the reaction between these antibodies and the substances with which they interact, called antigens. These tests are critical in diagnosing many infectious diseases, but are also used for detecting autoimmune diseases (in which the body attacks itself), and also in diagnosing some cancers. The ability to detect the antibody against **Human Immunodeficiency Virus** was crucial to helping curb its spread. In fact, it is so important to be sure that this antibody test is as accurate as possible that it is composed of two tests. The first is very sensitive and will detect HIV quite well but will also produce some false positive results (showing up positive when HIV is not really present). All these positive results will then undergo a second test that is very specific and will help clarify which positives are truly HIV and which are mistakes.

DNA and Genetic Testing. Ever since the discovery of DNA in the 1950s, countless new techniques have been developed that can detect and describe the genetic material within human beings or within the pathogens that are infecting them. By using lab methods such as the polymerase chain reaction, or PCR, which can amplify even small amounts of DNA so that there will be more material to work with, and gel electrophoresis, which is used to separate various segments of the DNA on a gel plate, labs can now manipulate the genes of both humans and pathogenic agents. For example, a form of PCR called reverse transcriptase PCR can be used to quantify the viral load in HIV infections. Similarly, genetic tests in humans can help predict how a person's inherited genetic make up, or genes, predispose her to certain diseases, such as in certain types of cancer.

Hematological Tests. Much can be learned about the body through the blood. The complete blood count, or CBC, quantifies and qualifies the white blood cells (WBCs), red blood cells (RBCs), and platelets in the blood. A hematocrit, for example, is a common test used to describe the portion of the blood made up of RBCs. The blood is then put on a slide, stained, and observed under a microscope in order to determine the characteristics of the different blood elements. RBCs will be studied carefully for the presence of certain infections, such as in **malaria**, in which the diagnosis is actually made by observing the organism in the RBC. The WBCs can also be differentiated. The type of WBC that predominates may suggest the type of infection in the body: neutrophils may be elevated in bacterial infections like **meningitis**, lymphocytes in viral diseases, and eosinophils in parasitic diseases, such as in intestinal worms. Coagulation factor tests, such as the PT-INR and PTT describe how well the blood can coagulate, or become solid to form scabs and stop bleeding. In **Dengue fever**, the body's blood may get "thinner" thereby putting the body at risk for severe bleeding.

Histology and Cytology (Pathologic Examination of Body Tissues). A pathologist examines microscopic samples of potentially diseased body parts to help diagnose diseases. These samples could include a scraping of cells (cytology), such as from a "Pap smear" testing for **cervical cancer**, or a solid tissue biopsy (histology), such as the biopsy taken from an abnormal growth found in the body. Once removed, the sample will first be inspected grossly with the naked eye. It will then be stained with special dyes and sliced paper-thin so that when inspected under the microscope, many pathologic characteristics of the cells and tissue can be identified, such as whether the cells look cancerous or appear infected.

Microbiologic Tests. Various methods exist to grow and characterize the **viruses**, **bacteria**, and fungi that infect humans. Most samples are first stained with a dye, such as

the Gram Stain or Giemsa Stain, and then examined under a microscope. Cultures can be made by placing any body fluid sample on a culture medium in a Petri dish that allows the pathogen to multiply so it can be more easily identified. **Bubonic plague**, for example, can be diagnosed by drawing out pus from an infected “bubo,” staining it, and then culturing it to look for the bacterium *Yersinia pestis*. Cultures will often be tested to discover the sensitivities of the pathogens to various **antibiotics**. Diagnosing active **tuberculosis** still requires microscopic examination and/or subsequent cultures of sputum smears coughed up by an infected person. In areas where exposure to tuberculosis (TB) is not very common, a skin test called a Tuberculin PPD Test can be performed by injecting a small sample of TB protein under the skin and seeing if the body reacts to it. If it does, then the patient has been exposed to TB, but it may still be dormant in the lungs. A chest x-ray or sputum smear will help to distinguish whether the TB is active.

Radiology. Before imaging technologies were widely available, it was common to perform an “exploratory surgery” by opening a person’s abdomen from top to bottom to look inside for the problem with the naked eye and bare hands. Luckily, ever since the first x-rays, there has existed the ever increasing ability to take pictures of the deepest parts of the body without having to actually go inside. First, the x-ray is a common and affordable method used to create a two-dimensional image by penetrating the body part under study with radiation and then developing the picture that is made. In many parts of the world where tuberculosis is endemic, the chest x-ray is often the only radiology study readily available. For more detailed pictures, the computed tomography scan (CT scan) may be available. With this technology, the part of the patient under diagnosis is put into a donut-shaped machine that takes a series of x-rays all around the body. Then a computer synthesizes these many images to create a three-dimensional picture of what is inside. Magnetic resonance imaging, or MRI, provides greater clarity by using magnetic energy instead of radiation to draw the internal landscape. Ultrasound technology is an alternate imaging method that uses supersonic echoes to make a picture that is less clear. It has its advantages, though: it can be used at the patient’s bedside and can look at moving body parts in real time, such as the heart in an echocardiogram.

Nuclear Medicine Studies is a relatively new field within radiology that determines not only what a patient’s body looks like anatomically but also how it is functioning physiologically. In the WBC Scan, a sample of WBCs from the patient’s body are collected and labeled with a radioactive marker. When reinserted into the body, the cells travel to areas of inflammation or infection, thereby helping provide important clues to where exactly an infection is located. This could be critical when one suspects that there is an abscess causing a patient to be febrile, but traditional methods cannot reliably locate it.

Electrocardiogram, Electroencephalogram, Electromyogram. Much of the body works by electricity. As charged ions move across the membranes of nerves, heart cells, and muscle cells, the electrical charge that is produced can be measured by a probe that is placed on the skin directly above. If these probes are placed above the heart, the test result produced is called an electrocardiogram, or ECG; if above the brain, it is called an electroencephalogram, or EEG; if above or within a skeletal muscle, it is called an electromyogram, or EMG. Because the movement of these cells’ electricity produces recognizable patterns as they print out on a computer, any change in the functioning of the cells will also produce recognizable patterns of those diseased states. This technology provides doctors with a relatively inexpensive and noninvasive method of understanding how various parts of the body are functioning.

Endoscopy, Bronchoscopy, Otolaryngoscopy, Laparoscopy, Cystoscopy. The human body has a number of openings to the outside world. The ears, nose, mouth, urethra, vagina, and anus are all gateways to internal hollow spaces that can be explored with a camera on the end of an extension. The names of these techniques will usually begin with a Greek or Latin word naming the organ, which is then followed by the suffix “-scopy.” In this way, endoscopy is the exploration of the upper gastrointestinal (GI) tract; colonoscopy is the exploration of the colon, or lower GI tract; bronchoscopy is exploration of the lung’s bronchi, and so on. Newer equipment can also use extensions to take tissue biopsies and fluid samples, inject medicines, and even remove some cancers. Because this technique allows doctors to perform minimally invasive procedures on patients, it has improved the screening and treatment of many diseases. In AIDS, for example, immunocompromised patients can sometimes suffer a serious lung infection from an organism called PCP. A positive diagnosis is made by finding the pathogen in the sputum, but patients are often not able to produce a good sample by simply coughing. A bronchoscope greatly increases the sensitivity of this test because it can often collect a sputum sample from deep within.

An emerging field of diagnostic technology known as biomedical informatics involves the use of computers and other new information technologies to integrate, contextualize, and assess the diagnostic findings of multiple tests in support of the process of differential diagnosis and decisions based upon it. *See also* Corpses and Epidemic Disease; Diagnosis of Historical Diseases; Heredity and Epidemic Disease; Human Body; Human Immunity and Resistance to Disease; Medical Ethics and Epidemic Disease.

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DANIEL PALAZUELOS

DIAGNOSIS OF HISTORICAL DISEASES. Modern researchers have diagnosed historic diseases according to their similarities to modern illnesses. Medical historians obtain the evidence for the associations between past and present diseases by studying all types of literary, medical, administrative, and ecclesiastical (church) records, as well as relevant artwork and archaeological evidence from the period in question. For example, the numerous plague epidemics of the **second plague pandemic**, starting with the medieval **Black Death** and continuing well into the eighteenth century, have been mostly diagnosed as the **bacterial** disease **bubonic plague** because historical accounts mention lymphatic swellings (buboes) and the coughing of blood, which is believed to indicate the concurrent presence of the pulmonary variation of the disease, **pneumonic plague**. However, advances in theory and methodology of modern medicine have gradually altered the approach to afford less credible face-value diagnoses, especially when the nature of the disease in question is uncertain.

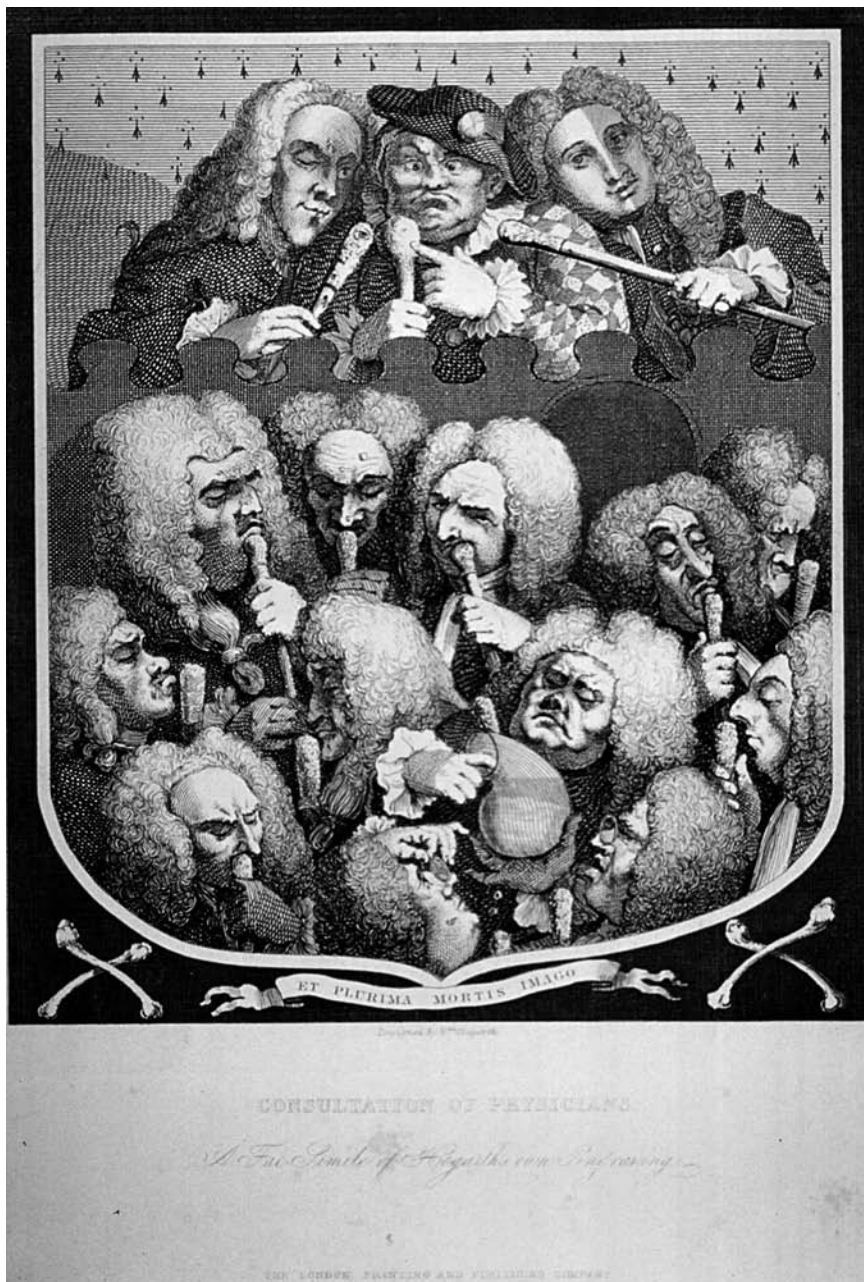
Nineteenth-century discoveries and advances in laboratory science proved **germ theory**, ushering in the modern age of medicine. This changed not only the understanding, prevention, treatment, and **diagnosis** of present diseases, but also the understanding and diagnosis of historic plagues. As the theory gradually became accepted, and the pathogens which cause some of the most infamous plagues, such as bubonic plague, **cholera**, **tuberculosis**, **typhus**, and anthrax were studied extensively, a renewed interest in the history of diseases was provoked, especially between the late nineteenth and mid-twentieth centuries, when the **third plague pandemic** gripped the world with the fear of another Black Death catastrophe.

As more information concerning current disease pathogens was amassed, specifically their behavior, ecology, and transmission vectors, the more such knowledge was applied to the diagnosis of historic plagues. For example, when it was proven that modern bubonic plague was spread by rats and that their fleas were the vectors by which humans were infected, historians easily saw rats and fleas as the cause of famous plague outbreaks like the **Plague of Justinian** and the Black Death.

For the most part, the matching of historic plagues with modern diseases remains popularly accepted and, in many cases, unchallenged. There is little doubt, for instance, that the disease which struck London in 1854, meticulously investigated and documented by the English physician **John Snow**, was an epidemic of **cholera**. We can be similarly certain that the great mortalities suffered by the natives of the New World after contact with Europeans in the sixteenth century were the result of the introduction of viruses like **measles** and **smallpox**. Diseases such as these have persisted into modern times and affected almost every area of human settlement at one time or another, engendering both a familiarity and reputation that serve to identify them almost beyond doubt.

However, history is full of many examples of plagues that modern medicine cannot diagnose with any real certainty. The mysterious plague that struck a Carthaginian army as its soldiers were laying siege to the Greeks of Syracuse in 396 BCE (Carthaginian Plague) remains unidentified. Similarly, medical historians have suggested that the **Great Plague of Athens** was variously measles, smallpox, bubonic plague, anthrax, typhus fever, or one of many others, without any consensus. The **Antonine Plague**, believed to have been brought back by Roman troops after campaigns in the East, was documented by the great **Galen**, but its nature remains a mystery. Similar in pathology was the Plague of Cyprian of the 270s. The medieval period is similarly dotted with mysterious illnesses, such as the unnamed epidemic that took disastrous tolls on the French army of King Louis VII (1120–1180) during the Second Crusade (1147–1149), whereas the early modern period witnessed another puzzling case for modern historians: the English **Sweating Sickness**. This malady appeared in the late fifteenth century, causing several terrible epidemics, most notably in England but also in Germany and parts of northern and eastern Europe, before disappearing completely by 1551.

Although several diagnoses have been suggested for these unknown plagues, none of them has been clearly identified. This is mainly the result of a lack of historical information or, as in the case of the English Sweats, the disease's apparent extinction. In the case of the Black Death, contention has recently developed because of the apparent marked differences between the medieval pestilence and the behavior of modern bubonic plague. Dilemmas such as the above have provoked new approaches to the diagnosis of historic diseases.



“Consultation of Physicians, or The Arms of the Undertakers’ Company,” by William Hogarth, 1736. Caricature of twelve physicians consulting on the contents of a urinal. Pictured above the group are, left to right, Dr. “Spot” Ward, Mrs. Mapp (known as “Crazy Sally”), and Chevalier Taylor (a well-known quack). Courtesy of the National Library of Medicine.

Since the mid-twentieth century, the theoretical approach to identifying historic diseases has changed considerably, albeit without significantly altering the traditional diagnoses already in place. Sir Frank MacFarlane Burnet (1899–1985), a prominent specialist in **immunology**, stated that historical diseases are best assessed by **epidemiology** rather than by interpreting the descriptions of symptoms contained in historical sources. This entails a move towards diagnosis by studying disease behavior in populations rather than in individuals.

Because epidemiology is a very broad discipline, including elements of mathematics, statistics, demography, and biology, as well as medicine and history, interdisciplinary approaches have been characteristic of recent attempts to diagnose historic diseases. In some cases, mathematical functions have been applied to historic population data to calculate accurately the transmission rates, incubation, and infectious period of the diseases that affected them. For example, an investigation of the parish records of baptisms, marriages, and deaths for the small northwest English town of Penrith during a sixteenth-century plague outbreak has revealed vital epidemiological information concerning the disease's behavior, indicating that it was most likely a virus—as opposed to bubonic plague, as previously diagnosed. Studies like this tend to be more localized, focusing on specific outbreaks as opposed to a whole series of epidemics, and they prove that with the right type of historical information and focus, the principles of epidemiology can ascertain the type of infectious disease affecting an historic population at any one time.

Because medicine and history are fields that are constantly evolving, the theories and tools by which historic diseases are diagnosed will continue to change as well. In recent laboratory tests, dental pulp from plague-era skeletons has been analyzed in the hope of finding traces of bubonic plague **bacterium** that could definitively prove the identity of the Black Death. To date, the results have been inconclusive, but if the technology is perfected, the future of historical diagnoses could be in the laboratory. *See also* Black Death: Historical Epidemiology, Modern Medical Debate.

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KARL BIRKELBACH

DIAGNOSTIC TOOLS. *See* Diagnosis and Diagnostic Tools.

DIET, NUTRITION, AND EPIDEMIC DISEASE. Diet and nutrition are linked to epidemic or infectious diseases in two main ways. First, foods can be vehicles for infections. Second, the quality of diets may influence the state of nutrition of the body, which may impact upon susceptibility to infections.

Foods as Vehicles for Disease. There are many different food infections, which differ greatly in terms of severity of the symptoms and in other ways. Food infections may amount to relatively mild forms of food poisoning involving vomiting and diarrhea, which are frequently dealt with domestically, without referral to a doctor. Therefore food poisoning statistics, where they are collected, usually only record a small proportion of cases. The symptoms of the milder forms of food poisoning usually arise from the irritation of the intestines by toxins produced by **bacteria** such as *Salmonella*. This organism was first identified in 1888, and since then the importance attached to food poisoning as a public health problem has varied geographically and over time. During the Second World War in Britain, for example, when the state became heavily involved in the purchasing and distribution of food, and in communal feeding, interest in food poisoning increased. In another example, upon the establishment of the British National Health Service in 1948, when, for the first time, all patients could consult a general practitioner free of charge about minor ailments, there appeared to be a rapid increase in food poisoning, leading to a series of food safety initiatives.

The incidence of food poisoning is closely related to food production, handling, and consumption methods. For example, during the post-World War II period, factory farming of poultry meat and eggs led to an increase in the consumption of these foods, whereas the advent of frozen poultry, microwave ovens, and fast food outlets, increased the risk of poisoning from infected products. In particular, by the late 1980s it was apparent that there was widespread contamination of poultry meat and eggs with *Salmonella enteritidis* phage type 4 (*S. enteritidis* PT4), a bacterium that is harmless to poultry but pathogenic to humans. Recent policies aimed at eliminating *S. enteritidis* PT4 in flocks (notably **vaccination**) have led to a decline in this form of food poisoning. Health education campaigns have also encouraged consumers to boil their eggs and cook their poultry meat thoroughly. At the same time, however, a new form of food poisoning, caused by *Campylobacter jejuni*, which was first discovered in the 1970s, has become widespread. Campylobacteriosis, like salmonellosis, is often a mild disease, but because of biological differences between the organisms, countering *Campylobacter* is currently proving problematic.

Common strains of *Salmonellae* can produce systemic disease (infection spread through the body), and even death, in the young, elderly, and immunocompromised, but such infections are usually associated with the microorganisms that cause the enteric fevers, and such organisms as *Escherichia coli* 0157. The latter was first identified as a threat to human health in 1982 and became known as the “burger bug,” in view of its association with ground beef. *E. coli* 0157 can cause hemolytic uremic syndrome, kidney failure, and death, and survivors may be brain-damaged or otherwise permanently disabled.

Other food-transmitted diseases include some that may only become apparent years or decades after consumption of the infective agent. These include bovine **tuberculosis**, which was common before measures were taken to eliminate the infection from dairy herds and to enforce the pasteurization of milk. Since the 1990s, much publicity has been given to variant-Creutzfeldt-Jakob Disease (vCJD), which is believed to be caused by an unusual infectious agent—a prion protein present in beef from cattle infected with Bovine Spongiform Encephalopathy (BSE). Only just over 200 known cases had occurred worldwide by April 2007, so, in spite of the massive disruption caused to the British and other national beef industries by measures to counter the spread of BSE and reduce the risk of vCJD, the disease can hardly be classified as “epidemic” in the usual sense of the term.

Diet, Nutrition, and Susceptibility to Epidemic Disease. The existence of these associations is widely assumed, yet the precise relationship between food intake and susceptibility to infection is unclear. Famine situations rarely provide clear-cut evidence as, quite apart from hunger, they usually involve large movements of people, overcrowding, and unsanitary conditions. Human feeding experiments often prove difficult to replicate, the relevance of **animal experiments** to humans can always be debated, and there are often alternative interpretations of epidemiological studies.

In 1902, Robert Hutchison (1871–1960), in *Food and the Principles of Dietetics*, opined that an insufficient supply of protein, as well as general underfeeding, lowered resistance to disease, citing the epidemics that followed the **Irish potato famine** as an example. He also remarked that exposure to infection was especially dangerous on an empty stomach, such as before breakfast, and that “the tubercle bacillus seems to find a specially-favorable soil in ill-nourished persons.” This latter point reflects general medical opinion of the period. During the late nineteenth and early twentieth centuries, a plentiful diet (along with fresh air and graduated exercise) was an important component of the new “open air” **sanatorium** treatment for tuberculosis. Sanatoria for wealthy, fee-paying patients were established at first, but later facilities were also created for working class people. Tuberculosis patients lost weight as the illness progressed, but gained weight as their condition improved. It was therefore assumed that the well nourished were less susceptible to the disease, and that a plentiful diet would enhance the resistance of the infected.

Certain foods, such as dairy products, cod liver oil, and fresh fruits and vegetables, were often regarded as being of special importance in the prevention and treatment of tuberculosis. But from the 1910s, such foods were also celebrated for other reasons by advocates of the “newer knowledge of nutrition,” who discovered that such foods could prevent specific noninfectious deficiency diseases such as rickets, beri-beri, and scurvy. These diseases, they believed, were caused by an inadequate intake of small quantities of certain organic constituents, which became known as “accessory food factors” or “vitamins,” which were only present in significant amounts in certain foods. Most of the early vitamin pioneers, including Frederick Gowland Hopkins (1861–1947), who shared a Nobel Prize for the discovery of vitamins, also considered that low vitamin intakes decreased resistance to infectious disease. Edward Mellanby (1884–1955), who was credited with showing that rickets was a vitamin deficiency, argued that vitamin A should be regarded as an “anti-infection” vitamin and claimed to have demonstrated its value in the treatment of puerperal fever and in animal experiments.

The notion that vitamins were connected with infectious as well as deficiency diseases was linked with the vitamin pioneers’ view that, in general, the role of nutrition in preventative and curative medicine had been neglected since the late-nineteenth-century bacteriological revolution. This view created common ground among the interwar nutrition enthusiasts, not all of whom thought that vitamins were of great practical importance. John Boyd Orr (1880–1971), for example, at the Rowett Research Institute in Aberdeen, considered that minerals were of greater importance than vitamins. And his research program included attempts to explore links between mineral intake and infections in both animals and humans.

Later in the interwar period, as others tested Mellanby’s and Orr’s hypotheses, it became clear that the links between nutrition and infection were not as simply demonstrated as these scientists had imagined, and evidence provided by practical experience during the

Second World War and its aftermath seemed only to confuse the issue further. In 1949 an editorial in the British medical journal *The Lancet* declared that “Every mother of a family, and every doctor in practice, firmly believes that the best bulwark against infection is good wholesome food.” However, in spite of the “appallingly low nutritional standards in Germany” at the end of the war, there had been no major epidemics, whereas experiments on antibody production by starving people also suggested that malnutrition did not “play as large a part in widespread epidemics as is generally supposed.” Similarly, children living in admirable conditions contracted childhood diseases, and the well fed were susceptible to colds and influenza. In addition, **poliomyelitis** seemed more common among young adults in excellent physical condition, in well-fed countries. But not all analysts of wartime health records failed to find links between diet, nutrition, and infectious disease. Isabella Leitch (1890–1980) showed that in populations in which energy and protein intakes were restricted, mortality from tuberculosis increased, reinforcing the rationale for the sanatorium dietary regimen and popular views of the benefits of a good diet.

Since the 1940s, the advent of **antibiotics** reduced the significance of many bacterial infections, but most “mothers” and “practicing doctors” have no doubt continued to regard good food as a precaution against infection. Popular nutritional preventative and curative strategies among Western populations, however, have increasingly involved vitamin supplements bought from **pharmacists**, health food shops, or supermarkets, as much as they have “healthy eating.” Besides multi-vitamin preparations and cod liver oil, large doses of vitamin C were commonly swallowed in the hope of combating the common cold and influenza, viral diseases that antibiotics are powerless to counter. This practice was encouraged by the publication of *Vitamin C and the Common Cold* by Nobel Prize winner Linus Pauling (1901–1994), in 1970.

Mainstream medical and scientific opinion never moved in favor of Pauling’s views, but there was, however, no practical and effective conventional treatment for the common cold and influenza with which the “megavitamin C therapy” competed. The situation was different in the case of the more recent Pauling-inspired approaches to **HIV/AIDS**. While official health agencies emphasised that good nutrition could help to preserve the quality of life of HIV-positive individuals, the claims of Matthias Rath (1955–), an associate of Pauling, that cocktails of micronutrients can combat HIV/AIDS as or more effectively than antiretroviral drugs, have been highly controversial. Rath accused the multinational pharmaceutical companies of profiteering from HIV/AIDS, and the approach of South African Health Minister, Manto Tshabalala-Msimang (1940–) to the prevention and treatment of the disease was much influenced by Rath. In 2003, after much criticism, the South African government agreed to make antiretrovirals available in the public sector, but Tshabalala-Msimang has been slow to implement this policy.

At the beginning of the twenty-first century the precise links between nutrition and susceptibility to epidemic disease remain unclear, although **historical epidemiology** is now beginning to provide some suggestive data—for which biomedical explanations are required. A recent analysis shows that during the Second World War, mortality from infectious diseases such as **diphtheria**, tuberculosis, **measles**, **whooping cough**, **dysentery**, bronchopneumonia, diarrhea, **typhoid**, and **influenza** increased in the Netherlands, especially in the younger age groups, but remained stable in neighboring Denmark. Both countries were occupied by Nazi Germany, but whereas the energy and animal-food content of the Dutch diet declined during the war, the Danish diet was relatively unaffected.

It has been suggested that the richer micronutrient (i.e., vitamin and mineral) content of the Danish wartime diet accounts for the difference, but a century after Frederick Gowland Hopkins published the first articulation of the vitamin concept, the precise nature of the links between diet, nutrition, and epidemic disease remain elusive. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Bioterrorism; Ergotism; Germ Theory of Disease; Greco-Roman Medical Theory and Practice; Human Body; Human Immunity and Resistance to Disease; Humoral Theory; Islamic Disease Theory and Medicine; Mallon, Mary; Pharmaceutical Industry; Poison Labels and Epidemic Disease; Protozoon, -zoa.

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DAVID F. SMITH

DIPHTHERIA. Diphtheria is a **bacterial** upper respiratory disease with high mortality rates in young **children**. At the end of the nineteenth century, microbiologists and public health experts successfully applied the principles of **germ theory** to the diagnosis, treatment, and prevention of diphtheria.

Diphtheria is caused by *Corynebacterium diphtheriae*, an organism with no known **animal** reservoir. *C. diphtheriae* is a thin rod that stains purple with the Gram stain (Gram-positive). With special stains, the bacteria show a characteristic club-like appearance with heavy uptake of dye at one or both ends (Greek *korynee*, club). With some stains, metachromatic granules (clumps of dye) are seen within the bacteria. *C. diphtheriae* will not grow on the usual agar medium used to diagnose streptococcal throat infections; special growth media are required. Four strains or biotypes of *C. diphtheriae* form distinct colonies called *gravis*, *intermedius*, *belfanti*, and *mitis*. As they divide in laboratory cultures, the bacteria arrange themselves at angles to one another, giving a "Chinese-ideogram" appearance under the microscope. Toxin-producing strains of *C. diphtheriae* produce an exotoxin responsible for most of the life-threatening symptoms of diphtheria; nontoxigenic strains cause less severe symptoms.

C. diphtheriae is spread through airborne respiratory droplets and nasal secretions or by direct contact with infected skin ulcers. During epidemics or in endemic areas, asymptomatic carriers can transmit the disease, presenting a public health risk. *C. diphtheriae* can live for weeks on fomites (inanimate objects capable of transmitting germs) such as dust particles, although this is rarely a route of human infection. A diphtheria-like illness has been linked to a related bacterium, *C. ulcerans*, transmitted through unpasteurized milk.

Clinical Picture and Treatment. In classic childhood diphtheria, toxigenic *C. diphtheriae* invades the upper airway, attaching to the mucosa (superficial membrane) of the nasopharynx, tonsils, pharynx, larynx, and/or trachea. After an incubation period of two to seven days, the child develops a sore throat with little or no fever. The bacteria release exotoxin, which binds to receptors on nearby tissues, causing localized inflammation and cell necrosis. In this environment, the bacteria continue to multiply and produce toxin, with the formation of pus-like exudate. The exudate congeals into a characteristic tough, grayish membrane that adheres to the tissues of the throat, soft palate, and larynx. Efforts to lift the membrane cause bleeding. Enlarged lymph glands in the neck may cause a characteristic “bullneck” appearance. In severe cases, the membrane and tissue swelling extend downward toward the trachea and bronchi, causing airway obstruction. In mild cases, the membrane begins to slough off after a week, and the patient recovers rapidly. In severe cases, the victim suffers death from asphyxiation within days of the onset of symptoms.

The spread of diphtheria exotoxin through circulation causes two major complications. In 10 to 25 percent of cases, exotoxin may attack the heart muscle causing myocarditis (inflammation of the heart). Untreated myocarditis has a high mortality rate as a result of irregularities in heart rhythm. Early in the illness, the diphtheria toxin may attack the myelin sheath that coats the nerves, causing muscle weakness in the face, eyeballs, and throat. Weeks to months later, transient paralysis may develop in the arms and legs. Recovery from neurological complications is usually complete.

Much of the diphtheria found in the United States today involves the skin (cutaneous diphtheria), often in adults. In these cases, *C. diphtheriae* invades neglected skin wounds or areas of infection, causing a deep, nonhealing ulcer with a grayish-brown membrane. Complications are rare, but the skin ulcers are a reservoir of infection and constitute a public health risk.

Laboratory confirmation of diphtheria takes several days, but **antitoxin** should be administered as soon as the disease is suspected. In the United States, antitoxin is obtained through the **Centers for Disease Control and Prevention (CDC)**. Delay in administering antitoxin increases complications and mortality. The dose of antitoxin depends on the severity of the infection. Because the antitoxin is prepared in horses, there is a risk of severe allergic reactions to the serum; procedures have been established for desensitizing patients who require antitoxin. **Antibiotics** such as **penicillin** or erythromycin eliminate the bacteria and are used in conjunction with antitoxin. Antibiotics without antitoxin are used for asymptomatic carriers and for those with cutaneous diphtheria. In severe cases with airway obstruction, an endotracheal tube is inserted into the airway, or a tracheostomy performed surgically until the patient improves. In recent outbreaks, mortality has ranged between 10 and 20 percent. Many people have some residual **immunity** from previous immunizations that may modify the course of the illness.

History. Diphtheria was probably recognized in antiquity, although distinctions among various types of throat infection were not clear at the time. In past centuries, deadly **epidemics** of childhood throat infections were referred to variously as *cynanche trachealis*, *angina* (inflamed throat) *maligna contagiosa*, *angina suffocativa*, sore throat distemper, membranous croup, putrid sore throat, *el garratillo* (Spanish, strangler), malignant ulcerous sore throat, and *morbus suffocans*. **Cotton Mather** described “a malady of bladders in the windpipe” in seventeenth-century Boston. A major epidemic swept the



Laboratory of Pasteur Institut (Paris), where diphtheria antitoxin is made. A man is shown using autoclaves to sterilize chicken broth in which to grow the antitoxin. January 3, 1895. Courtesy of the National Library of Medicine.

northeastern American colonies in the late 1730s, killing up to one-third of all children. Often, all the children in a family would succumb within days. Applications of antiseptics and harsh cauterizing solutions added to the suffering of the child with little benefit. In 1826 Pierre Bretonneau (1778–1862) in France clarified the clinical picture, distinguished diphtheria from scarlet fever, and gave the disease its name (Greek *diphtheria*, leather). Bretonneau and others pioneered the use of tracheostomy for airway obstruction.

In the nineteenth century, diphtheria became **pandemic**. Over 1,000 children died of diphtheria annually in New York City, a pattern that continued to the end of the century. In the early 1990s, widespread diphtheria epidemics (150,000 cases) occurred in the Newly Independent States of the former Soviet Union, generally among older children and adults who had previously been at least partially immunized; case fatality rates exceeded 20 percent in the worst affected areas.

Research and Control. Epidemic diphtheria was a terrifying prospect for parents and **physicians**. Progress in bacteriology and public health administration brought the disease under control within a few decades. In Berlin the bacterium was identified under the microscope by Edwin Klebs (1834–1913) in 1883 and grown on special culture media by his associate, Friedrich Loeffler (Löffler; 1852–1915) in 1884. Loeffler also identified the carrier state. *C. diphtheriae* was originally named the Klebs-Loeffler bacillus. In the late 1880s, bacteriologists Emile Roux (1853–1933) and **Alexandre**

Yersin at the Pasteur Institute showed that bacteria-free filtrates of diphtheria caused fatal disease in guinea pigs, proving that bacterial exotoxin was responsible for many of the symptoms of diphtheria.

In the 1890s, work by **Emil von Behring** and **Shibasaburo Kitasato** in Berlin, Roux in Paris, and other researchers led to the production of a diphtheria antitoxin in horses. The antitoxin-containing serum reversed the course of the disease and saved the lives of countless children. Health departments in New York and other American cities quickly began producing antitoxin in their own laboratories for distribution to physicians. A local diphtheria outbreak in Nome, Alaska, in the winter of 1925 was brought under control by serum rushed to the afflicted city by relays of dogsleds; the event is recalled by the annual Iditarod dogsled race from Anchorage to Nome.

In 1913, Hungarian pediatrician Bela Schick (1877–1967) developed a skin test for determining if a child was susceptible to diphtheria. In the 1920 and 1930s, research by Gaston Ramon (1886–1963) at the Pasteur Institute and by others led to the introduction of diphtheria toxoid (chemically modified toxin) and the development of an effective vaccine against diphtheria.

Immunization. Universal immunization with diphtheria toxoid has largely eliminated the disease in many countries. Despite universal childhood immunization recommendations, many children in the United States and other developed countries do not receive a full course of **vaccinations**. Many adults have waning levels of protective antibodies despite immunizations in childhood. Incompletely immunized travelers to endemic areas may contract diphtheria and become infectious to others.

Diphtheria vaccine is usually administered in a combined injection with tetanus and pertussis (**whooping cough**) vaccines. The CDC advises four doses of diphtheria toxoid in infancy with a booster at about age five and another at age twelve. Adults should receive booster shots, usually combined with tetanus toxoid, every 10 years for life. *See also* Contagion and Transmission.

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SANDRA W. MOSS

DISEASE IN THE PRE-COLUMBIAN AMERICAS. Prior to the arrival of the Spanish in the Caribbean in 1492, a variety of diseases endemic in the Old World were completely unknown among populations in the New World. These included **smallpox**, **measles**, and **bubonic plague**. After 1492 these three diseases and several others crossed the Atlantic into the Americas, devastating populations that had few immunological defenses as a result of lack of prior exposure. Within a century other diseases foreign to the New World would also arrive, leading to a massive population decline among indigenous peoples that did not subside until the mid-seventeenth century in Mesoamerica and the early eighteenth century in the Andes of South America.

The absence of Old World diseases from the New World was most likely the result of several factors. For one thing, many diseases could not survive or spread from person to person in the cold climate of the Bering Strait, the region through which the slow expansion of original populations from Asia into the Americas took place. To say that New World populations had no experience with certain diseases, however, should not be misunderstood to mean that they lacked disease altogether prior to 1492, or that they enjoyed an ideal of good health. For many years historians incorrectly believed that indigenous peoples in the Americas enjoyed exceptional health and had few problems with disease, but newer research in history, archaeology, and medical anthropology suggests that this was not so. We now know that such groups in fact suffered from a broad range of diseases and that epidemics periodically placed strains on many societies. Experiences with disease, moreover, varied widely according to the region and climate of the Americas where specific populations lived. Patterns of disease likewise varied according to whether populations were hunter-gatherers who migrated in search of food or sedentary agriculturalists who grew their own food and lived in relatively permanent settlements. Such populations grappled with disease in complex ways.

Diseases Present Before Contact. Some diseases appear very clearly to have been indigenous and unique to the New World. These include several **protozoan** infections including leishmaniasis and Chagas's disease, a kind of tropical illness common in Brazil. Although these diseases are considered lowland tropical infections spread by mosquitoes, colder and higher altitude regions also had their own specifically New World illnesses. These included Carrion's disease in northern South America's mountain valleys, among others. In this way, New World populations may have lacked exposure to several virulent diseases common in the Old World, but that did not mean they were without their own set of maladies.

For hunter-gatherers, scholars have drawn on archaeological records as well as contemporary ethnographic studies to suggest that such populations prior to 1492 likely suffered from a series of gastrointestinal and respiratory diseases brought with early populations across the Bering Strait. According to the historian Suzanne Austin Alchón, gastrointestinal disorders included bacterial and parasitic infections such as shigellosis, salmonellosis, tapeworms, hookworms, whipworms, and pinworms. In addition, infections of staphylococcal and streptococcal bacteria also led to skin diseases and potentially fatal respiratory diseases such as pneumonia and meningitis. Pneumonia appears to have been a common cause of death among both hunter-gatherer populations and sedentary agriculturalists.

Scholars speculate that respiratory infections and gastrointestinal diseases also served as the leading causes of death before 1492 among sedentary groups dependent on agriculture. One such respiratory disease, **tuberculosis**, emerged as an especially problematic illness

among dense populations. This is because the agent or bacillus that causes tuberculosis required the congregation of people in close spaces in order to spread from individuals who coughed to those in close proximity. Writing mainly about North America while discussing works on South America, the archaeologist Jane E. Buikstra (b. 1945) notes that skeletal remains reflect the presence of tuberculosis prior to the arrival of the Spanish. This is made evident by erosive spinal lesions, and some scholars such as M. J. Allison have also found pulmonary evidence of the disease on bodies excavated in Chile. The epidemiological patterning of these cases suggests that the disease was a mild form of tuberculosis.

Another disease that scholars believe was most likely present in the Americas before the Spanish arrived was **malaria**. Although there is some speculation that the Spanish brought malaria to the New World, it is also clear from native Mesoamerican sources that indigenous people were already familiar with the specific kinds of fevers associated with the disease. There are questions, however, as to how virulent malaria may have been among New World populations prior to 1492. If the mosquito-borne disease had been present in a particularly virulent strain, it would be reasonable to infer that the corresponding communities subject to infection would have had low population levels. But population density was in fact quite high in lowland coastal regions where mosquitoes transmit the disease, leading scholars to argue that the strain was mild.

Researchers have also long debated whether venereal **syphilis** was present in the New World prior to 1492, and whether it then spread into Europe via Spanish exploration and contact with natives. According to Jane Buikstra, certain lesions found on New World skeletons correspond to a set of related diseases known as treponematoses, which include venereal syphilis, yaws, and endemic syphilis. Disagreement persists, however, as to whether the skeletal evidence corresponds best with endemic syphilis and yaws or with venereal syphilis. Some scholars ask if venereal transmission of treponematoses originated in Europe after nonvenereal forms had spread there from the New World.

Pre-Columbian and early colonial texts suggest that indigenous populations experienced and feared epidemics in Mesoamerica and South America. Epidemics were a likely occurrence in North America as well. Often the writers of these texts and codices used vague language, discussing various “epidemics” and “plagues” that struck groups like the Aztecs in their early histories. As a result, we remain unable to identify many of these disease outbreaks. For example, the physiologist and historical demographer Sherburne Cook (1896–1974) wrote in 1946 that the Aztecs suffered from a disease they named *matlazahuatl*, which may have been **typhus**. Depictions of individuals suffering the fevers of *matlazahuatl* are present in one early colonial codex, but there is no way to link the condition to a modern disease typology with reasonable certainty.

Disease Variation across Populations. Patterns of disease distribution in the New World depended in large part on variations between particular environments and the different ways human populations interacted with those environments. The tremendous variation in regions and climates of the Americas makes it very difficult to generalize about specific diseases across populations. Diseases of tropical lowland climates, for example, tend not to spread into high altitude regions, where environmental conditions and the absence of specific disease vectors make their transmission difficult. In addition, human populations that developed sedentary agriculture and lived in dense urban settlements tended to experience a set of problems with disease different from that of nomadic, dispersed hunter-gatherer groups. The presence of epidemics among the Aztecs and the

Incas, two populations that developed large cities and depended on agriculture and animal husbandry for survival, attests to this difference. Animals such as the turkey, guinea pig, and llama often served as vectors for the transmission of diseases to humans.

Disease patterns and frequencies also varied according to differences in nutrition levels in various parts of the Americas. That is to say, certain diseases were more common in times of drought and famine, and other diseases could be the result of chronic malnutrition or vitamin deficiencies among different groups. These processes weakened the body's immune system in many cases and left it more vulnerable to diseases such as tuberculosis. It is also worth noting that the kinds of foods populations consumed varied tremendously in the Americas, leading to different health problems. Food and other offerings, moreover, were central to how groups carried out healing and ritualized beliefs about disease.

Aztec and Inca Understandings of Disease. Both the Incas and the Aztecs saw the body as reflecting the structure of the universe through its own organization and the functions of its parts. Moreover, they saw the body and the universe as connected. As a result, phenomena such as diseases that affected the body were seen not only as particular episodes of individual suffering, but also as events related to broader cosmological processes.

Among the Incas the structure of the body reflected the structure of the Inca Empire, which was divided into four quadrants just like the four limbs of the body. The universe followed a similar structure. In the case of the Aztecs, the historian Bernard Ortiz de Montellano writes that “astronomical events could affect bodily functions and, conversely, human behavior could affect the equilibrium and stability of the universe.” To treat, cure, or prevent disease thus often meant addressing both the specific afflictions affecting the individual patient and the wellbeing of the society through larger-scale rituals and cleansings. Moreover, both groups believed they could appeal to and appease their deities such that epidemics and illnesses could be prevented.

At the level of individual treatment, both the Aztecs and Incas relied on the expertise of herbalists, healers who drew on their knowledge of curative properties of plants and, to a lesser extent, animals to heal those suffering from disease. In the case of the Inca, different groups within the empire possessed knowledge of their own about medicinal herbs, though they also relied on traveling healers. One group in particular, a population known as the Kallawayas, possessed unusually effective medical knowledge of plants. As a result, they served as the official healers to the Inca state, traveling widely from the region around Lake Titicaca.

Like residents of the Inca Empire, the Aztecs and their imperial subjects also relied heavily on medicinal cures made from plants and animals. For the Aztecs milder diseases were treated with such medicines, whereas more severe conditions required complex, religiously based interventions. The emperor Motecuhzoma I (c. 1398–1469) established a botanical garden in 1467 for medical research, drawing on varieties of plants and knowledge about treatment from throughout the vast empire. General knowledge of herbal cures, however, predates that institution in Mesoamerica by centuries. It constituted a source of wonder for the Spanish, who wrote about Aztec medicine in works such as the *Florentine Codex* by Bernardino de Sahagún (1499–1590).

Both the Aztecs and the Incas also saw disease as reflecting relations between humans and the divine. For the Aztecs, diseases were caused by a mixture of supernatural phenomena linked to their religious beliefs and notions of deities, by magic or spells inflicted by sorcerers and others, and by natural or physical causes. Ortiz de Montellano argues, however, that the Aztecs did not see these categories of causation as separate, but rather combined and

integrated them in their explanations. Curing disease thus required addressing the immediate physical symptoms of the patient as well as the larger social and cosmological processes that had brought disease on the society. They drew on specialists called *nahualli* and *paini* in the Aztec language of Nahuatl to diagnose magical and supernatural causes of disease. To make such diagnoses, Ortiz de Montellano claims, the *nahualli* or *paini* often consumed hallucinogenic substances to communicate with supernatural beings.

The Aztecs themselves often saw diseases as working in the human body by causing changes in the strength and form of three animistic forces central to human life. These animistic forces were known as *tonalli*, *ihiyotl*, and *teyolia*. Although each had a specific function and occupied a different part of the body, *tonalli* in particular was central both to human life and to establishing links between individual human beings and their gods and universe. The imbalance between *tonalli* and other animistic forces and the loss of *tonalli* itself, which occupied the head near the forehead, were thought to bring on weakness and illness. Curing disease thus often required reestablishing lost *tonalli* in the patient through a variety of means.

The Aztecs treated diseases associated with divine causation through communal rituals and individual acts such as offerings and confession. Often they directed rituals to particular deities they believed were tied to specific diseases. For example, those affected with skin and eye diseases attributed their ills to a god named Xipe-Totec. Ortiz de Montellano writes that during the spring they would participate in a ritual wearing “the flayed skins of men who had impersonated the god (according to the Aztecs the men had *become* the god) and had been sacrificed.” Severe diseases were sometimes seen as having other kinds of complex causes (among them sin) that required ritualized treatments, such as confessions and incantations. The loss of animistic forces, in particular, could be interpreted as the result of immoral behavior. The treatment of disease thus often focused on establishing and practicing correct behavior to carry out therapy or preserve good health.

For the Incas, disease was also linked to questions of proper behavior, ritual purity, and relations between humans and the divine. The Incas saw disease as a source of significant concern that required both the healing of individual bodies and the healing of the body politic. This was in part because they believed disease was a reflection of sin, or *hucha* in their native language of Quechua. In order to cure people and eliminate disease, the sick had to confess their sins to special confessors known as *ychuri*, and a ritual cleansing known as a *citua* was carried out annually in the empire’s capital, Cuzco. According to the famous Jesuit missionary Bernabé Cobo (1580/2–1657), who wrote a history of Peru in the seventeenth century, the Incas celebrated the *citua* in August because it marked the beginning of a period when levels of disease tended to spike in the Andean highlands. Through the ritual the Incas asked one of their deities, the creator god Viracocha, to prevent illness from affecting Cuzco and the empire as a whole in the current year. They did this by expelling all dogs and non-Incas from the city, as well as those Incas who possessed physical deformities (which the Incas interpreted as resulting from moral fault). On the following day, the Inca royalty and nobility congregated with soldiers at Cuzco’s Sun Temple, where they held torches and waited for the new moon to rise. Cobo writes that upon seeing it, they cried out “diseases, disasters, and misfortunes, be gone from this land!” Others in the city left their homes and shouted repeatedly “May the evil go! Oh how we have wished for this festival! Oh Lord, let us live another year so that we may see another festival!” As they repeated these sayings, residents opened and shook their blankets and clothes, believing this would expel illness from their homes.

Different groups of Inca troops also congregated at Cuzco's Sun Temple and then in the city's main square as part of the *citua* festival of ritual cleansing. They did this to extend the process of cleansing and purification throughout the empire. At the temple they offered drinks in sacrifice before running from Cuzco in the direction of the empire's four quadrants, shouting as the moon rose "May the evil go!" Cobo claimed they ran in relays over long distances in the empire as an act of purification from disease. In this way, the rituals solidified the pre-Columbian belief that disease was to a large degree an expression of the relationship among mortals, the dead, and the divine. *See also* Astrology and Medicine; Diagnosis of Historical Diseases; Diet, Nutrition, and Epidemic Disease; Disease, Social Construction of; Environment, Ecology, and Epidemic Disease; Historical Epidemiology; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria in the Americas; Measles in the Colonial Americas; Religion and Epidemic Disease; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Syphilis in Sixteenth-Century Europe; Yellow Fever in Colonial Latin America and the Caribbean.

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ADAM WARREN

DISEASE, SOCIAL CONSTRUCTION OF. One of the keys to understanding the social construction of disease is the difference between illness and disease. Illness can be defined as the subjective physical process that people undergo, whereas a disease is the label that a person or group puts on that person's experience. In most of the Western world, the biomedical model of medicine is often seen as holding the key to the truth of many illnesses. In this system, the signs and symptoms of illness that a person presents

with, such as cough and fever, can be studied and then defined as a type of disease, such as **influenza**. A skilled health care practitioner usually makes this **diagnosis**. Similar to the scientific method, the diagnostic method involves creating hypotheses and testing them against observable, measurable data. The doctor who correctly diagnoses influenza uses this method, hypothesizing that there is influenza based on the symptoms the patient complains of, and then using the exam, lab tests, and centuries of knowledge from the medical community to verify her hypothesis. In this model, because diseases are conceptualized to have a cause that can be discovered, isolated, and then treated, modern biomedical medicine has cured some forms of cancer, eliminated diseases that once killed people in **epidemic** proportions, and even found pills that help to ease the pain of those diseases that cannot be cured.

The social construction of disease perspective, however, argues that although the diagnosis may seem to be an objective truth, it is really only a concept constructed by doctors working within one framework to describe a given phenomenon. This position does not argue that the symptoms of the illness are imagined or that the achievements of the treatment are not impressive. Instead, a social constructionist attempts to understand how the complex interplay of society, culture, and politics influences the way diseases (and their sufferers) are named, understood, and treated. The realizations that result from these questions help to place the diseases in their cultural, historical, and political contexts.

What one personally trusts to be true is largely a product of past experience and learning. In many societies across the world, and throughout the history of humankind, the diagnostic method has not been the primary method of diagnosis leading to treatment. Instead, people learned from their understanding and observations how rationally to construct other systems that addressed their illnesses. In many places, sophisticated methods very different from modern biologic medicine developed and spread because people experienced sustained health with these methods.

For example, Traditional **Chinese Medicine** (TCM) began thousands of years before the Western world developed the scientific method. In biomedicine, the goal is often to understand a disease as unfolding in a straight line—as being linear: if the cause is a specific **virus**, then the result will be influenza. In TCM, the cause and effect of illnesses are considered to be more wide ranging. From this perspective, illness and the body work not linearly, but through what has been called “the web that has no weaver.” Practitioners of TCM aim to consider all the factors that relate to the illness, such as diet, mental state, personality type, and so forth. The illness is not analyzed as a one-time problem, but as a result of patterns in the patient’s life. In fact, the aim of TCM is not always to cure diseases, but rather to realign the potential energy of the body, the *qi* (pronounced “chee”), so that it can heal itself, and the illness can no longer exist. Because this method cannot, by definition, isolate one specific cause of a person’s illness, TCM has not been as successful in treating specific diseases that have one cause, such as infections. But because it is more inclusive of many factors, it has been found to be very powerful in treating illnesses that have many factors, such as pain syndromes—diseases that western medicine is often unable to treat adequately.

There are countless other examples of different systems across the world that aim to define and treat illness. Sometimes, when people from different cultural perspectives are brought together to care for an illness, their separate mental constructions of what disease it is may collide. Anne Fadiman (b. 1953), in her book *The Spirit Catches You and You Fall*

Down, tells the story of a young Hmong girl who immigrated to the United States and was subsequently diagnosed with a brain disorder called epilepsy by her American doctors. Her family's cultural understanding of the illness differed radically, however, with the biomedical model proposed by the doctors. Whereas these doctors saw her illness as being caused by irregular electrical activity in the brain that could be medicated and controlled, the family saw her illness as a spiritual problem and attributed it to her wandering soul. Fadiman's story illustrates how the social construction of a disease can greatly affect a person's experience of her illness; the way that the reality of her illness weighed on them all, and their failure to comprehend the other's perspective, led to unfortunate consequences for the little girl.

Even within the same culture, however, conflict can occur when people of diverse genders, classes, or political standings construct diseases differently. As an example, when AIDS became prevalent in the United States, young homosexual men were affected first. The scientific medical system had not yet isolated the virus that causes the disease and the U.S. government avoided recognizing that people were dying from the disease. Gay men were often treated as shameful, second-class citizens. AIDS was socially constructed by many as a "gay disease," thereby enforcing the false belief that heterosexuals were safe. Some religious groups even claimed that the disease was a curse from God on homosexuals.

Feeling abandoned by their leaders and doctors alike, many homosexual men and other early infected groups, such as hemophiliacs, suffered tremendously at the sheer uncertainty of an awful disease that was quickly spreading. The play *Angels in America*, by Tony Kushner (b. 1956), explores this very question. In one scene, a powerful lawyer named Roy speaks to his doctor about his new and troubling symptoms. Roy has sex with men but does not want to call himself homosexual. In turn, what he chooses to call himself influences how he has constructed his relationship to not only the illness, but also the society in which he lives and has power:

Doctor [Henry]: Nobody knows what causes it. And nobody knows how to cure it . . . AIDS . . .

Roy [Lawyer]: Your problem, Henry, is that you are hung up on words, on labels, that you believe they mean what they seem to mean. AIDS. Homosexual. Gay. Lesbian. You think these are names that tell you who someone sleeps with, but they don't tell you that . . . homosexual is what I am because I have sex with men. But really this is wrong. Homosexuals are not men who sleep with other men. Homosexuals are men who in fifteen years of trying cannot get a pissant antidiscrimination bill through City Council. Homosexuals are men who know nobody and nobody knows . . . And what is my diagnosis, Henry?

Henry: You have AIDS, Roy.

Roy: No, Henry, no. AIDS is what homosexuals have. I have liver cancer.

Many activist groups interested in social change and social justice argue that the definition of who is sick and who is healthy is not always based on healing the individual patient, but rather, on defining social order and maintaining power differences between groups and individuals. Sometimes written into the very language of medicine are the assumptions and prejudices of the people who have the power to define

disease. If this process that allows mistaken prejudices to be tagged onto scientific thought goes unchecked, the disempowered individual or group will be isolated, as male homosexuals were during the first years of the AIDS epidemic. This may create a false sense of security for those who are considered “healthy,” but it provides no real safety. History later proved this right, as AIDS quickly spread to the very heterosexual populations that did not suspect that they were at risk. This same process is at work in other cases. For example, **tuberculosis**, though potentially dangerous to entire populations, has often been written off as a disease limited to the homeless, immigrants, and criminals. Diseases like alcoholism and drug addiction are often socially constructed as only affecting those who are amoral and weak. Countless epidemics that could have been diverted early on grew out of control because of such shortsightedness.

The definition of a disease is not always a matter of conflict between groups and cultures; sometimes it is a conflict across history as knowledge increases and opinions change. Even within the same culture, diseases can be redefined in dramatic ways. Stomach ulcers were once thought by western biomedicine to be the result of stress and diet, but as further study showed a type of **bacterium** called *Helicobacter pylori* to be the cause, the old philosophy quickly became obsolete. **Malaria** was once thought by the Romans to be spread by bad air, not mosquitoes: hence the name “mala aria.”

Understanding the social construction of disease is therefore a powerful way of analyzing how the phenomenon of illness is translated into the definition of a disease. It calls into question the very notions of truth, knowledge, power, and authority. A common criticism of this method is that it seems to imply that illnesses are imagined, but this is not accurate; it does not criticize people’s symptoms but rather questions how these symptoms are interpreted. For those interested in clinical medicine, the key lesson of social constructionist thought is that the notion of who is sick and who is well, who is safe and who is at risk, should always be considered in its cultural, historical, and political contexts. By doing this, one can better understand how people interact with their bodies, each other, their health-care practitioners, and their illnesses. *See also* AIDS, Literature, and the Arts in the United States; Astrology and Medicine; Ayurvedic Disease Theory and Medicine; Black Death, Flagellants, and Jews; Black Death and Late Medieval Christianity; Cinema and Epidemic Disease; Epidemiology; Greco-Roman Medical Theory and Practice; Humoral Theory; Irish Potato Famine and Epidemic Disease, 1845–1850; Islamic Disease Theory and Medicine; Leprosy, Societal Reactions to; Literature, Disease in Modern; Magic and Healing; Poison Libels and Epidemic Disease; Popular Media and Epidemic Disease: Recent Trends; Race, Ethnicity, and Epidemic Disease; Religion and Epidemic Disease; Scapegoats and Epidemic Disease; Sexuality, Gender, and Epidemic Disease; Syphilis in Sixteenth-Century Europe; Tuberculosis and Romanticism.

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DANIEL PALAZUELOS AND LINDSAY BROCKMAN

DISINFECTION AND FUMIGATION. Disinfection is the method of killing infectious disease agents outside the human body, typically with the use of chemicals. The related practice of fumigation is the use of gaseous chemical agents to kill microorganisms and pests (mosquitoes, body lice, rodents) that carry and transmit disease-causing microorganisms.

Early **miasma** theory identified filth and the noxious airs it created as the source of **epidemic** disease. During the **second plague pandemic** Europeans scrubbed the houses and furniture of victims with vinegar and fumigated houses by burning aromatic plants and firing guns. They also smoked tobacco to cleanse the air around them, held “plague infected” items—especially textiles—over fires, and set up smoky bonfires in city streets. The **sanitation movement** of the nineteenth century retained the theory and many of the processes. Sanitary hygienists emphasized cleanliness and the use of perfumes to neutralize the disease-causing foul airs. In the last decades of the nineteenth century, the laboratory work of **Louis Pasteur** and **Robert Koch** gave rise to the **germ theory of disease** which shifted attention from dirt and foul smells to microorganisms as the culprits in disease causation. Bacteriologists now emphasized that mere cleanliness was not enough, but that sanitation should employ disinfectants that would kill germs.

Following Pasteur’s work, Joseph Lister (1827–1912), an English **surgeon**, sought to develop a disinfectant to kill the germs that caused wound infections in hospitals. He used carbolic acid to disinfect surgical implements, and he also sprayed a mist of carbolic acid into the air over the operating field while he performed surgery, with the intention of destroying airborne germs. Influenced by Lister, hygienists started advocating the use of disinfectants as a precaution against disease. People were advised to use disinfectants to wash the bodies of people suffering from disease, to purify the air in the sickroom, and to fumigate and cleanse any items an infected person had touched. Manufacturers began to market a range of chemical disinfectants that they touted as “germ-destroyers,” although they were not necessarily effective. By the early twentieth century, manufacturers were also advertising products that could serve as personal disinfectants in the form of mouthwashes and skin cleansers that would kill the germs that cause disease.

As epidemiologists started to understand better the means by which germs were spread, they began to target those pests that were known as vectors or carriers of disease. For example, mosquitoes were known to spread the protozoa that caused **malaria** through much of the tropical world. In order to kill the insect vectors of disease and thus limit the potential for outbreaks of epidemics, public health officials fumigated homes and sprayed fields with insecticides in regions where malaria was prevalent.

Today, heat, radiation, and a variety of chemicals, including phenolic compounds and glutaraldehyde, are used as disinfectants and fumigants to kill germs and to disrupt vectors of disease. These methods of disinfection are employed widely in hospitals and agricultural and food production industries where infectious microorganisms could potentially spread quickly to a large population. *See also* Insect Infestations; Insects, Other Arthropods, and Epidemic Disease; Personal Hygiene and Epidemic Disease; Pesticides; Plague and Developments in Public Health, 1348–1600; Semmelweis, Ignaz; Yellow Fever Commission, U.S.



Truck equipped with disinfection tanks. Courtesy of the National Library of Medicine.

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WILLIAM H. YORK

DOCTOR. See Empiric; Physician; Quack; Surgeon.

DRUG RESISTANCE IN MICROORGANISMS. Killing disease-producing microorganisms with various substances is a major part of the battle against epidemic disease. Almost as soon as it was known that they could be killed, researchers discovered that some microbes could survive normally lethal doses of drugs. These microorganisms were commonly described as “drug-fast,” from the German suffix *-fest*, meaning *-proof*. These early studies interpreted the microbes’ resistance as “adaptation” to the toxic agents. By 1907, however, **Paul Ehrlich** focused on the concept of naturally resistant organisms, especially in the case of *Trypanosoma brucei* and *p*-roseaniline.

In 1913 Ehrlich clearly described drug action on microbes in Britain’s *The Lancet*: pathogenic microbes are only killed by substances with which they have a certain natural

relationship and through which relationship the germs are “fixed” (bound) by them. Once this “principle of fixation” was accepted, drug-fastness in a pathogen was readily explained as a reduction in receptiveness of the pathogen’s “chemo-receptors” for certain chemical combinations in the drug. In other words, the chemical connection between the pathogen and the drug that normally proved fatal to the pathogen could not take place. Already in 1913, the problem of clinical drug resistance was confronting the **physician** and microbiologist. Ehrlich discussed the problem of “relapsing crops” of parasites as a result of the biological properties of the parasites.

One corollary of the specific chemo-receptor hypothesis was that combined chemotherapy was best carried out with agents that attack entirely different chemo-receptors of the microbes. Using a military metaphor, Ehrlich urged the use of a “simultaneous and varied attack” on resistant pathogens. From the earliest days of chemotherapy, multiple drug therapy using agents with different mechanisms for connecting to a given pathogen was seen as a way to prevent emergence of resistant organisms.

From the mid-1930s until the early 1960s microbiologists contested and debated the central problem of “adaptation versus mutation.” Even those who viewed most microbial resistance (to chemicals and later to **antibiotics**) as some sort of inheritable change, or mutation, were divided on the issue of whether the mutations in pathogens arose in *response* to the chemical or antibiotic agent or occurred *spontaneously* and were simply observed after selection against the sensitive organisms.

As soon as a new antibiotic was introduced, reports of drug resistance appeared: sulfonamide resistance in 1939, **penicillin** resistance in 1941, and streptomycin resistance in 1946. Research focused on three major problems: (1) cross-resistance to other agents; (2) distribution of resistance in nature; and (3) induction of resistance.

In a major review in 1952, Bernard Davis (1919–1994) boldly (for the time) asserted that **bacteria** have nuclei, and that chromosomes within these nuclei apparently undergo mitosis. He went even further to note that some strains of bacteria are able to inherit qualities—including acquired drug resistance—from each of two parents, as do organisms generated by sexual unions. By mid-century, bacteria had come to be recognized as “real” cells, with conventional genetic properties, and it was only logical, Davis argued, to consider genetic mutations as the basis for inherited drug resistance.

The mid-century work in microbial genetics by Salvador Luria (1912–1991) and Max Delbrück (1906–1981), by Joshua (b. 1925) and Esther (1922–2006) Lederberg, and by David A. Newcombe (b. 1929) settled the matter of “induced versus spontaneous” mutations to drug resistance. They found that resistant organisms were already present in bacterial populations, having arisen by some “spontaneous” process; they were simply selected to survive and reproduce by the application of the drug. Because mutations to resistance to different agents were independent events (not resulting from use of a drug), Ehrlich’s concept of multiple drug therapy could be refined and made precise.

In the 1950s, especially in Japan, researchers noted the emergence of many strains of pathogens with resistance to several different drugs. The patterns of resistance were complex and did not fit a simple single mutation model. Careful epidemiological and bacteriological studies of drug-resistant strains in Japan led Tomoichiro Akiba (b. 1903) and colleagues, and Kuniyasu Ochiai and colleagues, to suggest that multiple drug resistance may be transmissible between bacterial strains both *in vivo* and *in vitro* by plasmids known as resistance transfer factors (RTFs) or R-factors. Because of the promiscuous

nature of R-factors, once a gene for drug resistance evolves, it can rapidly spread to the DNA of other organisms or even different species.

Knowledge of the mechanisms by which a drug worked with a pathogen often led directly to understanding the pathogen's mechanisms of resistance. Once it was known that penicillin killed bacteria by inhibiting the synthesis of certain cell-wall molecules that were found only in some bacteria (Gram stain-positive), one could understand that the Gram stain-negative bacteria were naturally resistant to penicillin. Likewise, inactivation of penicillin by a specific bacterial enzyme (beta-lactamase) aimed at a part of the penicillin molecular structure was discovered to be another key mechanism resistance to penicillin by certain bacteria. Such studies of antimicrobials have demonstrated the many ways in which microbial drug resistance evolves.

The production of antibiotics produces byproducts that are sometimes mixed into **animal** feed supplements, which therefore often contain the residues of the antibiotics themselves. The widespread use of such antibiotic-containing animal feed has led to a massive selection for resistant organisms in farm animals. The drug-resistance genes, unfortunately, are easily transmitted by R-factors into human strains leading to the widespread appearance of antibiotic resistance in human pathogens. This problem is especially common for the ubiquitous pathogen, *Staphylococcus aureus*, in which multiple drug-resistant isolates are frequently encountered.

Resistance emerges any time an antibiotic is used for any length of time, or is used in weak and clinically ineffective amounts. Widespread use of ineffective concentrations promotes emergence of drug-resistant populations. For these reasons, it is important to reserve application of new antibiotics to the infrequent cases where they are the only effective agents, as well as to employ sufficiently high and prolonged treatments to minimize the outgrowth of mutant bacteria with newly acquired resistance patterns. *See also* Hospitals since 1900; Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV)/AIDS; Immunology; Influenza; Malaria; Sulfa Drugs.

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WILLIAM C. SUMMERS

DYSENTERY. Dysentery (derived from the Greek *dys* "bad" and *enteron* "intestine") is a generic term for a group of diseases that cause inflammation and necrosis of the large intestines. All of these diseases are associated with bloody diarrhea and can be deadly,

depending on the source of the dysentery, as well as on available treatment. This type of diarrhea is distinctively different from the watery diarrhea commonly seen with **cholera**, not only in content but also with regard to the site of infection.

Dysentery is one of the most prevalent **epidemic** diseases in the world. Both infectious **bacterial** and **protozoan** agents, as well as certain chemical injuries, are associated with the development of dysentery. People throughout the world, of all socioeconomic classes and ages, are susceptible to developing dysentery; however, it is most often found in developing countries with poor waste management and inadequately treated water supplies. It should be noted that infected **children**, the elderly, and immunocompromised individuals have increased morbidity and mortality. Dysenteric epidemics affecting hundreds of thousands of people occur every year despite known effective treatments and preventive measures.

Biological Causes of Dysentery. Infectious bacterial agents that cause dysentery are varied and include *Shigella*, *Campylobacter*, *Escherichia coli*, and *Salmonella* species. In addition to bacterial infections, dysentery is often caused by infection with the protozoan *Entamoeba histolytica*. Infectious agents display some regional variation but all result in frequent and often painful diarrhea that contains mucus, pus, neutrophils, and exfoliated colonic epithelial cells. *Shigella* and *E. histolytica* are the most common causes of epidemic outbreaks.

Shigella is a Gram-negative, nonmotile bacillus of the taxonomic family Enterbacteriaceae (a family which also includes *Escherichia coli* and *Salmonella*). Japanese physician Dr. Kiyoshi Shiga (1871–1957) discovered this strain of bacteria over 100 years ago. Four species compose the genus *Shigella*: *S. sonnie* (serogroup D), *S. flexneri* (serogroup C), *S. boydii* (serogroup B), and *S. dysenteriae* (serogroup A). The basis for serogroup division is the differences detected in the O antigen which produces a variety of polysaccharide structures on the cell surface. These species can be further classified into 40 different serotypes.

Shigella infects and reproduces primarily in humans, but the organism has been recovered from the feces of captive primates. *Shigella* enters the body via fecal-oral transmission as a result of consuming contaminated food or water. Humans need only acquire 10 to 100 bacterial cells to become infected. Once in the digestive system, *Shigella* survives the low pH of the stomach as well as the immunological structures and digestive enzymes of the small intestine to reach the large intestine. Once in the colon, the bacteria are phagocytized by M cells found within the gut associated lymphoid tissue (GALT). The bacteria promptly escape the phagocytic vesicle, exit the M cell utilizing the cell's own cytoskeleton, and enter the surrounding epithelial cells via the basolateral surfaces of the cell. Additionally, *Shigella* invades local macrophages, thus evading the innate and acquired portions of the immune system. Within the epithelial cells, *Shigella* inhibits the cells' protein-producing machinery, effectively killing the cell while utilizing the space for reproduction. At this time, the more virulent *S. dysenteriae* begins to produce the Shiga toxin, which is a potent cyto- and neurotoxin. Through this and other toxins, *S. dysenteriae* causes the most clinically significant infectious complications. Both *S. dysenteriae* and *S. flexneri* can cause extra-intestinal complications that include congestive heart failure and/or hemolytic-uremic syndrome that can progress to renal failure. **Physicians** see greatly reduced infectious symptoms with an *S. sonnie* infection (typically only moderate diarrhea).

Physicians' choice of treatment for *Shigella* infection has often included ampicillin and trimethoprim-sulfamethoxazole accompanied with oral rehydration and nutritional supplements. However, **antibiotic** resistance to these drugs has fluctuated since about 1980.

The National Antimicrobial Resistance Monitoring System (NARMS) branch of the **Centers for Disease Control and Prevention** (CDC) reported in 2004 that the *Shigella* samples tested were highly resistant to ampicillin (77.8 percent), streptomycin (61.0 percent), sulfisoxazole (52.4 percent), trimethoprim-sulfamethoxazole (51.4 percent), and tetracycline (49.2 percent). Additionally, multidrug-resistant strains have been reported. Currently, quinolones, cephalosporin derivatives, and azithromycin are the drugs of choice. At this time, there is no available vaccine.

Amoebic dysentery is caused by the protozoan *Entamoeba histolytica*. Russian biologist Friedrich Losch (1840–1903) discovered the presence of the amoeba in 1873 and utilized dog experimentation to establish the relationship between the parasite and the disease in dogs. The Egyptian outbreaks of dysentery in 1885 and 1896 led Greek researcher Stephanos Kartulis (1852–1920) to detect a similar relationship between the parasite and disease in humans. Most medical information concerning *E. histolytica* was established by the end of the 1800s.

Because of specific species virulence factors, *E. histolytica* is the only one of nine common human protozoa that causes disease. In fact, it is a single-cell parasite that is the third highest cause of death from parasitic infection. Transmission of *E. histolytica* occurs by ingestion of the cyst form of the amoeba. Cysts are capable of surviving for long periods of time outside of the body and can even produce viable trophozoites (the mobile form of the amoeba) following exposure to chlorinated **water**. Trophozoites are the infectious and reproductive form of the organism. Within the distal ileum, trophozoites shed their cysts and can then colonize the intestines, reproduce via the formation of novel cysts, or cause infection as a result of a variety of virulence factors.

Infection within the colon typically manifests itself acutely in one of four ways: dysentery or bloody diarrhea, toxic megacolon, amoebic appendicitis, or amoeboma of the colon. Invasion of the intestinal lining is thought to occur through the induction of apoptosis followed by phagocytosis of host cells. This proposed path of infection might allow the parasite to kill neutrophils and other pro-inflammatory cells resulting in a minimal inflammatory response. Additionally, this path of invasion would explain the bloody diarrhea associated with parasitic infection. Extraintestinal infection can occur throughout the body but is typically found as liver abscesses because of direct access to the liver via the hepatic portal vein.

Currently, 90 to 99 percent of infected individuals are asymptomatic, which means that the body is capable of clearing the infection (usually within 12 months) and that not all sub-species of *histolytica* are invasive. Treatment options vary but often include two amoebicidal agents that will eliminate both the cyst and trophozoite forms. Additionally, supportive care is given to those with complications occurring because of infection.

Epidemiology. *Shigella* and *E. histolytica* are the most common causes of dysentery worldwide. In addition to causing similar symptoms, these organisms also share a common mode of **transmission**, via a fecal-oral pathway. Crowded areas in developing or socially disrupted countries with improper waste management and unsanitized water during times of drought and increased temperatures are the most likely places for epidemic dysentery. Until the late nineteenth century, dysentery was also very common in military camps and among troops on campaign, often taking more lives than action with the enemy.

The **World Health Organization** has estimated that 80 million cases of *Shigellosis* are contracted annually with 700,000 of these resulting in death. An overwhelming number of these cases are among children and the elderly. The most common cause of epidemic

infection is *S. dysenteriae* (Sd1) followed closely by infection with *S. flexneri*. Regional reports show that Sd1 ranges throughout the world with recent infections occurring in from 1969 to 1973 in Central America, from 1993 to 2000 on the African continent, and in 2000 in India. In North America, *S. sonnei* is the most common cause of *Shigellosis*. Infection with this serotype often produces acute, self-limited diarrhea but not deadly sequelae. In 2005 outbreaks in the United States occurred in Kansas, Kentucky, and Missouri daycare centers. Laboratory analysis confirmed close to 1,000 cases with a high degree of multiple antibiotic resistance.

A report in the *New England Journal of Medicine* suggested that there are 50 million cases of *Amebiasis* annually with 50,000 resulting deaths. One out of every ten infected individuals develops clinical symptoms. As with *Shigellosis* a large number of ill patients are represented by the young and the elderly. Southeast Asia and Central America are often plagued with outbreaks. In the United States, infections are often seen in immigrants. The last outbreak of *Amebiasis* as reported by the Centers for Disease Control and Prevention occurred in 1983 in Los Angeles, California, with close to 50 cases diagnosed but no common source of infection found. See also Drug Resistance in Microorganisms; Urbanization and Epidemic Disease; War, the Military, and Epidemic Disease.

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NICK RAGSDALE

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EARLY HUMANS, INFECTIOUS DISEASES IN. The long prehistory of infectious disease in humans extends back far beyond the pathogens that first emerged as infections in the hunter-gatherer ancestors of the *Homo* line around 2 million years ago. Those early prehumans bequeathed to us various “heirloom” infections, previously inherited from primate ancestors and retained by the early hominin line when it diverged 6 to 7 million years ago from the ancestral chimpanzee line.

The simplest category of heirloom infections comprised, presumably, the staphylococci, streptococci, and coliform **bacteria**—all families of bacteria that routinely coexist as commensals in and on humans. These bacteria can cause wound infections, throat infections, and diarrheal diseases when their micro-**environment** is disturbed or tissue is damaged. Soil-dwelling hookworms and the tetanus bacterium would also have been encountered often.

Over time, the succession of bigger-brained *Homo* species, eating increasing amounts of meat and using **animal** skins for rudimentary clothing and shelter, must have experienced new contacts with a wider range of bacteria and foodborne helminths (the various smaller enteric worms). Some evidence, though, indicates that nomadic humans are much less likely to harbor helminths, which depend on a fecal-oral transmission pathway, than are human communities living in settled, more crowded conditions. Larger gut-infesting worms, including tapeworms, are a very ancient group of commensal organisms with few retained independent capacities—they have evolved to be able, with minimal metabolic effort, to absorb nutrients passively through their outer coat. Early humans would have encountered them often in undercooked or raw meat from animal prey.

Various **viruses** able to persist or lie dormant for decades, such as the ubiquitous Epstein-Barr virus and a range of herpes and **hepatitis** viruses, also infected hunter-gatherers. The herpes virus group illustrates well a long parasitic history in both apes and hominins. These viruses could achieve unhurried vertical transmission, between generations, sometimes

via processes of reactivation after several decades of dormancy. Later paleoanthropological evidence, from the past several hundred thousand years, suggests that our *Homo* cousins, the Neanderthals, who occupied Europe and western Asia for much of the last quarter-million years, were also afflicted with dental cavities and infective arthritis.

The majority of newly-evolved human infections come from animal sources, via initial zoonotic infection. Others come from soil, such as the **Legionnaires' disease** bacterium, or from **water**, such as the **cholera** bacterium. Zoonotic infections would have occurred sporadically in hunter-gatherers, from locally circulating infectious agents in wild animals. Predation by early hunters was one direct route of acquisition. Other pathogens, such as simian **malaria** (in monkeys) and **trypanosomiasis** in antelope and buffaloes, require an **insect** vector for transfer from animal to human. Most such infectious contacts would have been transient because few zoonotic agents have the innate capacity to persist within tiny nomadic bands. Further, most pathogens cannot persist within humans without a sufficient sustained supply of susceptible young hosts with immature immune systems. Nevertheless, recent scares over the **Ebola** and **Marburg** viruses, both apparently acquired from tropical forest animal sources, underscore the occasional potential virulence of such agents.

Most of today's well-known common diseases did not exist in hunter-gatherer times. Indeed, the "crowd" diseases (such as have become prominent in later millennia: **measles**, **smallpox**, **influenza**, and many others) did not enter human populations until their progenitor microbes had an opportunity to "jump" from domesticated and pest animals into humans in the new ecological setting of **Neolithic** settlements. Further, the early human hunter-gatherers, living in small, isolated, and mobile groups, could not have sustained the endemic circulation of acute infectious diseases of that kind.

This radical shift toward farming, herding, and settled living emerged gradually, from around 10,000 to 11,000 years ago. This occurred in the wake of the warming and environmental changes that followed the retreat of the last 80,000-year-long glacial period. Fossil and pollen records show that this transformation in global climate decimated and displaced many species of edible animals and wild plant foods. In low to middle latitudes, humans responded by relying more on growing plants and herding animals. As food yields slowly increased so, inevitably, did localized human populations increase in size, in accord with available food supplies.

Those settlements created a new ecological niche for microbes. Indeed, this was a major "transition" in the human-microbe relationship—it allowed the proliferation of rodents, mosquitoes, and other pest species that were able to contribute new infectious pathogens to the early agrarians, whereas the closer and repeated contact with animals allowed the emergence of many novel zoonotic infections. This process thus ushered in the consequent rise of various human-adapted infections (malaria, **schistosomiasis**, **tuberculosis**, **leprosy**, influenza, smallpox and many others). Roundworms (nematodes) also thrived as human intestinal parasites now that people in settled communities were much more likely to make contact with and ingest fecally infected material—soil (especially young children) and plant foods. In particular, the roundworm *Ascaris lumbricoides* has been a human pathogen for many millennia. Overall, this radical change in human ecology greatly affected the pattern of disease. **Paleopathological** studies, comparing preagrarian and postagrarian skeletal remains, have shown that the early farmers were shorter, and shorter-lived, than their immediate hunter-gatherer forebears; they were generally less well fed and more exposed to infectious diseases.

This gradual and multicentered agrarian transition was the dominant source of today's familiar infectious diseases—that is, diseases able to establish themselves as endemic infections within populations and, in many cases, able to move between populations in epidemic fashion. This category includes acute viral diseases like measles, mumps, chickenpox, and influenza, and bacterial diseases such as tuberculosis, leprosy, and **syphilis**. Today, we think of those infectious diseases as part of the “natural order.”

The zoonotic origins of these “crowd” diseases are legion and fascinating. Smallpox arose via a mutant pox virus from cattle. Measles is thought to have come from the virus that causes distemper in dogs, leprosy from water buffalo, and the common cold from horses. Lesions in skeletons from the Middle East indicate that tuberculosis may have afflicted humans from at least 6,000 to 7,000 years ago. Dating from later millennia, tuberculosis-like lesions have been identified in the lungs of ancient mummies from Egypt and Peru. *Mycobacterium tuberculosis*, now adapted to humans, and *Mycobacterium bovis*, from cattle, are genetically very closely related, and this, and cross-infection from cattle to human, accords with the general thesis that the “crowd” infectious diseases of humans arose via zoonotic infection from cohabiting animals. In an uncomfortable reprise of this cattle-to-human transition, the bovine spongiform encephalopathy (BSE, or “mad cow disease”) prion found its way into humans sometime in the 1980s.

The list of cross-species transfers from animal sources to humans is long—and lengthening, as we acquire new zoonotic infections such as **HIV**, **SARS**, and the Nipah virus. Some historians consider that Asia, characterized by early large agrarian populations, may have been the main source of the infectious diseases that derived from domesticated and pest animal species, whereas Africa was the cradle of vector-borne infectious diseases from wild animal sources, including malaria, **Dengue** fever, and African trypanosomiasis (sleeping sickness). Malaria most probably gained its foothold as a human infection from early forest clearing and farming in western Africa. Later, irrigated agriculture afforded increased opportunities for various disease vectors and intermediate hosts: water-breeding mosquitoes, the water snails that spread schistosomiasis, and the guinea worm.

The animal-to-human passage of zoonotic infectious disease occurred widely around the world, in centers of agriculture and **urbanization**. South America's **Chagas's disease**, for example, entered human populations several thousand years ago, probably in Brazil, via domestication of guinea pigs by Amerindians. Chagas's disease is transmitted by a trypanosome (a **protozoan** cousin of the African trypanosome) via the blood-feeding triatomine bug that lives naturally in the earthen walls of guinea-pig burrows where it transmits the infection among guinea pigs. Mummies from northern Chile provide evidence, dating back several millennia, of organ damage from Chagas's disease and of the presence of the triatomine bug itself. The bug adapts readily to the earthen walls and thatching in poor rural housing where it transmits the trypanosome between humans. Today it infects a huge 15 to 20 percent of the population in the “southern cone” countries of South America, causing thinning and, often, rupture of the walls of the heart, colon, and esophagus.

As villages evolved into larger towns, and higher-order city-states and civilizations followed, so did the skeletal evidence of social stratification become stronger. Rulers, priests, warriors, merchants, laborers, and peasant-farmers became the defining basis of political structures, power, and privilege. Much of the evidence indicates that infectious diseases took their greatest toll on the poor and the peasantry. Adult height, estimated from skeletal remains, was greater in the urban wealthy than in the rural workforce. Some

of this differential reflected nutritional deprivation, some of it chronic and repeated infections.

It is important to remember that the many and various mutant microbes that early humans acquired from animal sources all have, themselves, very much longer ancestries. The mammals and **birds** from which we have recently acquired so many of our infectious diseases are themselves late-stage hosts in these long-running narratives. Indeed, bacteria and viruses predate the evolution of multicellular life by a billion years or so and spent eons learning, via the dispassionate processes of biological evolution, to infect one another and to acquire ways of adapting to hostile biochemical warfare (i.e., nature's **antibiotics**). They therefore have a genetic flexibility and fast-breeder survival capacity that we have only recently begun to fully recognize. *See also* Diagnosis of Historical Diseases; Historical Epidemiology.

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ANTHONY MCMICHAEL

EBOLA. *See* Hemorrhagic Fevers; Hemorrhagic Fevers in Modern Africa.

ECOLOGY. *See* Environment, Ecology, and Epidemic Disease.

ECTOPARASITES. Ectoparasites are organisms that live on the surface of other animals and depend on their hosts in order to complete their own life cycle; hosts can range from other **arthropods** to birds, fish, and mammals. Ectoparasites with human hosts include mites, lice, fleas, and ticks. Though other arthropods, such as tsetse flies and mosquitoes, feed on human blood and may thereby transmit disease, they do not abide on or very near the skin and are therefore not considered ectoparasites. Although these creatures usually trigger only itching, rash, or allergic reaction to their saliva or feces, they are sometimes infected with parasites of their own that can cause diseases ranging from **typhus** to **bubonic plague**. As a result, ectoparasites are significant vectors of human disease.

Mites. Mites are tiny arthropods related to spiders and ticks. Scabies, an infestation by the mite *Sarcoptes scabiei*, causes great discomfort although not serious disease. Adult mites, less than half a millimeter in length, dig burrows in the outer layers of the epidermis, where they lay eggs that hatch in three to four days. Intense itching and burning is caused by the secretions of the parasites, which prefer to live in the moist folds of the body such as between the fingers and the toes and in the groin area. Scratching can sometimes lead to staph or other secondary infections.

Scrub typhus is caused by *Rickettsia tsutsugamushi*, **bacteria** that live within the cells of mites or chiggers and are spread to humans through their bites. It occurs primarily in Southeast Asia and the Pacific, and affected thousands of Allied soldiers and marines during World War II (1939–1945). Symptoms include high fever, profuse sweating, and

swelling of the lymph nodes. Another disease associated with mites, the rarer but less serious rickettsial pox (*Rickettsia akaria*), is also spread through mite bites and produces a skin rash and mild fever.

Lice. Lice spend their entire life cycle on host animals, which can include birds and mammals. There are three varieties of lice that live on humans: *Pediculus humanus capitis*, or head lice; *Phthirus pubis*, or pubic lice; and *Pediculus humanus humanus*, or body lice. Although all cause severe itching and rash, the body louse can also serve as a vector of disease, spreading pathogens responsible for illnesses including epidemic typhus, trench fever (Werner-His disease), and louse-borne **relapsing fever**. Typhus and trench fever are spread through infected lice feces and relapsing fever through the body fluids of crushed lice. Lice are spread through close contact with an infested individual, or the sharing of clothing or bedding; infestations are most common under crowded, unsanitary conditions that make good hygiene difficult.

The adult body louse, a wingless insect from 2 to 4 millimeters in length, normally lives not on the skin of its host but on clothing, visiting the host only to feed. A female louse will lay nine or ten eggs per day, cementing them to clothing or bedding. The eggs, or nits, hatch within a week into nymphs, which grow to adulthood in about 16 days. Nymphs and adults feed on the blood of their hosts. Adults can live up to 40 days on a human host but will die within a few days if deprived of the ability to feed.

The most serious human disease transmitted by lice is **epidemic typhus fever**, which is caused by bacteria in the Rickettsia family, *Rickettsia prowazekii*. Although less well known than typhus, epidemic relapsing fever and trench fever have both caused millions of human deaths. An outbreak of relapsing fever in Eastern Europe killed an estimated 5 million people between 1919 and 1923. Trench fever, so named because it was first identified among soldiers in the trenches of the western front during World War I, killed more than 800,000 during the course of that war. The disease reemerged during World War II and then largely disappeared; a variant known as urban trench fever has become prevalent since the 1990s among urban homeless populations in Europe, Africa, and North America.

Fleas. Fleas are small, hard-bodied wingless **insects** (order Siphonaptera) that subsist as adults on the blood of their mammal or bird hosts, although they can survive for long periods of time without feeding if no hosts are available. Their powerful legs allow them to jump from host to host and to avoid attempts by the host to remove them. Most fleas are not host specific, and there are more than a dozen species that will feed on humans.

Fleas are carriers of two major pathogens affecting humans. Infected rat fleas (particularly *Xenopsylla cheopis*) can transmit the bacterium *Yersinia pestis*, and thus bubonic plague, to humans. Murine (or endemic) typhus fever can also be spread by fleas infected by *rickettsia typhi* bacteria.

Ticks. Ticks, small arachnids of the order Acarina, come in two varieties—hard ticks, or Ixodidae, and soft ticks, or Argasidae. Ticks spend a portion of their life cycle on a host animal, feeding on its blood. Hard ticks may remain attached to hosts for days as they continue to feed but soft ticks feed in a matter of minutes. Ticks, because they often harbor pathogenic parasites that are transferred to humans through their bites, are vectors of a number of human diseases, including **Lyme disease** (caused by bacteria), Rocky Mountain spotted fever (*Rickettsia* bacteria), **babesiosis** (protozoa), Q fever (bacteria), Crimean-Congo **hemorrhagic fever** (virus), and tick-borne relapsing fever (bacteria). Rocky Mountain Spotted Fever, the most serious tick-borne disease in the United States, is a

sometimes-fatal disease characterized by flu-like symptoms—fever, chills, muscle ache—and a rash. Lyme disease, the most common disease transmitted by ticks in the United States, begins with flu-like symptoms and a characteristic circular rash. If left untreated, the infection can spread to the joints, causing arthritis and severe joint pain, and/or the nervous system, causing numbness, tingling in the extremities, and memory problems. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Colonialism and Epidemic Disease; Contagion and Transmission; Disinfection and Fumigation; Environment, Ecology, and Epidemic Disease; Hemorrhagic Fevers in Modern Africa; Personal Hygiene and Epidemic Disease; Pesticides; Typhus and Poverty in the Modern World; Typhus and War.

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TERESA LESLIE

EHRlich, PAUL (1854–1915). Paul Ehrlich was the founder of modern chemotherapy and also made important contributions to the study of the immune system, blood, and cancer. Born on March 14, 1854, in Strehlen, Germany (now Strzelin, Poland), Ehrlich received his medical degree from the University of Leipzig in 1878. Upon graduation, he went to work at the Charité Hospital in Berlin, where he developed a method of staining the tubercle bacillus newly discovered by **Robert Koch**. In 1891, he joined the staff of Koch's newly founded Institute for Infectious Diseases in Berlin. Ehrlich became director of a laboratory for serum research and testing at Steiglitz in 1896. A new Institute for Experimental Therapy was created for him in Frankfurt in 1899, and he remained as its director until his death on August 20, 1915. From 1906 on, he was also head of the Georg-Speyer Haus, a laboratory for experimental chemotherapy built adjacent to the Institute.

From Ehrlich's days as a medical student, he was intrigued by the concept that drugs and chemicals had a particular affinity for specific organs and tissues. In the 1890s, his attention was focused on **immunology** when his colleague at Koch's Institute, **Emil Adolf von Behring**, discovered an antitoxin to combat the toxin produced by the **diphtheria** bacillus. Ehrlich played a significant role in assisting von Behring in the development of a standardized and sufficiently potent antitoxin preparation for use in the treatment of diphtheria patients. In order to explain the fact that the antitoxin specifically combined with the toxin molecule, Ehrlich developed his side chain theory. He theorized that the diphtheria toxin has the ability to combine with and poison specific molecular structures ("side chains" or "receptors") in the cell. As the cell compensates, some of the excess side chains produced are released into the bloodstream where they serve as antitoxins, specifically combining with and neutralizing the toxin. This concept paved the way for the emergence of the modern receptor theory of drug action. Ehrlich shared the Nobel Prize in Medicine or Physiology in 1909 for his contributions to immunology.

In the early twentieth century, Ehrlich began experimenting with dyes and other substances searching for chemical agents that could act with the same specificity as the

antitoxins. He reasoned that one could cure infectious disease by finding chemicals that would specifically attack and destroy pathogenic microorganisms within the body without harming the human host cell. He and his coworkers synthesized and modified the structures of numerous chemicals, testing the activity of these compounds in experimental animals against diseases caused by microorganisms known as trypanosomes. Later they also tested these compounds against **syphilis**. They soon focused on organic arsenic compounds. In 1909 they discovered that the 606th chemical that they tested, later trademarked Salvarsan, was effective against syphilis in animals. Although Salvarsan was not an ideal therapeutic agent because of its toxic side effects and the prolonged treatment required, it was the first drug that was truly effective in treating syphilis. It provided Ehrlich with a practical demonstration of the value of his concept of chemotherapy and helped to stimulate the search for other chemical agents against infectious diseases. See also Human Immunity and Resistance to Disease; Tuberculosis.

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JOHN PARASCANDOLA

EMPIRIC. Empiric refers to a wide range of European medical practitioners—women as well as men—who lacked the formal university medical training and guild membership of physicians and were not **surgeons**. "Empirical" denotes their general method of learning, which depended upon the observation of medical practice (as well as a certain degree of trial and error) rather than on the reading and interpretation of medical texts, which was the standard mode of learning in the universities. More importantly, however, "empiric" can also be applied to those who devalued book-learning in favor of hands-on experience and medical knowledge acquired by doing, a stance taken by **Hippocrates**, **Galen**, and the controversial **Paracelsus** in the first half of the sixteenth century. These opposing philosophies led to a long-running antagonism between empirics and **physicians**, with the latter often labeling empirics as fraudulent **quacks** or charlatans. Nevertheless, empirics occupied an important niche in the medical marketplace, offering an alternative set of regimens and remedies that could differ markedly from the more traditional, Galenic **humoral** treatments and remedies offered by university-trained physicians. This became especially prominent in the sixteenth and seventeenth centuries, when empirics became almost synonymous with proponents of **Paracelsian** or chemical medicine.

Empirics were, in some ways, well situated to deal with **epidemic** diseases such as **smallpox**, **syphilis**, and **bubonic plague**. This was the result of their common presence in both urban and rural areas, of the much smaller fees they generally charged, and of the fact that wealthy traditional physicians were often among the first people to flee when plague struck. Because many empirics claimed proficiency in treating internal disorders—traditionally the prerogative of the physician—they were a logical choice for beleaguered

towns and villages thus deprived of their local doctors (itself a label indicating formal education).

As this pattern was repeated during the sixteenth and seventeenth centuries, empirics established important footholds in many urban centers at the expense of their university-trained cousins. Their social and professional importance rose to such a degree that, shortly before the **Great Plague of London** (1665–1666), a number of English empirics banded together to establish the Society of Chemical Physicians in London, a short-lived rival to the Royal College of Physicians. Members of the Society openly advertised prophylactics and cures for plague during the epidemic. That they did a brisk business in treating plague victims may be inferred from the fact that 40 of the 50 practicing physicians in the Royal College fled London. Though the Society did not survive, its establishment was made possible in part by the repeated outbreaks of plague suffered by western Europe in the early modern period. Empirics continued to play a prominent role in the treatment of epidemic disease and made notable contributions to medical science and procedure well into the eighteenth century. *See also* Apothecary/Pharmacist; Folk Medicine; Medical Education in the West, 1500–1900; Paracelsianism; Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Scientific Revolution and Epidemic Disease.

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MARK WADDELL

ENCEPHALITIS. Encephalitis is a condition of the brain that involves swelling and inflammation. It can be triggered by **nonepidemic** reactions to such things as complications following a **vaccination**, mumps, chicken pox, or herpes. However, in the twentieth century encephalitis also took on an epidemic form caused by a viral infection often carried by an **insect** vector, especially mosquitoes. This type of disease has been labeled an arbovirus or **arthropod**-borne virus. Its effects cover a wide and varying range of symptoms, but there is a basic pattern. Most types of encephalitis cause high fever, very severe headaches, stiff necks, irrationality, irritability, mental confusion, and a semi-comatose state that can continue for years. Because of this last symptom, encephalitis has been mistakenly called a "sleeping sickness." For some victims the infection can lead to death. The mortality rate for epidemic encephalitis can range from 5 to 75 percent, depending on the strain, with the normal range being roughly 15 to 20 percent.

Analysis of blood and cerebrospinal fluid collected with a lumbar puncture will determine the presence of the disease. Mild encephalitis may disappear rapidly with simple bed-rest and analgesics for the pains, whereas more serious infections, determined with encephalography and magnetic resonance imaging, may require observation in a hospital

and treatment with appropriate antivirals such as amantadine or acyclovir, corticosteroids, or drugs to prevent seizures.

Two main types of the disease have been observed since World War I (1914–1918). The first broke out during the **war** and continued into the next decade. It was originally diagnosed by the Austrian medical researcher Constantin von Economo (1876–1931) who determined that it represented a new, but unidentified, viral infection that would soon be called “encephalitis lethargica.” Its cause was, and still is, unknown. By the late 1920s it had disappeared as mysteriously as it had arrived. Although the Matheson Commission in New York City had systematically studied it during the decade, the **virus** was not isolated, so despite its virulent impact that caused thousands of deaths, its nature remained obscure. Its aftereffects were most disturbing, as many survivors continued on in a somnolent, trance-like state. This long-term condition would eventually be analyzed by Dr. Oliver Sacks (1933–) in the 1960s and would become the source material for both a book and a motion picture entitled *Awakenings* (1990).

In the early 1930s another form of epidemic encephalitis appeared, first in Paris, Illinois, but more spectacularly in St. Louis, Missouri. The 1933 St. Louis epidemic made headlines because it was an unknown disease that was similar to lethargica but had many different aspects. The new strain killed older people, occurred in the spring and summer, and did not have as many debilitating aftereffects as the earlier encephalitis strain. It would be given the name St. Louis encephalitis, and this form would continue to appear from the 1930s into the 1980s. Other strains of encephalitis were discovered in various parts of the world, such as Japanese B in Asia; Murray Valley in Australia; and a horse-based form, Venezuelan, in South America. The equine connection also has a history in North America, having been reported during the nineteenth century as an epizootic known as “blind staggers.” This type, called eastern or western equine encephalitis depending on location, could infect humans on occasion. The first of the eastern outbreaks in humans took place in Massachusetts in 1938. This epidemic featured symptoms that differed from all the previous encephalitis types. Although the number of victims was relatively small, the mortality rate was a shocking 74 to 75 percent, and the primary targets of the disease were children under 10, including a significant percentage of infants. In addition, the effects on those who survived included severe brain damage and permanent mental retardation. Similar, but less virulent, attacks of this eastern equine strain continued to target humans on into the 1950s, especially on the east coast of North America.

The Virus and Its Transmission. The viruses for all of the encephalitis strains since 1933 have been isolated, starting with the St. Louis type discovered by pathologist Margaret Smith (1896–1970) in that city. For many years, however, the disease’s means of transmission were unclear. Back in 1933 a set of failed human experiments that had unsuccessfully attempted to prove a mosquito carrier was involved led public health officials to look elsewhere for a **transmission** medium. During the 1940s, however, the mosquito vector theory was reexamined and soon verified. What had been missed earlier was the presence of a necessary bird host that mosquitoes had to first bite in order to spread the disease. This discovery came about as a result of the work of William McDowell Hammon (1904–1989) and William C. Reeves (1917–2004) in the Yakima Valley of Washington state. Based on their research, the mosquito-bird-mosquito cycle of epidemic encephalitis transmission was accepted. Human beings, it was discovered, were simply occasional and accidental dead-end hosts who contracted the virus only under a

very specific set of environmental conditions. Humans could not pass on the disease to other humans.

Therefore, by the 1950s and 1960s, the main outlines of the encephalitis arthropod-borne virus had been mapped. Health officials knew what they were dealing with and how to combat it, although certain questions about the disease still remained unanswered. For instance, it was never clear at the start of an epidemic which mosquito breeds were implicated, because the study of mosquito types and breeding places was still underdeveloped. Even more difficult to determine were the types of birds that served as hosts. They could be domestic fowl or endemic wild species or, even more likely, migratory birds just passing through the area. Migratory species might, it was believed, become infected in one geographic area, and then fly into another area that had, up to that time, been free of encephalitis virus. They would serve as the reservoir that would be bitten by local mosquitoes that would then spread the epidemic in its new location. Also unknown was the mechanism by which the virus could survive the cold winter months. It has been suggested that occurs in the body of a hibernating mosquito, but this remains a matter of scientific debate.

Because of its mosquito-bird-mosquito cycle, epidemic encephalitis is an environmentally driven disease. It requires a pattern of weather, bird, and insect interactions for it to spillover to either horses or humans. It needs a wet, rainy season followed immediately by a dry period that creates stagnant breeding pools for vector mosquitoes. There have to be very large numbers of mosquitoes emerging from these pools, as well as wind currents that can spread them to a wider geographic area. An equally large bird population must be available to act as hosts, and both the type of bird and the type of mosquito have to be carriers or reservoirs acceptable to the encephalitis virus. Epidemics can also take place in regions that do not at first appear likely, such as the High Plains of Texas, where human-made environmental changes can establish the necessary natural conditions. Thus, the digging of irrigation canals in an arid area or the creation of catch-basins from water drained out of sewerage treatment plants can provide the required breeding grounds for mosquitoes and even wetlands for birds. It is this general environmental nature of encephalitis that necessitates an epidemiological investigation that includes a range of scientific specialties such as **ecology**, mammalogy, ornithology, veterinary medicine, and agricultural studies in addition to the expected fields of **epidemiology** and virology.

There is no cure for viral encephalitis nor is there any effective immunization. People who live in regions with high mosquito counts and a large bird population can protect themselves by wearing appropriate clothing and by applying insect repellent to ward off mosquitoes. The only systematic method of combating encephalitis either before or during an epidemic is to kill off either the bird hosts or the mosquito vectors. Because many different bird species may be involved in the infection cycle and because mass killing of birds is both unfeasible and socially unacceptable, it is the mosquitoes that are attacked. A typical anti-encephalitis campaign from the 1950s to the present involves the use of significant amounts of **insecticide**, originally DDT, now a diluted form of malathion, that is either sprayed from airplanes or, more likely, belched from the back of a slow moving street fogging truck. Also part of such a campaign is the draining of stagnant water from empty lots and receptacles in people's backyards that may serve as breeding pools. Ponds and ditches are usually treated with larvicide. Therefore, ironically, the methods to deal with an environmentally caused outbreak of encephalitis involve altering or destroying aspects of that environment, a fact that can sometimes lead both to natural degradation

and to political controversy. *See also* Encephalitis, Epidemic Outbreaks in the Twentieth Century; Gorgas, William Crawford; Yellow Fever Commission, U.S.

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ERIC JARVIS

ENCEPHALITIS, EPIDEMIC OUTBREAKS IN THE TWENTIETH CENTURY. Encephalitis is an inflammation of the brain occasionally triggered by such things as post-**vaccination** reactions, mumps, or herpes. Its symptoms can include sudden fever, severe headaches, irrationality, drowsiness, and at its worst coma that can lead to death. In the post-World War I era, encephalitis assumed a new viral **epidemic** form that led to outbreaks around the world.

Its first and most notorious form became known as *encephalitis lethargica*. It was originally noticed in 1915, while the war was still raging, and after the war it spread dramatically until roughly 1926, when it disappeared as mysteriously as it had appeared. It seemed to be linked somehow to the great **influenza pandemic of 1918–1919**, except that it had begun before the influenza outbreak, and its worst impact occurred in the winter of 1919–1920. It was initially studied by the Austrian medical scientist Constantin von Economo (1876–1931), who believed that the disease represented a new viral strain, even though the **virus** was never discovered. It eventually killed thousands of people and could affect survivors by placing them into a coma-like trance. This led to the disease often being incorrectly called "**sleeping sickness**," even though it had no relation to the African illness of that name. Lethargica has remained a controversial and unknown disease to this day.

In North America, viral encephalitis did not return until the 1930s. It, however, proved to be a type different from lethargica, with somewhat varied characteristics. This new type made a brief appearance in Paris, Illinois, in 1932 and then assumed an epidemic form in St. Louis, Missouri, during the late summer and fall of 1933. It became known as St. Louis encephalitis or SLE. Initially it was believed to be a return of encephalitis lethargica, but it struck at a different time of year, attacking different age groups with a set of less severe long-term effects. As a result, public health officials soon realized that they were dealing with a different strain. This time the virus was isolated, but the disease's cause and its mode of **transmission** could not be determined. It eventually spread throughout the city and its surrounding county until it ultimately ended with the advent of colder weather. The city suffered nearly 1,200 cases, with 221 recorded deaths.

In 1933 the speculation surrounding its transmission focused on the role of mosquitoes as probable carriers, especially since St. Louis was swarming with mosquitoes that summer. However, following a set of experiments utilizing **human subjects**, the mosquito theory was dropped. A group of physicians and then convict volunteers allowed themselves to be

bitten by mosquitoes that had just bitten encephalitis victims. None of them contracted SLE. This led investigators to turn to other theories of contagion. What they had not realized was that the mosquitoes had to bite an infected **bird** host and that the disease could not spread from person to person directly. Only under a specific set of **environmental** conditions involving climate, mosquito breeds, and precise types of migratory birds could SLE spill over to infect humans, who served only as dead-end hosts.

This picture finally became clear during the 1940s, and as a result St. Louis encephalitis was placed into a group of similar viruses known as **arthropod**-borne viral encephalitis, or arboviruses. SLE continued to break out during the 1950s in cities such as Louisville, Kentucky, and in unexpected places such as the High Plains and the Lower Rio Grande Valley of Texas. By the time of the Texas outbreaks, the mosquito-bird-mosquito cycle theory was generally accepted but was still being tested. By the next major outbreak, in St. Petersburg, Florida, in 1962, the only unknowns were the types of mosquitoes and birds that were involved. Health authorities battled the epidemic the only way they could: by killing the mosquito carriers with the use of clouds of insecticides from mobile fogging machines. Similar outbreaks of SLE occurred in Houston (1964) and Dallas (1966), whereas it emerged in Memphis, Tennessee, in 1975, and in the Canadian provinces of Ontario and Manitoba in 1975.

Other strains of viral encephalitis evolved in various parts of the world. For instance, there was a type known as Japanese B encephalitis; it was discovered in 1924 and its virus isolated in 1935. It was similar to SLE but was more dangerous, with a death rate of 50 to 70 percent; the rate for SLE was generally 15 percent. Japanese B occurred in Japan in the 1930s and spread to other Asian nations such as Taiwan, Korea, and India right into the twenty-first century. Yet another type of encephalitis appeared in Australia in 1917 called Murray Valley encephalitis. It also had a high mortality rate and continued to break out during the 1920s, the 1950s, and into the 1970s. Beyond these varieties of the disease, there were also types that were known to attack primarily horses. These strains of equine encephalitis could, on occasion, attack humans also. One of the most serious was Venezuelan equine encephalitis that occurred throughout parts of Latin America. In North America another strain, Eastern Equine encephalitis, also claimed human victims, particularly among young **children**, for the first time in Massachusetts in 1938. It reoccurred in other parts of the eastern United States into the 1950s.

Epidemic viral encephalitis was never the killer that **yellow fever** had been, but it was yet another mosquito-carried disease that could kill and seriously injure. There is still no cure nor any preventative. The only method of combating viral encephalitis remains that of killing the insect carriers. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Disinfection and Fumigation; Pesticides.

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ERIC JARVIS

ENDERS, JOHN FRANKLIN (1897–1985). The worst **poliomyelitis** epidemic in the United States occurred in 1952, when 57,000 people were stricken. John Enders and his team discovered that the **virus** that causes polio could be grown rapidly, and in a variety of different tissues, opening up the field of human virology. Medical historian John Simmons summed up their importance: “Their discovery of tissue culture technique is often lauded as a classic instance of scientific intuition combined with careful experiment leading to a medical breakthrough.” These mass production techniques meant that American microbiologists **Jonas Salk** and **Albert Sabin** could go forward with their polio research and develop a vaccine.

Enders was born in Hartford, Connecticut. Though he was a graduate student in English, a friend who was in a microbiology program influenced him to change his major. He received a doctorate in bacteriology and **immunology** from Harvard University, where he was a student of microbiologist and **typhus** expert Hans Zinsser (1878–1940).

Enders, who began his career working with viruses in animals and developing animal vaccines, was asked to set up an infectious disease laboratory at Children’s Hospital in Boston, Massachusetts, in 1946. In his early experiments, he found a way to grow the mumps virus in a tissue culture made up of fragments of chick embryos. During an experiment with the chicken pox virus, Enders and his team found that they had culture, composed of human embryo tissue, left over. So that the tissue would not go to waste, they tried growing polio viruses in it, using **antibiotics** to kill any contaminants. It had been previously thought that the polio virus would only grow in nervous system tissue, which had to be obtained from the brain or spinal cord of monkeys and could potentially be contaminated. But they found that they could use many different types of human tissue, including foreskin tissue from infant circumcisions and embryonic tissue from miscarriages. Using a new test tube technique, they were able to see how the polio virus killed the cells in the tissue.

Enders turned down the opportunity to develop a virus vaccine because his lab was not set up for vaccine production, and he felt that it would be better for private industry to develop a vaccine. Both he and Sabin believed that a live virus vaccine (made of live microorganisms that have been weakened but still maintain their ability to give immunity) would provide the best form of protection against polio.

Enders received the Nobel Prize in Physiology or Medicine in 1954 and was adamant that his team members Drs. Thomas Weller (1915–) and Frederick Robbins (1916–2003) share the honor equally with him. Enders developed a **measles** vaccine that was marketed in the early 1960s, and in his retirement, he investigated **HIV**, the virus that causes AIDS. *See also* Human Immunity and Resistance to Disease; Measles, Efforts to Eradicate; Poliomyelitis, Campaign Against; Vaccination and Inoculation.

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MARTHA STONE

ENTERIC FEVERS. “Enteric” means “pertaining to the intestines,” and the historic term “enteric fever” refers to two diseases characterized by fever and intestinal symptoms. These are now known as **typhoid** and paratyphoid and are caused by different **bacteria** of the salmonella group, paratyphoid being the milder disease. They have probably been human diseases since prehistoric times and are still common in many less developed countries. Unlike other salmonellosis, these are not zoonoses: there is no **animal** reservoir of the microbes that cause these diseases. Excrements (usually feces, but occasionally urine) of either healthy carriers or active or recovering cases are always ultimately responsible for outbreaks, with the vehicle of infection normally being food or drink. Outbreaks are often small and localized, but they can also be large, as when public **water** supplies are contaminated, and they may occur far from the original source—for example, when contaminated foodstuffs are transported across or between countries. Where typhoid is endemic, the incidence of the disease tends to peak in the summer months. Enteric fevers can attack people at any age, but younger people and in-comers to endemic areas are often especially susceptible. The precise demographic characteristics of outbreaks are frequently understandable in terms of the vehicle of infection and the eating and drinking habits of the victims. Historically, typhoid outbreaks occurred when sanitary conditions were poor and **personal hygiene** difficult, such as in besieged cities or overcrowded prisons. Recently, it has been claimed that the **Plague of Athens**, which killed about a third of the population of the city and its leader, Pericles, was a typhoid **epidemic**. Historians debate the precise role of the outbreak in ending the war with Sparta, but it is generally agreed that the loss of the war was the beginning of the end of Athenian hegemony of the ancient world. Much later, sanitary conditions prevalent during the early period of European global colonization were conducive to the spread of typhoid. Between 1607 and 1624, over 6,000 settlers died from typhoid in Jamestown, Virginia. The unplanned or badly planned **urbanization** in the eighteenth and nineteenth centuries also created conditions favorable to enteric fevers, and their control was one of the aims of the public health and sanitation reforms that followed.

Evidence of typhoid in the ancient world appears in the Hippocratic corpus. In *Of the Epidemics* (400 BCE), a case is described in which “Silenus” developed small red spots, a classic sign of typhoid. The evidence that the Plague of Athens was typhoid comes from the analysis of ancient microbial DNA extracted from teeth recovered from the mass grave at the Kerameikos ancient cemetery in Athens. Although some features of the disease described by the historian Thucydides (460–400 BCE), such as its sudden onset, differ from those seen today, the DNA sequences observed are sufficiently similar to those of the modern typhoid germ to allow the conclusion that the plague was either typhoid or a very similar disease. It is recognized that there are many different strains of the typhoid germ, which cause outbreaks in which different symptoms are prominent, and that the impact of the disease also varies according to the population attacked.

The interpretation of the DNA as typhoid, however, has been challenged. On the basis of a description of symptoms by the Greek historian Arrian of Nicomedia (c. 87–147), it has also been suggested that typhoid was the cause of death of Alexander the Great (b. 356) in 323 BCE. The Roman Emperor Augustus (63 BCE–14 CE) also appears to have suffered from the disease, which was treated by cold baths by Antonius Musa, a first-century Roman physician, a treatment that was still used in the nineteenth century.

Enteric fevers are distinguished from ordinary microbial food poisoning in that the former generally have a longer incubation period—at least 7 and often 20 days—with microbes carried from the gut by the blood to invade and disrupt numerous organs. In other words, enteric fevers are “systemic” infections. The symptoms of microbial food poisoning, in contrast, can appear within hours of eating the implicated food and are usually confined to inflammation and irritation of the gut. The attack rate in enteric fevers (number of cases among the population exposed to the contaminated food or beverage) depends upon the number of bacteria ingested but also varies according to the strain involved. The main clinical features of typhoid are usually a slow-onset prolonged fever, along with such symptoms as abdominal pain and digestive problems (diarrhea or constipation), headache, cough, and lethargy. The characteristic “rose spot” rash and liver or spleen enlargement are present in a minority of victims. Those who recover normally do so in about 28 days, but about 2 percent continue to pass the typhoid organism in their feces, with the gall bladder and the tube that transfers bile from the gall bladder to the intestine being the usual site of continued infection. Older women are most susceptible to becoming carriers. Possible complications of typhoid include **meningitis** (inflammation of the lining around the brain and spinal cord), osteomyelitis (bone infection), endocarditis and myocarditis (which affect the heart), bleeding from or perforation of the gut, and pneumonia. Before the availability of **antibiotics**, some 12 to 16 percent of victims died from these complications.

The distinction between typhoid and paratyphoid was not made until the era of bacteriology. The bacterium associated with typhoid had already been described in 1880 (now known as *Salmonella typhi*). In 1896, however, another bacillus was isolated that caused an illness similar to typhoid, apart from variations in the clinical signs and source of infection. This disease was named paratyphoid, and the associated organism, *Salmonella paratyphoid*, of which three forms were subsequently identified, labeled A, B, and C, which have different geographical distributions. In paratyphoid, the intestinal changes are more diffuse than in typhoid, whereas the skin eruptions are larger and more extensive. Paratyphoid is also rarely spread by water.

Enteric fevers continue to be a serious health problem in less developed countries, where public sanitation and water filtration, treatment, and sterilization remain inadequate. Patients also tend to delay seeing a doctor, and antibiotics are often not easily available in these countries. Typhoid resistant to chloramphenicol, the usual antibiotic treatment, and multiple **drug resistance** have caused increasing concern in recent years. Occasionally, chloramphenicol-resistant strains had been encountered from as early as 1950, but it was not until the early 1970s that a large outbreak of chloramphenicol-resistant typhoid occurred. This took place in Mexico, where the incidence of typhoid had declined for some 20 to 25 years as sanitary conditions were improving. Nevertheless, a massive epidemic began explosively in 1972 in Mexico City and the State of Hidalgo, soon spreading to the Central Valley and beyond. There were an estimated 10,000 to 15,000 cases during 1972, and the fatality rate, 13 percent at first, was unusually high. It emerged that 96 percent of the strains involved in the epidemic were chloramphenicol-resistant. The authorities responded with health education and the regulation of food markets, along with some 5 million doses of vaccine. The epidemic subsided in 1973 but lasted until 1975. As time passed, for poorly understood reasons, the proportion of the chloramphenicol-resistant strains involved declined. It proved surprisingly difficult to pinpoint the vehicle of infection, although for some geographically self-contained



First typhoid inoculation. United States Army Medical School, March 1909. Courtesy of the National Library of Medicine.

outbreaks within the overall epidemic, contaminated water was certainly involved. Bottled beverages came under suspicion, but it was concluded that, unusually, direct person-to-person spread was an important feature.

In 1984 it was estimated that globally there were 16 million cases of typhoid illness and 600,000 deaths annually. It has been estimated that, during 2000, there were 21,650,974 cases of typhoid illness and 216,510 deaths, and 5,412,744 cases of paratyphoid illness. However, in view of the shortage of laboratory and surveillance facilities in many of the countries where typhoid remains endemic, the reliability of the methodology upon which these data are based is uncertain. In countries such as Egypt, India, and Chile, where sufficient data are available, a downward trend in the incidence in typhoid is apparent, consistent with improvements in sanitary conditions in these countries. But some regions, especially south-central and southeastern Asia, continue to have a high incidence of enteric fevers. *See also* Colonialism and Epidemic Disease; Diagnosis of Historical Diseases; Diet, Nutrition, and Epidemic Disease; Hippocrates and the Hippocratic Corpus; Sanitation Movement of the Nineteenth Century; Typhoid Fever in the West since 1800; Vaccination and Inoculation.

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DAVID SMITH

ENVIRONMENT, ECOLOGY, AND EPIDEMIC DISEASE. Like various other large mammals, *Homo sapiens* is a patch-disturbing species. Over tens of thousands of years, humans have encroached upon and changed the natural environment and have done so at an increasing scale and with growing intensity. This encroachment has, inevitably, disturbed or disrupted many ecosystems and interspecies relationships, thereby affecting the ecology, geographic range, and activity of infectious agents. There are, we presume, tens of millions of different species and types of **bacteria**, **viruses**, and other microbes "out there" in the natural world. Hence, a major part of human experience—both biological-evolutionary experience and cultural experience—has been to encounter an increasing number of these infectious agents as human populations have spread and diversified around the world.

History might be told as a series of major transitions in the ever-changing relationship between the human and microbial worlds: **Neolithic** agrarianism, contacts and conflicts between adjoining empires, transcontinental explorations and conquests, and **industrialization** and **urbanization**. Today we are adding a new and momentous layer to that story of environmental exploration and encroachment and microbial mobilization. Many of the

large-scale environmental changes that humankind is now imposing on the biosphere, such as changes in the pattern and scale of land use, the use of waterways, and global climate change, have great implications for the pattern of infectious disease occurrence and **transmission**, now and in future.

Land Use and Environmental Change. Several decades ago the eminent twentieth-century microbiologist Rene Dubos (1901–1982) noted that throughout history humans have always substantially changed the environment in which they live. Many of these changes, he pointed out, affected the ecology and the occurrence of infectious diseases. The main human-induced environmental changes that affect infectious disease risk today include the following: land clearing, especially tropical deforestation; road building; irrigation; dam building; changes to regional climate; intensified crop and animal production systems; urban growth and sprawl; continuation of poor sanitation practices; and the pollution of coastal **waters**.

In the early 2000s, a working group of several dozen scientists from around the world reviewed what is known from published research about how patterns of land use affect the emergence of new infectious diseases. They ranked the land-use activities with greatest impact, in descending order: agricultural development; urbanization; deforestation; population movement and displacement; introduced species/pathogens; biodiversity loss; habitat fragmentation; water and **air** pollution (including heightened respiratory susceptibility); road building; impacts of **HIV/AIDS** on human resources for farming and land management; climatic changes as a result of human generation of greenhouse gases; and hydrological changes, including construction of dams.

The following examples illustrate some of the different ways in which various human environmental impacts affect emerging infectious diseases.

Altered Environment and Habitat with Increased Population Sizes of Either “Reservoir” Host Species or Vector Species. Forest clearance, with road building, ditch construction, and subsequent damming and irrigation, has diverse impacts on anopheline mosquito species—the species whose members are vectors for **malaria**. Cleared land and the creation of ditches often enhance breeding opportunities for local anopheline mosquitoes. Recent studies in the Peruvian Amazon have clearly shown a strong positive relationship between the intensity of forest clearance and the abundance of malaria-transmitting mosquitoes. On the other hand, land clearance and habitat disruption may eliminate some local mosquito species and thereby open a niche for an invasive anopheline mosquito species.

The rodent-borne **hantavirus** provides an illustration of how regional fluctuations in climate (whether natural or human-amplified) can disturb relationships among species within ecosystems. This virus occurs widely in rodent populations in agricultural systems in South America and East Asia and in arid grasslands in North America and elsewhere. In mid-1993, an unexpected outbreak of a mysterious viral infection occurred in humans in the Four Corners region of the southwestern United States. The infection caused acute respiratory distress and had a high fatality rate. This novel disease was eventually traced to infection with a previously unrecognized hantavirus, maintained primarily within the reservoir population of native deer mice. The disease was duly called “hantavirus pulmonary syndrome.” Human infection by this virus can apparently occur by the inhalation of wind-blown dried excretions of infected mice.

Why did this disease emerge in 1993? Researchers surmised that the El Niño meteorological event of 1991–1992, with its unseasonably heavy summer rains in the American

Southwest, had caused a great increase in the local rodent populations and had thus made the 1993 outbreak possible. Populations of deer mice were reported to have been more than 10 times greater than the previous 20-year seasonal average.

Biodiversity Change and Habitat Fragmentation. Deforestation with fragmentation of habitat increases the “edge effect” the extent of interspecies contacts at land-use boundaries—which increases pathogen-vector-host interaction. This process has contributed, in recent decades, to the emergence of a number of viral **hemorrhagic fevers** in South America: in Argentina (Junin virus), Bolivia (Machupo virus), and Venezuela (Guanarito virus).

These hemorrhagic fever infections typically occur in outbreaks ranging from a few dozen to thousands of cases. They are caused by arenaviruses for which wild rodents are the natural hosts. Outbreaks have mostly occurred in rural populations, when people become infected by contact with contaminated rodent excretions. This is well illustrated by the Machupo virus. The clearing of forest in Bolivia in the early 1960s, accompanied by blanket spraying of DDT to control malaria mosquitoes, caused both an infestation of the cropland by *Calomys* mice and the DDT poisoning of the usual predators of those mice (the village cats). The consequent proliferation of mice led to the emergence of a new viral fever, the Bolivian (Machupo) Hemorrhagic Fever, which killed around one-seventh of the local population.

Ecosystem Changes, Loss of Predators, and Host-Species Imbalance. Tick-borne **Lyme disease** in the northeastern United States illustrates this type of complex influence on infectious disease occurrence. This bacterial disease was first identified in the American Northeast in 1976 in the town of Old Lyme, Connecticut. The disease is spread by black-legged ixodic ticks that are infected with the spirochete *Borrelia burgdorferi*. The ticks normally feed on mammalian species, especially deer and white-footed mice, with the latter being the more likely source of the infective agent; that is, the mice are considered the more “competent” host species for transmission of the spirochete.

The tick has a three-stage life cycle: larva, nymph, and mature adult. Transmission of the spirochete is influenced by temperature and rainfall, which affect both the geographic range of the intermediate host mammals and the speed of maturation of the immature (larval-nymphal) tick. The temperature-dependent synchrony of blood feeding by both the larval and nymphal stages of the tick is an important requirement for maintenance of infection within the maturing ticks. In the northeastern United States, the tick is predominantly infected by feeding on spirochete-infected white-footed mice.

The tick, however, can also feed on other small mammals, most of which do *not* carry the spirochete. Hence, in depleted local ecosystems with few mammalian species, the tick-nymphs will be more likely to feed on infected mice, and so the proportion of infected ticks will be much greater than when the ecosystem has a diversity of food sources for ticks. In fact, forest fragmentation and hunting in the northeastern United States have reduced biodiversity in this ecosystem. This has entailed the loss of various predator species—wolves, foxes, raptors, and others—and a resultant shift of tick-feeding from the less to the more competent host species (i.e., white-footed mice). This example illustrates how a range of environmental and ecosystem changes in response to land-use and species eliminations, along with middle-class suburban sprawl into woodlands, can combine to influence the occurrence of an infectious disease.

Niche Invasion. The emergence of some infectious diseases results from a pathogen invading a newly created, or recently vacated, ecological niche. A good example of the

former is the Nipah virus, which first emerged as a human disease in Malaysia in 1997–1998.

Human contact with this naturally bat-borne virus followed the establishment of pig farms, constructed in combination with fruit orchards within newly cleared areas of tropical forest in central-northern Malaysia. It is thought likely that the unusually intense El Niño event of those same years, 1997–1998, and the associated extreme forest fires and smoky haze in Southeast Asia, impaired forest fruit yields, and that this forced the fruit-bats to seek food further afield. This they apparently did, especially from the newly available fruit orchards. Consequently, thousands of pigs were infected, often fatally, and over 100 infected pig handlers and slaughterhouse workers died from this new zoonotic viral infection.

The emergence of the Nipah virus in humans was, in summary, associated with a combination of environmental changes—forest clearance, unusual fires, and smoke—that caused a marked decline in forest fruit yield. This caused a displacement of fruit bats to a new food-source niche, which opened up new cross-species opportunities for the fruit bat virus.

Global Climate Change. The advent of human-induced global climate change is a major, momentous, new category of environmental change and ecological disturbance. Most infectious agents, their vector organisms, and their nonhuman reservoir species are sensitive to climatic conditions—as well as to many of the other environmental changes that will result (e.g., changes in vegetation and, hence, in vector-insect populations). Hence, it is widely expected that climate change will, via changes in both average climatic conditions and climatic variability, affect the spatial-temporal patterns of many infectious diseases.

The common microbial causes of food poisoning, including *Salmonella* and *Campylobacter* organisms, are known to be sensitive to temperature. Most food poisoning cases occur in the hotter months of the year and in the hotter countries of the world. The reported incidence of food poisoning has risen in many developed countries (which have systematic reporting of these diseases) in recent decades, but this has many plausible explanations. One possible contributor is the underlying warming that has occurred. There is a need for careful research on this topic.

Meanwhile, some tantalizing reports are appearing, as recently occurred for foodborne *Vibrio parahaemolyticus*, a major bacterial cause of seafood-associated food poisoning. In summer 2004, a major outbreak of this disease occurred on a cruise ship off northern Alaska after passengers had eaten oysters. The record showed that mean coastal-water temperatures had increased by 0.2°C per year since 1997—and, in particular, that 2004 was the only year when the critical temperature of 15°C had been exceeded throughout the July–August oyster harvest season. Researchers concluded that “rising temperatures of ocean water seem to have contributed to one of the largest known outbreaks of *V. parahaemolyticus* in the U.S.,” and they concluded that, with global warming, this elevated risk is likely to persist in the future.

Overall, there is increasingly suggestive evidence that the climate change that has occurred over the past three decades or so has influenced at least a handful of climate-sensitive infectious diseases. These include the northward extension of the tick that transmits tick-borne **encephalitis** in Sweden over the 1980s–1990s in association with warming winters, and an apparent increase in the human disease itself; the ascent of high-land malaria to higher altitudes in parts of eastern and southern Africa in association with

local warming; and the recent northward drift of the January winter “freezing zone” that limits the survival of the water snail that transmits *schistosomiasis* in eastern China.

Conclusion. Human intervention in the environment has been an age-old source of exposure to new microbes. The experience of the past several decades has underscored more clearly just how rapidly and adroitly microbes are able to take advantage of new environmental niches and altered ecological configurations. This newer understanding should have a steadying effect on our approaches to environmental disturbance, especially environmental changes now occurring on an unprecedented scale as we begin to change natural systems, such as climate systems, at regional and global scales. As we escalate our repertoire of environmental “patch disturbances,” we can expect to see, and to experience, an increase in the rate at which new and resurgent infectious diseases appear and spread. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Black Death: Modern Medical Debate; Colonialism and Epidemic Disease; Diet, Nutrition, and Epidemic Disease; Disease in the Pre-Columbian Americas; Early Humans, Infectious Diseases in; Epidemiology; Greco-Roman Medical Theory and Practice; Insect Infestations; Irish Potato Famine and Epidemic Disease, 1845–1850; Latin America, Colonial: Demographic Effects of Imported Diseases; Malthusianism; Pesticides; Poverty, Wealth, and Epidemic Disease; Sanitation Movement of the Nineteenth Century.

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ANTHONY MCMICHAEL

EPIDEMIC AND PANDEMIC. The *Dictionary of Epidemiology* defines the term “epidemic” as “the occurrence in a community or region of cases of an illness, specific health-related behavior, or other health-related events clearly in excess of normal expectancy.” “Pandemic” is defined as “an epidemic occurring over a very wide area and usually affecting a large proportion of the population.” A pandemic is thus simply a very large epidemic. The term “outbreak,” on the other hand, usually indicates a small epidemic. Clearly there is a good deal of subjectivity in these terms; different authorities may refer to the same event using different designations, and it is not infrequent that a single authority, in a presentation or manuscript, will refer to an event as an “epidemic” in one place and an “outbreak” in another. Although, like its counterparts, “pandemic” is sometimes used loosely, it usually indicates an event that is either global or at least covers a continent or major region of the world (e.g., the 1918 “Spanish influenza” pandemic). Similarly, the term “outbreak” is used preferentially when the health event in question is localized in time or place and limited in its impact upon a larger population (e.g., an outbreak might occur in a school, factory, or military unit).

The word “epidemic” is derived from the Greek root words for “on or about” (*epi*) “the people” (*demos*). Samuel Johnson’s 1755 dictionary (London) contains the word “epidemick,” apparently a fairly new word at the time; by the early nineteenth century it had strongly taken hold in English (minus the terminal “k”). “Epidemic” eventually replaced the earlier term “epidemy,” from the medieval “ipedemye,” spelled in various ways, and related to the Greek “epidemia.” Cognates of “epidemy” have been retained in other languages, for example, the German (*epidemie*) and the French (*épidémie*).

Corresponding terms referring to animal diseases are “outbreak,” “epizootic,” and “panzootic.” Even epidemiologists occasionally refer to animal outbreaks as “epidemics,” despite its nonsensical meaning, and also refer to epizootiological aspects of animal diseases as “epidemiological,” perhaps because the latter is more easily pronounced or more widely understood. America’s first great epidemiologist, Noah Webster, eventually became the nation’s first prominent lexicographer. It is of interest to note that in early editions of *Webster’s Dictionary* (e.g., New York, 1828) he defined the noun “epidemic” as “a disease generally prevailing,” and one that “seizes a great number of people at the same time.” He also listed two interchangeable adjectives, “epidemic” and “epidemical,” to be used in distinction to “endemic or local.” Before “epidemic” and its cognates became popular, an infectious epidemic disease might be called a “plague” or “pestilential disease” (*pest* and *peste* in German and French/Italian/Spanish, respectively) or a “*loimos*” (λοιμοζ) after the Greek term for plague.

In modern English usage, “epidemic” is commonly applied in a broad sense to refer to infectious, chronic, and lifestyle-associated diseases (e.g., SARS, diabetes mellitus, and obesity). It also enjoys popular usage as an all-purpose indicator of frequency (e.g., in referring to an epidemic of school tardiness). Until recent decades, however, an epidemic was almost always taken to mean a widespread acute disease, and in that sense it is the product of a long history of terms and concepts used to describe severe “pestilential” occurrences, almost all of which were infectious (with a few historical exceptions, such as outbreaks of **ergotism** or mercury poisoning).

History. Under whatever terminology, epidemic infectious diseases have been recognized since ancient times. Indirect lines of evidence suggest that in **early humans’** hunter-gatherer days large epidemics were unlikely to occur for the simple reason that small nomadic kinship groups had only occasional contact with each other, limiting the spread of microorganisms. Crop cultivation and animal domestication, which began about 10,000 years ago with the **Neolithic Revolution**, supported early **urbanization** with large concentrations of stable populations capable of sustaining widespread **transmission** of microorganisms. Moreover, it is probable that during this era many epidemic infectious diseases arose when animal organisms learned to switch hosts to infect, and to be transmitted among, humans (e.g., **measles**, **smallpox**, and **tuberculosis**).

By Old Testament biblical times, epidemics and epizootics were apparently common (e.g., the Pharaonic “plagues” in the *Book of Exodus* [c. 1552 BCE], some of which are now speculated to have been infectious). An epidemic was also described in *The Iliad* (events occurring around 1250 BCE). By the fifth century BCE, epidemic descriptions entered a new era of sophistication with the **Hippocratic corpus**, which described a number of epidemic diseases, such as mumps. The **Plague of Athens** (430–426 BCE), which occurred during the Peloponnesian Wars and may have brought about the end of Greece’s Golden Age, was vividly described by Thucydides (c. 460–400 BCE). Although the disease has not been conclusively linked to any disease known today, Thucydides’ account is

a landmark in epidemic history, representing the first disease characterized as a distinct entity on the basis of its clinical and epidemiologic pattern. Thucydides' description remained highly influential for centuries and formed the centerpiece of and often model for thousands of written histories of other epidemic diseases, which were typically compared to the Athenian disease, which served as a benchmark.

During the Renaissance and early Enlightenment (c. 1400–1800), it was common practice in writing treatises and dissertations to assemble epidemic chronologies that spanned recorded history, sometimes running into hundreds of entries. The Enlightenment featured attempts to distinguish one disease from another, at first on nosologic (naming) grounds that drew upon minor clinical and epidemiological differences to create charts that supposedly displayed relationships and differences among diseases and types of disease. Although ultimately unscientific, these nosologies did encourage rational observational study of epidemics and epizootics, a process aided by recognized epidemics of noninfectious diseases for which an etiology could be found (e.g., lead poisoning of wine and other drinks).

By the late 1700s infectious disease outbreaks and epidemics were being studied rationally and reported in the medical literature. Among these were naval outbreak investigations, delineation of complex diseases like anthrax by clinical-epidemiologic means, and investigation of cattle epizootics including rinderpest throughout the eighteenth century. In 1776 King Louis XVI (1754–1793) set up an international disease outbreak surveillance and investigation system in France and its overseas possessions, representing the first national governmental epidemic disease unit. During the 1832 cholera pandemic, epidemiologic methods based on statistical analysis of **demographic** risk factors (age, socioeconomic status, population density, etc.) finally brought the study of epidemics into a rational framework capable of contributing to the microbiologic breakthroughs that occurred in subsequent decades.

Modern Epidemic Concepts. A 1992 report of the U.S. Institute of Medicine has added a new concept and new vocabulary to epidemic diseases. Entitled *Emerging Infections*, this influential report has categorized epidemic diseases into those that have newly emerged and those that continue to reemerge (e.g., **HIV/AIDS** [newly emerging in 1981] and **Dengue** fever [reemerging/resurging over recent decades]). A third category “deliberately emerging” was later coined to address **bioterrorism**. More important than nomenclature, this report has reorganized scientific thought about infectious disease epidemics by emphasizing the many risk factors that influence emergence/reemergence, including risk factors related to the microbial agent (e.g., genetic mutation, host adaptation), the host (e.g., immunodeficiency), and the environment (e.g., crowding, travel).

Today epidemics and pandemics are routinely investigated and reported by local and national governments, and by international agencies such as the **World Health Organization** (WHO). For example, WHO has been involved in international planning for an **influenza** pandemic, recognizing that based upon historical evidence new pandemic strains arise periodically, on average every 30 years or so over the last three centuries. WHO also played a leading role in the 2003 SARS epidemic, which threatened to become pandemic when cases were exported from Hong Kong to a number of other countries. In the United States (for example) epidemic surveillance and outbreak investigation is conducted by all 50 states and by the Commonwealths and Territories, as well as by major cities and some county health departments. These activities are supported by, and

to some extent coordinated by, the federal U.S. **Centers for Disease Control and Prevention** (CDC), which also provide epidemic response backup to states. In addition, the United States and many other developed countries assist other countries and the WHO in support of epidemic activities, including outbreak investigation, **diagnostic** assistance, and provision of laboratory materials. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Biblical Plagues; Chadwick, Edwin; Cholera: First through Third Pandemics, 1816–1861; Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Environment, Ecology, and Epidemic Disease; Epidemiology; Epidemiology, History of; Historical Epidemiology; Human Immunity and Resistance to Disease; Snow, John; Virchow, Rudolf.

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DAVID M. MORENS

EPIDEMIOLOGY. Epidemiology has been eclectically defined over its brief—less than two-century—history, and its meaning is apparently still evolving. The *Dictionary of Epidemiology* (2004) defines epidemiology as “the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to health problems.” It further adds, more coherently, that epidemiology is “that branch of medical science which treats of epidemics.”

A wise and anonymous epidemiologist once observed that epidemiology “is all things to all men . . . The plethora of definitions is the very heart of the problem . . . a structure sturdy enough to . . . shelter **physicians**, dentists, veterinarians, and **nurses**; very small (micro) biologists and fat chemists; mammalogists, bugmen, birdmen, and spacemen; traffic directors and city planners; engineers mechanical, sanitary, electrical, stationary, and human; sociologists, psychologists, and anthropologists, cultural and otherwise . . . everything!” Indeed, the first of the above definitions, derived from earlier constructions, is steeped in the political correctness of modern public health (e.g., epidemiology should not study just diseases but also health). Moreover, it is often said (illogically) that epidemiology cannot really be epidemiology unless its findings are actually *applied* to health problems, casting it firmly as a proactive tool of public health. Epidemiology thus tends to be defined differently by those who wish to use it to achieve different aims.

The many and often tortured current definitions of epidemiology reflect confusion, particularly in the United States, where epidemiologic approaches are aggressively being taken up and adapted by professionals in a variety of disciplines, are being applied to new and different problems far removed from actual epidemics and infectious disease epidemics in particular, are being infused with methodological and theoretical complexities,

and are being taught increasingly in graduate schools to students without grounding in the medical arts or biomedical sciences.

These changes have led to a diffused professional body of epidemiologists distanced from epidemiologists of earlier generations in their emphasis on mathematical and theoretical study of data sets, trying to tackle the arguably more complicated problems of chronic and lifestyle-related diseases, which have become the major causes of morbidity and mortality in developed nations. This has led also to a generational and professional divide within epidemiology; it is unclear how or whether this will be reconciled. The new era of genomics, proteomics, and bioinformatics is likely to affect the future evolution of epidemiology in ways that are yet unknown.

Without taking a position on how epidemiology should be defined, it is worth noting that the word and concept came largely out of the study of pestilential and other infectious diseases. The origin of the term “epidemiology” has not been identified, but it was first used in its modern sense in continental Europe in the 1830s and 1840s in forms such as *Epidemiologie* (in Germany) and *épidémiologie* (in France). Appearance of the cognate in English may have occurred around December 1849 during the first planning sessions for what became, several months later, the Epidemiological Society of London. As many of the founding members of that society read the French medical literature regularly, a plausible argument could be made that “epidemiological” and “epidemiology” were imported from the French language directly into English. It is curious to note, however, that during the early decades of epidemiology, its practitioners did not call themselves “epidemiologists.” When “epidemiologist” did catch on, about a decade later, it was not in reference to a professional discipline but to a side-interest of physicians and occasionally others who drew upon their eclectic professional skills to serve the public health.

History. Although “epidemiology” and its cognates may have been new in the 1830s, the idea of examining and recording the occurrences and patterns of epidemic diseases was by then at least 3,000 years old. An ancient example is the **biblical plagues** of Egypt recorded in Exodus, written circa 1552 BCE. The ancient Greeks made major conceptual contributions to what might best be called “proto-epidemiology” (epidemiological ideas and activities undertaken before the word and concept had come into existence). Such observations were recorded in the **Hippocratic corpus**, as outlined in *Airs, Waters, Places*. Here the author posits that epidemic diseases are distinct entities appearing in patterns of either pathognomonic (characteristic of a single disease) or constellationary (occurring together in a pattern) clinical signs/symptoms, and under particular conditions of season, weather, and geological events. Democritus (c. 460–370 BCE) proposed that contagious diseases are spread by tiny invisible particles. And the still-unidentified **Plague of Athens** (430–426 BCE), described by Thucydides (c. 460–400 BCE), is a recognized landmark in the study of epidemics because it represents the first known characterization of a disease as a distinct entity on the basis of its clinical and epidemiologic pattern.

Many other epidemics were described and catalogued between Greco-Roman times and the eighteenth-century Enlightenment. But without an understanding of modern **germ theory** or infectious disease etiology, or any rational way to distinguish one disease from another, proto-epidemiology had difficulty moving beyond mere descriptions. During these centuries, occasional proto-epidemiologic investigations of occupational outbreaks were conducted (e.g., of lead poisoning), but these seem to have had little influence on epidemiologic thought. Even so, progress was gradually made by recording the

patterns and features of one disease at a time, without any awareness of movement toward overarching concepts of disease occurrence.

A critical first step in the development of epidemiology was disease distinction: without it there could be no basis for studying disease determinants or distributions. Persian-born physician **Rhazes** clearly distinguished **smallpox** from **measles**, and later observers eventually proposed other distinct contagious diseases (e.g., the Scot Bernard de Gordon [c. 1260–1318], who drew upon Rhazes and the Persian **Avicenna**, to list eight distinct diseases he thought were communicable [most of them correctly]).

During these many centuries there seems to have been no concept or term that corresponds closely to any modern concept of “epidemiology.” “Loimologia,” “loimology,” and “loimographia,” used in the seventeenth century, referred to the centuries-old chronicling of *loimos* (λοιμοζ), an ancient Greek term corresponding roughly to major epidemic/pandemic diseases. “Epidemical” and “epidemia,” popular in the late 1700s and early 1800s, were adjectives applied to infectious disease epidemics. The Latin term *epidemiologia* appeared as early as 1802 (*Epidemiologia española*), but the book’s subtitle (*ó Historia cronológica de las pestes, contagios, epidemias y epizootias*) makes clear that this “discourse about epidemics” applied only to the centuries-old practice of compiling chronological lists of important epidemics. This activity was, by the late eighteenth and nineteenth centuries, transformed into medical geography, as practiced, for example, by Noah Webster (1758–1843), August Hirsch (1817–1894), and Charles Creighton (1847–1927), and it spilled over into medical history, as practiced by physicians like Justus Friedrich Karl Hecker (1795–1850).

As the Enlightenment ended and the **Industrial Revolution** began, urban population concentration led to increasingly severe epidemics, but also to counteractive **sanitary movements**, to development of mortality, morbidity, and other **demographic data** systems, and to the appearance of vital statisticians and preventive medicine physicians. In the early years of this new industrial age, a generation of physicians returned to their European homes from the **Napoleonic wars**, many influenced by the radically new subjects of public health and social medicine, to address disease prevention in all segments of the population, prominently including the urban poor. These so-called “hygienists” studied the incidence and prevalence of various health conditions in populations, making use of census data and medical arithmetic, and identifying disease-specific demographic risk factors such as sex, age, locale, occupation, crowding, socioeconomic status, and others. In essence, these physicians systematically studied the distribution and determinants of diseases in open populations, the first true epidemiology. Their work can best be seen in the voluminous literature of the 1832 Parisian **cholera** epidemic. A generation later, the establishment of a national Register of Births and Deaths in England and Wales, coupled with the almost universal adoption of national censuses, led to further advances in epidemiology, as in the groundbreaking work of **William Farr**, William Budd (1811–1880), and **John Snow**. Snow’s separate investigations of cholera incidence rates by contaminated and uncontaminated London **water** supplies, and of cholera contamination at Soho’s Broad Street pump, were eventually recognized as landmarks in epidemiology and are taught to all epidemiologists today.

Modern Epidemiology. Throughout the nineteenth century, epidemiology was strongly oriented toward infectious disease outbreak/epidemic investigation and control, as it had been for centuries. The 1920s, however, saw epidemiology develop in new direc-



Lantern slide illustrating elements of epidemiology during third plague pandemic, c. 1900, Old Bengalpura Street, Mumbai, India. Wellcome Library, London.

tions, including such infusions of expertise from the social sciences as better standardized methodologies to link disease risk factors to diseases by comparing incidence rates in exposed and unexposed persons (cohort studies), and by comparing prior exposure frequencies in ill and well persons (case-control studies). In the United States, these developments were heavily influenced from about 1920 to about 1980 by the national experiment in establishing numerous schools of public health in universities. Throughout much of the twentieth century the United States was a leader in all forms of epidemiology, but this era now seems to be rapidly ending as the value of epidemiology has become more widely appreciated.

Although epidemiology is still subject to a bewildering array of definitions, it remains possible to identify some of its most visible practitioners. The term “epidemiologist” is generally used only to describe persons with doctoral degrees (M.D., Ph.D., Sc.D., Dr. P[ublic] H[ealth], etc.) who have had specific academic or practical training. Epidemiologists often work in national health agencies, such as the U.S. **Centers for**

Disease Control and Prevention and the U.S. National Institutes of Health, in state and local health departments, as faculty in Medical Schools and Schools of Public Health, as Preventive Medicine officers in the military, in industry (working with drug and vaccine development, and sometimes in occupational health), and in many other positions. People with masters and other degrees concentrating in epidemiology are often referred to in health department practice as “epidemiology specialists,” or by a similar term. In addition to health department work, they are also employed by industry and in academic research support positions.

As epidemiology evolves, it is probably best to view it not as a professional discipline but as an approach to public health problem solving, in which the methods and approaches are less important than the ultimate effect on population health. Indeed, until recent decades, virtually all epidemiologists were credentialed in another discipline (often medicine) and tended to view epidemiology as one of a number of “tools” (alongside, for example, clinical skills, microbiology, biostatistics) to be drawn upon in order to solve practical public health problems. Epidemiologist David Fraser has proposed that epidemiology be viewed as a liberal art, an idea that has taken hold in some academic institutions, the subject and principles now being taught to undergraduates and even to high school students. Increasingly, epidemiology and epidemiologists are the subjects of books and films, with the diseases they study serving as plot devices. This phenomenon seems to reflect public awareness and interest, a desirable occurrence given that however far removed from the “real world,” epidemiology must inevitably return to the problems of real human beings affected by real health problems. *See also* Epidemiology, History of; Historical Epidemiology; Measles, Efforts to Eradicate; Public Health Agencies in the West before 1900; Sanitation Movement of the Nineteenth Century; Smallpox Eradication.

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DAVID M. MORENS

EPIDEMIOLOGY, HISTORICAL. *See* Historical Epidemiology.

EPIDEMIOLOGY, HISTORY OF. Whereas the complex statistical methods and concepts in use by epidemiologists today are relatively new, the study of population-level disease phenomena can be traced back to ancient times. “**Epidemiology**” stems from the Greek “logos” (the study of) and “**epidemic**,” which in turn is derived from “epi” (upon) and “demos” (people).

Greek **physician Hippocrates** is often described as the first epidemiologist. He reportedly traveled extensively, treating the sick, teaching young doctors, and meticulously

recording his observations. His *On Airs, Waters, and Places* provides an early conception of epidemiology: “Whoever wishes to investigate medicine properly should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces for they are not at all alike, but differ much from themselves in regard to their changes. Then the winds, the hot and the cold,” the qualities of the **water** and soil, as well as the behaviors of the inhabitants, including “whether they are fond of drinking and eating to excess.” Extensive observation of these factors would, in turn, reveal patterns in the behavior of epidemics.

Although many of Hippocrates’ conclusions appear erroneous today, his great innovations were in emphasizing observation as the primary route to scientific knowledge and the identification of natural, rather than supernatural, causes of epidemics. Greek philosophers were prone to reduce complex phenomena to the invisible actions of a few simple elements (earth, **air**, fire, and water), but Hippocrates rejected metaphysics in favor of empirical observation. This empirical approach was subsequently stifled, however, by dogmatic adherence to **Galen’s humoral theory**, which dominated medical thinking for some 1,600 years.

Beginning in the sixteenth century, the early **Scientific Revolution** brought about a more robust empirical approach to scientific knowledge, rooted in observation and experimentation, and began the challenge to Galenic medicine. Meanwhile, an infrastructure for collecting census data was being developed in England and Wales; in 1538, Thomas Cromwell (c. 1485–1540), King Henry VIII’s (1491–1547) chancellor, ordered all parishes to keep a register of baptisms, marriages, and burials. In London, death statistics were published as the London Bills of Mortality—a practice pioneered by Milan and Venice—which by 1629 began to include causes of death. Two seventeenth-century figures, shopkeeper and amateur scientist John Graunt (1620–1674) and economist and philosopher Sir William Petty (1623–1687), saw the value in such data and developed early methods for utilizing it. In his book *Natural and Political Observations . . . upon the Bills of Mortality* (1662), Graunt used this data to demonstrate that mortality was very high in infancy and higher in the country than in the city.

Two broader developments in the eighteenth century proved important for the development of statistical medicine. The growth of **hospitals** during this period greatly increased the opportunities for clinical investigation, as physicians could now observe a larger number of patients with similar ailments and make comparisons. At the same time, the mathematical theory of probabilities was being developed and applied to a wide range of phenomena, including medicine. French mathematician Pierre-Simon Laplace (1749–1827) published a series of papers in the 1770s that attempted to capture human judgment in mathematical terms, and he recommended that physicians apply the calculus of probability in making clinical decisions. Parisian clinician Pierre-Charles-Alexander Louis (1787–1872) at La Charit  hospital advocated what he called the “numerical method” of analysis, which consisted of systematic record keeping and statistical comparisons to evaluate different treatments. This theoretical framework was crucial for the development of statistical methods for epidemiology.

It was in the nineteenth century that epidemiology as a discipline came into its own, furthered by Victorian enthusiasm for both quantification and social reform. The General Register Office was founded in 1836 to carry out civil registration of births, marriages, and deaths in England and Wales. **William Farr**, who had studied medicine and statistics with Pierre Louis in Paris, joined the Office as a compiler of statistical abstracts. During

his 40-year tenure at the office, he played an essential role in gathering and analyzing data for epidemic investigations and developed systems of disease classification. Additionally, during this time, in 1850, the London Epidemiological Society was formed “with the specific purpose of determining the causes of and methods of preventing **cholera** and other ‘epidemic diseases.’”

Today, every introductory epidemiology textbook relates the story of how London physician **John Snow** demonstrated that cholera was transmitted through contaminated water, rather than by changes in local atmospheric conditions (or miasma). After an 1854 outbreak in London, Snow plotted the houses of cholera victims on a map, illustrating how they clustered around a water pump on Broad Street. But Snow’s most ambitious and ingenious study—a model for the developing discipline of epidemiology—was a large-scale natural experiment in which he mapped out the source of the water supplied to neighborhoods in South London by rival water companies. Lambeth Waterworks Company took its water from the Thames upstream of London, beyond the reach of most of London’s sewage. Snow found that households served by competitor Southwark and Vauxhall Company, which took its water directly from the Thames in central London, had six times as many cholera cases as did the households served by its rival.

Snow’s evidence was indeed persuasive, but it was not the entire story. Critics pointed out that the neighborhoods served by the two companies differed in other ways as well—Southwark and Vauxhall served poorer households in more crowded areas closer to the river. Farr conducted the most thorough analysis of data from the cholera epidemic in nineteenth-century Britain, looking at age, **sex**, temperature, weather conditions, property values, and domestic crowding, along with countless other variables. His key finding was a consistent inverse relationship between cholera mortality and soil elevation. This finding supported the view of Farr and other leading public health experts at the time that cholera epidemics were precipitated primarily by changes in local atmospheric conditions. The ongoing debate provided the impetus for the development of novel methods for gathering and analyzing data and testing hypotheses, and Farr later came to accept Snow’s theory based on the extensive evidence.

With the advent of **germ theory** in the late nineteenth century, the microbiologist in the laboratory became the center of medical discovery, as the **microscope** revealed causative agents of anthrax, **tuberculosis**, and other deadly diseases. German physician **Robert Koch’s** postulates set out conditions for identifying pathogens with a particular disease: the organism must be found in all animals with the disease, but not in healthy animals; the organism must be isolated from a diseased animal and grown in pure culture; and the organism should cause disease when reintroduced into a healthy animal. With further study of **viruses** in the early twentieth century, however, it became clear that Koch’s postulates could not be met for all diseases. **Wade Frost**, the first American professor of epidemiology, maintained that, in the absence of experimental evidence, epidemiologists must proceed “inductively,” accumulating observations from a variety of sources and piecing them together into a coherent explanation of the role of a microorganism in a specific disease.

The debate over the relationship between smoking and health in the 1950s, although it focused on chronic disease, had an enormous impact on the discipline of epidemiology. In 1950 five case-control studies revealed that hospital patients with lung cancer, compared to individuals who were healthy or had an unrelated condition, were more likely to

be smokers. However, skeptical scientists, including some prominent biostatisticians and epidemiologists, challenged the methods employed in these studies and suggested alternative interpretations of the results. For example, legendary statistician R. A. Fisher (1890–1962) hypothesized the existence of a common cause behind both cancer susceptibility and the urge to smoke. This debate, in turn, provided an impetus for the development of new statistical methods to analyze epidemiologic data and for the undertaking of large cohort studies, such as the American Cancer Society study that tracked 188,000 middle-aged male smokers and nonsmokers. By 1964 the evidence from over 30 case control studies and 7 large cohort studies was overwhelming, and the conclusions of the Surgeon General’s committee on smoking and health affirmed that epidemiology could provide sufficient evidence of cause and effect to guide medical and public health decisions.

Epidemiology has evolved dramatically from its early development as a diversion for curious physicians into a highly specialized discipline. Epidemiologists today receive rigorous training both in statistical methods and in biomedical science, typically specializing in a particular disease area. Nevertheless, at the same time, the discipline remains inherently cross-disciplinary, as contemporary epidemiologists must understand and piece together information from the molecular and genetic level to that of human populations in order to understand the causes and determinants of patterns of disease. *See also* Cholera, First through Third Pandemics, 1816–1861; Demographic Data Collection and Analysis, History of; Plague in Britain, 1500–1647.

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MARK PARASCANDOLA

ERGOTISM. Ergotism is a generic term for three distinct human diseases resulting from the ingestion of cereal grains, most notably rye, that have been infected with the fungus *Claviceps purpurea*. *C. purpurea* produces spore bearing stalks (sclerotia) that contain a variety of chemicals, known as alkaloids, several of which are hazardous to humans and animals. The three best-known alkaloids are ergotamine, ergonovine, and lysergic acid hydroxyethylamine. Ergotamine can cause blood restriction to certain parts of the body producing a condition known as gangrenous ergotism. Ergonovine can cause spontaneous abortions in women. Lysergic acid hydroxyethylamine can cause a condition known as convulsive ergotism with symptoms ranging from hallucinations, to vomiting,

diarrhea, and lethargy. All ergot alkaloids have been synthesized in the laboratory, with much of the early work done by Sandoz Pharmaceuticals.

C. purpurea is an ascomycete, a sac fungus. In the spring and early summer it produces the sclerotia, which may germinate into as many as a dozen stalks that contain pollen. Windblown pollen may land on grass or grain and there germinate. The spores quickly colonize the host. The fungus sclerotia then emerge where the grain would normally form. Harvested fields may contain both healthy grain and grain infected with the ergot fungus. Fields that are somewhat moist are especially conducive to infection. Grains such as rye or barley are particularly susceptible to colonization. When cleaned properly, the grain is suitable for consumption, but if not, then various ergot alkaloids will be present in the grain when it is consumed, even as baked goods.

Gangrenous ergotism often leads to a loss of blood in the extremities, which can lead to loss of nails or even of feet and hands. Before the loss of sensation, the disease often produces feelings of intense heat in the affected extremities. In the Middle Ages this latter sensation caused the disease to be referred to as St. Anthony's fire. There are several documented medieval outbreaks of ergotism, most often in central Europe, with the first occurring in the ninth century. Outbreaks continued well into the nineteenth century in central Europe with children being particularly affected. In the Middle Ages and early modern era, gangrenous ergotism was sometimes coupled to convulsive ergotism with its resulting hallucinations and bizarre behavior, a combination that further emphasized nonphysiological aspects of St. Anthony's fire.

Some folk medical practitioners recognized the hazard but also the benefits that ergot could produce, although using too much of an ergot compound could prove dangerous. From the eighteenth century, midwives often used ergot compounds that contained ergonovine to induce childbirth, a practice that found its way into orthodox medicine for a time. An increased dosage of the compound, however, could be used to induce an abortion earlier in a pregnancy. Other compounds containing ergotamine were used to lessen the chances of hemorrhaging after delivery.

The convulsive ergotism produced by lysergic acid has produced several episodes of mass hysteria, the most notable occurring in Pont-St.-Esprit, France in 1951. During this episode some people jumped off the roofs of their houses believing they were pursued by demons. Although the cause of this episode has never been conclusively determined, most investigators believe it was caused by ergot-infected rye flour from a nearby mill. Convulsive ergotism has also been advanced as an explanation for witch accusations in the early modern era, most notably the Salem, Massachusetts, episode in 1692. Although several of the girls who were accusers of the Salem witches ostensibly exhibited symptoms similar to those of convulsive ergotism, most scholars do not accept this explanation, turning instead to social and cultural explanations. The advocates of convulsive ergotism as an explanation for witchcraft accusations tend to focus solely on the medical symptoms of the accusers and ignore all other aspects of the witch panic.

During his work synthesizing ergot alkaloids in 1943, the Sandoz chemist Albert Hoffman (1906–) turned his attention to the lysergic acid compounds. As he progressed through the compounds, he found one, LSD-₂₅, that produced intense hallucinations when ingested, something that Hoffman first experienced as he rode his bicycle home from work. Sandoz patented LSD-₂₅ and initially marketed the new drug as an aid to medical health professionals. Several health care professionals began to engage in research using the new drug in the early 1950s, and it was prescribed in several mental hospitals

for a variety of mental problems. Another group also took an interest in LSD-₂₅. The Central Intelligence Agency began experimenting with the new drug as an aid to interrogation or for use in creating chaos in a hostile population. In the 1960s the MK-Ultra program sponsored by the CIA and military intelligence soon progressed to field trials on sometimes unsuspecting populations. Some civilians also turned to LSD-₂₅ as a recreational drug calling it an aid to consciousness expansion. The Harvard psychologist Timothy Leary (1920–1996) became a noted exponent of the value of LSD. Both uses of LSD helped to produce a backlash, and Congress passed legislation criminalizing the manufacture or possession of LSD-₂₅.

Ergotism continues to pose a potential health hazard as *C. purpurea* remains in some grain supplies. Although present in all parts of the world, ergotism has been more of a problem in central Europe than elsewhere, and much of the work designed to control ergot infections is centered there. The principal means of preventing ergot infections continues to be rigorous cleaning of grain supplies to remove the ergot spores. Medical practitioners continue to be interested in ergot alkaloids. Ergotamine is marketed under several trade names as a means for controlling migraines. There is even some renewed interest in experimenting with LSD-₂₅ as a means of dealing with some mental disorders. Ergotism illustrates the old truisms that one amount of a drug can be a cure and another amount can be a poison. *See also* Biological Warfare; Diet, Nutrition, and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Folk Medicine; Human Subjects Research; Pharmaceutical Industry; Social Psychological Epidemics.

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JOHN M. THEILMANN

ETHNICITY. *See* Race, Ethnicity, and Epidemic Disease.

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FARR, WILLIAM (1807–1883). A pioneering English statistician and health researcher, William Farr was a creator of the modern life table, a statistical tool for predicting the lifespans of groups of people, and an important advocate for the systematic collection and application of health statistics. He served for 40 years in the General Register Office (GRO), created in 1839 to collect birth and mortality data in Great Britain. Not only was he a seminal figure in the development of the state's collection of health-related data, but he was also a researcher who made important contributions to both medicine and statistics.

Born in 1807, the eldest son of a Shropshire laborer, Farr was apprenticed at the age of eight to a patron who encouraged him to professional studies. Aged 19, Farr was apprenticed to a **surgeon**, first as a wound dresser and then as a dispenser of drugs. Thanks to a bequest from his patron, in the 1820s Farr studied medicine in Paris where hygiene and medical statistics were evolving as cutting edge medical subjects.

Returning to England in 1832, Farr briefly practiced as an **apothecary** while writing articles on medical statistics and their collection and application. Hired by the GRO in 1839, Farr was intimately involved in a range of initiatives to assure the collection of accurate statistical data. The resulting data was used by Farr and other officials as well as made available to other researchers interested in the study of health and disease. His development of a new system for the classification of disease (nosology) for use on death certificates helped Britain reform its system of health reporting.

Farr's masterwork, a study of England's **cholera** outbreak in 1848, was described by the *Lancet*, then as now a preeminent British medical journal, as "one of the most remarkable productions of type and pen in any age or country." Titled *A Report on the Mortality of Cholera in England, 1848–1849* (1853), its 100 pages of dense type were complemented by 300 pages of supporting charts, diagrams, maps, and tables that describe the epidemic in terms of incidences of illness (morbidity) and of death

resulting from it (mortality) cross-referenced economically, geographically, and socially. His conclusions on the 1854 cholera epidemic clashed with the insights of Dr. **John Snow**, and Farr's argument that cholera was airborne rather than waterborne was eventually proved incorrect. Even so, his work remains a model of epidemiological research and perhaps the most rigorous study of the potential for atmospheric diffusion of pathogens in the nineteenth century. During the 1866 cholera outbreak in East London, Farr harnessed his earlier lessons, accepted Snow's finding of waterborne causation, and quickly exposed the source of the pollution. He served as Compiler of Abstracts at the GRO until 1880. *See also* Cholera: First through Third Pandemics, 1816–1861; Demographic Data Collection and Analysis, History of; Public Health Agencies in Britain since 1800.

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TOM KOCH

FERNEL, JEAN (1497–1558). Born at Montdidier near Amiens, Fernel entered medical training quite late because of uncertainty as to where his true talents lay. After publishing three promising mathematical works, he turned to medicine and received his M.D. in 1530. Dissatisfied with the institutionalized version of medicine he had been taught, he pursued his own course of study. This led him to write a work that pointed the way to the reform of medical theory, *On the Hidden Causes of Things*, in about 1538. Aware of its radical nature, Fernel suppressed this book while he prepared the first major summary of the anatomy and physiology of the ancient medical authority, **Galen**, which formed the basis of all **medical education** (and from which Fernel wanted to depart). This was published in 1542 as *On the Natural Part of Medicine*, but later appeared as the *Physiologia*, accompanied by the *Pathologia*, and the unfinished *Therapeutice*, in his *Medicina* (1554). *On the Hidden Causes of Things* was published in 1548. Fernel also rose to become one of the best practitioners in France and spent the last two years of his life as the royal **physician**. He should be recognized as one of only three would-be reformers of medicine in the sixteenth century, alongside **Paracelsus** and **Girolamo Fracastoro**.

On the Hidden Causes of Things is concerned with three sorts of diseases with "hidden causes": poisonous, contagious, and pestilent. All three present the standard physiological concept of disease of the Galenic tradition with severe difficulties. The unvarying pattern of such diseases, such that all patients irrespective of body type or temperament respond in essentially the same way, seemed to belie the physiological view of disease based **humoral theory**. Consequently, Fernel offered his own

alternative account. Diseases of these types were held to act not on the humors, but on the substantial form or “total substance” of the body. Furthermore, they acted by means of some occult (hidden) power. A substance entering the body from outside, either through a bite or a wound, or by ingestion or inhalation, could wreak havoc in a healthy body, and so quickly that corruption of the humors—the traditional explanation—could hardly have taken place. If nothing else, Fernel pointed the way to a concept of diseases as entities in their own right, not merely collection of symptoms caused by humoral imbalances. He tried to provide details of the occult powers that could cause such rapid deterioration (drawing chiefly on **astrology** and alchemy). His considerable influence was eclipsed, however, when the advent of new mechanical philosophies of the seventeenth century rejected explanations that relied upon occult powers. *See also* Contagion Theory of Disease, Premodern; Paracelsianism; Scientific Revolution and Epidemic Disease.

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JOHN HENRY

FILM. *See* Cinema and Epidemic Disease.

FIRST PLAGUE PANDEMIC. *See* Plague of Justinian.

FLAGELLANTS. *See* Black Death, Flagellants, and Jews.

FLIGHT. Since the earliest times, flight has been one of the most commonly practiced individual responses to **epidemic** disease throughout history. People have resorted to flight as a means to protect themselves from outbreaks of disease and the horrors that sometimes accompany them. Even before the etiology of epidemic diseases and the exact nature of **contagion** were accurately understood, popular wisdom suggested that physical proximity could induce disease **transmission**; changing places was therefore considered a means for protection. Early theories of **miasma** that posited “corrupted air” as the cause of disease also recommended flight from affected areas.

Ancient medical systems had varying degrees of awareness regarding disease transmission and a variety of attitudes toward flight. In traditional **Chinese disease theory**, it was common understanding that people could transmit their sickness to others, and flight was therefore seen as useful. Similarly, ancient Indian **Ayurvedic** medicine vaguely recognized the transmissibility of epidemic diseases like plague and warned against the danger of remaining in an area where such a disease broke out, therefore encouraging flight. In the same way, ancient Greco-Roman medical theories that held that disease could either be transmitted by interpersonal contact or through fetid air considered flight a legitimate means to avoid disease.

Islamic teaching, on the other hand, prohibited flight from plague-stricken areas based on a tradition of the Prophet Muhammad (570–632), who advised: “If you hear that plague has broken out in a country, do not go there; if it breaks out in a country where you are staying, do not leave it.” This principle was further confirmed by Muslim scholars who warned that traveling would cause fatigue and make one more vulnerable to disease. Islamic plague literature, mostly written by legal scholars during and after the **Black Death** (1347–1352) legitimized this prohibition by maintaining that the plague was a blessing or mercy of God and a means of martyrdom for the believer. Therefore, Muslims were to be patient in times of plague and not flee: first because they believed that there is no way of escaping death that is sent by God and second because by fleeing plague, a Muslim would lose the status of martyr and thus the eternal reward of heaven. In practice, however, flight in search of a place free from the disease was common throughout the Islamic world during plague episodes. Sultans in the Islamic world would move their courts and entire households from plague-infested cities like Cairo to disease-free areas, staying away until the disease abated in the city.

During the recurrent outbreaks of plague following the Black Death, flight gradually became more of a routine practice for urban communities in the Islamic world, who would move to their countryside residences in times of outbreaks. This is also reflected in the changing attitudes of Islamic legal scholars to the issue. Although the major works concerning the topic of plague written by Islamic scholars during the fourteenth century did not authorize leaving plague-infested cities, works written in the Ottoman Empire from the fifteenth century onward have a dramatically different legal viewpoint on proper conduct during times of plague. Sixteenth-century Ottoman plague literature granted legitimacy to the need to exit a plague-infested city in search of clean air and legally authorized it.

Flight was also common practice in Europe, especially during and after the Black Death. European plague literature, both popular and medical, enthusiastically recommended flight as a first resort. Popular wisdom decreed that one should flee early, go far, and come back late. However, in practice, flight was not an option for all. Often only the affluent had the means to leave plague-stricken cities for the countryside. Especially after the initial wave of the Black Death, when recurrent outbreaks became more or less routine, the affluent urban dwellers would move to their permanent countryside residences where they would stay until the end of the outbreak. During violent plague outbreaks, city officials, doctors, and clergy left, whereas lower class individuals who could not afford to leave were bound to stay in cities. As a result of deaths and flight, deserted cities offered reduced taxes to attract newcomers from the countryside as laborers.

Although the European medical literature recommended flight as the foremost prophylaxis, Christian teaching denounced this practice, and instead preached repentance, patience, and prayer for protection from divine wrath. Those who fled were heavily condemned for further increasing God’s wrath and anger. Poet Giovanni Boccaccio (1313–1375) used the theme of flight as a moral critique of the fourteenth-century Florentine society in his *Decameron*, a literary treatment of flight from disease wherein ten young Florentines leave for the countryside to escape the plague in the city and entertain themselves by telling each other stories for 10 days. Throughout the Second Pandemic, preachers and moralists slammed **physicians**, community officials, and clergy who fled plague-stricken towns for their own safety when their services were needed most. Some cities fined absent civic officials, and King Charles II (1630–1685)—who had fled with his court—rewarded those who stayed put during London’s Great Plague in 1665.

One major problem with flight was that it could and did spread disease from its source. By the seventeenth century country folk shunned and even drove away refugees from plague-wracked cities, sometimes leaving the sick to die along the roadside. From the time of the Black Death, refugees were stopped at city gates and refused entry, and many states and locales required **quarantine** to guarantee the healthiness of those admitted. Immigration quarantine facilities at Grosse Île in Canada and in eastern port cities like New York and Boston were swamped with the disease-ridden **Irish** who fled the potato famine and epidemics in the later 1840s. Governments developed increasingly sophisticated **cordons sanitaires** to block the entrance of suspect travelers and those who were fleeing from infected areas into their own territories, or to keep their own victims isolated within a limited zone.

In the modern era, although there are national and international laws for declaring and enforcing public health measures like quarantine and isolation, flight is still extensively practiced. During the **Pneumonic Plague in Surat, Gujarat, India, 1994**, hundreds of thousands of people fled the city and further spread the disease to a wider geographic area. Similarly, in China, when Beijing was hit by **Severe Acute Respiratory Syndrome (SARS)**, over a million migrant workers left the city for their hometowns in rural areas in 2003, considerably extending the areas affected by the disease. Likewise, in Africa, thousands of people fled their homes in Congo-Brazzaville in 2003, in fear of the Ebola virus. More recently, in 2007, tens of thousands of Iraqis left their homes fearing the further spread of **cholera** in northern Iraq.

Flight has been and still is a factor for the spread of epidemic diseases around the globe. With the advanced travel technologies of the modern world, flight presents an extraordinary risk for disease transmission on both national and international levels. The recent implementation of the International Health Regulations (2005) by the **World Health Organization (WHO)** is an effort for international cooperation against the global risks of pandemics. *See also* Geopolitics, International Relations, and Epidemic Disease; Historical Epidemiology; International Health Agencies and Conventions; Medical Ethics and Epidemic Disease; Personal Liberties and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Public Health in the Islamic World, 1000–1600; Trade, Travel, and Epidemic Disease; War, the Military, and Epidemic Disease.

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NÜKHET VARLIK

FLU. *See* Influenza.

FOLK MEDICINE. Folk medicine may be considered the oldest form of medical practice because its roots can be traced to the earliest forms of human culture. Practitioners of folk or “traditional” medicine use locally available plants; animals (alive and as ingredients); and rituals, charms, and magic (“passing through” ceremonies, the spiritual healing system known as *curanderismo* in Latin America, faith healing) to cure their patients.

REMEDIES FROM ACROSS THE AGES

Nineteenth-century rural Egypt: "For those who are leprous they use a recipe very well-known among the 'old women' from ancient times. It is to eat every morning for ten days the heads of scorpions dried over the fire. The patient will be cured—if Allah permits—or else he will perish at the hands of the minions of Satan the Accursed."

From John Walker, *Folk Medicine in Modern Egypt* (London, 1934), p. 23.

Historically practiced within isolated agrarian communities and among the peasant class, it continues to be used today by groups geographically or economically isolated from the medical mainstream. Whereas professional medicine generally entails a course of formal training in prevailing mainstream medical models, folk medicine has traditionally been transmitted orally among community members, and practitioners are accorded author-

ity based on their accumulation of knowledge or on tradition (in some traditions the seventh son of a seventh son was supposed to have powerful healing talents). In Europe many folk practitioners were women, often called "root wives," "cunning women" (from *kennen*, to know), or "healers." Any given system of folk medicine is founded on the values, beliefs, and customs of the community that uses it. Although some folk medical practices have been partially accepted by professional medicine today, many are considered unscientific at best, or at worst, potentially harmful. Mainstream cultures have often perceived folk medicine practitioners as witches.

Folk medical responses to **epidemic** disease tend to be preventative (prophylactic), palliative (reducing symptoms), or curative. An African American method for preventing **tuberculosis** involved letting a cat sleep at the foot of one's bed. Palliative treatments included salves made with animal fat and used to minimize the scars caused by **smallpox**. Lady Frances Catchmay (fl. 1615–1630), a practitioner in early seventeenth-century England, claimed that she had cured over 300 victims of **syphilis** with an herbal drink and a special diet.

Some folk remedies mirrored major breakthroughs in mainstream medicine. It has been shown that long before Lady Mary Wortley Montagu (1689–1762) imported the practice of **inoculation** for smallpox from Turkey to Britain in the early eighteenth century, the practice of placing smallpox pus under the skin of a healthy person was used in ancient China and India. However, there is also evidence of its use by folk practitioners in Africa, as well as evidence that slaves brought knowledge of it to Boston before local physicians practiced inoculation.

Elements of the folk herbarium have found their way into the modern pharmacopoeia as biochemical researchers discover the healing properties of traditional medicinal herbs and other plants. Today, recognizing that traditional medicine is often the only source of medical attention for many of their citizens, some African governments have taken steps to foster collaboration between traditional practitioners and mainstream medical workers. The **World Health Organization** (WHO) notes that certain plants used in traditional African medicine are being tested as treatments for symptoms of **HIV/AIDS**. Groups such as the Consortium of Academic Health Centers for Integrative Medicine (CAHCIM) seek to systematize the integration of traditional ideas into mainstream medicine, but, as folklorist Wayland D. Hand (1907–1986) argued, some of the magical aspects of folk medicine may be ultimately incompatible with mainstream medical practice. *See also* AIDS in Africa; Apothecary/Pharmacist; Black Death (1347–1352); Disinfection and Fumigation; Empiric; Flight; Magic and

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MELISSA SMITH

FRACASTORO, GIROLAMO (ca. 1478–1553). Girolamo Fracastoro was an Italian humanist physician and poet who offered a new explanation of **contagion** for the transmission of diseases like **syphilis**, **typhus**, and the **Black Death**. He was born in the city of Verona in the Republic of Venice and studied mathematics, philosophy, and medicine at the University of Padua, receiving a B.A. degree there in 1502. Thereafter, he served as poet and physician to a number of leading Venetians until he was summoned to serve as physician to the members of the Council of Trent (1545–1563) under Pope Paul III (1468–1549). His two best-known works, *On Contagion and Contagious Diseases and Their Cure* (1546) and the poem, *Syphilis or the French Disease* (1530), from which the name of the venereal disease derived, were both concerned with the causes of infectious diseases and their treatment.

In the second century, **Galen** had mentioned the possibility that "seeds of disease" were responsible for the spread of contagious diseases, but he had given precedence to the theory that disease was spread by noxious airs or miasmas, rather than by human-to-human contact. According to miasmatic theory, putrefied airs act like poisons and cause a **humoral** imbalance and illness in those who inhale them and are constitutionally predisposed for the disease. In *On Contagion*, Fracastoro proposed a new explanation of contagion, arguing that imperceptible particles or "seeds" spread contagious diseases. He contended that these seeds were passed from an infected person to a new victim in three ways: directly by touch, indirectly by seeds called "fomites" which were carried by an intermediary object like clothing, or at a distance through the **air**. Furthermore, Fracastoro maintained that each disease was caused by a different kind of seed which was normally generated inside a sick person, but which could also originate as a result of an unfavorable planetary alignment.

Fracastoro's concept of disease-causing seeds coincided with efforts during the Renaissance to explain natural phenomena that occurred without direct physical contact

(like the attraction of iron shavings to a magnet) without postulating “occult” (hidden or spiritual) causes. In this case “seeds” provided a physical, *material* cause that explained human-to-human contagion via direct and indirect contact or at a distance. Although Fracastoro’s theory might appear to prefigure modern **germ theory**, it was not incompatible with miasmatic theory, nor did his contemporaries perceive it as revolutionary. Indeed, Fracastoro’s **contagion theory** was easily reconciled with the theory of bad airs, and many physicians even suggested that the seeds were responsible for putrefying the air. See also *Astrology and Medicine; Medical Education in the West, 1500–1900; Plague in Europe, 1500–1770s; Syphilis in Sixteenth-Century Europe.*

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WILLIAM H. YORK

FRENCH DISEASE. See Syphilis.

FROST, WADE HAMPTON (1880–1938). Wade Hampton Frost was a critical figure in the transformation of nineteenth-century “sanitary science” into the twentieth-century discipline of public health. As a **physician**, researcher, and teacher, he exemplified the increasingly specialized skills of public health experts in the first half of the twentieth century. Born to a country doctor, Frost received his medical degree from the Medical College of Virginia in 1903. The following year he passed the examination for the Public Health and Marine Hospital Service—later the Public Health Service (PHS)—where he began more than 20 years of service beginning in 1905.

Frost was involved as an investigator in a range of studies, including works regarding issues of **water** quality and its effect on disease. In 1905, for example, Frost was a critical federal investigator of a virulent New Orleans **yellow fever** epidemic, and in 1909 he was instrumental in the analysis of a waterborne **typhoid fever** outbreak in Williamson, Virginia. Across his public health career, he was principal in the research into a series of **epidemic** and **pandemic** outbreaks. In these studies his careful examination contributed to an understanding of diseases whose etiology was then unknown, including **poliomyelitis** in 1910–1912 and the **1918–1919 influenza** outbreak in the United States.

After his work on the 1918–1919 influenza outbreak, in which he and an economist determined the effect of the epidemic on U.S. cities, he was hired by the new School of Hygiene and Public Health then being established at Johns Hopkins University in Baltimore. He was hired originally as a “guest lecturer,” and he remained a commissioned officer in the PHS, albeit on detached service, through the 1920s. During this period his

first duties at Johns Hopkins were to teach **epidemiology** and disease studies through the case study method. He encouraged the adoption of epidemiology as a scientific study, as was the case with medical research, and his clear, precise methods of study laid the foundation for the future of epidemiology. He also introduced biostatistics as an important tool for judging confidence in data. In 1927 Frost published a “state of the art” text that defined the evolving science of the epidemiologist and focused on disease studies, along with public health promotion from the perspective of the public health practitioner. *See also* Influenza Pandemic, 1918–1919; Poliomyelitis, Campaign Against; Public Health Agencies, U.S. Federal; Typhoid Fever in the West since 1800; Yellow Fever Commission, U.S.; Yellow Fever in the American South, 1810–1905.



Wade Hampton Frost. Courtesy of the National Library of Medicine.

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TOM KOCH

FUMIGATION. *See* Disinfection and Fumigation.

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GALEN (129–ca. 217). Claudius Galenus of Pergamum, or Galen, one of medicine's most influential figures, was a **physician** who lived through the devastating **Antonine Plague** of the Roman Empire. Prolific, pedantic, and ruthlessly self-promoting, Galen authored about 350 works and created the framework of medical ideas and ideals dominant in the West until the eighteenth century.

Galen was from a prominent family of Pergamum (Bergamo, Turkey). His father Nicon, a cultured architect, immersed Galen practically from birth in the finest education available and, because of a dream, directed Galen at 16 toward medicine. When Nicon died three years later, he left Galen ample means to continue a lavish and lengthy education, traveling and studying a wide range of subjects with experts at Smyrna (Izmir, Turkey) and Alexandria (Egypt). After a prolonged stay in Alexandria, he returned home in 157 to take a prestigious job as **surgeon** for a troop of gladiators. Galen's ambitions, however, outgrew Pergamum, and he moved to Rome in 162. His connections, education, and flair served him well in the theatrical and highly competitive practice of treating Rome's affluent class and brought him to the attention of the imperial court. Emperor Marcus Aurelius (121–180), on campaign in the east, summoned Galen (who was in Pergamum at the time) to his service in 166. After returning to Rome, another opportune dream kept Galen from accompanying the emperor on campaign; he was, instead, assigned to safeguard the health of the emperor's son, the future infamous emperor Commodus (161–192). Except for one other trip to Pergamum, Galen remained in Rome and associated with Rome's imperial elite past the turn of the century.

Galen encountered an epidemic in Rome while he was with Marcus Aurelius in Aequilia in 168–169. Although he wrote late in life that he had left Rome in 166 to avoid the pestilence, he earlier had claimed that he had left for fear of his rivals. His comments on the epidemic are thus secondhand, scattered throughout his works, and they focus

more on individuals' symptoms than on overall generalizations (except with regard to fever). They appear to indicate **smallpox**, although **measles** has also been suggested. Galen thought, according to his own theories of the role of *pneuma* (breath), that treatment entailed purifying poisoned **air** within the body. In *Theriac to Piso* he suggests *gelenê* (a multi-ingredient antidote and tonic) as a prophylactic and remedy, making an analogy with the famous story of **Hippocrates** burning agents to purify the air during the **Plague of Athens**; in *Method of Healing* Galen observes that "drying drugs" were effective for a young man, perhaps reflecting the common theory that plague existed in overly dense and wet air. Galen's observations and theories on epidemic plagues long remained authoritative. His copious writings shaped **Islamic disease theory and medicine**, as well as that of the Christian West so powerfully that "Galenic" defined Western medicine until the **Scientific Revolution** and the development of **germ theory** overthrew his authority. See also Greco-Roman Medical Theory and Practice; Humoral Theory; Medical Education in the West, 1100–1500; Medical Education in the West, 1500–1900; Paracelsianism; Paracelsus; Smallpox in the Ancient World.

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ERIC D. NELSON

GEOPOLITICS, INTERNATIONAL RELATIONS, AND EPIDEMIC DISEASE.

History is replete with examples of **epidemic** diseases that have shaped, and in turn been shaped by, geopolitics—the intertwining of geography, political, and economic relations. The **Black Death** of the Middle Ages spread from Central Asia to Europe via **trade** routes, killing so many that Europe's social and political structures were irrevocably altered. European conquest of the "New World" was enabled by raging epidemics of **measles**, **smallpox**, and other infectious diseases, which—combined with **warfare**, forced labor, and displacement—killed between one-third and one-half of the indigenous population. Proliferation of international commerce and migration was again fundamental to the global pandemics of **cholera** that occurred through the 1800s, facilitated by rapid transport via steamships and the opening of the Suez Canal.

Cholera outbreaks, together with **yellow fever** and the reemergence of the **bubonic plague**, motivated the first international health meetings, treaties, and organizations in the late nineteenth and early twentieth centuries in Europe and the Americas. These efforts called for mutual notification of epidemic diseases and inspection and **quarantine** of both humans and goods, with the aim of safeguarding international **trade** and protecting home populations.

On another front, military action also spurred epidemics and their control: partly spread via troop movements, the **influenza pandemic of 1918–1919** killed upwards of

50 million people, far more than World War I (1914–1918), and was itself a deciding factor in several battles. As these various examples show, the emergence and transmission of epidemic disease is interconnected with global trade, migration, militarism, and international relations.

Geopolitical matters also shaped the first international disease campaigns. In addition to fears that disease outbreaks would interrupt the profitable transfer of goods and resources, Europe's imperial powers were concerned that disease problems could threaten colonists, provoke unrest, and reduce worker productivity in profitable plantations, mines, and other industries. Britain's colonial office, for example, sought to control **tuberculosis** among African miners and **malaria** among Asian agricultural workers. U.S. geopolitical interests in Latin America also shaped disease control efforts. The U.S. spearheaded the creation of the world's first international health agency, now known as the Pan American Health Organization, in 1902: for decades the organization was focused almost exclusively on stopping the spread of epidemics through commercial routes.

Precursor to today's **World Health Organization** (WHO), founded in 1948, the League of Nations Health Organization (LNHO), established after World War I, was launched by a commission to forestall the threat to Western Europe of **typhus** and other epidemics in Eastern Europe. The LNHO also became involved in cooperative efforts to address epidemics, such as infant mortality, that were rooted in poor social conditions. Following World War II (1939–1945), the WHO pursued a series of technical disease campaigns framed by Cold War politics. The WHO's Global Malaria Eradication Campaign, started in 1955, sprayed DDT against malaria-bearing mosquitoes but also used it as a strategy in the Cold War. The campaign's funders, primarily the United States and other Western countries, believed that malaria-free populations would be less attracted to communism. Subsequent campaigns against vaccine-preventable diseases, first smallpox, then **polio** and measles, followed.

Today, as in the past, international economic, political, and social relations and structures facilitate the (re)emergence and spread of both old and new pathogens and shape the ways in which epidemics are addressed by multinational entities, including public, private, and civil society agencies. Two intertwined sets of factors, both of which have intensified over the past decade, are central: globalization and renewed attention to global health governance, including the prominence of health on the foreign policy agendas of many countries.

Epidemic Disease and Globalization. Globalization refers to the growing political, economic, social, and cultural connections among individuals, communities, and countries that occur as business interests, people, goods, ideas, and values travel around the globe. In many respects, today's epidemic disease threats stem from the increased pace and intensity of global trade, financial transactions, travel, communication, and economic integration that have occurred over the past two decades. Economic globalization—the development of an increasingly integrated global economy via the removal of barriers to free trade and capital flow—is particularly important in explaining current patterns of epidemic disease.

Although international exchange and interdependence have occurred as long as global trade has existed, today's globalization is exceptional because of the unprecedented worldwide integration of markets and the increased role of transnational corporations and international financial institutions in social policy making. The World Bank (WB), International Monetary Fund (IMF), and World Trade Organization (WTO)—together

with corporate interests writ large—have enormous influence over global and domestic social and economic policymaking; international health policy is, in turn, dominated by a market-led paradigm that fosters privatization and overlooks the underlying determinants of disease.

For much of the post–World War II period, it was assumed that economic development and technical progress would eliminate the problem of infectious disease; global life expectancy has indeed increased, and there have been some key advances in disease control (most notably, the **eradication of smallpox**) as a result of international cooperation. However, not all attempts at disease control have been so successful. Many diseases once thought to be in retreat, including malaria, cholera, and tuberculosis (TB), have reemerged in recent decades, partly as a consequence of current global economic patterns and policies. New diseases, such as **HIV/AIDS** and **Severe Acute Respiratory Syndrome (SARS)**, are also linked to economic conditions and global interrelations.

For both new and reemerging diseases, the privatization and dismantling of government-funded social protections and programs that have accompanied economic globalization—in many developing countries via the Structural Adjustment Programs (SAPs) of the World Bank and IMF—have increased vulnerability to disease for marginalized groups.

As an example, the resurgence of cholera in South America in the early 1990s began with a freighter ship's discharge of cholera-infected ballast water from China off the coast of Peru. The cholera *Vibrae* infected local shellfish and entered the food supply, reaching the Peruvian population. Thereafter, the **bacteria** spread rapidly through overcrowded slums (economic conditions having forced many to migrate to urban areas in order to find work). Government cutbacks in public health, sanitation, and infrastructure—imposed by IMF and World Bank loan conditionalities starting in the 1980s (following the Latin American debt crisis, yet another feature of geopolitics)—enabled the disease to spread unchecked, killing thousands in Peru and neighboring countries.

Political and economic upheaval is a key factor in today's disease epidemics. Following the breakup of the Soviet Union in 1991, Russia has experienced increased unemployment, **poverty**, and inequity, which, together with the collapse of public health and social security systems, has resulted in escalating TB rates, particularly among the homeless, migrant workers, and prisoners. Russia's severely overcrowded and underfunded prison system has become a breeding ground for multidrug-resistant (MDR) TB, which is now spreading to the general population, with the poorest and most vulnerable least able to access treatment.

Like mass refugee movements in war-torn African nations, the trade, travel, and economic development accompanying contemporary globalization have exposed new disease reservoirs and expanded opportunities for exposure between pathogens and people. Today's mass movements of people and goods increase the chances of disease vectors being introduced into areas where they previously did not exist. The large-scale exploitation of natural resources leads to human encroachment on previously uninhabited areas where they may be exposed to pathogens to which they have no immunity. In central Africa, for example, logging, and consequent road construction, has brought people into contact with the **Ebola virus** via an increase in bush meat consumption. In many other areas of the world, clear-cutting, farming, and urban sprawl have enabled diseases such as **Dengue fever**, malaria, yellow fever, and **West Nile virus** (all spread via mosquito vector) to spread into human settlements. Climate change, also linked to **industrialization**, has also

contributed to the transmission of **insect**-borne diseases, as warmer temperatures have expanded vector habitats.

Perhaps the most visible link between globalization and the spread of disease is the increased speed and volume of global travel. As demonstrated by the SARS outbreak of 2003, an infectious agent appearing anywhere in the world can circulate around the globe in a matter of days, with health and economic consequences for both individuals and countries. SARS also illustrated the ability of globalization to help contain disease; the speed of global communication enabled accurate surveillance, reporting, quarantine, and eventual containment, especially because the threat appeared imminent to the well-off.

Globalization has also affected nutritional patterns, interpersonal violence, medical practices and personnel, and environmental health problems such as pollution. In some cases, rapidly diffused information helps to address disease, for example through the sharing of medical information and techniques via open source journals and international training programs. But in other ways, the work and living patterns of a “globalized world” increase people’s susceptibility to disease as a result of work stress, consumption of unhealthy food, and exposure to pollutants in the home, workplace, and surroundings.

Under-nutrition remains a major issue in much of the developing world, but obesity is also a growing concern. Diabetes and cardiovascular disease, conditions previously associated with affluent societies, have become global epidemics, posing great challenges to countries with weak health infrastructures (7 of the 10 countries with the largest numbers of diabetics are in the developing world). These chronic disease epidemics are attributed to globalization, in that trade liberalization has brought processed food and drinks and sedentary lifestyles to the developing world. Yet the relationship between globalization and chronic disease epidemics is more complex than the simple transmission of lifestyle and individual nutrition “choice.”

Although many societies—and even public health authorities—blame poor diets on individual choices and lack of education, these problems are rooted in the mass production and marketing of food products. Dietary patterns derive from tradition, culture, and household resources, but are also increasingly influenced by the industrialization of food production. Despite its complex production, marketing, and distribution chain, processed food has become far cheaper per calorie than fresh produce and basic foodstuffs in most cities—and even rural areas—around the world.

Along with increasing exposure and susceptibility to disease, globalization has also limited governmental capacity to address ill health. The migration of doctors and nurses from developing to wealthier countries—the “brain drain”—is a key factor here. Drawn by higher wages, improved working conditions, and better supported health care systems, thousands of health-care workers trained in developing countries (usually with public resources) have emigrated to wealthier nations, worsening the human health-care resources deficit in their home countries and widening health-care inequities worldwide.

The supremacy of trade liberalization has also limited governments’ abilities to address epidemic disease, as international trade agreements promote profits over human wellbeing. The WTO’s agreement on Trade Related Intellectual Property Rights (TRIPS), negotiated in 1994, has exacerbated the impact of diseases such as HIV/AIDS in low-income countries by protecting profit-making, patented pharmaceuticals,

effectively blocking treatment for millions of people. The WTO's 2001 "Doha Declaration" affirms the rights of states to protect public health in emergency situations, transcending TRIPS requirements. Many developing countries, however, lack the capacity to adopt the Doha provisions of compulsory licensing (local manufacture of drugs) and parallel importing of patented pharmaceuticals. Moreover, many developing countries are pressured to avoid adopting measures to protect public health in order to safeguard trade interests.

Marginalized populations—the poor, migrant workers, refugees—bear the brunt of (re)emerging epidemic disease, but in a globalized world everyone feels threatened. This perception of threat—often fuelled by overblown media coverage of remote risks such as "mad cow disease"—has led to the intensification of health diplomacy and the formalization of foreign health policy on the part of many nations in both the developed and developing world.

Epidemic Disease and Foreign Policy. Because epidemic disease does not respect borders, it has long been a focus of diplomatic concern. Health cooperation—the provision of funding, materials, and/or human resources to address health needs—has occurred as long as international relations have existed. But efforts to address epidemic disease are motivated by goals beyond improving health conditions. Since the 2001 terrorist attacks on the United States, the ubiquitous concern with national security has extended to epidemic disease. The potential intentional spread of infectious disease, such as the use of anthrax or smallpox as a bioweapon by terrorists, is considered a national security concern. Disease is also understood as a contributing factor to conflict around the world because disease and premature death are a potential cause of economic and social instability. War and social disorder in turn foster the conditions in which further epidemic disease can flourish.

In order to protect domestic health and national security, an increasing number of governments, in particular those of the United States and the United Kingdom, are providing aid to prevent the emergence and spread of epidemic disease. Within this larger foreign policy context, health aid is understood to confer a number of advantages on donor countries, including protecting the health of their own citizens; promoting political stability, economic productivity, and a vibrant civil society; and encouraging research, debt relief, and primary care. The pursuit of such goals results in donor priorities dominating aid agendas and, often, in a failure to address questions of social conditions and resource distribution in development assistance strategies.

A growing number of developing and emerging countries are also engaged in government-to-government health cooperation, including Taiwan, the Czech Republic, Iceland, Korea, Latvia, Lithuania, and the Slovak Republic. Various countries, such as China, Turkey, Saudi Arabia, and Brazil, are both aid donors and recipients. Perhaps most notably, since the early 1960s, dictator Fidel Castro's Cuba has sent medical missions to over 100 countries in Asia, Africa, and Latin America providing disaster relief, medical personnel and training, and health systems policy advice, as well as training thousands of foreign doctors in Cuba as a way of enhancing its international image.

Other kinds of cooperation among nations of the southern hemisphere (South-to-South cooperation) are also materializing. South Africa provides aid to Mali and the Democratic Republic of the Congo, and in turn receives aid in the form of ophthalmologists from Tunisia to eliminate its cataract backlog. The "Bolivarian Alternative for the Americas" is a regional group that includes Bolivia, Venezuela, Cuba, and Nicaragua. Member

states contribute funds, goods, and services to be used by other members. The India–Brazil–South Africa (IBSA) trilateral agreement, which promotes South-South dialogue, cooperation, and common positions on issues of international importance, includes a working group on health focused on epidemiological surveillance; sanitary regulations; traditional medicines; and Intellectual Property Rights.

Geopolitics and the Fight Against Epidemic Disease. The rapid spread of diseases across national boundaries underscores the need for global collaboration in fighting epidemics beginning with international systems of disease surveillance and reporting. International agreements to monitor and prevent the spread of disease have existed since the 1892 adoption of the International Sanitary Conventions that evolved into the World Health Organization's International Health Regulations (IHR) in 1969. Updated in 2005, the new IHR was implemented in 2007; 192 countries are currently party to the regulations, which require member governments to inform the WHO of any reportable diseases within a specific timeframe, but do not require further action.

Today, much global health funding and activity is led by interested parties beyond traditional state players and the WHO, including private foundations, **non-governmental organizations**, international financial institutions, multilateral organizations, and business groups. Private funding, led by the Bill & Melinda Gates Foundation, now accounts for one-fourth of all development funding targeted at health. Combined with an overall rise in health-related development assistance funds in the majority of donor nations since 2000, this means that more money is currently directed at global health challenges than ever before.

The adoption of the United Nations' Millennium Development Goals (MDGs) in 2000 has been a key impetus behind the increased funding for global health. Although not legally binding, the 189 signatory nations agreed to work toward the achievement of eight development goals, three of which are directly health related (reducing child mortality; improving maternal health; and combating HIV/AIDS, malaria, and other diseases), by 2015—a deadline that most experts agree is unlikely to be met.

Whereas the MDGs embody broad development objectives, most of the initiatives implemented to meet them have very narrow targets. For example, reducing epidemic disease is approached on a disease-by-disease basis, a strategy that obscures the contributions of the global political economy and related poverty and inequity.

In sum, global public health efforts, reflecting geopolitical power, are not democratic. Priorities to address epidemic disease are almost inevitably set by donors, be they foundations, multilaterals, or governments. Diseases that receive media attention in rich countries garner the most funding (e.g., the Global Fund to fight AIDS, Tuberculosis, and Malaria); currently, HIV/AIDS drives most global health spending. Although all killers are undoubtedly worthy of attention, high-profile diseases draw resources away from competing health concerns.

Recent increases in both public and private funding for global health, along with new attention to disease on foreign policy agendas, suggest that the political will to address epidemic disease exists. Success requires greater coordination among donors, meaningful involvement of aid recipients, and, above all, attention to the underlying environmental factors of disease. Increasing aid alone will never solve global epidemic disease problems. Vanquishing epidemic disease must be understood not simply as a goal in itself, but as an essential component of improving global health. *See also* Capitalism and Epidemic Disease; International Health Agencies and Conventions.

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KLAUDIA DMITRIENKO AND ANNE-EMANUELLE BIRN

GERM THEORY OF DISEASE. The germ theory of disease, also known as the pathogenic theory of medicine, proposes that microorganisms too small to be seen by the naked eye are the cause of many diseases. After decades of research and observation suggested that living organisms could be responsible for disease, the theory became generally accepted in the scientific community by the end of the nineteenth century, with profound effects on medical treatment and our cultural response to illness. Highly controversial when first proposed, germ theory is now the fundamental basis for clinical microbiology and, indeed, for all of modern medicine. Our understanding of the role of microscopic organisms in human suffering and death has led to the extensive use of **antibiotics**, immunity-producing **vaccinations**, and disinfectants; a much greater investment in sanitation; and an increased concern for **personal hygienic** practices almost everywhere. As a result, germ theory is perhaps the most important contribution to the improvement of health and the extension of life expectancy among people around the world.

Early Explanations for Disease. The significance of the germ theory of disease is best understood when compared to earlier explanations. Although previous accounts turned out to be inadequate, they each foreshadowed the direction medical science would later take in its search for the cause of human illness. For example, **humoral theory**, the leading Western concept for over two millennia, suggested that diseases were caused by substance imbalances within the body of the patient. This theory identified such crucial substances, or "humors," as blood, phlegm, yellow bile, and black bile, and each of these was in turn associated with a major organ in the body, such as the heart, brain, liver, and spleen. Its adherents emphasized diet, exercise, and rest for retention of good health. A second theory explained the suffering and death created by epidemics, focusing largely on the presence of "miasmas," or poisonous **airs**, as the proximate cause of the spread of disease. Although addressing what appeared mysterious at the time, miasmatic arguments emphasized what we would today think of as **environmental** factors in disease causation. It led people to drain swamps, burn refuse and human waste, and otherwise dispose of or neutralize these sources of unseen "miasmas." Finally, there were hypotheses that suggested that diseases might be spread by "contagia"—agents that could be passed from one person to another through air, water, clothing, bedding, or cooking utensils. Although the precise cause of disease was clearly not understood, it was apparent that many diseases followed a course of **contagion** from one individual to another, and this thinking found its best expression later in the germ theory of disease.

Developing the Germ Theory. Although earlier theories of the cause of human and animal diseases may seem quaint and primitive today, some suggested that living organisms like tiny seeds or spores could be related to disease. During the second half of the

nineteenth century, observers came to exactly that conclusion. The French chemist and microbiologist **Louis Pasteur** led the way when he determined the cause of rabies, cholera, anthrax, and silkworm disease. In the 1860s Pasteur's work also led to the development of several effective vaccines, and his efforts set the stage for modern biology and biochemistry. Central to Pasteur's work was his discovery that microorganisms are present in the air but are not created by the air—a critical challenge to earlier theories of the spontaneous generation of disease. He did this by proving that broth became contaminated when exposed to the air but, once sanitized by boiling, the same broth did not reveal the contaminants. He also discovered that fermentation, for example turning grape juice to wine, was a biological process carried out by microorganisms and concluded that if germs could cause fermentation, they might just as well cause diseases; if so, then the laboratory manipulation of the germs that caused diseases could be used to immunize people and animals.

In the 1870s the German physician **Robert Koch** firmly established the practice of bacteriology when he purified the anthrax bacillus and demonstrated that it created endospores that, once caught in the soil, could cause “spontaneous” outbreaks of the disease. Koch also showed that the organisms could be seen in every instance of the disease, that the germ could be produced in a pure culture, that the disease could be reproduced in experimental animals, and that the organism could be retrieved from the inoculated animal and grown again in another culture. Koch also created a series of techniques still used today, including the staining and purification of samples, the development of bacterial growth media, and the use of the Petri dish and agar plates for specimen samples. Using these methods, he later demonstrated the bacterial roots of the devastating disease **tuberculosis**, and identified the *Vibrio* bacterium that caused cholera. For these discoveries, Koch later received the Nobel Prize in Medicine.

Joseph Lister (1827–1912), a British physician and Professor of Surgery at Glasgow University, noticed that many people survived the trauma of surgery but then died later from “ward fever.” Lister believed that microbes in the air of the **hospital** caused the disease to spread in the recovery wards, and that people who had been operated on were especially susceptible to illness, as surgery had left them weak, and their open wounds provided an entry point for the germs. His experiments included the careful cleaning of the wounds of patients who had suffered compound fractures and risked the onset of gangrene. He dressed the wounds with thin layers of lint covered in carbolic acid, and enjoyed an immediate increase in the survival rate of these patients. Lister established beyond doubt the relationship between poor sanitation and the spread of disease, especially in the hospital setting, and he established careful procedures for sanitizing surgical and other treatment equipment. Among other honors received in his lifetime, modern-day mouthwash Listerine offers tribute to Lister's contributions to sanitation and health.

By the end of the nineteenth century it was clear that earlier theories explaining the cause and spread of disease were either incomplete or wrong, and the germ theory of disease came to play a crucial role in our understanding of human suffering and death. Once the presence of pathogenic agents had been established, researchers armed with increasingly sensitive **microscopes**, dyes to stain biological samples, and other tools launched a series of discoveries that continue to determine our understanding of medicine today. In the 1890s **Alexandre Yersin**, a student of Pasteur, and **Shibasaburo Kitasato**, one of Koch's protégés, simultaneously discovered the bacterium that caused the dreaded plague, and Yersin worked to develop a serum to combat it. Scientists, physicians, and the general

public rightly celebrated these developments, and the evidence is indisputable that each new discovery marked an increase in the quality of human life. The germ theory of disease led to the theoretical foundations of the modern science of **epidemiology**, inspired the development of newer and more effective antibiotic drugs, established principles for hygienic practices in hospitals and other medical care facilities, and informed our understanding of public sanitation, wastewater treatment, and a host of other practices.

Once controversial, germ theory is now accepted by virtually everyone associated with modern medicine, although we are well advised to recall that a complex network of factors also play a significant role in the rise and spread of disease. For example, environmental exposure to materials such as asbestos, benzene, tobacco, and lead has also produced human suffering on an unprecedented scale. *See also* Contagion Theory of Disease, Premodern; Fracastoro, Girolamo; Human Immunity and Resistance to Disease; Immunology; Protozoon, -zoa.

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BART DREDGE

GONORRHEA AND CHLAMYDIA. Gonorrhea is an infectious inflammatory disease that primarily affects the urethra but may involve the genitalia, joints (arthritis), skin, eyes, and occasionally other organs. It is caused by a specific **bacterium**, the gonococcus. This Greek term literally means “discharge of seed”; its earlier designation, “*blennorhea*,” means discharge of mucus. Involuntary urethral discharges were referred to in ancient writings, but because of the absence of associated pain, it is unlikely that gonorrhea was being described. London **physician** Andrew Boorde (1490–1549) cited a painful condition that resulted from “meddling with a harlot” and could be transmitted to another woman. Uro-genital symptoms in women are generally less severe, and diagnosis was not recognized in women for another 200 years. Furthermore, gonorrhea was considered to be a symptom of **syphilis**, rather than a discrete disease. The differentiation made by Benjamin Bell (1749–1806), a Scots **surgeon**, in 1793 was accepted only gradually.

The Gonococcus. In 1879, when Albert L. Neisser (1855–1916) was a 24-year-old trainee in the dermatology department of the University of Breslau (Prussia), he made microscopic examinations of secretions from typical cases of gonorrheal urethritis (inflammation of the urethra), neonatal infections, and ophthalmia (eye inflammation) of adults.

He stained the microscopic slides with methyl violet dye and in each case observed structures having a similar appearance. At the time only two diseases had a proven bacterial cause; hence, even Neisser was uncertain of the significance of his observation. He was unsuccessful in finding a medium on which to grow these presumed bacteria. In 1882 he described these structures in more detail and called them "gonococcus," even though he remained uncertain about whether they were the actual cause of the inflammation at the various locations. Two problems impeded research on this question. No animal was found that could be infected with this germ, and it was difficult to grow in an artificial medium. Culturing first succeeded in 1885, and research into how to grow this bacterium reliably continued for the next 70 years.

The genus of bacteria to which the gonococcus belongs is called *Neisseria* that includes not only the meningococcus that causes spinal meningitis, but also nonpathogenic bacteria that occur in the human mouth. The simplest way to identify the gonococcus is to apply the Gram stain to secretions that have been dried on a microscope slide and to find stained round bacteria, usually in pairs, within leukocytes (white blood cells). If no gonococci can be detected, but symptoms are suspicious of gonococcal disease, then fresh secretions must be placed on a specialized culture medium, preferably with added carbon dioxide. After at least two days of incubation, any growth is examined. Growth requirements of gonococci are more complex than those of meningococci.

Symptoms of Gonococcal Infection. All extra-genital complications of gonorrhea were recognized before their etiologic relationship with gonococcal infection, or the discovery of the gonococcus itself. In the early nineteenth century, gonococcal **conjunctivitis** was confused with trachoma, and the possibility that they were separate diseases hinged on giving credence to trachoma patients who stated that they had not been sexually active. Although any joint may be involved, arthritis usually affects only one or two joints, particularly the knee and ankle. Because joint pain is such a common symptom, it appeared likely that its occurrence in a person with gonorrhea was a coincidence. Proof of the causative relationship was obtained by injecting synovial fluid from an inflamed joint of men who had gonorrhea into the urethra of healthy men. The development of typical gonorrhea proved the identity of the cause. Before there were **antibiotics**, the vast majority of gonococcal arthritis cases were men, but since the 1960s most have been women. The probable explanation is that because silent, untreated gonococcal infection is more common in women, their risk of an eruption of symptoms is more persistent.

Uro-genital symptoms in men usually begin two to five days after having become infected. If a woman becomes symptomatic, this begins about 10 days after having been infected. Between 10 and 20 percent of infected women develop pelvic inflammatory disease, which may cause sterility as a result of scarring of the fallopian tubes. Once the body harbors gonococci, various extra-genital manifestations may occur, either from direct contact or from dissemination through the blood. Since the advent of antibiotic therapy, these events have become less frequent and occur mainly in persons who lack recognized symptoms of the genital infection. Manifestations as a result of direct contact are pharyngitis from fellatio ("oral sex"), proctitis from anal intercourse, and conjunctivitis from inadvertently touching the eye with a contaminated substance or finger. The most frequent manifestations of gonococci disseminated through the blood are arthritis and dermatitis; involvement of the liver or heart is rare. Pain may be limited to a tendon, but more often a few joints become inflamed. Arthritis tends to occur during the latter

half of pregnancy. The most typical skin eruption consists of tiny red spots, some with blistering, mainly on the hands and feet. Skin and joint symptoms often occur simultaneously.

Treatment. The first successful treatment that pertained to gonococcal infection was aimed at preventing the blinding of the eyes of newborns who had been infected in the birth canal. In 1880 Carl S. Credé (1819–1892), a German obstetrician, introduced placement of a 2 percent solution of silver nitrate into the eyes of newborns. This practice gradually became routine, and by 1910 the ocular manifestation of gonorrhea had virtually been eliminated from newborns.

Injection of silver nitrate or potassium permanganate into the urethra of symptomatic men became the main treatment among many that were tried. Vaccines prepared from gonococci had no effect on the disease. Arthritis was treated by inducing fever or by locally heating affected joints. However, the first reliable eradication of gonococcal infection occurred in 1938 with sulfanilamide. This required 4 grams of pills per day for at least three weeks and cured about 80 percent of cases. The bacteria soon became resistant to sulfanilamide, but the infection would temporarily respond to one related sulfa drug after another. The real breakthrough occurred in 1943 when it was found that one injection of a small dose of **penicillin** would be curative, even in patients whose **sulfa drug** treatment had been unsuccessful. However, strains of gonococci that required increasingly large doses of penicillin for cure became more frequent. In about 25 years, the curative dose of penicillin increased some 60-fold to 4.8 million units. Tetracycline taken by mouth was shown to be effective, and between 1962 and 1972 it was replacing penicillin in the treatment of gonorrhea. Resistance to tetracyclines developed more rapidly than it had to penicillin. Consequently, new chemically unrelated antibiotics have been introduced every few years. Cephalosporin was the favorite antibiotic in 1990, and since then drugs in the fluoro-quinolone group have in part replaced it. It has been found that after a once-effective antibiotic has fallen into disuse for some years, the prevalence of resistant strains of gonococci diminishes, so that it again becomes possible to treat initially with the least expensive antibiotic, penicillin. If this is not rapidly successful, other agents are available.

The problem of antibiotic resistance in the United States has two causes: adaptation of local strains to various antibiotics and importation of resistant strains, mainly from Southeast Asia and Africa, by infected people who are returning from these areas.

Differential Diagnosis: Chlamydia Trachomatis. The most frequent microbe in the differential diagnosis of gonococcal infections is *Chlamydia trachomatis*. This is a peculiar bacterium that survives only within cells of certain species. Dr. Julius Schachter, of the University of California San Francisco, discovered it in humans in 1966. Identification is ordinarily made by immunologic methods performed on urine, rather than by culture. Chlamydia is present most frequently in sexually active young women.

This infection may be cured by several antibiotics. Azithromycin in a single oral dose or doxycycline for one week are currently favored in most circumstances. Erythromycin is preferred for neonates. The development of resistance to initially effective antibiotics has been less of a problem with Chlamydia than with gonococci.

Epidemiology of Gonococcal and Chlamydial Infection. With recognition of the importance of infection with Chlamydia, gonorrhea has fallen to become the second most prevalent venereal disease in the United States. The actual prevalence of both infections can only be estimated because as many as half of the cases of gonorrhea and

even more with Chlamydia are not reported to health departments. According to a report from 2003, a peak prevalence of gonorrhea occurred in 1978, with a steady decline until 1995, when this disease leveled off. In 2005 more than 330,000 cases of gonorrhea and more than 900,000 cases of infection with Chlamydia were reported to U.S. health departments. According to a population survey, rather than health department data collection, of the 14–39 year age group, conducted during 1999–2002, these events have become less frequent: the mean prevalence of gonorrhea was 0.16 percent in males and 0.33 percent in females; Chlamydia was found at a rate of 2 percent in males, 2.5 percent in females. Of those with Chlamydia, 2.7 percent of males and 6.8 percent of females also had gonorrhea. In a larger national survey conducted in 2001–2002, 70 percent of individuals with gonorrhea were also infected with Chlamydia. Both infections have been detected substantially more frequently in African American than in other racial cohorts. The availability of effective treatment has reduced the occurrence of complications.

Persistence of Symptoms. The symptoms that used to be called post-gonococcal urethritis usually reveal a Chlamydial infection that was masked until the gonococcal infection had been cured. Chlamydial infection has a longer incubation period than gonorrhea and may require a different antibiotic for treatment.

Reactive arthritis (formerly called Reiter's disease) is believed to result from an immunologic reaction to various bacteria, but predominantly Chlamydia. The typical patient develops urethritis, followed by conjunctivitis and arthritis or tendonitis, thus closely mimicking symptoms of disseminated gonococcal infection. This syndrome occurs predominantly in men and does not respond reliably to antibiotics. *See also* Drug Resistance in Microorganisms.

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THOMAS BENEDEK

GORGAS, WILLIAM CRAWFORD (1854–1920). William Gorgas, whose use of sanitation techniques to rid Panama of mosquito-borne **malaria** and **yellow fever** resulted in the successful completion of the Panama Canal in 1914, "found himself leading the most costly, concentrated health campaign the world had yet seen," as historian David McCullough (b. 1933) expressed it.



William Crawford Gorgas. Courtesy of the National Library of Medicine.

Gorgas was born near Mobile, Alabama, and though he was unable to realize his dream of attending West Point military academy, the medical degree that he received from Bellevue Medical College in New York City allowed him to enter the military as a **physician**. After being sickened by yellow fever and developing immunity, he was posted to Havana, Cuba, as chief sanitary officer. He arrived at the close of the Spanish-American War of 1898, which had placed Cuba under American control. Many diseases, including **dysentery** and **typhoid**, were raging. At that time, Gorgas believed that unsanitary conditions caused yellow fever, and though Havana was thoroughly cleaned, yellow fever persisted.

In 1884 French physician **Alphonse Laveran**, working in Algeria, suggested that malaria was a mosquito-borne disease, and around the same time, Cuban physician Carlos J. Finlay (1833–1915) theorized that the mosquito transmitted yellow fever. In 1899 British tropical medicine specialist **Ronald Ross** discovered that the parasite that causes malaria is transmitted by the bite of the *Anopheles* mosquito, and the following year, American physician **Walter Reed's** experiments showed the involvement of the mosquito now known as *Aedes aegypti* in yellow fever transmission, confirming the theory that Finlay had been unable to prove.

Gorgas was then able to bring the diseases under control within 18 months by hiring a large staff of inspectors to locate and cover or eliminate all mosquito breeding grounds, enforce fines for harboring mosquitoes or mosquito larvae, fumigate homes, enforce the use of netting, **quarantine** the sick, and deal with city residents' resentment and suspicion.

Desiring a quicker sea route from the Atlantic to the Pacific Ocean, a French engineering company had begun to build a canal across the Isthmus of Panama in the 1880s. Mainly because of the high death rate from malaria and yellow fever, they were unable to continue and sold the unfinished canal to the United States. The digging resulted in unfinished sewage drains and shallow trenches that collected water and were breeding grounds, but government officials did not believe that the **insects** were the cause of these diseases. When Gorgas was made Panama's chief sanitary officer, he was able to turn to President Theodore Roosevelt (1858–1919) for support, and, using measures similar to those proven in Cuba, the diseases were entirely eradicated within eight months.

Gorgas was made Surgeon General of the U.S. Army and, after he retired, served as a consultant on the control of malaria and yellow fever in Brazil and South Africa. He died suddenly in England, however, before he could carry out his plan to study outbreaks of yellow fever in West Africa. See also *Malaria in Africa; Sanitation Movement of the Nineteenth Century; War, the Military, and Epidemic Disease; Water and Epidemic Diseases; Yellow Fever in Latin America and the Caribbean, 1830–1940.*

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MARTHA STONE

GREAT PLAGUE OF LONDON. See London, Great Plague of (1665–1666).

GREAT POX. See Syphilis.

GRECO-ROMAN MEDICAL THEORY AND PRACTICE. The medicine of classical antiquity, though not a single intellectual tradition, formed the medical knowledge of the medieval West, the Islamic world, and some modern medicine into the Enlightenment. The Greek medical tradition arose around the same time as the Pre-Socratic natural philosophers in Attica and the Aegean Islands: the fifth century BCE. The earliest extant Greek medical texts are called the "Hippocratic corpus" in reference to **Hippocrates**, the (probably legendary) author and **physician**, who was considered the founder of the school that produced these texts. Although many folk medical traditions already existed, such as the cult of the healing god Aesclepios, the Hippocratic texts provide the earliest evidence of a medical system organized around observation and analysis. Hippocratic medicine claimed that explicable natural phenomena underlay illness, and physicians seeking to heal diseases must understand their natural causes.

Greek **humoral theory**, derived from the Hippocratic corpus, viewed health as the equilibrium of fluids in the **human body** called humors; it was believed that if these became imbalanced, illness resulted. The humors—blood, yellow bile, phlegm, and black bile—were often associated with particular organ systems and used for their classification. Whereas medieval physicians fixed the number of humors at four, the Hippocratic authors give no set number. These early theories developed from the observation of sick patients, but little dissection or anatomical study occurred. Hippocratic medicine emphasized the role of the environment in the development of plagues and asthma. Greek physicians correlated both meteorological and astrological influences with the epidemic diseases of populations. Plagues were viewed as the consequence of many natural factors converging on a location; thus, epidemics were believed to result from temporary conditions acting on specific places.

Ancient physicians were aware of the limitations of their art. They could observe the course of a disease, predict its worst moments (crisis), and estimate the point beyond which recovery was unlikely or impossible, but rarely could they effect an immediate cure. Fevers and the healing of wounds modeled the course of illness generally. Prediction was vitally important to ancient physicians because their ability to attract clients depended on their skill in predicting an accurate outcome to illnesses. Diagnosis was based on systematic observation of the patient, the taking of the pulse in various locations, and the examination of urine (uroscopy) and of the complexion. Once a doctor decided that a patient's condition had a remedy, he would design treatment for that specific patient. Treatment regimens often included carefully chosen **diets**, because diet was believed to affect the humors. Most drugs were derived from herbs, though some were mineral or animal products. Following humoral theory, the goal of a treatment regimen was the restoration of humoral balance. To this end, purges, controlled bleeding, baths, and similar cures were prescribed. Although the Hippocratic Oath delineated surgery as separate from medicine, many physicians performed surgical procedures, along with cleansing wounds with wine and wrapping them, setting fractures, and making braces to correct the posture. Healers who were not physicians, known as **empirics**, also performed many of these procedures. The efficacy of Greek practice varied greatly, with better results for chronic than acute diseases. Because there was no precise pharmaceutical knowledge, categories of drug therapy were often vague, and whenever possible, physicians adjusted their care to the changing needs and illnesses of the patient. The wealthy were treated in either the home of the physician or that of the patient, whereas the poor often traveled to healing shrines. Although the knowledge of **quarantine** existed to some extent, ancient medicine encouraged those suffering from plague to flee the location where they were stricken, and thus escape to places with better "air."

Aristotle's biological and psychological writings significantly affected medicine and physiology in the Greek world. Aristotle's detailed zoological writings contributed anatomical detail to the often-hazy anatomy of the Hippocratics, and his hierarchy of functions for the heart, brain, lungs, and liver became part of standard Greek physiology. Though rival schools held different hierarchies for organ function (Plato's followers believed the brain was the central organism against Aristotle's claims for the heart), none of them approached Aristotle's level of systematic study. The rise of Alexandria, Egypt, as a center of Greek culture and learning during the Hellenistic Age led to new advances in medicine. Ptolemaic Egypt produced innovative physiologists, particularly the fourth-century anatomist Hierophilus and early-third-century Erisistratus. Systematic human dissections were performed for the first time in this city in the third century BCE, and the wide cultural exchanges in the city led to many new treatments being added to the Greek pharmacopoeia.

During the Hellenistic Age, Greek medicine was introduced into the Roman Republic. The Latinization of Greek medicine is the principal cause of its survival as the bedrock of Western medical thought into modernity. As Rome expanded and came to dominate the Mediterranean, Greek culture became a large influence in Roman intellectual and social life. Wealthy Romans consulted medically trained Greek slaves and freedmen, and Hippocratic-Alexandrian medicine began to replace traditional Roman healing methods in urban centers, if not in rural regions. Also, the Roman army routinely employed Greek surgeons by the first century CE. The great army doctor

Dioscorides (c. 40–90), for instance, wrote influential guides to pharmacology. Whereas some traditional Romans were bothered by the alien nature of Greek natural philosophy, most physicians who criticized Greek medicine followed basic humoral theory in their own texts.

Galen was the greatest physician of the classical world. His theories changed Greco-Roman medicine immensely. Innate bodily heat was one of his key concepts. Galen thought it was the difference between living and nonliving matter, maintained by the heart, which received blood from the liver and *pneuma* (air and “spirit”) from the lungs. He believed, in opposition to Aristotle, that there was no “chief” organ, but that the brain controlled behavior, the liver digestion, and the heart the innate heat. Galen’s work on the nervous system introduced the relationship between nerves and muscular movement into Greco-Roman medicine. The medieval inheritance of classical medicine was largely shaped by Galenic language and concepts, especially the doctrine of innate heat. *See also* Apothecary/Pharmacist; Avicenna (Ibn Sina); Ayurvedic Disease Theory and Medicine; Black Death (1347–1352); Chinese Disease Theory and Medicine; Contagion Theory of Disease, Premodern; Environment, Ecology, and Epidemic Disease; Epidemiology, History of; Islamic Disease Theory and Medicine; Magic and Healing; Malaria in the Ancient World; Medical Ethics and Epidemic Disease; Plague of Athens; Plagues of the Roman Empire; Plagues of the Roman Republic; Rhazes; Smallpox in the Ancient World; Surgeon.

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DENNIS GREGORY CARAMENICO

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HAFFKINE, WALDEMAR MORDECHAI (1860–1930). Waldemar Haffkine, who began his career as a zoologist, developed the first vaccine for **bubonic plague** and one of the first vaccines for **cholera**. He understood how to translate laboratory findings into effective means of disease control in humans.

Haffkine was born in Odessa, Russia, where he received his doctoral degree in natural sciences and became involved in anti-Czarist revolutionary causes. He studied under Russian zoologist and microbiologist Elie Metchnikoff (1845–1916), who assisted him at critical times in his career. He was invited to Paris where he became bacteriologist **Louis Pasteur's** assistant, began to study **typhoid fever** and **cholera**, and experimented with inoculation against cholera using attenuated (weakened) **virus**. In 1883 German bacteriologist **Robert Koch** had identified the **bacterium** that causes cholera, but scientists dismissed the idea of an anticholera vaccine after Catalan bacteriologist Jaime Ferran y Clua (1852–1929) refused to cooperate with various scientific organizations that were investigating his cholera vaccination program, and his results were dismissed as invalid.

Haffkine studied cholera in laboratory animals and inoculated himself and three of his friends before reporting his findings and declaring that his vaccine was safe for humans. In 1893 he was invited by the Indian government, at Pasteur's recommendation, to help control a cholera outbreak there. He faced problems ranging from dosage variations to fatal attacks of cholera after inoculation. Though Haffkine's vaccine was weak and only moderately effective, statistics indicated that it lowered the death rate significantly.

In 1896 India announced an outbreak of plague, and Haffkine was asked to develop a vaccine, following the discovery of its cause by French Swiss bacteriologist **Alexandre Yersin** and Japanese bacteriologist **Shibasaburo Kitasato**. Haffkine's vaccinations were carried out in many stricken Indian cities, but he was often thwarted by the government's sanitarian approach to the illness, which involved the removal of patients from their homes and forced admission into hospitals, as well as many residents' resistance to **vaccinations**.

Haffkine had to battle complicated political intrigue for many years, when a laboratory accident resulted in the death, from tetanus, of 19 people who were being immunized against the plague. After an enquiry, Haffkine was eventually exonerated, thanks in part to the efforts of tropical medicine specialists **William Simpson**, from Scotland, and **Ronald Ross**, from England. His career, however, did not recover, and some believed that he had not used correct scientific methods, though, as scholar Ilana Lowy wrote, “Haffkine tirelessly asserted his right be recognized as the true pioneer of scientific vaccination.”

Though Haffkine was unable to regain his influence, the laboratory where he had worked in Bombay (now Mumbai), India, was renamed the Haffkine Institute in 1926, 11 years after he retired, and is still in existence. *See also* Cholera: Fourth through Sixth Pandemics, 1862–1947.

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MARTHA STONE

HANSEN, GERHARD ARMAUER (1841–1912). In 1873 Norwegian **physician** and researcher Gerhard Armauer Hansen discovered the bacillus that causes **leprosy**, which would become known as Hansen’s disease. Through clinical observation and epidemiologic study, he had developed the conviction that leprosy was an infectious disease with a specific causal agent, rather than the product of **heredity** or **environmental** factors, the conclusion of most experts at the time. The bacilli Hansen observed in the diseased cells of leprosy sufferers demonstrated for the first time that a microorganism could cause a chronic disease.

Born in Bergen, Norway, Hansen trained in medicine at the University of Christiania in Oslo. In 1868 he returned to Bergen, Europe’s center for the study of leprosy, to study the disease under Daniel C. Danielssen (1815–1894).

Hansen’s research soon departed radically from his mentor’s, which was premised upon leprosy’s hereditary transmission. Early studies in which Hansen observed yellowish, granular masses within leprous nodules, along with his clinical observations, suggested to him a different etiology. In 1871 Hansen began conducting epidemiologic studies in western Norwegian districts where leprosy affected many, and in 1872 he published a report asserting that the disease was infectious. Referring in detail to the observations he had made among lepers and their families, he systematically dismantled the arguments in support of heredity, constructed his argument for contagion, and pointed toward his microbiological findings. In 1873, using a primitive staining process, Hansen revealed the rod-shaped bacilli that came to be known as the cause of leprosy. In 1875 he was appointed Norway’s Chief Medical Officer for Leprosy.

Controversy arose when Albert Neisser (1855–1916), a German researcher, used a more sophisticated technique to demonstrate the microorganism’s existence even more

clearly and claimed primacy for his discovery. Ultimately, however, the overwhelming majority of Hansen's professional peers credited him with the discovery.

Having identified the bacillus, Hansen worked to prove that it was the etiologic agent for leprosy and to dispel persistent skepticism about communicability. He traveled to the United States to conduct studies among leprosy Norwegian emigrants, a population uniquely useful for epidemiologic observation, as the disease had not previously existed in the area. He also unsuccessfully sought to cultivate the bacillus and transfer it to animals or people in order to demonstrate pathogenesis. In 1879 he inoculated a patient ocularly with leprosy material against her will and was found guilty of the act in a court of law. The court stripped him of his position as resident physician at the Bergen Leprosy Hospital, but he remained Chief Medical Officer for Leprosy until his death in 1912. As such, he served as the president of the Second International Congress on Leprosy held in Bergen in his honor in 1909.

Hansen convinced Norwegian authorities to enforce mandatory isolation of the most contagious leprosy patients. Previously, admission to hospitals had been voluntary for leprosy sufferers, and usually only the most debilitated presented themselves. Hansen used data from the National Leprosy Registry to demonstrate that incidence of the disease had diminished most appreciably in regions with strictly enforced hospitalization. Hansen's work ultimately resulted in widespread recognition that leprosy was a contagious disease, if not a highly contagious one, the transmission of which could be controlled by aggressive public health measures. *See also* Demographic Data Collection and Analysis, History of; Leprosarium; Leprosy in the Premodern World; Leprosy in the United States; Leprosy, Societal Reactions to.

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AVA ALKON

HANSEN'S DISEASE. *See* Leprosy.

HANTAVIRUS. *See* Hemorrhagic Fevers; Hemorrhagic Fevers in Modern Africa.

HEMORRHAGIC FEVERS. The term hemorrhagic fevers describes a broad group of human illnesses caused by **viruses** from four families: Arenaviridae (including Lassa and New World Arenaviruses), Bunyaviridae (including Hantavirus), Filoviridae (including Ebola and Marburg viruses), and Flaviviridae (including the viruses responsible for **Yellow Fever** and Dengue fever). All hemorrhagic fever viruses (HFVs) have RNA for their genetic material, and all are enveloped in a fatty (lipid) covering. Although there is significant variation from virus to virus, in general they can cause a severe, potentially fatal illness affecting several different organ systems. The severity of the illness depends on several factors, including the type of virus, the size of the dose, and the route of infection.

After exposure, the virus incubates for 2 to 21 days and then attacks cells in the bloodstream, typically white blood cells (macrophages) and their predecessor cells

(monocytes), leading to general fever and aches in the early stages of illness. From the blood, the infection can spread to a number of different organs including the kidneys, liver, and lungs. In many cases, as the disease progresses it damages the smallest blood vessels, the capillaries, causing fluid leakage into the surrounding tissues. It may also cause significant internal and external bleeding (hemorrhage), from which viral hemorrhagic fevers take their collective name. In severe cases, patients may bleed from the skin and eyes and may excrete copious amounts of blood through vomiting and diarrhea. Death can result from several causes, including heart or kidney failure, blood loss, pulmonary distress, seizure, or shock.

All viral hemorrhagic fevers are of animal origin (zoonotic). Ordinarily the virus replicates in a host species, typically a rodent or arthropod, which suffers few if any ill effects from the infection. Hemorrhagic fever viruses are therefore geographically restricted to the areas inhabited by their host species. Infection of the **human body** results from close contact with the host species. HFVs can be spread to humans via bites, as is commonly the case when arthropods such as ticks or mosquitoes are the host species. When rodents are the host, the virus is usually secreted in saliva, droppings, or urine, which can then dry and become airborne as dust particles. In some cases, the primary host may spread the virus to other animals such as livestock, which then pass the virus on to the humans who care for or slaughter them. Because HFVs exist normally in an animal reservoir, human outbreaks are sporadic and very difficult to predict.

Transmission. The jump from host species to human is called primary **transmission**. Many hemorrhagic fever viruses are incapable of spreading from person to person, and their outbreaks are caused entirely by primary transmission. However, some HFVs can be spread from person to person in a process called secondary transmission. Secondary transmission occurs via direct contact with infected blood or other bodily fluids. There is little evidence that HFVs are normally transmitted via coughing or sneezing, although such a means of spread cannot be ruled out entirely. Secondary transmission can occur through the skin if infected fluid contacts a cut or other break in the surface. Puncturing the skin via a needle stick allows the virus direct access to the bloodstream and is therefore a particularly dangerous mode of transmission. In numerous documented cases, the repeated use of syringes under conditions of poor hygiene has served to amplify naturally occurring outbreaks of HFVs, contributing to both the spread and the lethality of the illness. HFVs are probably not transmissible from person to person before major symptoms have manifested themselves.

Because poor public health practices have contributed so significantly to the emergence of viral hemorrhagic fevers, it follows that good public health has been the most effective way to halt outbreaks. In cases of secondary transmission, quick identification, followed by **quarantine** of suspects and isolation of infected individuals has been successful. For some such outbreaks, the introduction of basics for **personal hygiene** such as clean water, soap, gloves, and appropriate clothing has been sufficient to halt secondary transmission of the illness via contact with infected fluids. Proper use and disposal of equipment such as needles and thermometers is essential. In cases of primary transmission via rodents, controlling the host population through trapping or poisoning has been effective, as have efforts to eliminate rodents from human dwellings and food sources where their urine and feces readily come into contact with people. When arthropods serve as the host, measures such as **fumigation**, wearing of proper clothing, and use of nets, screens, and other barriers are effective.

Treatment. There has been little opportunity to observe most hemorrhagic fevers in a clinical setting, so evidence regarding individual treatment is sketchy at best. For all hemorrhagic fevers, treatment consists of supportive therapy—the administering of fluids and electrolytes to ensure that blood pressure and circulatory volume remain high enough to allow the body's defenses to deal with the infection. Careful observation must accompany fluid treatment, as damage to blood vessels can permit the leakage of added fluids from the circulatory system into surrounding tissues causing complications such as pulmonary edema, the swelling of lung tissue leading to suffocation. In the case of Lassa fever, the use of antiserum derived from the blood of previously infected patients has been effective in early stages of the disease, but this necessitates prompt and accurate diagnosis, which often is not available in early stages of hemorrhagic fever outbreaks. Trials have shown that treatment with the drug ribavirin after infection may reduce the mortality rates of several hemorrhagic fever viruses. There are no known treatments for illnesses caused by the Filoviridae and Flaviviridae families. With the exception of yellow fever, there are no licensed vaccines for any hemorrhagic fever viruses.

HFVs as Biological Weapons. Since the 1990s hemorrhagic fever viruses have received considerable public attention as potential weapons in **biological warfare** or **bioterrorism**. There is some justification for this concern. Outbreaks of the Ebola virus in 1976 killed between 53 percent and 88 percent of infected persons, and in Angola, an outbreak of the closely related Marburg virus killed 235 of 257 infected individuals in 2005 (a 91.4 percent mortality rate). In addition, both the Soviet Union and the United States worked on weaponizing various HFVs during the Cold War, and the Soviet Union is known to have worked with Ebola and Marburg. Studies carried out in former Soviet bioweapons facilities have demonstrated that high concentrations of these agents in aerosolized form can cause illness in guinea pigs and nonhuman primates. In addition, a nonvirulent strain of the Ebola virus, dubbed Ebola Reston, may be somewhat transmissible in aerosol form. This evidence suggests that although HFVs such as Ebola and Marburg are not ordinarily very infectious, they are a short evolutionary leap away from high infectivity. The lethality of these viruses coupled with the lack of any effective therapy would make such a modified form a devastating weapon. Accordingly, in 1999 the **Centers for Disease Control and Prevention** (CDC) in Atlanta classified hemorrhagic fever viruses as Category A bioweapon agents.

Families of Hemorrhagic Fever Viruses

Arenaviridae. Arenaviruses are spherical and have a grainy appearance under the electron microscope. The host species for arenaviruses are rodents. There are four strains of arenavirus in the Western Hemisphere, which cause Argentine, Bolivian, Venezuelan, and Brazilian hemorrhagic fevers. All four of these hemorrhagic fevers tend to occur in limited, sporadic outbreaks. The best-known arenavirus causes Lassa fever, which is endemic in several countries of western Africa. In approximately 80 percent of patients, Lassa fever shows few if any observable symptoms. In the remaining 20 percent, the virus causes a severe disease that may affect the liver, spleen, and kidneys. For approximately 1 percent of all infected individuals, death occurs within 14 days of infection. Approximately 300,000 to 500,000 cases of Lassa fever occur each year in West Africa, with about 5,000 fatalities. Lassa may be spread from person to person via direct contact with infected fluids, but there is no definitive evidence to support direct airborne transmission of the virus. The animal reservoir for the Lassa virus consists of several closely related species of rat; because these rats have a wide geographic distribution, the Lassa virus may have a

wider range than is currently believed. Treatment with ribavirin in the early stages of infection may reduce the mortality rate in Lassa fever outbreaks.

Bunyaviridae. Bunyaviridae is a large family of viruses including five genera, each with many different serotypes. Bunyavirus diseases have been documented throughout much of the world, including Africa, Asia, and most recently North America. In Africa, the primary Bunyavirus diseases are Rift Valley Fever (RVF; genus *Phlebovirus*) and Crimean-Congo Hemorrhagic Fever (CCHF; genus *Nairovirus*). In both cases the animal host of the virus is an arthropod—mosquitoes in the case of RVF and ticks for CCHF. RVF is confined to Sub-Saharan Africa. Mosquitoes transmit the virus to both people and livestock, which then pass it on to humans. In most people RVF causes a mild illness with few if any symptoms, but in some patients the disease can progress to hemorrhagic fever accompanied by **encephalitis** and eye damage, including **conjunctivitis**. Approximately 1 percent of infected humans die of the disease. In late 2006 and early 2007, the **World Health Organization** (WHO) reported outbreaks of Rift Valley Fever in the United Republic of Tanzania, Kenya, and Somalia, all of which had extremely high mortality rates ranging between 23 percent and 45 percent, but this is at least partially attributable to the fact that surveillance was only able to detect severe cases of the disease. In contrast, CCHF is endemic throughout Africa, Asia, the Middle East, and Eastern Europe. Ticks transmit the virus for CCHF to humans and many other species of mammal. CCHF often causes death from liver, kidney, or lung failure, with a mortality rate of approximately 30 percent. The use of ribavirin in the early stages of infection may reduce the mortality of both illnesses.

The third genus of Bunyaviruses that cause hemorrhagic fever in humans are the Hantaviruses. In Asia, Hantavirus infections often lead to kidney failure and are thus referred to as hemorrhagic fevers with renal syndrome. These illnesses have been known in China and Russia for centuries; they received international attention during the Korean War, when thousands of UN troops became ill with Hantavirus infections. The virus was not identified until 1976, followed by identification of the main host species, the striped field mouse, several years later. Recently a new form of Hantavirus endemic to the southwestern United States has been discovered, one that causes an immune reaction producing very fine damage in the capillaries, which allows fluid but not cells to leak out. Consequently the lungs of victims fill with liquid while the blood congeals, leading to rapid death from pulmonary edema. By 1995, 115 cases of this new Hantavirus disease had been confirmed, most in the four corners region of the southwestern United States; the mortality was a very high 51.3 percent. The host animals for this virus are also mice. There is evidence that Asian Hantaviruses respond to treatment with ribavirin, but there seems to be no treatment other than supportive therapy with careful observation for the American Hantavirus.

Filoviridae. Filoviruses are the most recently discovered family of hemorrhagic fever viruses, having first been observed in 1967. The name means threadlike or filamentous, describing the threadlike structure of the viral particles. There are two genera of filoviruses, Marburg and Ebola, and Ebola has four sub-types, three of which cause severe hemorrhagic fevers in humans. Marburg virus was discovered in 1967 when workers in Marburg, Germany, were exposed to the virus via a shipment of green monkeys from Uganda. In this initial outbreak, there were 31 confirmed cases in Germany and Yugoslavia, of which 7 (23 percent) were fatal. Ebola first became known through two unrelated but simultaneous outbreaks in Zaire (now Democratic Republic of Congo) and Sudan in 1976. Each outbreak resulted in approximately 300 confirmed illnesses. The

mortality rate for the Sudan epidemic was 53 percent; that of Zaire was 88 percent. There was another major Ebola epidemic in Congo in 1995, leading to 316 illnesses and a 77 percent mortality rate. The most recent epidemic, as noted above, was an outbreak of Marburg in Angola in early 2005, which killed a staggering 235 of 257 known cases (91.4 percent mortality).

The courses of all filovirus infections are similar. After an incubation period of 2 to 21 days, in which the virus infects the macrophages and monocytes, the illness spreads to other tissues such as the kidneys and spleen. Victims suffer high fevers and excruciating pain. In later stages the viruses cause capillary damage resulting in massive internal and external hemorrhaging. The cause of death is typically described as terminal shock. Filoviruses are spread via direct contact with infected fluids. Airborne spread has not been observed among people, but laboratory research suggests it might be possible. Poor public health has been a significant factor contributing to the secondary transmission of filovirus infections. In all three major Ebola outbreaks, hospitals have served to amplify rather than reduce the incidence of the disease by reusing syringes, needles, and other medical equipment without sterilization. There is no known treatment for filovirus infections other than supportive therapy. The natural range for most filovirus strains appears to be Africa, but some strains (such as the Reston strain) occur naturally in Asia and the Philippines. The animal host of filoviruses is currently unknown, but evidence is increasingly pointing toward bats as the host species. The mode of primary transmission from host to human remains unknown.

Flaviviridae. Viruses of the Flaviviridae family cause four hemorrhagic fevers in human beings: **yellow fever**, Omsk Hemorrhagic Fever, Kyasanur Forest Disease, and Dengue fever. Omsk Hemorrhagic Fever and Kyasanur Forest Disease have ticks as their host species and have a limited impact on human health. Of the four, Dengue fever poses the greatest public health threat. Dengue may be caused by one of four closely related types of flavivirus. In most cases it causes a severe flu-like illness, but in a minority of cases the fever leads to symptoms consistent with other HFVs—high fever, liver damage, internal and external bleeding, and death as a result of general shock. Dengue is a very widespread disease, endemic in more than 100 countries, particularly in Southeast Asia and the western Pacific. The incidence of Dengue has increased dramatically in the past two decades. Currently, WHO estimates that there may be 50 million cases of Dengue infection worldwide every year, with approximately 500,000 cases requiring hospitalization. Dengue is most prevalent in urban and semi-urban environments, affects children under the age of 15 preferentially, and is the leading cause of hospitalization and death among children in several countries. Dengue viruses are transmitted via the bites of infected female mosquitoes. There is no treatment for Dengue fever, but proper supportive therapy can reduce mortality to 1 percent or lower. There is no vaccine, and the only current method for controlling the spread of Dengue is to combat the mosquitoes that transmit the virus.

Future Research. Currently, far more is unknown than known about hemorrhagic fever viruses, leaving all major areas of research open. Much more needs to be done in the identification of host species and determination of ranges of the viruses. The same is true for modes of transmission, primary and especially secondary. Greater opportunity for clinical observation is necessary for improving our understanding of the course of the diseases. Finally, the overall lack of drug therapies and effective vaccines indicates that these areas also await extensive further investigation. *See also* Air and Epidemic Diseases;

Animal Diseases (Zoonoses) and Epidemic Disease; Diagnosis and Diagnostic Tools; Diet, Nutrition, and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Epidemiology; Hemorrhagic Fevers in Modern Africa; Human Immunity and Resistance to Disease; Insects, Other Arthropods, and Epidemic Disease; International Health Agencies and Conventions; Pesticides; Pharmaceutical Industry; Poverty, Wealth, and Epidemic Disease.

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JEFFREY LEWIS

HEMORRHAGIC FEVERS IN MODERN AFRICA. Hemorrhagic fevers are human illnesses caused by **viruses** that result in damage to the blood vessels, making them more permeable and potentially resulting in internal bleeding. Hemorrhagic fevers are distributed throughout the world, but those that are found in Africa include Ebola, Marburg, Lassa, Crimean-Congo, Dengue, and Hantavirus. Outbreaks of Ebola and Marburg have primarily taken place in Central Africa, including the Democratic Republic of Congo (Congo Kinshasa), the Republic of Congo (Congo Brazzaville), Uganda, and Sudan, whereas outbreaks of Dengue have taken place not only in Africa but in other tropical regions of the world, including Asia, the Pacific, Australia, and the Americas.

Although the occurrence of Marburg and Ebola hemorrhagic fevers are considered rare when compared to illnesses caused by other viruses such as **Human Immunodeficiency Virus** (HIV), they are important illnesses because when they do strike, the consequences are devastating. Furthermore, there is evidence that outbreaks of Ebola, for example, have been occurring with increasing frequency since the mid-1990s. In the case of Marburg hemorrhagic fever, whereas in earlier years there were only a few documented outbreaks, in 1998 a large outbreak occurred in the Democratic Republic of Congo (DRC) resulting in a case fatality of 83 percent. The deadliest outbreak of Marburg to be recorded occurred in Angola in 2005 where it claimed at least 300 lives.

Indeed, Marburg and Ebola hemorrhagic fevers have arguably caused the most terror and are considered the most severe of the hemorrhagic fevers because of their ability to spread through large populations in a short period of time if not contained, and also possibly because our knowledge of the viruses that cause these illnesses is limited. Our

knowledge of viral hemorrhagic fevers is indeed small when compared to our knowledge of other viral infections such as HIV.

Dengue hemorrhagic fever, although having a good prognosis if treated early, can also be fatal. It is also one of the most common viral illnesses spread by mosquitoes, with hundreds of thousands of people becoming ill every year. In the early 2000s, there have been more frequent **epidemics** of Dengue hemorrhagic fever occurring in major cities in the tropics, causing this illness to become a major public health concern.

Outbreaks of Ebola have been common in Central African countries such as the DRC and the Republic of Congo, claiming the lives of scores of people. Examples of prominent outbreaks of Ebola hemorrhagic fever included the outbreak in Yambuku, Northern Zaire in 1976, which later spread to Southern Sudan. This was the first outbreak of Ebola to be well documented.

Outbreaks of these hemorrhagic fevers are unfortunately not history. Since the 1976 outbreak of Ebola Hemorrhagic fever, there have been scores of epidemics in various countries in Africa. In October 2007, the **World Health Organization (WHO)** reported an ongoing outbreak of Ebola confirmed in the previous month, in which there was a total of 25 out of 76 suspected cases from a province in the DRC.

Since the 1976 Ebola outbreak in Zaire (DRC), researchers, health-care providers, public health experts from agencies such as the World Health Organization and the **American Centers for Disease Control and Prevention (CDC)**, and government officials have made great strides in ensuring the accurate and systematic documentation of outbreaks. Wherever outbreaks of these three hemorrhagic fevers have occurred, there has been efficient communication among various international bodies and important parties. Necessary personnel have been deployed to the areas not only to assist in containing the virus causing the hemorrhagic fever but also to document relevant information pertaining to how the outbreak began and how it spread, in an effort to gain a better understanding of these deadly diseases and to prevent future outbreaks.

These diseases are especially dangerous when they reach epidemic levels on the African continent, given the many challenges faced by the African countries where these hemorrhagic fevers tend to occur. To give an example, the likelihood of death resulting from Ebola in Africa is 50 to 90 percent, with health-care providers directly involved in caring for those infected being at great risk of contracting the virus. Indeed, the mortality rate for medical workers who contract Ebola is 50 percent. While the likelihood of death from Marburg is lower than that of Ebola—about 25 percent—both diseases may spawn complications, a few of which include liver inflammation, inflammation of the spinal cord with possible permanent paralysis, and, in men, inflammation of the testicles.

The prognosis of a patient suffering from Dengue fever is better than that of Marburg and Ebola, with most patients recovering from Dengue fever if health care is provided promptly and in an aggressive manner. Nevertheless, half of the patients suffering from Dengue fever who are not treated go into shock and die.

To date, there is neither a cure nor a vaccine for these easily transmittable deadly hemorrhagic fevers, with exposure occurring through contact with body fluids. Infected persons are isolated and provided with supportive treatment and care, which means that they receive fluids and electrolytes to maintain hydration and medications to help relieve the symptoms of the disease and treat resulting complications. Furthermore, little is known about how the animal host transmits the virus to the human host. As such, the

need for further research that would yield information critical to the development of a cure or even a vaccine is essential.

With the world becoming more and more of a global village and with people traveling with ease from one part of the globe to another, there is need for the understanding of such diseases that have the potential to spread among scores of people within a very short time frame. Diseases that once only occurred in a remote African village can now be easily transported through a human host traveling from Central Africa to the Americas to be transmitted to someone else in that part of the world. It is therefore critical that any outbreaks of hemorrhagic fevers on the African continent be speedily curbed as a way of not only protecting the health of Africans but also that of citizens of other countries in the world.

Challenges for African Countries. The African countries that have experienced epidemics of hemorrhagic fevers are also some of the very poorest countries in the world. Many lack the infrastructure, as well as the health and social services personnel, to care adequately for those who are infected. Take, for example, the DRC, which has a gross domestic product (the total market value of all final goods and services produced within a country in a year) per capita of \$123, compared to that of the United States, which is \$11,004. The poor economy of the DRC has undoubtedly limited domestic funding for the establishment of health-care infrastructure, as well as for the education, training, and adequate compensation of health-care personnel necessary for the containment of outbreaks of deadly diseases.

Limited Medical Supplies. In resource poor countries, containing epidemics resulting from hemorrhagic fevers can indeed be challenging. Because the diseases are transmitted through contact with bodily fluids, including contact with equipment such as needles that have been used on or handled by an infected person, it is important to take strict precautions when handling anything that has come into contact with the infected person. As such, it is recommended that those coming into contact with the infected person's body fluids or anything else that the person has been in contact with put on gloves, gowns, goggles, and masks, items that are often not readily available in hospitals or clinics in the African countries affected by these epidemics. It is also recommended that needles that have been used on infected persons be sterilized or disposed of appropriately using standard protocols. In the 1976 epidemic of Ebola hemorrhagic fever in Yambuku mission hospital in Northern Zaire, it is clear that inability to contain the virus effectively through proper sterilization of needles and syringes contributed to the rapid spread of the virus, which eventually claimed the lives of 280 of the 318 people infected. It is documented that at the time of the outbreak, the routine was for five needles and syringes to be issued to the nursing staff every morning for their use on the hospital units. These needles and syringes were rinsed between patients with warm water and sometimes boiled at the end of the day.

Today, we know that because these viruses are spread through direct contact with infected body fluids, nondisposable protective equipment such as gowns or masks must not be reused unless they have been properly disinfected. Moreover, needles and syringes that have been used on the infected person are definitely not to be reused. The Centers for Disease Control and Prevention report that contaminated needles and syringes have played a significant role in spreading infection where outbreaks of Ebola hemorrhagic fever have occurred. Clearly, even today, poor African countries such as the DRC can ill afford adequate disposable needles and the equipment necessary to ensure proper and

continuous sterilization of needles. Neither can they afford to dispose of important protective gear.

Lack of available medications also complicates the delivery of efficient and much needed health care to victims of epidemics of hemorrhagic fevers. Basic medications that are sorely lacking in hospitals when there is no outbreak, such as fever-reducing medications, become all the more needed when there is one.

Limited **diagnostic tools** that would allow for the prompt identification and isolation of cases are also in short supply, making it difficult to contain the virus following prompt identification, thus resulting in amplification of the virus leading to outbreaks. Early detection and containment of the viruses causing hemorrhagic fevers are further made difficult because the signs and symptoms of hemorrhagic fevers, such as headache, fever, and vomiting, are very similar to those of other diseases such as **malaria**, **dysentery**, and **influenza** commonly present in Central Africa. During the Ebola epidemic in Kikwit in the DRC in 1995, laboratory tests were unavailable, and patients exhibiting fevers were empirically treated with antimalarials and **antibiotics** rather than the medications indicated for Ebola.

Infrastructure. Isolation of infected persons, required to ensure the effective containment of the viruses causing hemorrhagic fevers, is a challenge when there is limited infrastructure to house those infected. During the Ebola outbreak of 2003 in the Republic of Congo, one of the rural hospitals had only two rooms available for use as isolation rooms. These two rooms had a metal cot with no mattress, a bucket, broken windows, and no running water or toilets.

Health-Care Personnel. In addition to the need for infrastructure, in order to save the lives of those already infected, aggressive treatment is essential. As mentioned earlier, treatment involves fluid replacement therapy and administration of medications that will help treat the signs and symptoms of the disease as well as the complications resulting from the disease. In cases of an outbreak, there is therefore an urgent need for health-care personnel who will not only provide such aggressive treatment but also ensure strict monitoring of patients for prompt identification of complications and rapid ensuing medical response. Yet in African countries that experience outbreaks of hemorrhagic fevers, there is routinely a dire need for health-care personnel. To give an example, according to the **World Health Organization**, the DRC had an average of 0.53 **nurses** and 0.11 **physicians** per 1,000 population in the year 2004. This need naturally intensifies when there is an outbreak of a hemorrhagic fever.

The short supply of health-care personnel engaged in the treatment and the containment of outbreaks of hemorrhagic fevers such as Ebola and Marburg face not only the risk of acquiring the viruses themselves as they tend to patients with limited supplies but also the stigmatization by other members of the community and from their own families. Further complicating the situation faced by health-care providers when such epidemics occur in African countries are the two very divergent sociocultural models used to curb the spread of hemorrhagic fever epidemics: On one hand, there is the Western biomedical model in which Westerners respond to the epidemic with the provision of important resources, assistance in isolating and providing treatment to the sick, and conducting of hygienic rituals such as bagging infected **corpses** for appropriate handling. Such actions of Westerners in response to epidemics of hemorrhagic fevers on the African continent are viewed from a different perspective by the observing Africans who may have a limited understanding of Western infection control procedures. On the other hand, for the

Africans, there is the traditional model in which African peoples in the midst of an epidemic offer their own explanations for what is taking place in their communities, based on their own frame of reference and their traditional medical and religious beliefs.

African health-care providers find themselves caught in the middle of these two different and sometimes conflicting models. Often they do not reveal what occurs in the African context to the Western health-care providers for fear of being labeled backwards and ignorant. At the same time, they are mistrusted by their fellow Africans who associate them with the Westerners whom they do not understand and perhaps also do not trust. One important issue to note is that although some of the indigenous practices used by Africans in an effort to contain the spread of a hemorrhagic fever epidemic may serve to amplify the outbreak, other practices complement those instituted by Western health-care professionals. The two cultures, although different, can negotiate, and a common ground, more collegial in nature, can be discovered to strengthen the response to fever epidemics on the African continent.

Although much has been said about the challenges faced by resource-poor African countries in which outbreaks of these deadly diseases occur, there is also much to be said about the unity, cooperation, and resilience of human beings when epidemics such as Marburg and Ebola occur. For instance, on August 31, 2007, the World Health Organization reported an outbreak of an unknown illness in the province of Kasai Occidental in the DRC, with 50 percent of the cases identified as children less than 10 years of age. An investigation team that included officials from the ministry of health in the DRC, WHO officials, and those from other agencies took important measures, such as obtaining clinical samples for laboratory testing, mobilizing support for epidemiological investigation and logistics, ensuring the provision of supplies and safe **water**, promoting safe burial practices, and strengthening infection control. Clinical samples were also sent to the CDC in Atlanta, Georgia. Less than two weeks later, the Ministry of Health of the DRC confirmed that laboratory analysis performed at the Centre International de Recherches Médicales de Franceville in Gabon and at the CDC in the United States indicated that the unknown illness in the province of Kasai Occidental was an outbreak of Ebola hemorrhagic fever. The prompt response of both national and international officials to the needs of an African nation with limited resources in the midst of such a crisis is a testimony to the results yielded by human cooperation and unity. This is only one example that indicates that with each subsequent outbreak of hemorrhagic fever and with the acquisition of more knowledge and experience, national and international teams of health-care experts and social scientists become better organized in their clinical management and documentation of cases, and the mortality rates resulting from the epidemics are consequently lower.

The commitment of local nurses during the outbreaks occurring in the DRC in 1995, in Uganda in 2001–2002, and in the Republic of Congo in 2003 also speaks to the resilience and commitment of health-care providers who often place their own lives at risk while prioritizing the lives of others in the midst of a deadly outbreak.

On the Frontiers. Over the past decade, significant progress has been made through various studies that have increased scientists' understanding of the molecular mechanisms that are involved in the **transmission** of viruses from the host cells and the processes that lead to hemorrhagic fevers themselves. One of the most important advances in combating these viruses through research is evidenced through the extraordinary successes of two vaccine platforms that have proven to be capable of completely protecting nonhuman primates against some strains of the Ebola and Marburg viruses.

Swift measures in the detection and treatment of the viruses causing Marburg, Ebola, and Dengue hemorrhagic fevers and continued investigation into the disease source and the disease process through research speak to the international unity and cooperation among organizations and countries that is necessary for not only the containment but ultimately the elimination of these deadly hemorrhagic fevers. *See also* AIDS in Africa; Animal Diseases (Zoonoses) and Epidemic Disease; Folk Medicine; Geopolitics, International Relations, and Epidemic Disease; Non-Governmental Organizations (NGOs) and Epidemic Disease; Pharmaceutical Industry; Trade, Travel, and Epidemic Disease.

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LUCY MKANDAWIRE-VALHMU

HENDERSON, DONALD AINSLIE (1928–). As head of the **World Health Organization's** (WHO) worldwide **smallpox eradication** program from 1966–1977, Dr. Donald A. Henderson led the only successful disease eradication program to date. This unprecedented triumph marked the containment of a **virus** that had plagued humankind for millennia (killing 300 million people in the twentieth century alone) and established Henderson as a key figure in the history of global public health.

Born to Canadian parents in Lakewood, Ohio, Henderson earned his Masters in Public Health degree from Johns Hopkins University in 1960. Initially employed by the **Centers for Disease Control** (CDC) in Atlanta (first as chief of the **epidemic** intelligence service from 1955–1957, then as chief of the surveillance section from 1960–1966), he was recruited as WHO's chief medical officer for the smallpox eradication campaign in 1966.

As head of the program, Henderson oversaw the thousands of public health workers who carried out the massive **vaccination** campaign. Using a combined approach of mass vaccination and surveillance and containment (or "ring vaccination"), Henderson and the national eradication teams that made up the worldwide campaign were able to prevent the spread of—and eventually vanquish—the disease. Such a successful outcome had eluded eradication efforts against hookworm, yellow fever, and malaria earlier in the century.

In speaking about eradication initiatives, Henderson cited several advantages in the case of smallpox: there was an effective, easily administered, and inexpensive vaccine

available for a disease with no animal reservoir, and the political will existed to achieve the goal. Henderson's own determination and initiative were also key factors in the victory. For example, he befriended Emperor Haile Salassie's personal physician in order to ensure Ethiopia's participation in the face of fiscal concerns and traveled to Moscow (against orders) personally to demand improved quality of vaccine donated from the USSR. In recounting the campaign, Henderson describes smallpox eradication as a "Cold War victory" noting that the atmosphere of international competition helped to drive the success of the program. Nonetheless, Henderson was also critical of the neglect and underfunding of other pressing health issues beyond smallpox that occurred as a result of the eradication campaign, leading him to argue against future disease eradication attempts in later years.

Knowing that the eradication program was almost complete, Henderson left the WHO to become Dean of the Johns Hopkins School of Public Health (1977–1990), just prior to the report of the last natural case of smallpox in Somalia in 1977. Following his role in the smallpox eradication campaign, Henderson has continued to be involved in public health and disease eradication/control issues in both academic and government settings, serving as White House science advisor (1991–1993) and deputy assistant secretary for health and science for the federal Department of Health and Human Services (1993–1995). Henderson is the recipient of numerous international awards and honorary degrees, including the Presidential Medal of Freedom (received in 2002), the highest civilian honor in the United States.

Although smallpox was officially declared eradicated in 1980, Henderson continues to be troubled by the virus and its potential role in **biological warfare**, a concern that resulted in his appointment as founding director of the Center for Civilian Biodefense Strategies at the Johns Hopkins School of Public Health in 1997. His work on bioterrorism and public health security has continued via his 2001 appointment as head of the federal Office of Public Health Preparedness and 2003 transfer to the Center for Biosecurity at the University of Pittsburgh Medical Center. Rather ironically, Henderson currently spends much of his time making public health contingency plans in the unlikely event of intentional reintroduction of the very disease that he helped to wipe out.

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KLAUDIA DMITRIENKO AND ANNE-EMANUELLE BIRN

HEPATITIS. The word hepatitis is a catchall term that refers to any inflammation (–itis) of the liver (*hepar*) and does not imply a specific cause or connote contagiousness. Inflammation of the liver is defined as an irritation or swelling of liver cells. Hepatitis is a

term that encompasses many different causes. Only hepatitis caused by a **virus** (viral hepatitis) is potentially infectious to others. Consequently, hepatitis from causes other than viruses, such as alcohol (alcoholic hepatitis) or fat (fatty liver hepatitis), cannot be spread through food or by interpersonal or sexual contact.

Hepatitis is generally described using two broad categories. One category refers to how long a person has hepatitis, and the other category refers to what factor caused the hepatitis. Inflammation of the liver that lasts less than six months is known as acute hepatitis. Within six months, people with acute hepatitis are completely healed. The liver typically self-repairs any short-term damage it may have suffered, and no long-term consequences are suffered. Viral hepatitis A is an example of acute hepatitis.

Inflammation of the liver that lasts longer than six months is known as chronic hepatitis. People who progress from acute hepatitis to chronic hepatitis are at risk of developing cirrhosis (severe scarring of the liver that is typically irreversible) and the complications of cirrhosis, such as liver cancer, internal bleeding, and liver failure. Viral hepatitis B and viral hepatitis C can lead to chronic hepatitis.

Hepatitis is also described by its cause. Although hepatitis is most frequently caused by viruses, other stimuli may cause forms of the disease. These include autoimmune liver disease (autoimmune hepatitis), obesity (nonalcoholic fatty liver hepatitis), alcohol (alcoholic hepatitis), and some medications and herbs (toxin-induced hepatitis). This entry only discusses potentially infectious viral hepatitis. A virus is a tiny microorganism that is much smaller than **bacteria**. Its main activity and goal consists of reproducing more viruses and causing damage. A virus is capable of growth and multiplication only once it has entered a living cell. The main goal of the hepatitis virus is to enter a liver cell, reproduce more hepatitis viruses, destroy the cell, and move on to attack the next liver cell.

The History of Viral Hepatitis. Viral hepatitis can be traced back to ancient times, when it was believed by scientists that some type of virus existed that attacked the liver, resulting in a yellow discoloration of the skin and eyes, now known as jaundice. From the late 1800s to the early 1900s, scientists believed that there were only two forms of viral hepatitis: infectious hepatitis and serum hepatitis.

In 1963 a major breakthrough in research occurred—the cause of serum hepatitis was identified, and the virus was given the name hepatitis B virus (HBV). It took an additional 10 years for scientists to isolate the cause of infectious hepatitis. This virus was given the name hepatitis A virus (HAV). Around this time, medical researchers realized that other forms of viral hepatitis must exist that were not caused by either HAV or HBV because there were still so many cases of hepatitis that were not the result of one of these two viruses. These cases of unknown viral origin were lumped into the category of non-A non-B (NANB) hepatitis. In 1989 the virus that caused the majority of NANB hepatitis was identified through cloning experiments and was named the hepatitis C virus (HCV).

Although the three most common viruses causing hepatitis are hepatitis A, B, and C, other hepatitis viruses also exist. The hepatitis delta virus (HDV), first isolated in the mid-1970s, was shown to exist only in the presence of HBV. The existence of another hepatitis virus, which is similar to HAV, was suggested throughout the 1980s but was not successfully cloned until 1990, at which point it was named the hepatitis E virus (HEV). Evidence of the existence of a hepatitis F virus (HFV) is, at present, only anecdotal. Hepatitis viruses that do not appear to be significant causes of liver disease are the hepatitis G virus (HGV), discovered in 1995; the transfusion-transmitted virus (TTV),

identified in 1997; and the SEN-V, identified in 1999. Other viruses, such as herpes simplex virus and Epstein-Barr virus, can also attack the liver. However, since the liver is not the principal organ damaged by these viruses, they are considered not to be a significant cause of viral hepatitis. Because approximately 10 percent of hepatitis cases still do not have an identified cause, researchers suspect that one or more as yet unidentified hepatitis viruses may exist.

Incidence and Prevalence. In the United States, HAV is the most common cause of acute viral hepatitis. Each year, approximately 134,000 Americans are infected with HAV. In fact, around 33 percent of all Americans have at some point been infected with HAV. Almost 100 percent of people who live in U.S. communities with substandard **water** and sewage sanitation systems, in addition to people living in economically developing countries such as Africa, Asia, and Latin America, have been infected during **childhood**.

Approximately 2 billion people worldwide have been infected by hepatitis B, and almost 400 million people worldwide, including 1.25 million people in the United States, are chronic carriers of this virus. Approximately 65 million of those chronically infected will die of the disease. HBV is the single most common cause of cirrhosis and liver cancer worldwide. Hepatitis B is endemic in Southeast Asia, China, and Africa. In these areas of the world, more than 50 percent of the population has been exposed to HBV at some point in their lives. The virus has a relatively low prevalence in North America, Western Europe, and Australia, and accounts for only 5 to 10 percent of all chronic liver diseases in these areas.

HCV is the most common cause of chronic liver disease in the United States. It is estimated that almost 5 million Americans (over 2 percent of the U.S. population) and more than 1 percent of the world's population are infected with HCV. Although the incidence of people becoming acutely infected with HCV is decreasing, approximately 8,000 to 12,000 deaths are attributed to hepatitis C each year.

How Hepatitis Viruses Are Transmitted. Hepatitis A virus is transmitted by the enteric or fecal-oral route. Enteric transmission consists of introduction of a virus into the body by way of the digestive tract. It occurs when a virus is present in the feces (fecal) of an infected person, and is then transmitted to another person via ingesting (oral) a small amount of infected stools. HBV, HDV, and HCV are transmitted via the parenteral route, meaning that these viruses are introduced into the body by any way other than via the intestinal tract. HBV is transmitted either through contaminated blood, during sexual contact, or from mother to child during childbirth. HDV only occurs in individuals who already have hepatitis B. HCV is transmitted only by blood-to-blood contact. This includes intravenous drug use, blood or blood product transfusions prior to 1992, and possibly tattoos and body-piercings. Sexual **transmission** of HCV is very rare, and transmission from mother to child at childbirth occurs in only 3 to 5 percent of cases.

The Symptoms and Physical Signs of Hepatitis. These may vary greatly. At one extreme, some people are very ill, with jaundice, fever, decreased appetite, abdominal pain, nausea, vomiting, and fatigue. At the other extreme, and more commonly, people with hepatitis may be totally asymptomatic—meaning that they have no symptoms—or may have vague, nonspecific symptoms, such as mild fatigue or flu-like symptoms. The severity of symptoms that a person is experiencing often bears no correlation to the amount of damage done to the liver.

Diagnosing Hepatitis. The only way to determine the type of hepatitis one has, what caused it, and how much damage has been done to the liver, is through a combination of tests. These include blood tests, such as liver function tests (LFTs) and hepatitis-specific blood tests (such as antibody and antigen tests); imaging studies done by a radiologist, such as a sonogram; and a liver biopsy (removal of a tiny piece of liver tissue using a special needle).

Treatment and Prevention. Medications used to treat viruses are known as antivirals. Treatment of acute hepatitis, such as hepatitis A, is mostly supportive. This means that treatment is based upon the symptoms being experienced, and no antiviral medication is typically needed.

Treatment of chronic hepatitis, such as chronic hepatitis B or C, is more complicated and depends on numerous factors. Treatment of hepatitis B may include an injectable medication known as interferon, or one or more oral medications either alone or in combination, known as nucleoside and/or nucleotide analogues. Typically, hepatitis B cannot be cured, and treatment is life-long. Treatment of chronic hepatitis C involves the use of pegylated interferon (a once-a-week injectable medication), in combination with an oral medication known as ribavirin, which is taken daily. Treatment lasts for 24 to 48 weeks. Hepatitis C is the only virus that can potentially be cured, with recovery rates greater than 55 percent.

Prevention is, of course, the best treatment for any disease, and fortunately, hepatitis A and B **vaccinations** are available. The development of the hepatitis B vaccine represents one of the most important advances in medicine. This is the first and only vaccine in history that can simultaneously prevent liver cancer, cirrhosis, and a sexually transmitted disease. This vaccine has been incorporated into the immunization programs of more than 80 countries, and routine hepatitis B vaccination of all newborns in the United States has been in mandatory since 1999. The hepatitis A vaccine has been available since 1995. There is currently no vaccination for hepatitis C. *See also* Human Body.

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MELISSA PALMER

HEREDITY AND EPIDEMIC DISEASE. Humans differ significantly in their susceptibility to **epidemic** diseases. These disparities are the result of a wide range of biological, developmental, geographical, social, economic, cultural, behavioral, and psychological factors. Recent studies have confirmed what **physicians** and patients, ancient and modern, have generally believed: that hereditary variations can play a key role in determining who does or does not succumb to a given disease. Long before the advent of gene studies of twins and adoptees, for example, medical writers used such terms as

diathesis, constitution, or hereditary predisposition to denote the way in which certain kinds of illness seemed to “go by blood.” Not until the mid-1700s, when Pierre-Louis Moreau de Maupertuis (1698–1759) studied the **transmission** of polydactyly (extra fingers or toes) in a German family, did the role of heredity in the onset of disease or abnormality start to emerge as a field of scientific inquiry. And it took the twentieth century’s development of improved statistical techniques, advances in our understanding of twinning and genetic relatedness, and the advent of genomic analysis for robust data to emerge. As genotyping becomes quicker and easier, more and more genes are being identified that can reduce or enhance an individual’s infectivity and her chances of overcoming infection.

The high level of polymorphisms among genes involved in immune function, not least the human leukocyte antigen (HLA) genes, reveals the intense selective pressure humans have been exposed to from disease. Often as a result of genetic variations, some individuals and groups have a heightened resistance to infection. Members of the Fulani tribe of West Africa, for instance, seem to have a high frequency of genes conferring a degree of resistance to the *Plasmodium* parasite that causes **malaria**. Members of African populations with hemoglobin C also appear to enjoy a raised level of protection against severe cerebral malaria. And those who lack the Duffy blood group on their red blood cells may have complete resistance to *vivax* malaria.

Genetic linkage studies, including some genome-wide scans, have recently identified a number of chromosomal regions bearing genes that are likely to confer enhanced disease resistance. Certain HLA alleles have been shown to correlate with the rapid clearance of **hepatitis B** infections in the Gambia, Europe, and Korea. Non-HLA genes have been implicated in protection against **leprosy** and **tuberculosis**; in the latter case, the Vitamin D receptor gene may play an important role. And it has been established that between 5 and 21 percent of Caucasians carry a mutation, $CCR5\Delta32$ (Δ =delta), which means that their macrophages and lymphocytes lack a coreceptor that certain HIV strains require for entering them. This can give homozygotes protection against HIV infection and can afford heterozygotes a delay in the onset of full-blown AIDS.

In addition, selection for certain blood types may have been related to infectious disease. The occurrence of Blood Group O, for example, is especially high among those suffering from severe forms of **cholera**, indicating that other blood groups might have evolved to confer resistance to such deadly infections. Yet epidemic diseases typically exert less intense selective pressures than endemic infections like malaria, leprosy, or tuberculosis. Specific outbreaks can, of course, be devastating—for instance, bubonic plague during the Middle Ages in Europe. Nevertheless, the cumulative death toll from infections like plague, **typhoid**, and cholera tends to be far less than that from endemic infections that kill persistently over successive centuries. Even so, some investigators associate the high frequency of certain mutations with past epidemics. It has been suggested, for example, that the $CCR5\Delta32$ mutation was selected for as a result of the bubonic plague outbreaks of the Middle Ages. There is, however, some dispute as to whether the selective pressures would have been adequate to produce the observed frequency of the gene among modern Caucasians. Other researchers have argued that $CCR5\Delta32$ was an adaptation for combating **smallpox**, a disease that was undoubtedly a potent selective force, killing countless people before reproductive age. Such debates are difficult to resolve partly because other factors might also account for the frequency of the genes in question.

Less benign genetic mutations certainly confer selective advantages against disease. The benefits for people in malarial regions of carrying single recessive genes for sickle-shaped hemoglobin, α -thalassemia, or β -thalassemia are well known. Mutations that are highly deleterious in homozygote form may also have evolved to help combat epidemic diseases. The high rates of the recessive gene for cystic fibrosis (CF) in western Europe suggest that heterozygote carriers once enjoyed some level of **immunity** against one or more major killers. The frequency of the main CF gene does not in itself prove that it conferred a survival advantage. But there is evidence that CF genes could have provided protection against typhoid: the mutation causing CF appears to make it harder for the bacteria responsible, *Salmonella typhi*, to enter the body's cells. Other groups of researchers have suggested that CF genes gave a heterozygote advantage against cholera, diarrhea, or tuberculosis.

Conversely, certain alleles are associated with increased susceptibility to infectious disease and/or a lowered ability to fight against an existing infection. Twin studies have demonstrated high levels of concordance in cause of death between parents and children for such infections as tuberculosis, leprosy, and **poliomyelitis**. More recently, researchers in many countries have identified genes that are disproportionately common among those suffering from various, though typically endemic, infections. For example, the study of HLA alleles has revealed an association between specific mutations and susceptibility to tuberculosis and leprosy in Indian populations. Moreover, separate studies among Brazilian and West African families indicate the presence of a mutation on chromosome 5, in a region associated with immune response, which may lessen resistance to **schistosomiasis**.

The identification of genes or gene complexes involved in disease susceptibility has vastly improved in recent years. In particular, the ease of genotyping has now made genome-wide linkage studies more viable. Researchers in the field are confident that in the coming years a far more complete picture will emerge of the links between human genetics and the incidence of disease. It is also hoped that a fuller understanding of the genetics of susceptibility will contribute to the development of more effective therapies and vaccines. See also Human Subjects Research.

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JOHN WALLER

HIPPOCRATES (ca. 460–375/350 BCE) AND THE HIPPOCRATIC CORPUS.

Although Hippocrates is widely regarded as the father of western medicine and is famous for treating a plague in antiquity, we actually know very little about him or this incident. Plato (428–348 BCE; *Protagoras* 311b–c) and Aristotle (384–322 BCE; *Politics* 1326a14), in the fourth century BCE, recognized him as a **physician** of some renown, but by the first century BCE, he had become a heroic figure associated with many deeds, beliefs, and texts. **Galen**, physicians of the Renaissance and Enlightenment (such as **Paracelsus** and **Thomas Sydenham**), and even contemporary medicine have looked back to Hippocrates as a foundational hero in their own image. In short, Hippocrates became, from very early

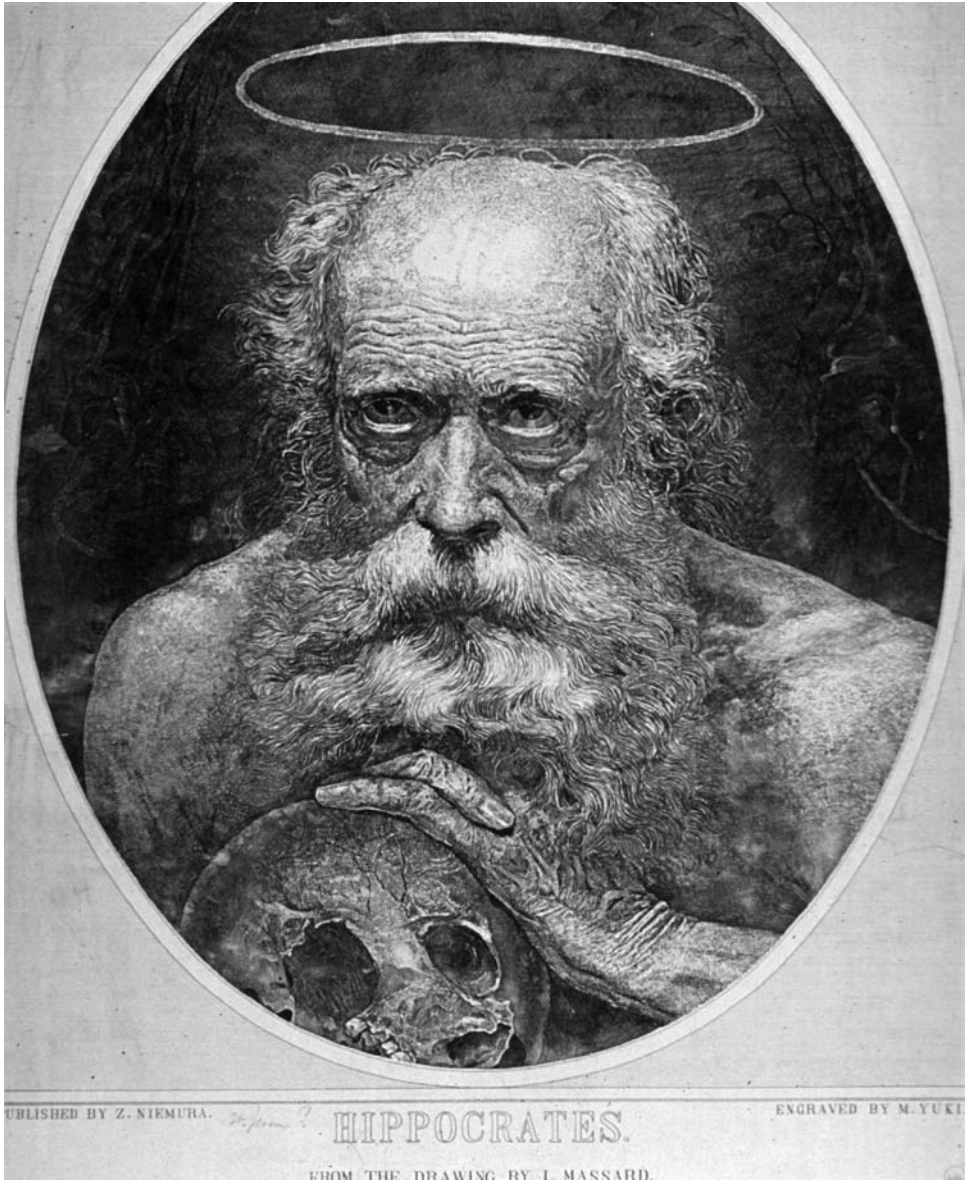
on and through a process that we do not fully understand, an iconic figure onto whom people throughout the ages have projected their own ideas of the best of medical knowledge, practice, and ethics. He has gained the status of the principal figure in the fifth-century rationalization of Greek medical theory and practice. Hippocratic medicine attributed disease to purely natural, rather than religious or magical, causes and sought natural preventive measures and therapies.

Hippocrates was born on Cos, a Greek island just off the present-day coast of Turkey. He was a member of the Asclepiadai (“Sons of Asclepius”), a clan that claimed descent from both Asclepius (the god of healing) and Heracles (Hercules). He seems to have been active as a physician and teacher primarily in northern Greece in the last half of the fifth and early fourth centuries BCE. His son Thessalus, a son-in-law Polybus, and grandson Hippocrates (physician to Alexander the Great [356–323 BCE]) also reportedly became famous physicians. However, specific traditions about Hippocrates’ life are mostly later fictions, and what he actually believed is disputed even by ancient authorities. Plato (*Phaedrus* 270c) says that Hippocrates thought it important to consider “the whole” (although what this means has been of debate since antiquity), whereas Aristotle (according to the Anonymus Londinensis papyrus, whose source appears to go back to Aristotle’s pupil Meno) and Galen present differing versions of Hippocrates’ core beliefs.

Similar uncertainty attends the “Hippocratic Question,” namely which—if any—of the works of the “Hippocratic” Corpus (a group of about 65 medical texts assembled in Alexandria in the third and second centuries BCE) Hippocrates actually wrote. These works cover many different subjects and come from a variety of sources and authors with differing medical beliefs. The seven books entitled *Epidemics* are not about **epidemics** in the modern sense of a widespread occurrence of a common disease, but contain individual case studies and generalized observations concerning patients and locations mostly in northern Greece. Among these, however, a plague at Thasos near Lemnos appears in *Epidemics* 3.3–4, and cases and observations concerning **malaria**, and possibly **influenza**, occur in *Epidemics* 1 and 2.

Hippocrates’ earliest extant association with epidemic plague (or *loimos* in Greek) comes from two works of the pseudepigrapha (texts written to appear to be something else, such as letters or speeches composed as if they were written by a famous person) found at the end of the corpus: the “Presbeutikos,” a fictitious oration composed between 350–250 BCE, and the “Decree,” a fictitious Athenian honorary decree composed shortly thereafter. They credit Hippocrates with diagnosing a plague in the late fifth century BCE and with saving Greece by circulating an effective therapy. In this early version, envoys from the Barbarian kings of Illyria and Paeonia (roughly modern Albania and Kosovo) arrive at Hippocrates’ residence in Thessaly (northern Greece) and promise him great riches if he comes to help them. Hippocrates questions the envoys and, once he has learned enough of the disease, pretends to be unable to travel and sends the envoys away. But he then composes a therapy, distributes it throughout Greece, and sends his sons and pupils to take it to various areas (it is unspecified, however, just what this therapy entailed). When he finally arrives in Athens, the Assembly honors him and his son Thessalus.

By the first century BCE, this episode had become widely associated with the famous Athenian plague of 428–427 BCE deemed incurable by the historian Thucydides (460–400 BCE; *The Peloponnesian War* 2.47–54). The Roman historian Varro (116–27 BCE; *On Rural Farming* 1.4.5) credits him with saving “many cities,” and Pliny the Elder (23–79 CE; *Nat-*



Hippocrates. Engraved by M. Yuki. From the drawing by L. Massard. Courtesy of the National Library of Medicine.

ural History 29) repeats the assertion, found in the “Presbeutikos” and “Decree,” that he was honored for this service. In these and some other versions of the story, such as those by Galen (“Theriac to Piso” 16), Plutarch (46–127; “Isis and Osiris” 383c) and Aetius Amidenus (6th century CE; *Tetrabibloi* 5.95), Hippocrates used a bonfire composed of various materials to dry and correct the imbalances in the **air** thought to cause plague according to the prevailing

theories of the time. This tale survived through the Renaissance in medical literature and art, and is featured on the cover of the famous 1588 Venice edition of the corpus.

Another famous story, found first in the pseudepigrapha (Letters 1–9) and in several later accounts (“Vita Hippocratis Secunda Soranum,” Suda, Johannes Tzetzes [1110–1180]), involves a request made to Cos by the Persian king Artaxerxes II (c. 436–358 BCE). With a plague ravaging his army, the king sends for Hippocrates, promising him riches and honors. Hippocrates, supported by Cos, refuses to aid an enemy of the Greeks. Although Greek writers (and others) saw this as an example of Hippocrates’ patriotism, courage, and character, the Roman Cato (95–46 BCE; Pliny, *Natural History* 29.13–14; Plutarch, “Cato” 23) may have had this story in mind when he criticized Greek doctors and warned his son that “they have sworn to kill all barbarians with medicine, and to charge a fee for it as well.” See also Avicenna (Ibn Sina); Environment, Ecology, and Epidemic Disease; Greco-Roman Medical Theory and Practice; Islamic Disease Theory and Medicine; Medical Education in the West, 1100–1500; Medical Education in the West, 1500–1900; Medical Ethics and Epidemic Disease.

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ERIC D. NELSON

HIPPOCRATIC CORPUS. See Hippocrates.

HISTORICAL EPIDEMIOLOGY. As one of the sciences of public health, **epidemiology** is concerned with the descriptions and explanations of the origins, etiologies, and **transmission** of diseases in populations. Historical epidemiology is the description, analysis, and explanation of patterns of epidemic diseases and their consequences in historical populations. A rather new field of study, historical epidemiology is interdisciplinary: it uses the traditional tools of social history, as well as the techniques of modern epidemiology, medical demography, medical geography, evolutionary biology, and genetics. Historical epidemiology can help researchers form a more complete understanding of the current trends in infectious, chronic, and reemergent diseases facing the world today.

The origins of the discipline of epidemiology help to explain the scope of historical epidemiology. Although the field has older roots, as a branch of medical science, epidemiology can be dated to the founding of the London Epidemiological Society in 1850. The founding members of this public health–minded group included William Budd (1811–80), Richard Bright (1789–1858), **John Snow**, and **William Farr**, the Statistical Superintendent at the Registrar General. From its inception, the aim of the society was, “to endeavor, by the light of modern science, to review all those causes which result in the manifestation and spread of epidemic diseases . . . to collect together facts, on which

scientific researches may be securely based.” Although epidemiologists and historical epidemiologists still investigate the major infectious diseases, the domain of the discipline has shifted to recent trends in the changing relationship between human hosts, disease pathogens, and the environment.

Historical epidemiology plays a vital role in public health and the history of disease. By analyzing changing disease patterns over time and the impacts of public health responses on the health of populations, historical epidemiology helps to develop a more complete picture of the long term impacts of modern medicine and public health policies. The most important focus has been the impact of social reforms, environmental interventions, technological changes, and advances in medical knowledge on the development of the modern world. The study of the history of public health has also been widely influenced by historical epidemiology. For example, decreases in mortality and morbidity have increasingly been related to triumphs of public health in the late nineteenth and early twentieth centuries, as well as to the modern transition to preventive medicine in western societies. In this way, historical epidemiology’s focus on changes in the health of populations can better delineate the impact of modern medicine on infectious and chronic diseases, changes in the environment, diet, and nutrition.

The Demographic Transition. Historical epidemiologists recognize that epidemics help define social relationships, cultural norms, and political practices. Thus, the study of changing demographic patterns has occupied a central role in this field of study. One of the most interesting questions that has vexed historical epidemiologists is the occurrence of what has been called the “demographic transition”—the transition from the high birth rates and death rates of preindustrial societies to the low birth rates and death rates of industrial and postindustrial societies. The outcome of this demographic change has been a dramatic and continuing increase in world population. The demographic transition has left many questions unanswered: what is the relationship between economic modernization and the demographic transition? How did rising living standards affect this change? What were the effects of technological, scientific, and curative or preventative medicine? These are the types of questions that historical epidemiologists have sought to answer.

Understanding the demographic transition has both important historical implications and current applications. By the early twentieth century, in most European and North American countries, the collective population had begun to experience health and disease on terms dramatically different from those of previous centuries. As many epidemic diseases such as cholera, typhoid, and scarlet fever entered a period of relative stagnation and ultimate decline, adults started to live longer, and infant and child mortality rates steadily declined. Historically human population had grown very slowly, but this pattern was disrupted in the last two centuries by exponential human population growth. In 2007 the world population exceeded 6.5 billion and is projected to continue to grow throughout this century. Historical epidemiologists have been at the center of answering the complex questions of why this transition occurred.

Of the many historical epidemiologists to examine the modern rise of populations, the Irish-born physician and professor of Social Medicine at the University of Birmingham, Thomas McKeown (1912–1988), is perhaps the most important. In a body of research developed from the 1950s to the 1980s, McKeown argued that the growth in modern populations from the eighteenth century was the result of broad improvements in overall standards of living, particularly improved diet and nutrition. Using historical data on

changes in death rates, McKeown noted that population growth was primarily affected by a decline in mortality from infectious disease. The basis for this decline, according to McKeown, was improved economic conditions that followed as a result of the Industrial Revolution. These changes led to rising standards of living that enhanced nutrition and strengthened human resistance to disease. Although the above formulation was the crux of his argument, McKeown also noted that other developments also contributed to the demographic transition, such as public health reforms, the enlargement of preventative and curative medicine, and the decline in virulence of infectious organisms. These last three factors were seen as minor contributors to the demographic transition particularly before the twentieth century.

The essential question that McKeown's research has raised is whether human agency, in the forms of medicine and public health or changes in economic growth, stimulated the rise of modern populations. The implications for this research are immense: should public health be directed at specific interventions or broader measures to reorganize the socioeconomic determinants of health? McKeown's stress on broad social and economic changes, as opposed to specific public health and medical interventions, has remained highly controversial and largely unresolved. Although his methodology has been called into question, the main complaint that has been generated against McKeown is the little weight given to medical science in contributing to the mortality decline before the twentieth century. Recent research has suggested that inoculation, vaccination, local public health efforts, and improvements in medical prevention perhaps played a much larger role in the mortality decline than has been suggested. An important instance is the experience of Britain. John Snow's epidemiological research on the mode and transmission of cholera in mid-nineteenth-century London, the growth of state medicine under the public health officer John Simon (1816–1904), and the numerous Parliamentary public health acts all facilitated the improvement of water supplies and methods of sewage disposal. By the beginning of the twentieth century, public health in Britain occupied a central role in British government and society, and directly influenced the control of epidemic disease.

Although a great deal of work in this field still remains, new epidemiological methods and disease ecology modeling are promising for the future. Although numerous scholars have since discredited McKeown's findings, his ideas have shaped the direction of subsequent research both in Western countries and in the developing world.

The Epidemiological Transition. Epidemic disease has played a key role in the demographic development of all societies. Throughout history, frequent mortality crises caused by epidemics of plague, cholera, typhoid fever, and smallpox have been the determining factor in demographic growth and decline. Related to the demographic transition, one of the other chief areas of focus for historical epidemiologists has been the "epidemiological transition," which can be defined as the general shift from acute infectious pandemics and deficiency diseases to chronic noncommunicable and degenerative diseases. Examination of this phenomenon lies at heart of the interests of historical epidemiologists: specifically, the interactions between disease patterns and their demographic, social, and economic consequences.

Historical epidemiologists have identified three stages of the epidemiological transition. The first is called "The Age of Pestilence and Famine." This stage describes most preindustrialized societies and is characterized by high mortality rates and low life expectancy, somewhere between 20 and 40 years. The major causes of death in this stage were epidemics, famines, and wars. A good example is the epidemiological work of the

seventeenth-century London statistician and pioneer epidemiologist John Graunt (1620–1674). By analyzing London's Bills of Mortality (lists of the numbers who died by cause of death printed weekly by the Company of Parish Clerks), Graunt demonstrated that nearly three-fourths of all deaths were attributed to infectious diseases, malnutrition, and maternity complications. Other more chronic conditions such as cancer were responsible for less than 6 percent.

"The Age of Receding Pandemics" is the second stage of the epidemiological transition. During this stage, mortality rates began to decline progressively in relation to the decreased frequency and virulence of epidemics. The average life expectancy increased to somewhere between 30 and 50 years. This stage characterized most western countries in the late nineteenth and early twentieth centuries. Better nutritional standards, increased economic prosperity, and more vital and sustained public health activities all contributed to the changes during this phase. Nonetheless, rapid **industrialization** and **urbanization** also took their toll in the forms of increased crowding, and air and water pollution. By the end of the nineteenth century, however, increased public health efforts in most Western countries led to improved sewer systems, drainage, and the provision of clean, filtered water. In countries of the developing world where public health reforms have been delayed, mortality rates remain high, particularly from waterborne and deficiency diseases.

"The Age of Degenerative and Human-Made Diseases" is the third stage, in which mortality rates stabilized at a fairly low level and the average life expectancy increased to beyond 50 years. Sustained economic improvements coupled with massive industrialization and urbanization during this stage led to an increase in chronic diseases. As behavioral changes such as increased caloric diet and lower daily caloric expenditure occurred and were accompanied by an increase in activities such as smoking, the kind of diseases experienced dramatically changed. Some researchers have recently added a fourth stage, in which major technological advances in medicine lead to a delay of death from chronic cardiovascular diseases and cancer.

The demographic transition and the epidemiological transition are subject to regional variation because of differing social, economic, demographic, and environmental forces. They occur at different times in different places. The factors that influence the changes broadly described by these transitions are complicated. They involve the ecological and biological determinants of mortality, namely the complex balance among disease agents, fluctuating levels of host resistance, and the ever-changing environment.

The historical relationship between demographic changes and patterns of disease is complex. It involves a dynamic, continuously changing process whereby some diseases disappear and others appear for the first time, reemerge, or mutate from existing species. Recent projects in the genome sequencing of both humans and diseases indicate that this process is not unidirectional. The emergence of new infectious diseases like AIDS is one prime example. Recent work in historical epidemiology has suggested the need for a change in the global approach to the emerging problems of changing patterns of disease. See also *Demographic Data Collection and Analysis, History of*; *Diagnosis of Historical Diseases; Epidemiology, History of*; *Paleopathology*.

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JACOB STEERE-WILLIAMS

HIV/AIDS. See Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS).

HOSPITALS AND MEDICAL EDUCATION IN BRITAIN AND THE UNITED STATES. According to European hospital historians, the role of hospitals in medical education seemed assured as early as the 1770s. Medical education, formerly conducted in medical school classrooms or on a one-to-one basis between master and apprentice, was literally brought into hospitals in the mid-eighteenth century. Links between the two institutions only grew stronger over the next hundred years. Although appearing both inseparable and essential to the education of medical practitioners, the combination of medical education and hospital instruction was not yet a reality on both sides of the Atlantic. Though clinical clerking had become a common experience, even a right, at many European medical schools, American schools, like their German counterparts, rarely provided such extensive hands-on ward instruction. Instruction continued to be provided by part-time teachers, whereas preclinical courses more quickly came under the influence of scientific ideas than did clinical training. As a result, by the late nineteenth century, the hospital school of medicine lost ground to the university as the favored site of medical instruction. Reformers tackled these and other disparities in the first decades of the twentieth century. By the end of the century, clinical instruction in a hospital setting was firmly embedded in the medical curriculum in both England and America.

Significant progress in clinical teaching had been made at American medical schools since the Civil War (1861–1865). The period devoted to clinical subjects had grown to two years, and section teaching had brought students into the hospital wards. As in the United Kingdom, specialization only increased in pace during this period, with the proliferation of both specialist hospitals and specialist clinics in general hospitals. However, teaching remained largely demonstrative. Few students learned practically by carrying out tasks in hospitals. Patients were cared for in the presence of students, but they were not cared for by students. Reformers aimed to rectify this through the introduction of clinical residencies (clerkships in Britain), requiring students to spend significant periods of the day addressing their patients' needs, rather than collectively walking the wards for an hour. According to William Osler (1849–1919), who was engaged in and understood both the North American and English systems of medical education, all other forms of clinical instruction were "bastard substitutes" for the residency. Though common practice at Johns Hopkins, where Osler had been based between 1889 and 1905, and moderately successful at other schools, such as Western Reserve University, Jefferson Medical

DURING THE FRENCH REVOLUTION, FRENCH MEDICAL EDUCATION REFORMER PHILIPPE PINEL ENCOURAGES “THE CLINICAL TRAINING OF DOCTORS” (1793)

Medicine must be taught in the hospitals—The healing art should only be taught in hospitals: this assertion needs no proof. Only in the hospital can one follow the evolution and progress of several illnesses at the same time and study variations of the same disease in a number of patients. This is the only way to understand the true history of diseases. In these shelters for suffering humanity, young students can analyze the influence of the seasons and of each year’s medical constitution. And only in a hospital can the physician be certain that patients receive the specific diet and medication he prescribes, and that nascent symptoms are carefully observed.

Need for an appropriate teaching hospital— . . . all modern medical schools have emphasized observation as a characteristic aspect of medicine when it is viewed as a major branch of the natural sciences. Leyden [The Netherlands], Edinburgh [Scotland], Vienna [Austria], Pavia [Italy], etc, have stressed the need of selecting a small number of patients for didactic purposes and grouping them on teaching wards. This offers the advantage of focusing the students’ attention on a small number of well-defined cases, without neglecting any aspect of cleanliness or health.

Project for a teaching hospital: Proposal by the Society of Medicine—At a time when education is being restored in France and public instruction organized, the Society of Medicine turns its attention to a matter of supreme importance, the creation of teaching hospitals. Only clinical teaching can spread knowledge of the healing art in a uniform manner and restore the rigorous, oft-neglected principles of observation. All other public teaching of medicine by the lecture method is pointless and unproductive.

From *The Clinical Training of Doctors: An Essay of 1793*, edited and translated by Dora P. Weiner (Baltimore: Johns Hopkins University Press, 1980).

College, and the universities of Pennsylvania and Michigan, the practice of residency was struggling for survival when Abraham Flexner’s (1866–1959) report on medical education appeared in 1910. As a result, the famed survey of 155 North American medical schools indicted clinical teaching more severely than all other branches of American medical education. Even where residencies existed, usually only a fraction of medical students could be accommodated by limited ward places. Most attended outpatient clinics where opportunities for observing acute patients were limited. Equally limited were possibilities of following the daily course of diseases and therapies. Further progress required providing students direct participation in the management of patients.

Residency continued to struggle until American medical schools attained some control over affiliated teaching hospitals. Although most schools were associated with such clinical facilities, they often had very little control over hospitals. Johns Hopkins was one of few schools that exercised control over its teaching hospital, a point recognized by Flexner. Though bedside instruction in hospitals has been traced to fifteenth-century Europe, many hospital governors continued to tolerate teaching in the wards as long as it was strictly regulated and did not interfere with daily hospital activities. Unlike in London, where hospitals gradually developed their own schools during the eighteenth and nineteenth centuries, American medical schools and hospitals developed separately from

one another. By the late-nineteenth century, it had become clear that hospitals in the United States would have to become more closely associated with medical schools, especially during the clinical years of training. For many schools, the answer lay in building their own hospitals.

Although the English system allowed for the appointment of clerks and dressers in the wards, as became common at St Bartholomew's for example in 1865, the need for further progress in clinical education was recognized. The Haldane Commission, the British equivalent of the Flexner report, highlighted the key deficiencies in the British context. Established in 1909 and published in 1912, the Commission found fault with clinical medicine carried out by physicians and surgeons whose main interest lay in private practice. Given the length of the inquiry, by the time of its publication, the commissioners had become greatly influenced by Flexner's report. Equally influential was William Osler, Regius Professor of Medicine at Oxford from 1905 to 1919, who called for a full-scale invasion of hospitals by the universities. In their report, the Commissioners advised the establishment of professorial units in clinical medicine and surgery. Quoting Osler, the report suggested that only such units would allow a professor to carry out the three-fold duty of curing the sick, studying the problems of disease, and giving students a university education in the science of their profession. The advent of the British University Grants Committee after the First World War transformed some of these ideas into reality. Academic units with professors at the head became the general rule for the preclinical subjects, and some teaching hospitals experimented with full-time professorial units in medicine and surgery. Nevertheless, the bulk of clinical teaching remained, as it does today, in the hands of part-time visiting staff, and only 13 full-time clinical chairs were established in Britain's medical schools before World War II. As a result, experimental science was more often encountered in laboratories than in hospital wards, where staff employed traditional methods of observation and undertook little clinical research.

Rectification of the key deficiency in American medical education involved building hospitals and would cost schools considerably more than professorial units. Washington University contemplated building a teaching hospital in 1903, until it was estimated that it would cost \$1 million. Yale abandoned plans to build a hospital in 1910 when its projected cost reached \$3 million. Even a well-endowed university like Harvard abandoned plans to build a teaching hospital years earlier on the grounds of cost. Instead, many schools decided to form links with existing community hospitals. Before 1910 only Western Reserve University and Dartmouth College managed such affiliations. Other hospital boards, though managing vast clinical resources, permitted only demonstrative teaching. Most resisted the efforts of medical school staff to improve clinical teaching before 1910.

In the next decade, however, these difficulties were largely overcome. Most American medical schools managed to improve relationships with nearby voluntary hospitals. In 1910 alone, three significant unions occurred. These involved Columbia and Presbyterian Hospital in New York, Harvard Medical School and Peter Bent Brigham Hospital in Boston, and Washington University Medical School and Barnes Hospital and St Louis Children's Hospital in St Louis. In some instances, teaching hospitals had to be constructed at the taxpayers' expense. In each case, Johns Hopkins remained the model of best practice. In the case of Washington University Medical School, Flexner's report was particularly influential in provoking cooperation, though not at other institutions, where overlapping boards of trustees facilitated union.

Formerly hostile to clinical residencies, most American hospital trustees had become convinced that their institutions would benefit from association with a medical school. Besides better patient care, close association promised state-of-the-art care, including laboratories and the latest medical equipment, and enhanced their potential research output. The division of labor was also mutually advantageous. Like business corporations, unions between medical institutions promised to make medical schools and hospitals more efficient administrative units. Failure to acquire a teaching hospital, on the other hand, often resulted in the closure of a school. The difficulties facing rural schools were occasionally insurmountable. As a result, medical education became ever more urban as great numbers of rural schools disappeared. By 1921 every surviving American medical school had affiliated with a hospital that it either controlled or owned. In 1926 the American Medical Colleges announced that residencies had been introduced at all medical schools. With student numbers in decline during this period, schools found it easier to offer pupils residencies. Though a uniform system of residency remained to be created at the 76 medical schools in existence in 1930, subsequent changes were of degree, not kind.

Though the modern system of medical education in the United States had emerged by the 1920s, the relationship between medical schools and hospitals in the United Kingdom continued to be debated in the 1940s with the introduction of a National Health Service. The fullest expression of these discussions is in the report of the Special Commission on Medical Education, known as the Goodenough Report (1944), which was charged with a review of medical schools in the knowledge of impending government health legislation. Among other things, the committee found that accommodation for teaching and research fell below ordinary requirements at most teaching hospitals. Among its many recommendations was that students no longer be taught simply about sick people in hospital beds, but of the social and industrial causes of ill health. As a result, in contrast to American schools where education became ever more standardized, English medical schools began to offer an increasing number of electives. Recognizing the additional reality of specialization, the Goodenough Report also proposed a comprehensive system of postgraduate education, rather than leaving qualified practitioners to self-educate. Based less on examinations and professional associations than in the American case, this involved the establishment of a national system of specialized postgraduate institutes, organized around specialist hospitals. The four Scottish medical schools set up a joint body to organize postgraduate training, which in England was organized regionally. The British Postgraduate Medical Federation of the University of London was established in 1945 and integrated more than a dozen hospital-affiliated specialist units in the capital, including the British Postgraduate Hospital and Medical School at Hammersmith, which was established in 1935.

With the introduction of a National Health Service (NHS), the institutions of medical education in England were significantly reorganized. Instead of being under one of the fourteen regional hospital boards under the jurisdiction of the Ministry of Health, English teaching hospitals were placed under independent boards of governors responsible to the Ministry of Health from whom they were financed. Medical school, staff, and university were all represented on these boards. Rather than being handed to the universities, medical schools were also put under independent boards of governors responsible to the university from which they received their funding but on which the governing board of its teaching hospital was represented. In this way, each school was ensured some control

in the selection of staff and hospital policy, and each teaching hospital was guaranteed a voice in the election of staff and in control of the school's policies. The hospital provided the school with the necessary facilities for the business of medical instruction in return for the numerous services rendered by the high-powered scientific departments that the schools now maintained, subsidized by the university. The autonomy of teaching hospitals was removed in 1974 when the boards of governors were abolished and the hospitals placed under new Area Health Authorities. In the 1990s, trust status promised British teaching hospitals a return to the independence they lost in 1974.

Besides organizational issues, the advent of the National Health Service has had an impact on medical education and has accelerated changes in clinical teaching methods. Given the slow rate of hospital construction since the introduction of the NHS, facilities for clinical instruction began to fall short of the recommended bed numbers. Though the Goodenough Committee suggested 1,000 beds for each annual intake of 100 first-year, clinical students, the Ministry of Health limited hospitals to 800 beds for several years. As a result, students had to travel more extensively in the post-war period in order to obtain sufficient clinical experience, especially in obstetrics. Changes in the distribution of the population have further prevented teaching hospitals from offering the clinical work necessary for the education of students, whose numbers have only increased. Selective and controlled admission to suit teaching interests remains unrealistic. This has encouraged additional training in nonhospital environments, but reform has been limited. More often students enter nonteaching hospitals to escape the artificial atmosphere of a teaching hospital. In the 1960s, teaching hospitals more regularly appointed full-time staff in general medicine, surgery, and obstetrics, and not only in pathology, radiology, and anesthesiology. Funds for medical research more often came from private foundations than from research councils, and they increased exponentially in this decade.

Like the NHS, medical schools in the second half of the twentieth century grew dramatically in size and bureaucracy. English schools were also unusually concentrated in London. In 1965 there were 12 schools within five miles of Charing Cross, leading the Todd Report (1968) to suggest that schools be combined. Cuts in funding in the 1980s encouraged further mergers, and new provincial schools were created. In both the U.K. and U.S. contexts, the close union of medical schools and teaching hospitals brought science and medicine closer together, though students in Britain's two dozen medical schools often remained less aware of research undertaken in clinical departments. Many more had become aware of the fact that medical facilities of British universities were lagging far behind those in America. Instead of American medical students traveling to Europe to receive the best training, after World War I many more Europeans were choosing to attend North American medical schools. In Britain, the decline in medical facilities at universities was emphasized in the Porritt report (1963). Although much clinical research is still funded by notable individual benefactors, hospital policy now tends to be determined by medical boards, whose decisions trustees generally follow. The traditional conflicts between hospitals and medical schools continue to exist, but the reputations of both rely on affiliation. The tensions between education and patient needs have also been resolved in favor of education, which the public generally accepts. The patient, on the other hand, is no longer simply central to hospitals' teaching functions. With federal educational subsidies in decline since the 1980s, American teaching hospitals more often resort to aggressive marketing in order to attract patient revenue. Consequently, the language of clinical instruction in the teaching hospitals of the nation's 125 medical schools

more often signals the triumph of marketplace rhetoric and values than of prevention and the relief of suffering. Whereas the number of cases treated in hospitals only increases, the average length of stay has fallen, once again making it difficult for students to see patients. These changes encourage further rethinking of clinical education and generate additional critiques of hospital-based learning. *See also* Hospitals in the West to 1900; Hospitals since 1900; Medical Education in the West, 1500–1900; Medical Ethics and Epidemic Disease; Nurses and Nursing; Public Health Agencies in Britain since 1800; Public Health Agencies, U.S. Federal.

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JONATHAN REINARZ

HOSPITALS IN THE WEST TO 1900. The earliest known hospitals were examples of Christian charity. They were not exclusively meant to heal the sick but also to house the poor; they were “guesthouses” rather than hospitals in a modern sense, an idea that is expressed in the Latin term *hospitium*. Travelers, pilgrims, the disabled and injured, the infirm elderly, and those such as poor widows who lacked resources found shelter and sustenance. Over time the hospital evolved first into the social institution dedicated to the care of the chronically ill, and then into a more multipurpose care-providing facility.

Ecclesiastical authorities created shelters to house the needy and the sick in response to famine, **war**, and **epidemics**. Because of this close link with Christianity, prayer, religious rituals, and reflection were important therapies alongside rest, nutrition, and medication. The earliest such shelters were established in Byzantium (Constantinople) between the fourth and sixth centuries; the Gallo-Roman *hôtels-dieu* of the same period also fall in this category.

Non-Christian roots of the hospital include ancient Greek temples to the god of healing, Asclepius, which also served as healing places. In the Roman Empire, *valetudinaria* were shelters for injured or exhausted slaves. Islamic societies created “places for the sick,” the **bimaristan**; one of the earliest of which was established in Damascus, Syria, in 707.

Paralleling the development of hospitals were **leprosaria**, where chronic sufferers of **Hansen's Disease** and related maladies found shelter and care and isolation from the stigmatization of wider society. With the Black Death and subsequent plagues from the fourteenth through eighteenth centuries, many leprosaria and hospitals were transformed into short-term pest houses where victims of plague either recovered or died. Larger

hospitals set aside special wings or wards for infectious disease cases or appended outbuildings during local epidemics. In the sixteenth and seventeenth centuries, new or previously rare infectious diseases emerged: syphilis, influenza, typhus, and smallpox, among others. Hospitals wrestled with their obligations to their communities: the elderly and chronically ill who resided in most hospitals were threatened by the acutely diseased, though the mechanisms of disease transmission were but dimly understood. With the Renaissance in the sixteenth century and the **Scientific Revolution** in the seventeenth, hospitals became more closely related to medical education and primitive research. The ideas of philosophers of the Enlightenment made rulers and their medical doctors realize that healing could not exclusively be achieved on the basis of speculations. Hence, by the early nineteenth century, a new concept of the (poor) citizen-patient with a right to hospital care was emerging. The patient became an object of medical observation, **diagnosis**, and treatment. This new “rational” medicine was based on an empirical method that combined observation of the sick with systematic examinations of the deceased.

Large hospitals were an excellent place to put these ideas into practice. They acquired importance as clinical research centers, as they provided medical doctors and students with numerous cases of diseases to study, such as **tuberculosis**. In the United Kingdom, a hospital system had emerged in the eighteenth century that extended throughout the country. The Royal Infirmary in Edinburgh was established in the 1720s and became one of the foremost institutions for medical instruction in Europe. In France hospitals were reformed after 1789, in the course of the French Revolution. The General Hospital (*Allgemeines Krankenhaus*) in Vienna was a 2,000-bed facility inspired by Paris’s late eighteenth-century *hôtel-dieu*.

Yet unexplained in the period before the advent of **germ theory**, these large hospitals were feared by patients for their high mortality rates. These were often the result of inadequate hygienic and sanitary conditions—for example, in connection with autopsies and subsequent patient examinations that contributed to spreading of infectious diseases, a connection that was not yet understood.

In the nineteenth century medical innovations occurred in a transatlantic setting. For example, in the early 1800s medical students from all over Europe and America flocked to the huge hospitals in Paris and Vienna, whereas those of the late nineteenth century turned to Germany. Americans also contributed to the changing outlook of the hospital.

Moreover, **nursing** emerged as a skilled profession particularly for women, a development in which the British nurse Florence Nightingale (1820–1910) played a leading role. In contrast, in 1687 Elizabeth Cellier (d. c. 1688) had unsuccessfully petitioned English King James II (r. 1685–1688) for a College of Midwives. The professional nurse became a feature of the modern nineteenth-century hospital.

Hospitals were the sites of numerous new inventions that would ultimately serve the goal of diagnosing and fighting infectious diseases. In 1816 the French **physician** René Théophile Hyacinthe Laënnec (1781–1826) developed the stethoscope; a great help in diagnosing pulmonary complaints such as tuberculosis. In 1846 ether was first successfully used as anesthesia during surgeries in the Massachusetts General Hospital in Boston. The news soon spread to England. With the elimination of pain, longer surgeries on, for example, infected internal organs became possible.

Also in the 1840s the relationship between the performance of autopsies and high mortality rates in hospitals was discovered: when doctors and medical students proceeded from the dissection table to examining patients, they failed to scrub all “death matter” off

their hands. This endangered, among others, women who had just given birth. Puerperal fever was known as early as in ancient Greece, yet starting in the eighteenth century it became a major problem in maternity hospitals. In a way, the creation of big hospitals thus highlighted problems in transmitting infectious diseases that could subsequently be solved. Physicians Oliver Wendell Holmes Sr. (1809–1894) in New England and **Ignaz Semmelweis** in Vienna both understood the connection between childbed fever and autopsies; yet they were little successful in effecting changes.

Only with the birth of bacteriology did practices begin to change. In 1867 the British surgeon Joseph Lister (1827–1912) published his observations with regard to the antiseptic method. Lister had been inspired by **Louis Pasteur's** findings on fermentation. He concluded that microorganisms might be responsible for surgical infections and began using carbolic acid to disinfect wounds. Nonetheless, two or three patients occasionally shared a bed even in his day—a practice that disregarded the potential dangers of possible infections spreading among those convalescing from surgery. Ironically, at about the same time, physicians realized that it was most important to prevent germs from entering a surgical site. This could be achieved through the aseptic method, such as the sterilization of instruments with heat. Pasteur's English collaborator Charles Chamberland (1851–1908) developed this method. Hence, even though many revolutionary discoveries were made in the second half of the nineteenth century, implications for preventing the spread of contagious diseases were not always immediately recognized.

The late nineteenth century witnessed the establishment of new hospitals with research laboratories in addition to facilities for patient care, such as at the medical school of the Johns Hopkins University in Baltimore, Maryland, which was launched in 1889 and which, in the 1890s, first introduced rubber gloves as a means to increase hygiene. Further discoveries changed the routine at hospitals: German physicist Wilhelm Konrad Röntgen's (1845–1923) work on X-rays (1895) became an important means for diagnosis of diseases like tuberculosis. On the basis of the findings of Pasteur and **Robert Koch**, the 1880s marked the beginning of immunization as we know it today, to which **Emil Adolf von Behring** contributed when he developed an antitoxin for **diphtheria** in the 1890s. Hospitals could provide cures and therapies that could rehabilitate, and they were slowly losing their stigmata as warehouses for the poor and terminally ill.

With the prevention of the spread of infectious diseases and the advent of widespread **vaccination**, hospitals in the future would no longer serve primarily to receive hundreds of victims during the outbreak of an infectious disease, such as the **cholera** epidemic in Hamburg as late as in 1892. An awareness of germ theory and subsequent development of treatments, as well as improvement of living and hospital conditions, marked the beginning of a new area in the history of hospitals on the eve of the twentieth century. *See also* Disinfection and Fumigation; Hospitals since 1900; Medical Education in the West, 1500–1900.

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ANJA BECKER

HOSPITALS SINCE 1900. Over the past hundred years or so, hospitals have evolved from providing care (often long term) for the indigent patient with chronic infectious disease and the infirm elderly. With America in the forefront, hospitals have concentrated health-care functions and services as the medical profession has become increasingly specialized and reliant on technology. The revolution in prophylaxis and treatment of traditional epidemic diseases, with vaccines and antibiotics for example, has meant that hospitals in developed countries have acquired a new clientele. In developing countries, however, hospitals treat a wide range of complex conditions that often combine one or more infectious diseases with complications stemming from such factors as malnutrition, birth defects, and violence.

Western Hospitals. The current structure and function of hospitals are those of either a modern high-tech palace that focuses on short-term high intensity intervention, or a hospital for specialized care or long-term care of chronic conditions. Hospitals can be categorized by size (number of beds), teaching (university affiliated) versus nonteaching functions, privately owned versus government-owned status, general care versus specialized care (hospice, psychiatric care) provision, or length of care (acute care, long-term care) provision. Private hospitals can be either for-profit or nonprofit. Nonprofit hospitals are often associated with religious institutions. In the United States, most psychiatric hospitals are owned and operated by the state, whereas the federal government owns and operates military and veterans hospitals. Most **tuberculosis** (TB) hospitals were state-operated. In developed countries other than the United States and Canada, the government owns and controls the majority of hospitals. Most hospitals in the United States have up to 800 beds, those in Sweden up to 1,000 beds, and those in Russia up to 1,250 beds.

In the early 1900s, TB, pneumonia, bronchitis, **diphtheria**, and enteritis were major causes of death. For the first half of the twentieth century, infectious diseases were the most common cause for hospital admissions. TB hospitals (**sanatoriums**), in use up to 1960, often hosted patients for two years or more. Some hospitals had whole wards for treating **typhoid fever**, **smallpox**, or scarlet fever. In the early 1900s, **syphilis** was also common, until an effective treatment was discovered in 1909. General hospitals played a major role in patient care. For example, in 1943, general hospitals admitted

over 90 percent of all U.S. patients, even though they had only 40 percent of the total number of hospital beds.

Group hospitalization insurance was introduced by Baylor University Hospital in the United States in 1929 and was soon widely adopted. Prior to health insurance, patients paid for their care with their own resources or worked for the hospital after they recovered from their illness. Insurance induces demand for health care services, since the payer is a third party. As a result, hospital utilization grew. In 1945 about 30 million people in the United States had hospital insurance, and their rate of hospitalization was 50 percent higher than that of the population as a whole. The average cost per day per patient in 1910 was less than \$2, whereas in 2006 it was between \$900 and \$1800 depending on the level of care provided.

The Hill-Burton Hospital Construction Act of 1946 provided federal funds to build new hospitals, expand existing hospitals, and add new technology to hospitals. Medicare and Medicaid programs began in the 1960s. The number of hospital beds in the United States peaked in the 1960s, a time that was considered the golden era for hospitals. Between 1946 and 1976, as a result of specialization and technology, hospitals were at the center of American health care.

In 1973 the U.S. Congress passed the Health Maintenance Organization (HMO) Act to help finance the development of HMOs, and thus to control costs. In 1983 Congress introduced the diagnosis-related group (DRG) as a means to cut Medicare spending. This greatly reduced reimbursement payments of Medicare part A, the hospitalization portion of Medicare. In the 1990s, there were many hospital mergers and conversions of nonprofit to for-profit status. Many hospitals closed during this time. Also in the 1980s and 1990s, malpractice concerns forced many **physicians** to use more (often unnecessary) laboratory tests in practicing defensive medicine. Worldwide, beginning in the 1980s, health-care administrators focused on cutting costs, improving efficiency, and preventing the occurrence and spread of disease. In the United States, the average number of days (length of stay) for patients in the acute care hospital went from about 21 in 1910, to 9 in 1960, to 6 in 1994.

In most hospitals, nursing is the largest department, followed by dietary services, and then housekeeping. Other departments include laundry, medical records, pharmacy, laboratory, social services, respiratory therapy, patient education, and nutrition counseling. Identification and treatment of infectious agents, improved sanitation, infection control, and improved nutritional status of the patients all help to decrease the incidence and spread of infectious disease.

Hospitals and Epidemic Disease. Epidemic **typhus** was a major problem in World War I (1914–1918) and in World War II (1939–1945). **Measles**, mumps, and **meningitis** were also common in WWI, but overall improved hospital sanitation significantly reduced deaths from infectious disease. After WWI, the **Spanish influenza pandemic** (1918–1920) hit and killed more people than the war itself. During the pandemic, temporary hospitals were established to meet the sudden increase in need. One such hospital was the Emergency Influenza Hospital in Kirksville, Missouri, which was the Theta Psi Fraternity House at Southeast Missouri State College before being converted to the temporary hospital. Worldwide, nearly 20 million people died from this catastrophic pandemic. In 1957 the Asian flu pandemic hit many areas of the world, and a second wave occurred in early 1958. In 1968 the Hong Kong flu pandemic occurred, returning in 1970 and 1972. Regional epidemics of the flu occurred in 1976 with the swine flu, in 1977 with the Russian

flu, and in 1997 and 2003 with the avian flu. Since 2000 influenza has resulted in about 226,000 annual U.S. hospitalizations. Since the 1990s, multiple-drug-resistant TB has been spreading rapidly. In 1993 the **World Health Organization** (WHO) declared war on TB and initiated programs for TB identification, treatment, and control. Accordingly, hospitals are required to have isolation policies and procedures in place to deal with TB.

A major challenge facing hospitals in the later decades of the twentieth century is infections that are acquired in the hospital. In the United States, according to the **Centers for Disease Control and Prevention** (CDC), there are about 1.7 million cases and 99,000 deaths each year as a result of infectious diseases acquired while in the hospital.

About 32 percent of these infections are urinary tract infections (UTI), 22 percent are infections of surgical sites, 15 percent are pneumonias, and about 14 percent are blood-stream infections. Whereas the number of admissions, the average length of stay, the number of inpatient surgical procedures, and the total number of hospital-acquired infections have all decreased, the incidence of hospital-acquired infections in the United States has increased over recent decades.

In 1983 the CDC advised all health-care workers to use universal precautions to help decrease the spread of infectious disease and in 2007 recommended hospital infection-control report cards. Process measures such as timely administration of perioperative **antibiotic** prophylaxis, insertion practices of vascular catheters, and hand hygiene practices could be measured. Outcome practices such as intensive care unit infection rates associated with central vascular catheters and complications as a result of surgical-site infections could be measured and reported.

Hospital Quality. Technology dominates many hospitals today. Health-care consumerism in the community, a focus on costs from the health-care administration, and a lack of personal attention to patients are current challenges facing many hospitals. But issues of quality are far from new. Richard C. Cabot (1868–1939), the “father of medical social work,” wrote *Diagnostic Pitfalls Identified during a Study of Three Thousand Autopsies* in 1912, and five years later hospital reformer Ernest A. Codman (1869–1940) published *A Study in Hospital Efficiency*. These two men helped initiate quality control in hospitals by bringing to the attention of hospital trustees and medical professionals the identification and measurement of hospital treatment outcomes. In this vein, in 1918, the American College of Surgeons started a survey program to establish hospital standards. Also in the early 1900s, American registrars started using the International List of Causes of Death, which had been designed by the French statistician Jacques Bertillon (1851–1922).

U.S. hospitals are rated according to Avedis Donabedian’s (1919–2000) three-element model of health-care quality: structure, process, and outcome. Since 1990, *U.S. News & World Report* has annually published the list of “America’s Best Hospitals.” HealthGrades is a different, relatively new, grading system for U.S. hospitals. As a result of cost-containment strategies, health-care systems in developed countries seem to be moving toward increased delivery of services via clinics and other outpatient care settings. Because the greatest proportion of health-care spending is on hospital costs, the shifts in hospital marketing and management are geared toward cost reductions. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) and the Institute for Healthcare Improvement (IHI) support quality improvement by enhancing organizational learning, sharing lessons learned, benchmarking, and using the continuous quality improvement process to improve hospital quality.

Hospitals in Developing Countries. During the twentieth century, hospitals played a major role in the globalization of Western medicine. Charitable, mission-based hospitals in particular have introduced Western medicine and provided training to populations in developing colonial and postcolonial countries. Health care in these regions is predominantly curative rather than preventive, and centralized hospitals are usually in competition with primary care clinics for scarce health-care resources. From the 1970s the **World Health Organization** (WHO) has advocated a decentralized system focused on primary care in zonal and regional facilities. Urban political elites, however, tend to support the larger centralized systems. When reliant on local personnel, clinics tend to have minimally educated and prepared caregivers because those with options easily find work in larger cities or abroad. Yet even larger urban health centers have problems with sexism, low morale, and lack of adequate training, funding, supplies, and the confidence of the community. African traditional medicine, for example, still has sway among large segments of the population, and one of the challenges is to blend it with Western medical approaches to healing.

Care for children and responses to epidemic diseases such as polio, tuberculosis, plague, yaws, and cholera, as well as more recent pestilences such as HIV/AIDS and Ebola are serious issues for African hospitals. Initiatives tend to be reactive rather than pro-active, with few (but increasing) resources devoted to health education, public health initiatives, and preventive medicine. In 2000 and 2005, WHO published clinical guidelines for pediatric (children's) health care in areas and facilities with limited resources. Follow-up reports and studies from Asian, African, and Oceanic countries have shown that hospitals in developing countries have shown clear decreases in case fatality rates when guidelines like these are applied, along with greater attention to personnel training and resource management. See also Contagion and Transmission; Diagnosis and Diagnostic Tools; Drug Resistance in Microorganisms; Hospitals and Medical Education in Britain and the

EBOLA EMERGES ON WESTERN MEDICINE'S FRONTIER, 1976

The hospital conditions in Abumombazi were not as deplorable as in other parts of the country. A prominent Zairian general came from the region. He had the clout to attract a white doctor to the village, and there, with Belgian nuns, [Danish physician] Grethe [Rask] worked with what she could beg and borrow. This was central Africa, after all, and even a favored clinic would never have such basics as sterile rubber gloves or disposable needles. You just used needles again and again until they wore out; once gloves had worn through, you risked dipping your hands in your patient's blood because that was what needed to be done. The lack of rudimentary supplies meant that a surgeon's work had risks that doctors in the developed world could not imagine, particularly because the undeveloped part, specifically Central Africa, seemed to sire new diseases with nightmarish regularity. Earlier that year, not far from Abumombazi, in a village along the Ebola River on the Zaire-Sudan border, a virulent outbreak of a horrifying new disease had demonstrated the dangers of primitive medicine and new viruses. A trader from the village of Enzara, suffering from fevers and profuse, uncontrollable bleeding, had come to the teaching hospital for nurses in Maridi. The man had apparently picked up the disease sexually. Within days, however, 40 percent of the nurses in Maridi were stricken with the fever, transmitted by contact with the patient's infected blood either through standard care procedures or through accidental needle sticks.

Frightened African health officials swallowed their pride and called the World Health Organization, who came with a staff from the American Centers for Disease Control. By the time the young American doctors arrived, 39 nurses and two doctors were dead.

From Randy Schilt's *And the Band Played On: Politics, People, and the AIDS Epidemic* (New York: Stonewall Inn Editions, 2000) p. 4.

United States; Hospitals in the West to 1900; Nurses and Nursing; Pharmaceutical Industry; Sanatorium.

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MARK A. BEST

HUMAN BODY. This section will present the major systems of the body in a way that links the names of each individual part (or the anatomy of the system) to the way that they work together (or the physiology of the system). It is important to understand these details in order to appreciate how and why they can become diseased (the pathology of the system).

The Integumentary System. The largest organ in the body, the skin forms a protective layer between the body and the harsh world around it. One way it does this is by regulating the body's fluids and temperature. If hot, the skin has pores that open to release sweat and cool off the body as the sweat evaporates; if cold, blood vessels in the skin constrict, thereby diverting blood to the core of the body where it is most needed. In addition to sweat glands, oil glands next to the hair roots keep the skin supple and the hair lubricated. Different types of nerve receptors in the skin offer perhaps the greatest protection to the body: the abilities to touch, sense temperature, and feel pain. The skin has two different layers: the epidermis is the outermost section of skin made of piled up layers of cells, and the dermis, made up of thicker fibrous material, lies beneath it.

Unlike armadillos, which have a hard shell of skin protecting them, humans are incredibly soft and vulnerable to trauma. Because the skin barrier is so easy to breach, many serious infections can enter the body via this route. A simple cut, for example, can allow **bacteria** to enter and cause infections, such as a *cellulitis* (a superficial infection of the skin) or an abscess (a deeper, walled-off infection). **Insects** that bite the skin can introduce into the blood parasites that cause serious diseases such as **malaria** or Lyme disease. On the other hand, the so-called viral exanthems, diseases such as **measles** and rubeola, are caused by **viruses** that infect the entire body but make themselves present with a rash or "eruption" on the skin.

The Respiratory System. The lung can be thought of as a giant balloon that inflates and deflates more than 20,000 times a day. Unlike a hollow party toy, however, it is made up of millions of microscopic balloons called alveoli. These alveoli are like spring buds at the end of the branches of the respiratory tree, which starts at the trachea (windpipe) and branches out in the lungs into ever smaller bronchi, and then into bronchioles. Inhaled air is composed of a number of gases, but most importantly oxygen (O₂), which is the elixir that the body's cells need to burn energy, and carbon dioxide (CO₂), which is one of the by-

products created by the body in return. The alveoli absorb O_2 and expel CO_2 from the bloodstream through a net of thin-walled blood vessels that surround them, called capillaries. This exchange maintains the acid-base balance, or metabolic equilibrium, of all the body's processes. The proper passage of air through the lungs, and the effective transfer of gases, is therefore absolutely essential to life.

If the lungs become diseased, however, the essential process of gas exchange could be jeopardized. If the alveoli fill up with infection or fluid, such as with pneumonia or **Severe Acute Respiratory Syndrome** infection, oxygen cannot be absorbed, and carbon dioxide cannot be exhaled, putting the body at risk of complete respiratory failure. In **tuberculosis**, the lung architecture can be so severely damaged that those who survive the disease are sometimes left with considerably less lung function.

The Circulatory System. The main function of the heart is to squeeze bright red blood full of O_2 to different parts of the body. Blood makes this journey through different types of tubes that vary in composition and caliber. Starting from the most powerful chamber of the heart, the left ventricle, blood leaves through the largest artery in the body, the aorta. It then flows through smaller arteries, and then into even smaller arterioles. All these arterial blood vessels are relatively muscular and can contract or relax, depending on factors such as the blood pressure and temperature of the body. Following the arterioles, a network of capillaries penetrate deep into the tissues and organs of the body and allow for the easy transfer of O_2 as well as CO_2 and other toxins. Dark blue blood, full of these metabolic by-products, then travels back to the heart in the thin walled veins and venules of the venous system. From here, the blood collects in the right atrium, passes into the right ventricle, and is ejected into the lungs. Another vascular system in the lungs delivers blood to the single-cell-walled capillaries that line the alveoli so that effective gas exchange can once again occur. Upon leaving the lungs, the blood will collect in the *left* atria before entering into the left ventricle to begin the journey anew. Between the atria and the ventricles, and between the ventricles and the large arteries that take blood away from the heart to either the body or the lungs, there are four leathery valves that contain the blood in the proper heart chamber before it moves on. It is their opening and closing that produces the *lub-dub* sound of the heart beating. The heart beats because its rhythmic contractions are controlled by an electrical system that periodically produces a signal that travels from the sinus node in the right atrium down to the ventricles.

The Lymphatic System. Any fluid that squeezes out from the blood vessels is brought back to the venous circulation through a separate series of thin-walled conduits called the lymphatic system. This system is also important in the immune function of the body. It is composed of the lymph glands, which serve as docking stations for activated white blood cells; the thymus and tonsils, which also work with the immune system's white blood cells; and the spleen, which filters and purifies the blood. Each patch of lymph nodes has its own name, depending on where it is located and what area of the body it drains.

Swollen lymph nodes and an enlarged spleen usually suggest that the body is fighting off an infection. If most of the nodes that one finds are swollen and the spleen is enlarged, then the infection is likely a total body infection, such as **Human Immunodeficiency Virus** or mononucleosis. If only a small patch of lymph nodes are swollen, such as those under the neck, under the arm, or in the groin, a localized infection can usually be found by tracking back to where these lymphatic channels drain. In **bubonic plague**, the presence

of a large lymph node exuding pus, called a bubo, suggests that a flea carrying plague bacteria has bitten the skin that is drained by that lymph node.

The Hematologic and Immunologic Systems. Flowing through the arteries, veins, and capillaries of the body, the blood is full of specialized cells that perform different functions: red cells transport oxygen, white cells fight off infections, and platelets clog up ruptures that cause bleeding. All these are created deep within a latticework of dividing cells inside the bones, called the bone marrow. Many pathogens live or travel inside the bloodstream, and some parasites such as malaria's actually live inside the red blood cells. The importance of white blood cells in preventing infection is especially evident when they are compromised: the Human Immunodeficiency Virus (HIV) is a retrovirus that eliminates one of the most important white blood cells, the CD4+ T-cell, thereby putting the body at risk for countless infections. It usually is not HIV, per se, that kills the infected person, but the many other germs that the compromised immune system cannot control, a syndrome of diseases called **Acquired Immune Deficiency Syndrome**.

In addition, blood is full of many other proteins and dissolved molecules that help the body function correctly: there are proteins that fight off infections, called antibodies; proteins that work with platelets to stop bleeding, called coagulation factors; and excreted toxins that are by-products of metabolic processes. Diseases such as the **hemorrhagic fevers** Ebola and Dengue alter the coagulation factors such that the body cannot stop bleeding once it begins, often leading to the infected person's death.

The Endocrine System. Various organs throughout the body that form the Endocrine system secrete biologically active proteins called hormones into the blood so that their effect can be carried throughout the body. The main organs considered part of this system are the pituitary gland, the hypothalamus, the thyroid gland, the parathyroid glands, the insulin-producing cells of the pancreas, the adrenal glands, the ovaries, and the testicles. Each hormone produced has its own set of actions and helps to regulate processes as complex as menstruation and puberty. Even small alterations in any of these organs or hormones can have dramatic effects on the growth, development, and health of a human being.

The Digestive System. Once food is swallowed, a wavelike motion called peristalsis will pulsate through the esophagus, the tube of muscle that brings the food from the mouth to the stomach. Before entering the stomach, the food will meet a band of muscle that contracts or relaxes to control the flow of food, called the lower esophageal sphincter (LES). This pattern essentially mirrors the form of the entire gastrointestinal (GI) tract: a succession of tubes and sphincters that regulate the transport of food, altering it at each stage so that the body can absorb necessary nutrients. Once in the stomach, acid and enzymes dissolve and digest the chewed up food, especially proteins, but stop short of digesting the stomach organ itself because of a protective lining of mucous along the stomach wall. The stomach muscle simultaneously contracts powerfully so as further to mash the chewed up food mechanically. The stomach gets ulcers when the protective layer is damaged, usually by an infection, allowing the acid to burn the stomach wall. Once fine enough to move through the tight opening of the pyloric sphincter at the end of the stomach, the chewed up food, now called chyme, enters the small intestine, which has three parts. First, in the duodenum, carbohydrates are processed with a stew of digestive enzymes and anti-acidic solutions that pour out from a gland called the pancreas, and fats are processed with bile that comes from a collecting sack that sits just under the liver called the gallbladder. The other two parts of the small intestine, called

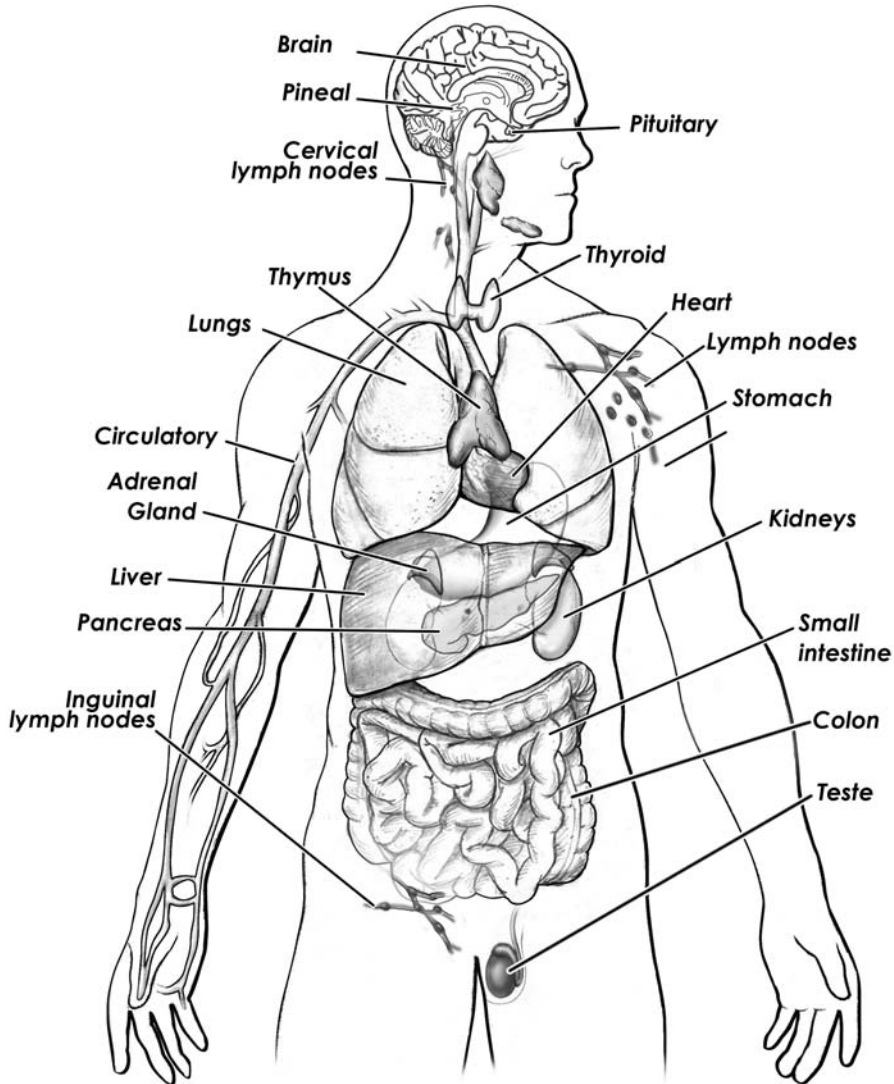
the jejunum and ileum, work with the duodenum to absorb nutrients into the blood through tiny finger-like projections, called villi, on their inner walls. As digestion progresses, carbohydrates are reduced to simple sugars, fats break down into fatty acids, and proteins are divided into their amino acids. All the blood of the intestines collects in what is called the portal venous system that passes through the liver so that the nutrients can be further processed, and toxins may be neutralized. Any medicines absorbed into the blood may also be altered as they pass through the liver. Once past the large intestine, the ingested food, now stool (feces), sits in the rectum until it can pass through the final sphincter, the anus.

When the process of digestion up to the point of the small intestine malfunctions, terrible consequences can happen to the body. For example, in many developing countries, parasitic worms, such as tapeworms, infect the small intestine and intercept the nutrients from consumed food before they are absorbed by the body. Sometimes worms such as roundworm grow and divide, becoming such masses that the entire small intestine plugs up and stops working.

Many diseases that cause infectious diarrheas work at the level of the large intestine by either breaking down the inner lining (the mucosa), thereby preventing it from absorbing water correctly, or by poisoning the cells themselves so that they secrete water. **Dysentery** is sometimes called a “bloody diarrhea” because the damage to the mucosa, or the inner lining of the intestine, caused by the toxins produced by the pathogenic bacteria cause it to bleed. **Cholera**, on the other hand, is one type of “secretory diarrhea” which does not destroy the mucosa, but yet can kill a human in only a few days because the amount of fluid lost through the poisoned and malfunctioning cells can fatally dehydrate the body. Oral Rehydration Therapy (ORT) is a simple but effective treatment that works to replace lost vital fluids by using both salt and sugar dissolved in water to help pull hydration back into the body. Its wide use has saved millions of lives to date and forms the cornerstone of any effective diarrhea treatment.

The Reproductive System. Despite being a source of embarrassment in many cultures, the human genitals play the most important role in the survival of our species: sex and reproduction. When a fetus is first forming, the tissues that change to become either male or female sex organs originate from the same dividing cells, and therefore, the female genitalia and male genitalia are very much alike. The most sensitive parts of the genitals are the tip of the penis, or the glans, and the front of the vagina near the pubic bone, or the clitoris. The shaft of the penis and the lips, or labia, of the vagina develop from the same folds of tissue, as do the scrotum and the mounds of skin next to the labia called the mons venus. A key difference though, is that the female gonads, or the ovaries, are internal, whereas the male gonads, or testes, are outside the abdominal cavity. During intercourse, once a man ejaculates semen into a woman’s vagina, the sperm from his testicles may combine with her egg, or *ovum*, that has come from the ovary down the *fallopian tubes*. The fertilized egg will usually implant in the woman’s *uterus* and, if successful, the fetus will grow, producing the same genitals that will someday start the process anew.

Sexual intercourse involves the exchange of fluids through these organs, so if one partner is infected with a sexually transmitted disease (STD), his or her sexual partner is also at risk of becoming infected. Different diseases infect people differently. **Syphilis** forms a painless ulcer on the external genitals, making infected people unaware that they are infecting their partners. Chlamydia and **gonorrhea** inhabit the sexual fluids, making



A cut-away drawing of major organs and glands in the human (male) head and torso. Courtesy of Megan Rojas.

them pus-like and contagious. HIV infects the blood and can enter the sexual fluids, but it can also infect someone through the exchange of blood, as can happen with blood transfusions or the sharing of needles during intravenous (IV) drug abuse.

The Muscular and Skeletal System. The human skeleton can be thought of as a puppet: the bones are like the sticks that play the arms and legs, and the muscles are like the strings that pull the sticks. Bones are connected to one another at the joints in different ways. The shoulder and hip joints, for example, have a ball-in-socket type joint that

allows for a full range of circular motion. The knee, on the other hand, is like a hinge and can move in only one path. Muscles are connected to bones by tendons, and bones are connected to other bones by ligaments. Each bone has a name, as does each muscle, ligament, and tendon.

The Urinary System. The kidney is made up of a complex network of cells, called nephrons, which concentrate salt and toxins in urine. By doing this, the kidney filters the blood, rids it of many impurities, and helps maintain the metabolic equilibrium of the body. Once the urine is produced, it flows out through the ureters into the bladder. The urethral sphincter will hold it back until it can flow out through the urethra. **Schistosomiasis** is a parasite that lives some of its lifecycle in the urinary system and is therefore passed onto other people who swim in fresh water in which an infected human host has urinated.

The Nervous System. The very design of the central nervous system works to resist damage. Protected by the thick skull bone of the head, called the cranium, the brain is composed of the cerebrum (the part that processes most thinking, from controlling speech to doing math calculations) and the cerebellum (the part that controls the body's coordination and balance). Both sit on top of the brain stem, which controls basic bodily functions like breathing and defecation. Entering at this level, the spinal cord is the long highway of nerves that brings messages back and forth from all parts of the body. Covering all of these parts is a bath of cerebrospinal fluid and a series of protective layers called the meninges. Entry into the brain space is therefore incredibly difficult; even the substances in the blood itself have to cross the so-called blood–brain barrier. If bacteria do happen to breach this barrier, they can cause a profound inflammation in the meningeal space, called **meningitis**. If the infection enters into the brain itself, it is called **encephalitis**. Depending on where it does damage, dramatic changes in bodily function and personality can occur. Indeed, there is a tremendous amount of specialization in each part of the nervous system, with different types of nerves bringing messages to different types of tissues in the body. Some nerves bring messages for skeletal muscle movement whereas others may bring messages for digestion. Similarly, the diverse lobes and folds of the brain work to control different aspects of various thoughts or actions. See also Antibiotics; Ayurvedic Disease Theory and Medicine; Chinese Disease Theory and Medicine; Contagion and Transmission; Corpses and Epidemic Disease; Diet, Nutrition, and Epidemic Disease; Germ Theory of Disease; Greco-Roman Medical Theory and Practice; Heredity and Epidemic Disease; Human Immunity and Resistance to Disease; Immunology; Islamic Disease Theory and Medicine; Personal Hygiene and Epidemic Disease.

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DANIEL PALAZUELOS

HUMAN IMMUNITY AND RESISTANCE TO DISEASE. A continual interplay occurs between microbes and our immune systems. Our immune systems have evolved to provide us with resistance to most microbes encountered throughout life. Yet pathogenic microbes evolve increasingly elaborate strategies to exploit weaknesses in our immune responses and cause disease. Defects in either innate or adaptive components of the human immune system can profoundly reduce a host's resistance to infection. Consequently, infectious microbes often suppress or evade aspects of the immune system in order to cause disease, for example during **bubonic plague, influenza, and tuberculosis**. The ability of the immune system to resist infection is also reduced in **AIDS** and is a major cause of morbidity and mortality in human immunodeficiency virus (HIV)-infected individuals.

Barriers to Infection. The initial barriers to infection are the epithelial surfaces of the body. These include skin and the mucous layers of the eyes, lungs, gut, and other body surfaces. The importance and strengths of these barriers are attested by the fact that billions of nonpathogenic microbes inhabit these epithelial surfaces every day of our lives without causing disease. Those few microbes that do manage to cross an epithelial barrier soon encounter immune cells—such as macrophages, dendritic cells, and neutrophils—that can eat (phagocytose) microbes or debris from damaged tissues. The immune cells also produce a variety of toxic products that directly damage or destroy invading microbes, as well as numerous secreted hormone-like products (cytokines) that recruit and activate other components of the immune system. Those few nonpathogenic microbes that happen to cross epithelial barriers are thus rapidly eliminated by our innate immune system.

In some cases, dendritic cells will transport invading microbes or their products to lymph nodes that drain the infected tissue. This enables the dendritic cells to present antigens that activate antigen-specific antibody-producing B lymphocytes and T cell receptor-producing T lymphocytes within the lymph node. Once activated, T cells contribute to the increased activation of macrophages and other immune cells through their ability to produce cytokines such as interferon gamma (IFN γ). IFN γ is also produced by natural killer (NK) cells in response to hormone-like cytokines produced by infected cells. NK cells can also respond to stress-induced changes in expression of molecules at the surface of infected cells. T cells and NK cells can also directly lyse (kill) infected target cells, thereby preventing the growth of viruses and other intracellular pathogens. B cells produce antibodies that recognize the pathogen or its antigens.

In contrast to harmless, nonpathogenic microbes, pathogenic organisms have evolved strategies to subvert or evade destruction by the innate immune system. One common mechanism used is to avoid destruction by phagocytes. For example, *Streptococcus pneumoniae* **bacteria** produce slippery polysaccharide capsules that interfere with the ability of phagocytic cells to internalize the bacterium. **Viruses** and some other bacteria do not prevent phagocytosis itself, but rather avoid destruction by a phagocyte once phagocytosed. For example, *Mycobacterium tuberculosis* is readily engulfed by macrophages, but in most cases it continues to live inside these cells without being killed. Other viruses and bacteria

have evolved strategies to prevent antigen presentation by cells they infect, so that T cell responses are not efficiently activated.

A common feature associated with a variety of antimicrobial immune responses is the formation of a structure called the *granuloma*. The granuloma is a collection of immune cells that forms to surround and wall off sites of infection within the body. Small cytokine-like molecules known as chemokines are crucial for recruiting the immune cells to sites of infection. These chemokines form a path leading out from the site of infection and bind to receptors on the surface of nearby immune cells. The immune cells then move along the path to the site of infection. Although granulomas can help to limit the dissemination of pathogenic microbes through the body, the collection of activated immune cells also causes localized tissue damage that may contribute to disease symptoms or severity.

Detection of Invading Microbes. In order to contribute to resistance against infection, phagocytes and other immune cells must be able to detect the presence of the invader. To do this, immune cells express a variety of “innate” receptors that play important and complex roles in the immune response.

One class of receptors is specific for the “Fc region” of antibody molecules. The Fc region is a conserved region found on the opposite end from the antibody antigen binding site. Because of this separation of the two regions, each antibody molecule can bind simultaneously both a microbial protein or particle and a host “Fc receptor.” In the case of cells that phagocytose microbes, binding of Fc receptors to antibodies bound to a microbe’s surface can enhance the ability of the leukocyte to eat that microbe. This process is called *opsonization*. The immune cells that are most capable of phagocytosis are macrophages, dendritic cells, and neutrophils. On other, nonphagocytic, immune cells Fc receptors can alter the function of the cell or cause the cell to release toxic products. For example, when an antigen and antibody triggers the Fc receptors present on a natural killer (NK) cell, this cell is triggered to kill infected cells. Conversely, Fc receptors on mast cells (that contain histamines) trigger the release of products that cause allergic-type reactions.

A second class of innate immune receptors detects microbes independently of antibodies. Rather, conserved components of pathogens are detected. These include components of the cell wall of bacteria, elements in virus particles, or material produced by **protozoan** pathogens. Examples of this class of receptors include scavenger receptors, Toll-like receptors (TLRs), and the related Nod-like receptors (NLRs). These receptors typically cause the release of cytokines, which regulate immune responses and enhance the ability of cells to kill phagocytosed microbes.

In addition to cells, conserved blood proteins also have a role in preventing the dissemination of invading microbes and/or in killing these microbes. Proteins involved in blood clotting are activated by microbes and can cause blood clots to form at sites of infection. These clots then physically wall off invading pathogens. Proteins of the “complement system” also recognize pathogens. “Complement” proteins bind to the pathogen and can cause death of the pathogen by breaking down the cell wall. Similar to antibodies and Fc receptors, complement can also cause opsonization of microbes, which are then more readily eaten and killed by phagocytic cells.

Impact of Immune Deficiency on Host Resistance. Animal models of infection have been crucial in defining components of the immune system that promote resistance to infection. Rendering mice deficient for specific immune cell populations, cytokines, or other killing mechanisms has enabled immunologists to make several generalizations with regard to which immune responses are most important for resistance to a specific

pathogen or class of pathogen. T cells are usually important for eliminating infections with intracellular pathogens, either through direct lysis of infected cells or production of cytokines that regulate innate immune cell functions. For example, animals rendered genetically deficient for $\text{IFN}\gamma$ or tumor necrosis factor (TNF)- γ are highly susceptible to infections by intracellular bacteria such as *Mycobacterium tuberculosis* and *Listeria monocytogenes*, as well as viruses like murine cytomegalovirus (MCMV). B cells and antibodies play a more substantial role in immune resistance to extracellular pathogens and toxins, such as *diphtheria* toxin, but can also contribute to resistance against viruses such as *influenza*.

Cytokines produced by T cells, NK cells, and other cell types also have diverse effects during antimicrobial immunity. For instance, in addition to activating antimicrobial killing mechanisms of macrophages, $\text{IFN}\gamma$ and TNF γ are thought to contribute to immunity by promoting granuloma formation and maintenance. Cytokines such as IL-12, IL-18, and IL-1 regulate the production of these cells and also influence more general host responses to infection such as fever. It is important to note that cytokines have numerous effects and sometimes can have opposite effects on infection with different microbes. For instance, type I IFNs can regulate the survival of infected cells as well as the ability of such cells to produce proteins that degrade nucleic acids in viruses. Mice deficient for type I IFNs are thus more susceptible to infections with several viruses, including MCMV. Yet, these same mice are considerably more resistant to infection with certain intracellular bacteria, such as *L. monocytogenes*.

With regard to humans, mutations in several genes have been shown to predispose one toward specific pathogens or classes of pathogens. For example, humans who lack expression of the receptor for $\text{IFN}\gamma$ or for IL-12 show increased susceptibility to infections with intracellular bacteria such as *Mycobacteria* and *Salmonella*. Mutations in the chemokine receptor CCR5 are associated with a reduced risk of **human immunodeficiency virus** (HIV) infection in otherwise high-risk individuals. This is at least partially because HIV exploits CCR5 for entry into infected cells. See also Contagion and Transmission; Drug Resistance in Microorganisms; Heredity and Epidemic Disease; Human Body; Immunology; Vaccination and Inoculation.

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LAUREL LENZ

HUMAN IMMUNODEFICIENCY VIRUS/ACQUIRED IMMUNE DEFICIENCY SYNDROME (HIV/AIDS). AIDS is a new infectious disease whose symptoms are the end result of infection with the Human Immunodeficiency **Virus** (HIV). In June 1981, AIDS was first recognized in the medical literature, but at that time, the causative agent of AIDS was unknown, so the disease was given several names describing either symptoms exhibited by patients or social characteristics of those patients. “Wasting disease,” “slim disease,” “opportunistic infections,” and “Kaposi’s sarcoma (KS),” were used singly or together to describe the symptoms. Because the disease was first recognized in the homosexual communities of large U.S. cities, “Gay-Related Immune Deficiency (GRID)” and

“Gay cancer” described a salient identity of patients. By 1984 medical researchers had identified a retrovirus as the causative agent in the disease. In 1986 this virus was named Human Immunodeficiency Virus (HIV), and in 1987 the disease AIDS was defined by the U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) as the end stage of infection with this virus—hence the name HIV/AIDS. HIV is transmitted by intimate contact between bodily fluids. Over 2 to 10 years, the virus kills key controlling cells of the body’s immune system until an infected person has no immunological defenses against many different opportunistic infections and cancers. Because infected and contagious people appear healthy for many years, HIV has spread rapidly in geographic locations where individuals engage in sexual relations with many partners, infected women become pregnant and transmit the virus unknowingly to their babies, and injecting drug abusers share needles. In areas of the world with large populations and few medical resources, the rapid spread of HIV and subsequent epidemic of AIDS has destabilized societies by killing the young adults most likely to become infected and thus leaving children without parents and communities without leadership.

The Virus and its Effect on the Human Body. HIV is a retrovirus, composed of ribonucleic acid (RNA). The term *retro* originates from the property of these viruses to transcribe themselves, via an enzyme called reverse transcriptase, into a DNA form that is then integrated into the invaded cell’s genome. The creation of new viruses then becomes a part of the cell’s own genetic instructions. In the early decades of the twentieth century, the AIDS virus mutated in West Africa from a form that infected only chimpanzees to one that could infect humans.

Retroviruses had been known to cause disease in animals since 1911, when Peyton Rous (1879–1970), a scientist at the Rockefeller Institute for Medical Research in New York City, discovered that a particular type of cancer in chickens could be transmitted by grinding up a tumor and injecting it into another chicken. By the 1970s, the molecular structure of retroviruses was known, but none had ever been identified as causing disease in humans. In 1980 Robert C. Gallo (b. 1937) and his colleagues at the National Cancer Institute, National Institutes of Health, in Bethesda, Maryland, demonstrated the existence of retroviruses that caused cancer in humans by triggering unchecked replication of T cells.

In contrast, HIV, the retrovirus that causes AIDS, kills the helper T cells that regulate the immune system, thus destroying the body’s natural defenses against opportunistic infections and cancers. When the initial infection takes place, HIV causes fever, headache, malaise, and enlarged lymph nodes—symptoms similar to those of many other virus infections. These symptoms disappear within a week or two, but the infected individual is highly contagious at this point, with HIV present in large quantities in genital fluids. For the next 10 years in adults (and approximately 2 years in infants infected at birth), there may be no disease symptoms at all. During this period, however, HIV is destroying the T cells that are the body’s key infection fighters, and this decline is measurable. Once the immune system has reached a certain level of disruption, the infected person begins to experience symptoms. Lymph nodes may enlarge again, energy may decline, and weight may be lost. Fevers and sweats may become frequent. Yeast infections may become frequent or persistent, and pelvic inflammatory disease in women may not respond to treatment. Short-term memory loss may be observed. Infected children may grow slowly or have many bouts of sickness.

The CDC defines the advent of full-blown AIDS as the moment when an individual infected with HIV experiences a T cell count below 200 per cubic millimeter of blood

(healthy adults have T cell counts of 1,000 or more). This is the point at which the immune system is so ravaged that it cannot fight off **bacteria**, viruses, fungi, parasites, and other microbes normally kept in check by the immune system. Symptoms of people with AIDS may include coughing and shortness of breath, seizures, painful swallowing, confusion and forgetfulness, severe and persistent diarrhea, fevers, loss of vision, nausea and vomiting, extreme fatigue, severe headaches, and even coma. Children with AIDS may experience these same symptoms plus very severe forms of common childhood bacterial diseases such as **conjunctivitis**, ear infections, and tonsillitis. People who develop AIDS also may develop cancers caused by viruses, such as Kaposi's sarcoma and **cervical cancer**, or cancers of the immune system known as lymphomas. Eventually, the person with AIDS is overwhelmed by the opportunistic infections and cancers and dies. Antiviral drugs are able to suppress the damage to the immune system but not to eradicate the virus. People living with AIDS must take antiviral drugs, which have many side effects, for the rest of their lives.

Transmission. HIV is not easily transmitted. It is *not* transmitted by hugging, kissing, coughing, using public toilets or swimming in public pools, or sharing eating utensils or towels in the bathroom. Transmission of HIV requires close contact between an infected person's bodily fluids and the blood or other bodily fluids of a noninfected person. The principal way in which AIDS is transmitted is through sexual intercourse—genital, anal, or oral. It is also transmitted easily when injecting drug users share needles, or when needles used in tattooing or body piercing are reused without being sterilized. HIV may be transmitted from mother to child before, during, or after birth, and it may be transmitted in breast milk. Before 1985, when a test for HIV was released, the AIDS virus was also transmitted through contaminated blood and blood products used in surgery or to treat hemophilia.

Education about the routes of transmission, programs to encourage abstinence from sex or faithfulness to one partner, the distribution of condoms and clean needles, and free testing so that people may learn their HIV status have been the major methods by which the transmission of AIDS has been slowed, when such methods have been utilized. Religious taboos against the use of condoms during sex and political views that oppose the distribution of clean needles to drug abusers have inhibited prevention efforts. Cultural resistance to permitting women to refuse unsafe sex and the existence of informal multi-partner sexual networks in which individuals do not think of themselves as promiscuous because they have sex with only a few people whom they know well have also hindered the interruption of transmission of HIV.

Epidemiology. As a new disease, AIDS was literally “constructed” by epidemiologists in the years after it was first identified in the medical literature. Between 1981 and 1984, epidemiologists had to answer many questions: What did it mean to have AIDS? How was the disease transmitted? What did the epidemiological data suggest about possible etiological agents? How much morbidity and mortality did the disease exact and over what time periods? How was the disease dispersed geographically? Which populations were most at risk for contracting the syndrome?

The first on-the-ground investigations of the new syndrome were done as collaborations between the CDC and state or local health agencies. Public health officials followed up every case they could find of KS and *Pneumocystis carinii* pneumonia (PCP). A 30-page, detailed questionnaire was developed that produced a picture of AIDS in the United States. By early 1982, statistics showed that the average age of patients was 35. All of the

patients were gay men, and they were living in the strong gay communities of San Francisco, New York, and Los Angeles, all areas of high opportunity for gay men. They had a large number of sexual partners. They all went to the same nightclubs and most used the drugs known as poppers (isobutyl nitrite or amyl nitrite).

By June 1982, however, information about cases of AIDS outside the gay communities had been collected, and the understanding of AIDS was broadened. AIDS was identified in injecting drug users and their sexual partners, in newborn babies, and in heterosexual patients who had undergone surgery. These new observations suggested a blood-borne pathogen. The discovery of cases in hemophiliacs reinforced the evidence for transmission via blood, like **hepatitis B**.

HIV infection and AIDS are concentrated in places where the methods of transmission are most prolific and where prevention methods are not employed. It was first identified in the United States, for example, in the gay communities of large cities, where frequent and unprotected sexual encounters took place, enabling rapid spread of the virus. Injecting drug users, communities of whom are often concentrated in large cities, spread the virus to one another through shared needles and to their sexual partners during sex. In much of Sub-Saharan Africa, in contrast, AIDS is more often transmitted heterosexually. HIV transmission is concentrated along highways traveled by men working far from home and seeking sex with female sex workers. Once infected, the men may unknowingly infect their wives. When the wives become pregnant, their unborn children may become infected as well. Cultural practices that discourage the discussion of sex may lead men to deny infection. Because women in many African cultures have no recognized right to demand that their husbands wear condoms during sex, they have almost no options to protect themselves from infection. A popular superstition that a man will be cured of his HIV infection by having sex with a virgin may lead men to have forcible intercourse with young girls, thus spreading the infection further. In Southeast Asia and in India, the sex trade in large cities has been a principal locus of HIV transmission.

Sociocultural Construction of the Disease. As a mental picture of AIDS was constructed by epidemiologists from the medical evidence they observed, the meaning of the disease was also constructed in the social, political, cultural, and religious contexts of the societies in which it existed. "Having AIDS" meant much more in all societies than mere infection with a virus and the physical consequences of that infection. Because HIV was transmissible sexually, views about marriage, homosexuality, adultery, and premarital sex all colored the perception of someone with AIDS. In cultures that had strong prohibitions against homosexuality, AIDS became a symbol of how God punished gay people. In cultures that held religious beliefs against the use of condoms during sex, that method of AIDS prevention was discounted as being of no importance. In cultures in which political leaders implemented pragmatic rather than ideological policies, strong prevention efforts such as education, condom distribution, and programs to distribute clean needles to addicts reduced the incidence of new infections.

History of Research on and Control of HIV/AIDS. As soon as epidemiologists understood that AIDS attacked the helper T cells that controlled the immune system, they urged virologists to search for a hitherto unknown virus that fit this description. The only viruses known to attack human T cells were the retroviruses identified by the Gallo laboratory at the National Cancer Institute (NCI) in Bethesda, Maryland. These viruses were known as Human T-Cell Lymphotropic Virus, Types I and II (HTLV-I and HTLV-II), which caused cancer in humans. Three groups of investigators began searching for

retroviruses as possible causative agents of AIDS. In addition to Gallo's group, there were virologist Luc Montagnier's (b. 1932) group at the Pasteur Institute in Paris and medical researcher Jay Levy's (b. 1938) group at the University of California San Francisco (UCSF). In 1984 Gallo's group published four papers in the journal *Science* that demonstrated a retrovirus as the cause of AIDS. They initially believed that it was in the same family as the other two HTLV viruses; hence, they named it HTLV-III. Montagnier's group at the Pasteur Institute and Jay Levy's at UCSF also identified the causative retrovirus of AIDS at about the same time. They named their viruses, respectively, lymphadenopathy associated virus (LAV) and AIDS related virus (ARV). Within a year, these viruses were shown to be identical. Because the AIDS virus caused destruction of infected T cells instead of the uncontrolled reproduction that occurred in cancer, it was deemed separate from the HTLV family. In 1986 an international group of scientists proposed that the name of the retrovirus that caused AIDS be changed to *Human Immunodeficiency Virus* (HIV).

The first medical intervention developed for the control of AIDS was a diagnostic test adapted from the laboratory assay that confirmed the presence of antibodies to HIV in cell cultures. This enzyme-linked immunosorbency assay (ELISA) can have false positives, however, so a second test, known as the Western blot, which assays for specific viral proteins, was used to confirm a positive ELISA test. In 1987 the U.S. Food and Drug Administration (FDA) required that both tests be used before someone would be told that he or she was infected with AIDS. Twenty-five years into the epidemic, these diagnostic tests arguably remain medicine's most useful interventions for addressing the AIDS epidemic because they provide a measurable, replicable means to identify infected individuals.

During the two years of intensive laboratory research during which HIV was identified and characterized genetically, information also emerged about the virus that helped suggest which preventive interventions by political and public health leaders might be possible. Within just a few months after HIV was identified, molecular biologists understood that it mutated far too rapidly—up to 1,000 times as fast as **influenza** virus—for a traditional vaccine to be made against it. Instead of being able to vaccinate against AIDS, political and public health leaders needed to use educational methods aimed at curbing high-risk behavior to slow transmission, a much harder task.

Molecular and genetic studies also identified the key points in the virus's life cycle, which, if interrupted, would halt the spread of the virus. The first was the CD-4+ receptor on the cell wall of the host cell to which the virus attached. Second was the point at which the enzyme reverse transcriptase caused the single-strand RNA virus to make a complementary copy that transformed it into double-stranded DNA. Third, the enzyme integrase caused the viral DNA to be spliced into the genome of the host cell. Finally came the point at which the enzyme protease cut newly constructed polypeptides into viral proteins in the final assembly of new virus particles. By 1986 intellectual strategies were in place to intervene in each of these four steps, but scientists were not technologically capable of implementing most of them, and a great deal of molecular information about HIV, such as the existence of necessary co-receptors in step 1, was not yet known.

In 1984 some drugs were known to inhibit reverse transcriptase, so this is where the work on an AIDS therapy began. Scientists utilized an anti-cancer drug-screening program at the NCI to identify potential drugs for use against AIDS. One of these that showed promise *in vitro* was azidothymidine, commonly called AZT. After truncated clinical trials in which AIDS patients showed a clear response to AZT, it was approved for use by the FDA in record time and sold under the brand name Retrovir or the generic name zidovudine. Within a few

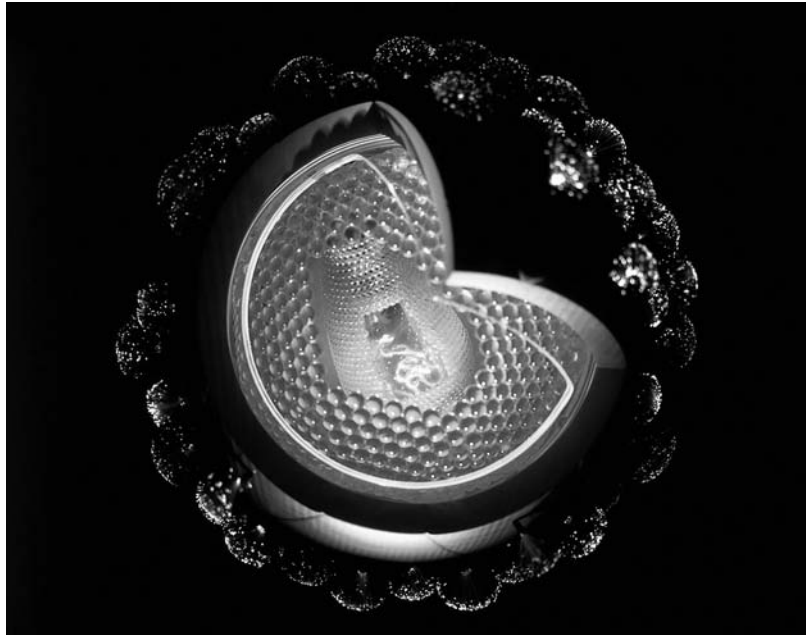
more years, two additional reverse transcriptase inhibitors, known in chemical shorthand as ddI and ddC, were approved by the FDA for treating AIDS. The reverse transcriptase inhibitors improved the condition of AIDS patients but had a number of toxic side effects and were subject to the development of resistance by HIV.

Other than these antiretroviral drugs, treatments for AIDS focused on existing drugs for treating the opportunistic infections and cancer that people with AIDS developed. In 1995 the first of a new class of antiretroviral drugs was introduced.

Known as protease inhibitors, these drugs interfered with the final enzymatic step in the viral assembly process. For a brief period, there was optimism that the protease inhibitors would “cure” AIDS because viral loads—the number of virus particles in a quantity of blood—disappeared. It soon became apparent, however, that HIV was only suppressed and that it rapidly rebounded if the drugs were withdrawn. These drugs, too, caused unpleasant side effects. The combination of reverse transcriptase inhibitors and protease inhibitors known as Highly Active Antiretroviral Therapy, or HAART, is nevertheless the most effective “cocktail” of drugs for long-term therapy against AIDS. Pharmaceutical research still works toward a rationally designed, molecularly based drug with minimal toxicity as a therapy for AIDS, but at present, that goal has not been attained.

Current Situation of AIDS. In November 2006, WHO reported that 2.9 million people had died of AIDS-related illnesses and estimated that 39.5 million people were living with HIV/AIDS. WHO also reported that there were 4.3 million new infections in 2006, 65 percent of which occurred in Sub-Saharan Africa. There were also important increases in Eastern Europe and Central Asia.

Research continues on a preventive vaccine and on new antiviral drugs. The most effective means for controlling the epidemic, however, still remains diagnosis of individuals infected with HIV, education about how the virus is spread, and public health efforts to change behavior to minimize the risk of infection. *See also* all AIDS-related entries; Animal Research; Capitalism and Epidemic Disease; Cinema and Epidemic Disease; Disease, Social Construction of; Human Body; Human Immunity and Resistance to



Cut-away model of the human immunodeficiency virus (HIV), the cause of AIDS. John Wildgoose.

Disease; Literature, Disease in Modern; Medical Ethics and Epidemic Disease; Personal Hygiene and Epidemic Disease; Personal Liberties and Epidemic Disease; Pharmaceutical Industry; Popular Media and Epidemic Disease: Recent Trends; Poverty, Wealth, and Epidemic Disease; Religion and Epidemic Disease; Sexual Revolution.

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VICTORIA A. HARDEN

HUMAN PAPILLOMA VIRUS AND CERVICAL CANCER. Many people consider **epidemic** diseases to be those that affect populations suddenly, accompanied by severe symptoms like diarrhea and rashes that are dramatic and strike quickly. A corollary might be that if an epidemic struck slowly, modern medicine could catch up to it and wipe it out. Cervical cancer is an epidemic disease that progresses gradually and can be detected and even cured if found early. But despite the opportunity to stop this epidemic, it continues to be a leading cause of cancer death among women in many developing countries.

It may seem unusual to think of cancer as an epidemic, but the remarkable distinction of cervical cancer is that it is caused by a **virus**, just like **influenza** or the common cold. The Human Papilloma Virus (HPV) in some forms causes simple warts, like those commonly found on hands or feet. The virus comes into contact with the cells in the topmost, or epidermis, layer of human skin, and causes the skin cells to divide and grow more than normal. On the hands, a little bump with a crown like a cauliflower will form; on the cervix of a woman, cancer can develop.

The cervix is a round lip at the end of a woman's uterus, which separates it from the vaginal canal. It is covered with skin very much like the skin anywhere else on the body. When cervical skin cells are infected with an HPV that is potentially cancerous, visible changes occur in how these cells look under a microscope. Normally, the cells look like clear bags with a stained circle in the middle of each cell. This dot is the *nucleus*, where the DNA of the cell is located. This DNA holds all the information on how the cell functions, divides, and dies. Once infected with HPV, the DNA changes; the nucleus may become larger in comparison to the rest of the cell, look darker, or look more irregularly shaped—all changes that are easily spotted under the microscope. There are many different types of HPV, and the most dangerous are four subtypes (numbered 16, 18, 31, 45) that hold oncogenes, the genes that affect the DNA and cause cancer.

In the United States and the rest of the developed world, cervical cancer used to be one of the leading causes of cancer death among women. All this changed when Dr. George Papanicolaou (1883–1962) developed a test in the 1920s that allowed health-care providers to look for the very changes mentioned. First, a small sample of cells from a woman's cervix is collected. Then, these cells are placed on a glass slide, stained with various dyes, and viewed under a microscope. If changes are found, then the infected cells on the cervix can be either cut out or burned off with a super-cold probe. The cervix does not have any pain nerves so this does not cause the patient pain. After many years of implementation, this procedure all but eradicated cervical cancer among the women with access to a Papanicolaou (Pap) smear test. If left alone to continue changing, however, the infected cells of the cervix can grow into cancer. They may continue to develop until they have invaded organs nearby; cancerous cells can even travel throughout the body to implant and grow in places far away from the cervix. This is called metastatic cervical cancer, and it is usually fatal.

A study of American women in 2003–2004, published in the *Journal of the American Medical Association* in February 2007, found that at any given moment 26.8 percent have some form of the virus. Other studies indicate that 80 percent of women will acquire the virus at some point, that 14,000 will develop cervical cancer each year, and that almost 4,000 American women will die of it each year. Worldwide estimates in 2004 were 493,000 new cases annually and 274,000 annual deaths.

The reason so many women continue to die of a disease that is entirely preventable has more to do with politics and economics than with science and medicine. Although it is a simple test that does not require much equipment, the Pap smear has some critical shortcomings. First, many women are unaware of the causes and dangers of cervical cancer and have never heard of it or have never been offered an explanation of it. Second, getting a sample is sometimes embarrassing or uncomfortable for women. It entails inserting a speculum into the vaginal canal, which spreads the vaginal lips so that the cervix can be seen and then sampled. Although most trained health-care practitioners can perform this exam while avoiding discomfort, the patient has to know and trust that all this is actually worth the trouble. Some traditional and modern societies highly value modesty, and a stranger, particularly a man, is not trusted to perform such a sensitive procedure. In addition, even if women want the test, in cultures in which men have control over their wives' and daughters' activities, women are not allowed to decide this issue for themselves. Third, Pap smear analysis and follow-up can be extremely difficult in developing countries. The slides from the Pap smear

must be transported to another doctor, who will examine the sample to see whether it is abnormal. If abnormal cells are seen, the patient must then be notified to return to the clinic for further care. In many developing countries, some women have to walk or ride for hours to get to the nearest clinic. The process of obtaining the results can take months if a good system of transport and analysis of the sample does not exist. Similarly, some countries have not been able to develop reliable laboratory systems that can provide accurate results in a reasonable amount of time. For example, some studies from Latin America show that a result may return as long as six months after the sampling date, and may have a false-negative rate of up to 50 percent, meaning that the abnormal cells were missed by the pathologist in up to half of the patients who actually had cellular changes. With a system that entails multiple visits to screen, receive results, and treat, cervical cancer prevention has not reached places that lack good roads, dependable lines of communication, and governments that choose to invest in these procedures.

In order to address this epidemic, some groups are trying different approaches. The HPV that causes cervical cancer is transmitted sexually, but studies show that condoms alone do not prevent the **transmission** of the virus from one person to another. Multiple new screening strategies have been developed. The goals of a good screening test are to catch all the people who have the disease and to minimize falsely diagnosing those who do not have the disease. The most promising alternatives have been Visual Inspection with Acetic Acid (VIA) and HPV testing. In VIA the cervix is coated with a vinegar-like solution and if there are areas that have been infected by the HPV, they turn white. In HPV testing, samples of vaginal fluids are taken and tested for the worst types of HPV.

To utilize these methods most efficiently, some groups are developing a system called the “one visit screen and treat” approach. In one technique, VIA is performed, and if positive many of the abnormal cells are treated by burning them off at the same visit. The benefit of this approach is that the women do not have to travel to the clinic more than once. Similarly, other groups have explored having patients self-collect vaginal samples to test for HPV. Some women have considered this preferable to a Pap smear because it may be less embarrassing and more comfortable. But if her test returns positive, a woman will still have to undergo a vaginal exam to have the precancerous cells removed. The one visit screen and treat approach has not yet proven to be as effective as the Pap smear in reducing the incidence of cervical cancer, although there is great potential.

The discovery of HPV as the cause of cervical cancer has led to a number of important advances, including the recent release of a vaccine that is able to prevent infection with the most dangerous types of HPV. Even this vaccine, however, is not a perfect cure: it is relatively expensive, lasts only a number of years, and is only helpful in women who are not yet infected with HPV. It is most promising for young women who are not yet sexually active, but it does not address the millions already infected.

Cervical cancer, a deadly disease affecting women, has a cure. This cure, however, is not available to everyone in the world, especially those women who are most commonly affected by this slow moving epidemic. New methods have been developed that may help these women access the screening process and subsequent treatment. The critical next step, however, is securing the health-care practitioners to perform the tests, along with the support necessary from their governments, to ensure that this process begins.

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HUMAN SUBJECTS RESEARCH. Scientists have included humans as the focus of both basic and applied research ranging from biomedical to behavioral studies, and despite the specific focus of a project, the general purpose of the research has been to extend human understanding beyond what is already known. As they gathered observable, empirical, and measurable evidence, scientists subjected their analysis to rigorous standards of reasoning and technical method, and new medical products, improved clinical procedures, and more sophisticated knowledge of physiology, pharmacology, biochemistry, and human behavior followed.

From the start, the scientific method distinguished itself from other means of establishing knowledge, and researchers developed specific hypotheses to explain natural phenomena as they designed experimental studies to test these predictions for accuracy and consistency. Today, the systematic observation, description, and measurement of data—as well as the exposure of experimental results to the critical scrutiny of other scientists—provide the fundamental bases of the modern sciences such as chemistry, biology, and psychology.

A human subject is typically a living individual who participates in scientific research by interacting directly with the investigator. For example, a human subject may surrender bodily materials such as cells, blood, or other tissues if required by the research design. In other cases, he or she may disclose personal medical, family, or psychological information to the scientist, or perform exacting tasks such as undergoing rigorous physical exercise or completing batteries of psychological tests. In larger epidemiological studies, scientists are concerned with the health and welfare of whole populations as they systematically collect and analyze data related to the frequency, distribution, and causes of human disease. No matter its specific focus, the application of the scientific method provides a variety of potential benefits such as the testing of new drugs, the discovery of new health products and technologies, the development of better diagnostic methods, and the improvement in comfort and quality of life. Though the causes of some epidemic diseases, such as bubonic plague, were discovered by studying dead victims, many more discoveries were the result of studying living victims. This is especially important for understanding the transmission, course, and other patterns of a given disease.

A good example of very early human subjects research was **Edward Jenner's** trials of cowpox vaccine in the late eighteenth century. Jenner kept careful and detailed notes on

those he vaccinated, the doses he used, and their reactions to the injections. This provided important information to later physicians. Later in the century, Dr. Eduard Arning (1855–1936) offered Hawaiian death row inmates the choice of execution or inoculation with potentially deadly leprosy material. He wanted to study the contagious nature of **Hansen's Disease**. Some early researchers used themselves as test subjects, as with members of **Walter Reed's yellow fever** team in 1900. In a second phase of his study Reed coupled inducements—including money—with early informed consent contracts that laid out the risks involved. These are at the heart of modern research approval processes.

The testing of the antibiotic streptomycin for use against pulmonary tuberculosis began in England in 1946. Researchers pioneered the double blind, randomized control clinical trial. One group of subjects received the drug, whereas a control group got the standard drug of the day. Patients were randomly assigned to groups, with neither the doctor nor the patient aware of who received which drug (double blind). This model has become one of the standards for pharmaceutical testing. In 1953 the U.S. National Institutes of Health (NIH) opened a 540-bed research hospital in Bethesda, Maryland, for subjects of their studies.

The inhumane “medical experiments” carried out by Nazi German and Imperial Japanese doctors in the 1930s and 1940s led to the establishment of **medical ethics** standards for researchers. In 1979 the NIH established written guidelines for ethical project design and conduct, a development followed by western European countries by the 1990s. The Council of International Organizations of Medical Science and World Medical Association ethics standards require that before any research may be conducted on human subjects, including vaccine trials, a research ethics committee (REC) or an institutional review board (IRB) must approve a formal proposal that outlines the proposed research and the protections offered to human subjects. The review committee is charged with determining whether the research is scientifically valid, whether the benefits to medical knowledge outweigh the risks to the subjects, and whether people participating in an experiment, or their surrogates, have been adequately informed of the risks and whether, knowing these risks, they have given their informed consent to participating as subjects. *See also* Epidemiology; Epidemiology, History of; Heredity and Epidemic Disease; Hospitals and Medical Education in Britain and the United States; Leprosy in the United States; Personal Liberties and Epidemic Disease; Pharmaceutical Industry; Poliomyelitis, Campaign Against; Public Health Agencies, U.S. Federal; Scientific Revolution and Epidemic Disease.

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BART DREDGE WITH ROBERT BAKER

HUMORAL THEORY. Developed in Classical Greece, humoral theory provided the basis for Western medicine from the fifth century BCE to the nineteenth century. According to humoral theory, the body contains four principle substances, or humors—blood, phlegm, yellow bile, and black bile—and good health requires a balance among them. This was first articulated in the writings of fifth-century BCE Greek physician **Hippocrates** and his followers, and then accepted by later intellectuals, including the Greek philosopher Aristotle (384–322 BCE) and the Roman **physician Galen**. The writings of these two men expanded upon the original theory and helped ensure it would become the standard explanation of health and disease in both European and Islamic civilizations until the nineteenth century.

The humors, like their corresponding elements of the natural world (earth, **air**, fire, **water**), combine the four principle qualities of hot, cold, dry, and wet: blood (air) is hot and wet, phlegm (water) is cold and wet, yellow bile (fire) is hot and dry, and black bile (earth) is cold and dry. Humoral theory held that all human bodies contain these four substances, though each person maintains a particular ratio among them. Each body's humoral balance is affected daily by external factors commonly known as the six non-naturals: air, food and drink, sleep and waking, exercise and rest, evacuation and repletion, and passions. Thus, illness is a result of imbalance in the humors, which can be restored to balance through manipulations of diet and lifestyle. In addition, balance may be restored through the removal of excess humors, principally through bleeding. One result of this theory was the perception of illness as a continuum of “nonhealth” rather than as a result of a discrete disease with a unique causative agent. **Diagnosis** of problems was therefore subjective, and physicians tailored therapy to each individual.

While humoral theory worked well to explain individual ailments such as fever or congestion, **epidemic** disease required a more intricate explanation to account for widespread (but not universal) experiences of similar symptoms. Of primary use for explaining epidemics was the first of the non-naturals—air. Corrupt or unhealthy air (miasmas) could spread a similar set of symptoms within a large population, particularly affecting those whose natural humoral balance left them susceptible to such contaminations. In this way, the ability of some in the population to escape an epidemic could be explained through either lack of sufficient exposure to the miasma or through lack of predisposition to the miasma.

Whereas popular ideas of **contagion** began to emerge in response to plague in the fourteenth century, coherent medical theories of contagion did not emerge until the sixteenth century with Italian physician **Girolamo Fracastoro**. These offered alternative explanations for some diseases, but did not seriously undermine the widespread acceptance of humoral theory in general. Challenged by **Paracelsianism** in the sixteenth and

seventeenth centuries, humoralism was finally supplanted by **germ theory** in the nineteenth century. See also Greco-Roman Medical Theory and Practice; Islamic Disease Theory and Medicine; Medical Education in the West, 1100–1500; Plague and Developments in Public Health, 1348–1600.

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KRISTY WILSON BOWERS



IMMUNITY. See Human Immunity and Resistance to Disease.

IMMUNIZATION. See Vaccination and Inoculation.

IMMUNOLOGY. Immunology is the scientific discipline that seeks to explain the human host immune system and its many roles in health and disease. The immune system has important roles in maintaining health and in fighting diseases such as cancer, autoimmunity, and infections.

At least as early as ancient Greece, it was recognized that humans who recover from some specific infectious diseases are resistant to a second attack of the same disease. We now know this is true because the immune system can recognize infectious agents or products of these agents (called antigens). This recognition leads to activation of an immune response and, frequently, to the elimination of these antigens or pathogens. The reason we avoid getting sick a second time is that our immune system “learns” from the first encounter and “remembers” how to eliminate the infectious agent before it can again cause disease symptoms. Importantly, this “immunological memory” is highly specific and is shaped by and adapted to the immunological experiences of each individual.

Beginning in the late 1800s, scientists discovered that the ability of our immune system to remember antigenic challenges is dependent on specific types of white blood cells and by one of their secreted protein products called antibodies. Antibodies are made by B lymphocytes (B cells). Antibodies recognize and bind with very specific sites (“epitopes”) on a pathogen or antigen. This binding can reduce the ability of the pathogen to cause disease by blocking the function of the antigen or causing destruction of the pathogen. Pathogen destruction occurs either directly, by a process called complement fixation, or indirectly by a process called opsonization. Opsonization occurs when an antibody coats a pathogen so that it can be detected and eaten by phagocytic cells. When eaten, the microbe is usually killed and digested.

Each antibody recognizes a distinct epitope with high affinity and exquisite specificity, as conferred by the antibody's unique antigen binding site. Because there is an enormous number of potential pathogens and antigens that might be encountered by each human or animal, the immune system has evolved a mechanism to generate millions of different antibody molecules. DNA rearrangements occur during the development of each B lymphocyte clone. These DNA rearrangements join together three individual DNA regions (V, D, and J) to form a single antibody-encoding gene. Because of imperfect joining and a large number of different V, D, and J regions in the genome, up to approximately 10^{10} distinct antibody molecules can theoretically be made within a given individual. A similar process of gene rearrangement occurs within T lymphocytes (T cells) in order to create a diverse array of cell-surface T cell receptors (TCRs). Whereas antibodies recognize the three-dimensional structure of an antigen, individual TCRs recognize peptide fragments of protein antigens that are displayed on the surface of infected cells. Some T cells can directly kill infected cells. They do this by recognizing host-derived surface proteins that are components of the major histocompatibility complex (MHC), which are able to bind and present small peptides that are processed from pathogen-derived antigens.

Because V, D, and J gene rearrangements occur separately within individual T cells and B cells that develop in the body, each cell produces a unique antibody or TCR. When an individual T or B cell senses an antigen that binds its TCR or antibody, it is activated to proliferate and mature into a more developed stage. A single T or B cell can thus quickly expand into a clonal population containing thousands of cells. These cells then produce antibodies or kill infected cells. After eliminating the antigen or infection, many of the responding T and B lymphocytes will die, but the remaining cells persist at a frequency 10 to 1,000 times greater than in the previously uninfected "naïve" individual. These cells also differ from their parents in that they respond more rapidly and efficiently to a second encounter with a given antigen. Thus, the ability of the immune system to prevent reinfection is the result of the persisting "memory" T and B cell populations that rapidly eliminate any reencountered antigen or pathogen.

The ability of the immune system to remember previously encountered antigens is the basis for vaccines and **vaccination**. The development of an effective vaccine by **Edward Jenner** ended a worldwide **epidemic** caused by **smallpox virus** and ultimately enabled humankind to eradicate this deadly disease. Similarly, vaccines developed against poliovirus by **Jonas Salk** and **Albert Sabin** have reduced the worldwide incidence of **poliomyelitis** to a point where this infection may also someday be completely eradicated. It is hoped that vaccines can be developed that will help eradicate other epidemic pathogens, such as **AIDS** and **tuberculosis**.

Immunologists often categorize the immune response into two phases: *adaptive* (acquired) and *innate* immunity. T lymphocytes, B lymphocytes, and the antibodies they produce are considered to participate in *adaptive* immunity. By contrast, *innate* immunity is comprised of other white blood cells; as well as the ermline- (genetically) encoded products of cells that promote immunity. Innate immune responses are not specific to a particular pathogen or antigen and do not undergo DNA rearrangements. Rather, they are more generic for broad classes of pathogens (e.g., Gram-negative **bacteria**) and are largely identical among different individual humans or animals of a given species.

In the absence of infection, most T and B lymphocytes circulate through the bloodstream and the lymphatics. The lymphatics are vessels that drain the fluid (*lymph*) that collects in tissues of the body. The lymph passes through a series of lymph nodes, which

are collections of immune cells that act to filter out microbes or antigens from the lymph. Antigens collected by dendritic cells or macrophages can trigger the activation of naïve T and B cells that transiently pass through the lymph node draining a site of infection. These activated immune cells then proceed to direct the adaptive and innate components of the immune response against the antigen or pathogen. The activation of an immune response can also cause the lymph node to swell. Swelling of lymph nodes is a common symptom of infection but is more pronounced during some specific diseases, such as **bubonic plague**.

Although our understanding of the immune system and its roles in health and disease is far from complete, studies of innate and adaptive immunity have enabled immunologists to understand how our bodies resist infection and re-infection. It is also clear that defects in one or more components of the immune system can strongly contribute to plagues, pestilence, and pandemics. *See also* Contagion and Transmission; Drug Resistance in Microorganisms; Heredity and Epidemic Disease; Human Body; Human Immunity and Resistance to Disease.

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LAUREL LENZ

INDUSTRIALIZATION AND EPIDEMIC DISEASE. The shift from hunter-gatherer living to early **Neolithic** farming and domestication of **animals**, which began around 10,000 years ago, created the first “big bang” opportunity for novel infectious disease agents to enter the human species. The settled and denser agrarian way of life allowed sustained and closer contacts with animals and their microbes, the proliferation of pest species (rodents, flies, etc.) as vectors of infectious agents, and, in due course for some infectious agents as towns and early cities formed, the opportunity for continuous circulation and survival in populations of sufficient size to sustain a supply of susceptible (non-immune) persons.

The second era of great new opportunity for microbes came with industrialization, initially in late eighteenth-century England; then in Europe, North America, Australia, and beyond; and now in many lower-income countries that have been undergoing industrialization in the late twentieth and early twenty-first centuries. Prior to the advent of industrialization, the human population was mostly rural, with fewer than 1 in 20 persons living in either town or city. When factories arose, and mechanized manufacturing, agriculture, and transport spread for the first time, there were large populations of densely crowded, impoverished, malnourished factory and sweat-shop laboring classes. This, of course, was an ideal “culture medium” for many potentially **epidemic** and endemic infectious diseases: hence the public health scourges of **tuberculosis**, **smallpox**, **measles**, **diphtheria**, pertussis (**whooping cough**), **cholera**, and others.

Tuberculosis (TB) has long been predominantly a disease of the poor and crowded segments of urban-industrial populations. It persists as a scourge in crowded shantytowns and slums around the world. In the early **Industrial Revolution** tuberculosis was rife, and in the nineteenth century it was known as “the white plague.” This disease, which was no respecter of persons and was readily transmitted by coughing, has also provided the stuff of much romance in the history and stories of nineteenth-century Europe.

Miasmas, Germs, and People. The biological nature of the often rampant “crowd diseases” of industrialization was not understood before the advent of the **germ theory** in the 1880s. The prevailing view in the earlier decades of industrialization was that epidemic diseases were spread by “**miasmas**,” foul airborne emanations from dank and dirty soil and rotting organic matter such as **corpses**. Highly visible air pollution from soft coal-burning homes and early factories, which were rarely far apart, seemed to substantiate the notion that “corrupted air” had deleterious effects on the human body. The miasma theory could also explain, for example, why cholera and other such diseases were epidemic in places where the **water** was undrained and foul-smelling.

The record of infectious disease impacts and societal responses is particularly well documented in England. There, miasma theory motivated the epoch-defining sanitary revolution beginning in the mid-nineteenth century. **Edwin Chadwick**, sanitary engineer and utilitarian, looms large in this story with his hugely influential 1842 *Report on the Sanitary Conditions of the Labouring Population of Great Britain*. Chadwick argued that the local miasmatic atmospheric conditions arising from putrefaction and excreta caused the “endemic and contagious diseases” that afflicted the populace, particularly in the poor and crowded sections of London. Disposal of sewage and wastes via public sanitation would rid society of this economically draining miasmatic scourge.

Late in the nineteenth century, germ theory was propounded, drawing on the work of **Louis Pasteur** in France and then **Robert Koch** in Germany. “Contagious” diseases came to be understood as being caused by “germs” via the process of person-to-person “infection”; they did not arise by themselves from miasmatic emanations. The retreat of cholera in England in the later decades of the nineteenth century, as both public sanitation and domestic hygiene improved, gave good corroboration to this ground-breaking theory—a theory that, during the twentieth century, would reshape much thinking, research, and practice within a new “biomedical” frame that would bring more reductionistic insights and perspectives to the study of causation and prevention of infectious diseases.

Food Production and Processing. As the twentieth century unfolded, other aspects of industrialization also began to affect patterns of infectious diseases. In particular, there have been many, and continuing, unexpected consequences of the intensification of food production methods.

The commercialization of poultry production in much of Southeast Asia appears to have contributed to the amplification of the spread, during 2004–2007, of the highly pathogenic H5N1 strain of **avian flu** (“bird flu”). This strain has killed, or prompted owners or authorities to kill, many millions of birds, both wild and domestic. By 2007 it had also infected more than 300 humans, with approximately 200 fatal cases, two-thirds of which were in Vietnam and Indonesia. The actual origin of the new strains of influenza is thought to lie in the small-hold farming practices of southern China and adjoining countries, but the opportunities for wider spread and for zoonotic transmission to humans are multiplied via the industrial-scale production of poultry for urban food markets.

The most notorious and exotic of zoonotic diseases occurred late in the twentieth century in the United Kingdom, when the nation’s “mad cow disease” disaster spilled over into the human population. This disastrous episode arose from the unnatural practice (introduced to accelerate productivity of dairy cattle and growth of beef cattle) of feeding cattle with industrially-treated proteinaceous and energy dense “bovine offal”—scraps of recycled meat, fat, gristle, and offal from slaughtered cattle. This resulted in the surprise occurrence of a “prion” disease that affected the bovine brain. The prion molecule, a type

of rogue protein molecule, has the unusual capacity to “multiply” by inducing normal protein molecules in the brain to undergo copy-cat molecular deformation. This caused cow “madness”—bovine spongiform encephalopathy (BSE)—by rendering the brain tissue spongy. Subsequently, and somewhat against expectations, prions were transmitted to human consumers of beef products in the United Kingdom and caused over 150 fatal cases of a degenerative brain disease called variant Creutzfeldt-Jakob disease (vCJD).

Less exotically, the reported rates of infectious food poisoning have increased markedly in Western countries during the past two decades. Several outbreaks of the potentially lethal toxin-producing *Escherichia coli* 0157 in North America and Europe in the mid-1990s originated in contaminated beef imported from infected cattle in Latin America. Inevitably, in an industrial era, in light of the modern scale of food production and the length of commercial supply lines from source to consumer, there are frequent outbreaks of gastroenteritis (food poisoning) as a result of faults or mishaps in the production and distribution of processed foods.

Concomitants of Industrialization: Infectious Disease Risks from Urbanization; Medical Technologies; Antimicrobial Resistance. The industrial age has entailed the rapid growth of cities as the engines of the modern economy, along with the evolution of a range of new technologies—for transport, workplace automation, health-care facilities, and other purposes. Cities have been described as “highways for microbial traffic.” The relevant features extend beyond the obvious influences of large numbers and crowding upon risks of infection. Urban living also typically entails a loosening of traditional family and social structures, and it allows a greater personal mobility with extended social networks. These features, along with access to modern contraception, have facilitated a diversification of sexual contacts and practices and, hence, the spread of sexually-transmitted infectious diseases (STDs). Around the world, the familiar STDs, **gonorrhea** and **syphilis**, persist widely. In many cities they are increasingly supplemented by chlamydia, herpes viral infections, and now **HIV/AIDS**. Sadly, the growth in sex tourism in today’s increasingly interconnected and mobile world—a form of tourism that capitalizes in an exploitative fashion on the desperation of migration and **poverty**—amplifies the risk of STD **transmission** in many of today’s developing countries. Cities are also the epicenters of the international drug trade and of illicit drug use. Intravenous drug injection has become a major source of spread of infection, including HIV/AIDS and **hepatitis B**.

The discovery of natural **antibiotic** substances in the mid-twentieth century spawned a new era of infectious disease control and a rapidly growing enterprise for the **pharmaceutical industry**. Some evidence of the evolution of bacterial resistance to **penicillin** appeared within a decade of its generalized use in health care. Nevertheless, the range and use of antimicrobials increased rapidly over the next few decades, not just to treat infectious diseases in humans, but also for enhancing the growth of livestock (including, more recently, aquaculture). This increasingly widespread use of antimicrobials has resulted in a serious spread of antimicrobial resistance, entailing threats of localized outbreaks of **hospital**-based “epidemics” of resistant strains of bacterial infections. Over two-thirds of the bacteria that cause hospital-acquired infections are now resistant to one or more of the usual antibiotics used to treat them.

Other modern medical technologies have also facilitated the spread of infectious disease agents. The unhygienic use of hypodermic needles for therapeutic injection can be one vehicle for transmission. Indeed, within the past decade there has been a tragic episode of widespread hepatitis C dissemination in Egypt as a result of the unhygienic use

of needles used for a campaign to control of bilharzia (**schistosomiasis**). Blood transfusion and organ transplantation also pose risks of infectious agent transmission. This furthermore raises the worrying prospect of the possible future entry into humans of occult (hidden) **viruses** via xenotransplantation—that is, organ transplants for humans from genetically bred pigs that naturally harbor a range of viruses.

Meanwhile, industrialization has conferred various benefits for the reduction of infectious disease risks in the health-care setting. Modern autoclaves and sterilizing procedures provide a far higher level of cleanliness in hospitals and clinical settings. Industrial production of medical instruments, diagnostic tools, and other hardware has provided practitioners around the world the highest quality of equipment in history. Likewise, reliance on handcrafted pharmaceuticals has been superseded by their production under standardized and quality-controlled conditions, making them more affordable, safer, and longer lasting. The provision of drugs and the means of administering them in large and reliable quantities made the **eradication** of smallpox and the elimination of **polio** in the United States possible, and they hold the promise of reducing and perhaps eradicating other infectious diseases. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Capitalism and Epidemic Disease; Colonialism and Epidemic Disease; Drug Resistance in Microorganisms; Pesticides; Poliomyelitis, Campaign Against; Public Health Agencies, U.S. Federal; Sanitation Movement of the Nineteenth Century; Smallpox Eradication; Tuberculosis and Romanticism; Vaccination and Inoculation; Venereal Disease and Social Reform in Progressive-Era America.

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ANTHONY MCMICHAEL

INDUSTRIAL REVOLUTION. Industrial revolution is the transformation from agrarian societies to industrialized market economies geared towards **capitalism** and profit making, which implies large-scale production in factories on the basis of new technologies. The origins of the modern Industrial Revolution can be traced back to seventeenth-century Europe, but major modifications of many aspects of life were not felt until the late eighteenth century.

Industrialization is an ongoing process rather than a singular event that triggered subsequent changes. In the Western world three waves of **industrialization** that constituted the Industrial Revolution may be identified: A first wave started with mechanization of eighteenth-century British textile manufacture. It spread to continental Europe and North America. Innovations in that early period included the invention of the steam

engine in 1690 and improvements to the weaver's loom with the result that more linen or cotton cloths could be produced with less human power. A second wave occurred in the mid-nineteenth century with the advent of large-scale steel production, railroads, steamboats, and steamships, which also promoted a transportation revolution. The introduction of the Bessemer process for steel making in the 1850s and new furnaces in the 1870s allowed the inexpensive and efficient production of a previously rare and precious product. A third wave of industrialization set in after World War II (1939–1945), spreading older and innovative industrial organization and processes that affected the whole world. Yet the Industrial Revolution had been an international phenomenon from the beginning, as the mechanized production process depended on functioning trade relations with countries all over the world from which raw materials were procured and to which products were sold.

From the beginning there existed an awareness of health hazards for human beings in the new production processes. In 1700 the Italian professor of medicine, Bernardino Ramazzini (1633–1714), published a book on the influences of particular trades on health, which was quickly translated into English. England pioneered in showing early concern about the “Sanitary Condition of the Laboring Classes,” as indicated by **Edwin Chadwick’s** 1842 report with that title. A few years earlier, the English **physician** Charles Turner Thackrah (1795–1833) had examined death rates in certain trades in Leeds. In the nineteenth century, a general concern with health problems as a consequence of **environmental** and living conditions—including **air** pollution, inadequate sewage disposal, tainted **water** supplies, poor ventilation, and crowded quarters—particularly in urban areas, also led to a growing interest in occupational diseases.

The combination of demand for labor in the new factories and improved infrastructure resulted in the migration of people from smaller communities to industrial centers. It also meant increasing emigration from Europe to America. The new means of transportation sometimes had positive effects. For example, the replacement in the mid-nineteenth century of sailing vessels with steamships not only shortened transatlantic crossings, but it also meant that travelers no longer had to wait for a suitable wind in unhygienic conditions that might expose them to new diseases. Then again, the increasing mobility also brought the danger of importing diseases: when immigrants arrived at U.S. ports such as Ellis Island in New York they were subjected to health examinations, and a considerable percentage were returned to their home countries.

Because industrial production was geared towards making profit, the health and safety of workers were of minor concern to factory owners, particularly because the causes of infectious diseases were unknown until the late nineteenth century. Workers labored in steel plants under harsh conditions twelve hours a day. Heat, fumes, and physically exhausting work provided numerous health hazards that resulted in greater susceptibility to disease and short life expectancies. Often urban families took boarders into their already crowded living quarters to supplement their income. Hence, in the industrial centers, overcrowded, ill-ventilated, and unsanitary living and working conditions favored the spreading of infectious diseases such as **tuberculosis**, **typhoid**, and **cholera**, which in early modern times had replaced the **epidemic** scourges of the Middle Ages.

Industrial or occupational medicine developed in the context of **industrialization** and discoveries in medical science in the late nineteenth century. For instance, the awareness of microorganisms that caused and spread disease led a new generation of middle-class people to educate the working class about sanitary living conditions and healthy nutrition.

Starting with Toynbee Hall in a slum in East London in 1884, college and university graduates initiated the settlement house movement. It soon became an opportunity for women to enter the professional sphere as social workers. The best-known institution in the United States was Hull House in Chicago. One of the residents was Alice Hamilton (1869–1970), a physician and pioneer of industrial medicine. Studying typhoid fever in Chicago around 1900, Hamilton pointed out the connection between disease and sanitation and called for public health reforms. In 1919 she became the first woman to earn professor rank at Harvard University.

However, with the development of bacteriology in the late nineteenth century, the focus of attention shifted to **germ theory of disease** and its implications for public health. For example, researchers studied pulmonary ailments that were caused and transmitted by germs in dusty air. Other causes for occupational diseases were regarded as less significant in the general excitement over the discovery of microorganisms. Still, infectious diseases such as cholera had declined in the Western world by the middle of the twentieth century. This decline was the result of new realizations, for example, that water containing germs caused the disease, and thus proper sewage would prevent spreading of the disease. Yet in the new and more hygienic surroundings, in which mild, routine childhood exposure to certain germs was greatly reduced, “cleanliness diseases” such as epidemic **poliomyelitis** emerged. *See also* Hospitals in the West to 1900; Pesticides; Pharmaceutical Industry; Poverty, Wealth, and Epidemic Disease; Trade, Travel, and Epidemic Disease; Urbanization and Epidemic Disease.

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ANJA BECKER

INFANTILE PARALYSIS. *See* Poliomyelitis.

INFLUENZA. In humans, influenza is a potentially lethal respiratory illness caused by a large number of closely related **viruses** of the family Orthomyxoviridae, whose genetic material is RNA (ribonucleic acid). Influenza viruses can infect birds as well as humans and other mammals. Influenza viruses evolve rapidly, resulting in new outbreaks of disease on a regular basis. Depending on the strain of the virus and the host species, influenza infections range from the benign to the highly communicable and pathogenic. There are three major categories of influenza viruses: A, B, and C. In humans, all three viruses can cause respiratory illness. Type C influenza can infect humans and swine; type B infects only humans; and type A can infect humans, swine, and other mammals, but is endemic in both domestic and wild birds. Type A influenza viruses also mutate much more rapidly than do types B and C. Because they evolve rapidly and are capable of cross-infecting different species, type A influenza viruses are responsible for new and highly contagious forms of the disease and are therefore of great significance from the perspective of public health and **epidemic** disease.

In birds, influenza ordinarily infects the gastrointestinal system, but in humans and other mammals it infects the respiratory system, making it very transmissible via coughing and sneezing. The disease incubates for approximately one to five days after exposure and may be transmitted before recognizable symptoms are apparent, making it one of the most contagious human diseases known. In this form, influenza often resembles a very severe cold. Symptoms include fever, sore throat, coughing/sneezing, and muscle aches but can also include headache, dizziness, vomiting, and diarrhea. It is therefore very difficult to diagnose influenza by symptoms alone.

Influenza often is not a direct cause of death but instead tends to encourage secondary **bacterial** infections by destroying the cells that line the nose, throat, and lungs and by weakening the immune system. These bacterial infections can lead to pneumonia, which is very often the direct cause of death during influenza outbreaks. Influenza death via secondary bacterial infection is most common in those in poor health or with weak immune systems; thus, the victims in most flu epidemics tend to be the very young and the elderly. In rarer cases, the virus can trigger an excessive immune system response, comparable to an allergic response, which causes massive damage to the lungs. Known as acute respiratory distress syndrome (ARDS), this condition can very quickly lead to death. In contrast to bacterial pneumonia, this condition occurs most often in relatively young people with strong immune systems. Influenza is seasonal, affecting the greatest number of people during the winter months. According to the **Centers for Disease Control and Prevention**, a typical flu season in the United States results in the hospitalization of approximately 200,000 people, of whom about 38,000 die. Between 1 and 1.5 million people worldwide die of the disease on an annual basis.

Structure. Viewed under very high magnification, the influenza virus resembles a spike-covered ball. The ball contains the viral RNA, which occurs in eight segments that are analogous to chromosomes in higher organisms. These eight segments produce a total of nine proteins, some of which structure the virus and some of which copy the viral RNA once in a host cell. The most common “spikes” on the surface of the virus are made of a protein called hemagglutinin (H). This protein allows the virus to attach itself to, and then enter, cells of the host organism. The other protein “spike” on the surface of the virus is neuraminidase (N). This protein is responsible for allowing newly created viral particles to break free from the surface of their host cells. These two proteins serve as the primary antigens by which the immune system of the host organism recognizes the virus. Currently 16 different strains of hemagglutinin proteins and 9 different strains of neuraminidase proteins have been identified.

The number of these two surface proteins provides a general naming system for flu viruses. For example, the virus that caused the devastating **influenza pandemic of 1918–1919** was covered with hemagglutinin 1 and neuraminidase 1 proteins, and is therefore known as H1N1. Avian influenza, which is currently a major public health concern, has the hemagglutinin 5 protein and is therefore H5N1. Historically, humans have been most susceptible to viruses with the H1, H2, and H3 antigens, whereas all 16 types are capable of infecting birds. There can also be significant variation within each type of viral surface protein, so in addition to the 144 major strains of influenza (16 H types x 9 N types yields 144 possible different HN combinations) there are hundreds of sub-strains. For example, a recent survey of influenza types among domestic birds in Guangdong province of China revealed more than 500 different strains of the virus, including 53 subtypes of the H9 strain. Among research and medical professionals, a more precise naming system is used to account for these sub-strains.

Mutability and Variation. The enormous number of influenza strains and sub-strains results from the extraordinary mutability of the virus, which ensures that novel forms and combinations of the HN surface proteins (antigens) emerge year after year. Two properties of the influenza virus account for this variation. The first is “antigenic drift,” which results from imperfect copying of the virus’s RNA genome. Influenza RNA is a single-stranded molecule, unlike DNA, which has two complementary strands, and therefore two copies of the information contained with the genetic sequence. This allows the cellular machinery to check one copy against the other and make corrections where necessary, resulting in very accurate copying of the genetic message. Organisms with single-stranded RNA genomes have no such mechanism for correction, and consequently the copying of their genetic messages during replication is much more error prone. In fact, relatively few of the copies made of an influenza virus will have the exact same genetic sequence, which has led researchers to think not in terms of populations of identical viruses, but instead in terms of swarms of closely related, but different, viral copies. Any of these copying errors has the potential to lead to a viable mutant sub-strain of virus slightly different from the parent strain. When such changes occur in the surface proteins of the virus, the immune system of the host organism may have a difficult time recognizing the new antigens, and the process of antigenic drift has taken place. This genetic variation drives influenza virus evolution at an extraordinarily accelerated rate—the virus evolves approximately 1 million times faster than the DNA-based life forms it infects.

Genetic reassortment is the second process that drives influenza mutation by splicing together genes from different influenza viruses, leading to the phenomenon known as “antigenic shift.” Genetic reassortment results from the coinfection of a host cell by more than one strain of influenza virus. During the process of copying and assembly of the viral components, there is sometimes an intermingling or reassortment of the eight RNA segments from the different viruses. When this happens, a new strain of hybrid virus can result. Such hybrids possess features of both “parent” viruses, but in a novel combination. Since viruses from different species can coinfect the same cell, reassortment offers the possibility for new strains of virus to cross the biological barrier between species. Reassortment is therefore capable of producing dramatically new populations of viruses in a short time. Thus, for many years researchers believed that reassortment/antigenic shift was responsible for all new epidemic forms of the disease, but recent research has shown that this is not accurate. In 2005 researchers working on the virus responsible for the global influenza pandemic of 1918–1919 demonstrated that it gained its virulence via simple genetic mutations (antigenic drift) instead of reassortment and recombination of human and bird influenza genes (antigenic shift).

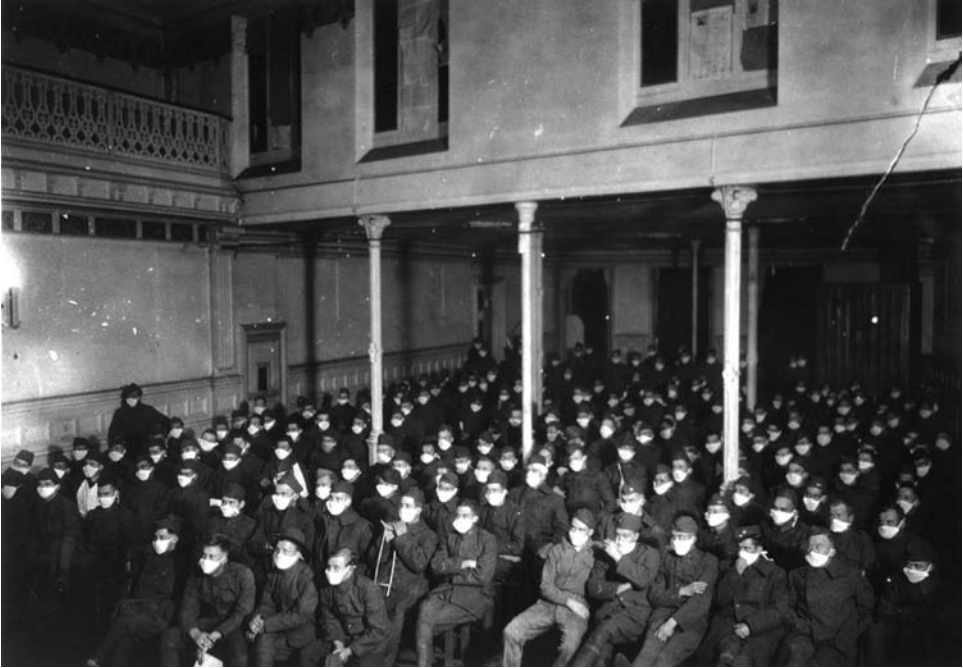
History. The rapid emergence of new strains of influenza virus enables the disease to reoccur on a yearly basis. In most years, the new strains of virus that infect human populations are not especially virulent, making the annual flu season somewhat manageable and predictable. However, extremely lethal strains also emerge regularly, albeit unpredictably. These strains result in global pandemics whose consequences dwarf those of the regular flu season. The most devastating pandemic in history was the 1918–1919 flu pandemic that probably killed 50 million or more people in about a year, 675,000 of them in the United States. Inaccurately remembered as the Spanish flu, the origins of this strain are not yet certain, although recent research suggests that it may have emerged at Army bases in the United States. It spread rapidly thanks to its own infectivity as well as the movement of soldiers and populations accompanying the end of World War I (1914–1918). The virus

was a strain of the H1N1 type and was unique in that it killed a large percentage of its victims directly via ARDS. Public health services in developed countries, which to that point had been making dramatic progress in the reduction of infectious disease, were helpless. They did not have the technical ability to isolate and identify viral pathogens, and the presence of secondary bacterial infections in the lungs of some (but not all) of the victims confounded the efforts of physicians to attribute the pandemic to a single causal agent. The virus was not identified until the early 1930s, and it was not until the post–World War II era that the mechanism of viral infection began to be unraveled. There have been two major global pandemics since 1918: the “Asian” or “Chinese Flu” (H2N2) of 1957–1958, which killed approximately 2 million people globally, and the “Hong Kong Flu” (H3N2) of 1968–1969, which killed about 1 million people.

In early 1976, David Lewis, a healthy 18-year-old private in the U.S. Army, died of influenza after an all-night training hike through winter weather. By February, public health officials were convinced that the strain that killed Lewis was very similar to the 1918 strain. Fearing a repeat of that pandemic, they convinced President Gerald Ford (1913–2006) to launch a costly and much-publicized program to vaccinate all Americans against this strain. Because new strains of influenza typically originate in their bird hosts and cross the species barrier to humans using pigs as intermediaries, the strain was identified in pigs and became popularly known as “Swine Flu.” The vaccine program was delayed by the reluctance of the insurance industry to underwrite it. By the time that trials of the new vaccine began in late summer, no new cases of the disease had been reported. The trials demonstrated that the vaccine was effective in adults but less so in children, raising concerns about its overall effectiveness. By the end of the year no further cases of the flu had emerged, but in a small number of patients the vaccine had contributed to the development of Guillain-Barré syndrome, a neurological condition that is potentially fatal. That December the **vaccination** program was ended, having become a public relations catastrophe for the presidency as well as for leading public health officials.

Treatment. As with all viral diseases, there is no effective **antibiotic** treatment for influenza, although there is currently an effective class of antiviral agents called neuraminidase inhibitors that can reduce influenza symptoms if taken after infection and may reduce likelihood of infection if taken as a preventative measure. The most commonly available is oseltamivir, available commercially as Tamiflu. The most effective route for combating influenza remains vaccination. Each year researchers must gauge which new influenza strains are most likely to infect humans; to do this they analyze strains that have already moved into swine populations, as these are the most likely to make the jump to humans. It takes several months to develop, test, and market a new vaccine. To ensure maximum efficiency, the annual flu vaccine is designed to confer **immunity** against the three most likely flu strains.

Avian Influenza. In 1997 the H5N1 strain of influenza began to receive widespread attention when it led to an unusually destructive disease in its bird hosts. It quickly became known as avian influenza, or “bird flu” for short. The virus was able to spread to humans where it also was very lethal—in this first outbreak, 18 human cases were documented, of which 6 led to death. Several sub-strains of the virus have caused subsequent outbreaks among birds and humans. As of August 2006, over 220 million birds had been either killed by the virus or deliberately slaughtered by people to end localized outbreaks. As of April 2007, there had been 291 laboratory-documented cases of H5N1 in human beings in 12 different countries; 172 of these cases (59 percent) have been fatal. This is an



U.S. Army Hospital Number 30, Royat, France. Patients at moving-picture show wear masks because of an influenza epidemic, 1918. Courtesy of the National Library of Medicine.

exceptionally high mortality rate for human influenza, exceeding by far that of the 1918 pandemic strain. The virus has not yet demonstrated the ability to be transmitted easily from person to person, although one case has been documented. Should the virus evolve in such a manner that it becomes easily communicable among people, it would become a public health threat of the highest order. Currently, it is impossible to predict when or if such a change in the virus might take place.

Future Research. There are many questions about influenza waiting to be answered. Understanding the relationship between the surface antigens and human disease, especially their role in transmission, is of great importance, as it may allow us to better anticipate the emergence of dangerous sub-strains. There is also a great deal of current research on new types of anti-viral drugs. Relying on one class of anti-viral drugs, the neuraminidase inhibitors, is risky as it is very likely that resistant forms of the virus will emerge. Finally, much attention is being paid to vaccine research. Here research is split between developing new vaccines and new processes for manufacturing vaccines. The goal is ultimately to develop vaccines that can be produced very quickly and can confer immunity against a range of potential viral sub-strains. *See also* Drug Resistance in Microorganisms; Influenza Pandemic, 1889–1890; Influenza Pandemic, 1918–1919; Severe Acute Respiratory Syndrome (SARS).

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JEFFREY LEWIS

INFLUENZA PANDEMIC, 1889–1890. During the summer of 1889, a severe **influenza epidemic** was reported in the Russian Empire's impoverished central Asian city of Bukhara (in modern Uzbekistan), to which destination Russia had just completed 900 miles of the Trans-Caspian Railroad. The associated high mortality of 5 to 8.75 percent (the norm is around 2 percent) suggests that if flu was involved, there may have been a coexisting disease such as **malaria**. Other sources give the **pandemic's** origin as western Siberia and northern Kazakhstan. By October the illness had traveled to Moscow and St Petersburg and thence into Poland, as well as along the highways, railroads, and rivers into Finland, Hungary, southern Russia, Germany, and Austria. In Western Europe it was named "Russian flu," but the Russians believed it was a **miasma** that had been wafted on pestilential breezes into the Empire from China, following the flooding, in 1888, of the Yellow River (Huang He), in which up to 2 million humans and animals were drowned. They called it the "Chinese cold." A popular French theory maintained that the Chinese cold was transformed into influenza by Russian peasants living in filth and squalor.

The citizens of Paris, London, and Edinburgh were laid low with flu by the end of October and into March the following year. Steamship traffic carried influenza across the Atlantic to the United States where, by mid-December 1889, it was reported in New York and Boston. By January it had crossed the Midwest and entered Canada. Simultaneously, it passed through the Mediterranean into North Africa, and via Atlantic and Pacific seaports (dock workers were often its first victims) into South Africa, South America, Japan, the west coast of the United States (January), China via Hong Kong, Singapore (February), India, Australia, New Zealand, and Indonesia (March). The secretary of the Illinois State Board of Health observed that in just three months influenza had encompassed the globe, whereas in 1843, just prior to the railroad and steamship age, its journey to and through the United States had taken six months. There were exceptions. Remote Kashmir was not affected until December 1890. Similarly, influenza's progress

along the circuitous **trade** routes of central Africa was slow, and it eventually reached British Nyasaland (Malawi) in September 1890. To black Africans, who claimed never to have experienced influenza, it was a disease of white colonization. Indeed, **colonialism** and globalizing trade links increased the volume and speed of international communications and therefore its spread. Throughout the world, the pattern of transmission was generally from large cities to small towns and thence into rural districts.

Most reports suggest that the largest group affected by influenza were those aged 15 to 40 years, followed by the elderly, who had perhaps gained some immunity from the pandemics of the 1840s but were in any case less socially active, and then children and infants. Most deaths, however, were among the elderly.

In Europe, the 1889–1890 influenza was the greatest single killer epidemic of the nineteenth century, claiming 270,000 to 360,000 lives, although the overall mortality rate was only 1 percent. In Britain, influenza interrupted the decline in adult deaths from infectious diseases that had for a generation accompanied rising living standards and sanitation reform. Deaths in London from **whooping cough**, pulmonary **tuberculosis**, bronchitis, **diphtheria**, **typhoid**, and **measles** were higher during 1889–1890 than the previous ten-year average, suggesting that influenza lowered resistance to other infections. Nevertheless, influenza killed by far a smaller percentage of Londoners (0.5 per 1,000) than Parisians (2.5 per 1,000) or the people of Lisbon (1.6 per 1,000). Influenza was also considered to be a major cause of nervous and **psychological** disorders by acting as a “devitalizing agent.” Descriptions of influenza sequelae included “depression,” “shattered nerves,” “neurasthenia,” and “despondency.” During 1890, for example, an unprecedented 140 melancholics afflicted with influenza “poison” were admitted to Scotland’s Royal Edinburgh Asylum. Coroners also cited influenza as a reason for “temporary insanity” in cases of suicide. Across Europe, rates of suicide (mostly male) and attempted suicide (mostly female) rose during the 1890s. In England and Wales, there was a 25 percent increase in suicides between 1889 and 1893. Paris witnessed a 23 percent rise during 1889–1890 compared with the average, and there were also increased rates in Germany and Switzerland.

The pandemic disrupted manufacturing, public services, and transport as workers fell sick simultaneously (the incubation period is one to four days). In Massachusetts, about 27 percent of the workforce in affected establishments was absent for an average of five days per employee. In London, during the Christmas mail rush, 1,346 post office workers (about 15 percent) went sick for an average of 15 days each. Two died. Next door to the city’s main post office was St. Bartholomew’s Hospital, which treated about 25 flu victims during the outpatient hour every working day throughout January and February. Winter sickness rates among the London Metropolitan Police were four times higher than usual, with 1,660 out of 14,000 (12 percent) succumbing to influenza in January alone. Even British Prime Minister Lord Salisbury (1830–1903) took to his bed. Among the eminent individuals who died of flu were the poets Robert Browning (1812–1889) and Alfred Lord Tennyson (1809–1892), and Queen Victoria’s (1819–1901) grandson, the Duke of Clarence (1864–1892). Post-influenza lassitude left many people unfit for work, and in an unprecedented move, Pope Leo XIII (1810–1903) granted a dispensation in the matter of abstinence to people suffering from flu during the Church’s penitential season of Lent. Sick pay for British workers was not universal, and those who were not covered or who were inadequately covered by insurance were often unable to pay their doctors’ fees. Indeed, local benefits clubs sometimes collapsed under the payouts for influenza and associated

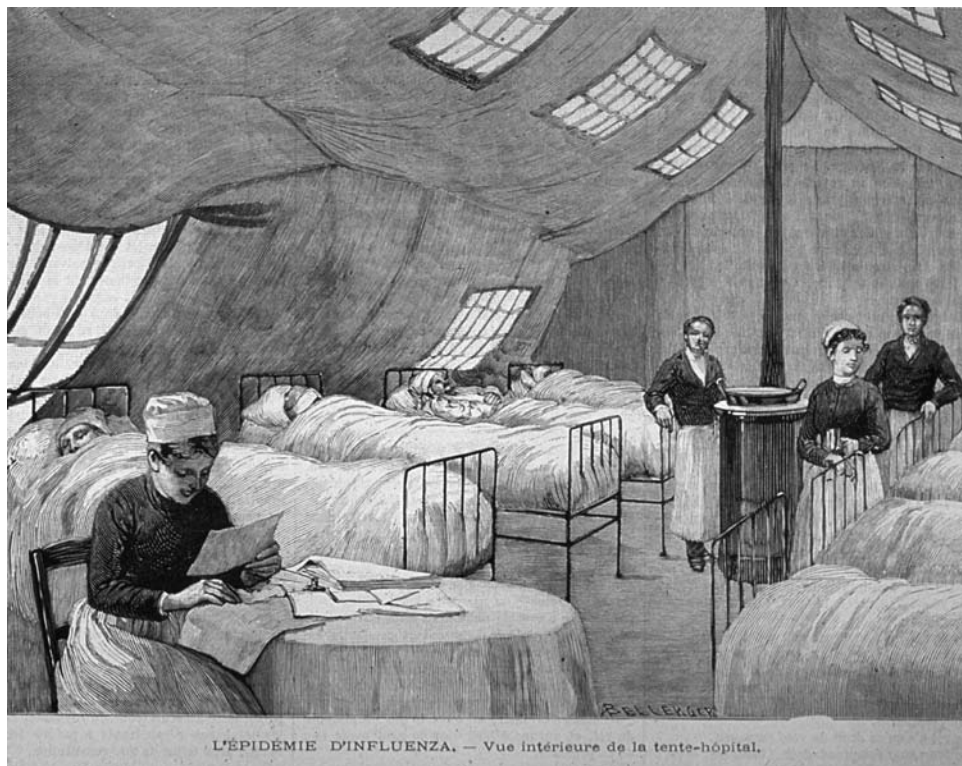
illnesses. Financial problems were enough to induce feelings of despair in poor and mid-dling workers even if suicide was not actually contemplated.

Physicians used the word “**virus**” to explain the immediate cause of influenza, although only in the sense of its being a hypothetical pathogenic microorganism. Many combined the new Pasteurian **germ theory** with traditional ideas about **contagion**, miasmas, constitutional disturbance, atmospheric influences, and local **environmental** conditions. A typical viewpoint, suggested by the physician to the Edinburgh Royal Infirmary, was that the influenza microorganism existed in all parts of the world but only under certain conditions did it become sufficiently active to cause severe symptoms in humans and animals. Like other doctors in the northern hemisphere, he commented on the unseasonably warm winter of 1889–1890, although influenza prevailed independently of season, climate, and weather, appearing in the cold of Russia and the heat of India. Others invoked high and low pressure atmospheric gradients, varying ozone levels, electrical storms, recent earthquakes, and volcanic eruptions across Europe, the United States, and the Pacific as material energizers of dormant germs, spores, or atmospheric “fomites.” Once the germs had been activated, according to these theories, they turned contagious and infectious and were able to pass from host to host in the usual way. Less plausible ideas about comets and meteors carrying poisonous gases from outer space nevertheless appeared in medical literature as well as the popular media.

Some military and naval surgeons believed that influenza was the tropical disease called **Dengue** or breakbone fever, modified by climate. The symptoms of aching joints and limbs were similar, and those who had suffered Dengue in the past believed they were experiencing relapses. The concept of vector-borne transmission, influenced by the recent work of **Patrick Manson** on mosquitoes, nematode worms, and elephantiasis, was proven immaterial in areas where higher than normal levels of **insects** were observed or where crop yields were poor, indicating infestation. Migrating birds were also proposed as carriers of the influenza agent, and in some locales there were excess deaths among fowls, cage birds, cats, dogs, and particularly horses. Epidemics of equine (“horse”; type A) influenza or “pink-eye,” a frequently fatal respiratory disease in horses, were observed during the early 1890s in Glasgow, Lisbon, and Warsaw, and there was a severe outbreak in St Petersburg in 1889, preceding the influenza. A century later, in 1989–1990, horses in northeast China were stricken with a similar respiratory disease. Mortality in some herds reached 20 percent. The causative virus was classified as an influenza H3N8 subtype that originated in birds.

Medical opinion, in general, was converted during the course of the 1889–1890 pandemic from a belief in the miasmatic origin of influenza to its being a communicable disease. The German bacteriologist Richard Pfeiffer (1858–1945; **Robert Koch**’s son-in-law) announced in 1890 his discovery of the influenza organism although attempts at replicating flu symptoms with “Pfeiffer’s bacillus,” and at producing an anti-flu serum, proved unsatisfactory. Nevertheless, “Pfeiffer’s bacillus” was still being discussed in the bacteriology literature of the 1920s. It subsequently proved to be *Haemophilus influenzae*, a bacterium implicated in some of influenza’s secondary infections. Proof of the viral nature of influenza did not occur until the development of the electron microscope in the 1930s.

Most physicians understood that the pandemic influenza of 1889–1890 was more virulent than ordinary sporadic influenza but that there were no specific treatments to shorten its duration. Bed rest, antipyretics, purgatives, and bland food were the usual recommendations. A plethora of patent remedies, preventives, and fortifying tonics appeared



Interior view of a supplemental tent hospital during the 1889 influenza pandemic, showing a nurse sitting at a table, several beds with patients, and nurses standing near a stove. Illustration from *L'Illustration*, January 4, 1890. Courtesy of the National Library of Medicine.

on grocery and pharmacy shelves, and it is likely that many sufferers resorted to these rather than consulting a doctor. Public opinion was against enforced **quarantine**, which was seen as official meddling with everyday business to contain what most regarded as a minor illness. In Edinburgh, where an isolation hospital *was* provided, not a single patient was admitted throughout the epidemic. Edinburgh physicians were disappointed at being denied an opportunity to study the disease, particularly because a scientific committee appointed by the Royal College of Physicians had been established for this purpose. The pandemic was extremely well documented worldwide, with many countries publishing detailed studies of their experiences. Maps and statistical tables were compiled, and this reflected the growing preoccupation of nations with their own vital statistics. Moreover, the growth of scientific medicine had resulted in the increasing publication of medical journals, which encouraged the reporting and international dissemination of such studies.

Influenza epidemics occurred in many countries during much of the decade following the 1889–1890 pandemic and were often associated with higher mortality than the initial pandemic. For example, the Irish death rate at 19.4 per 1,000 during the 1892 wave was the highest since registration began in 1864. Excess mortality in Chicago rose from

1,200 in 1890 to 2,000 the following year. In the northern English town of Sheffield, fewer than 5 people died of flu during one week in March 1890 compared with over 100 during the same week in 1891. This suggests that minor viral mutations (“drift”) of the pandemic strain continued to circulate around the world. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Demographic Data Collection and Analysis, History of; Human Immunity and Resistance to Disease; Influenza Pandemic, 1918–1919; Public Health Boards in the West before 1900.

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CAROLE REEVES

INFLUENZA PANDEMIC, 1918–1919. **Influenza** is a viral disease with a very high morbidity rate. Virulence varies from outbreak to outbreak because of the constantly shifting nature of the **virus**. Like all viruses, it reproduces itself by penetrating the cell of a host and using the host’s genetic material. The influenza virus, like other RNA viruses, is particularly adept at mixing its own genetic material with the host’s, reconstructing its own so that when the invaded cell bursts (the cause of being ill), large numbers of new variations are released. Most are not viable, but a few not only are but also have new biological characteristics. The result is that eventually, sometimes quickly, the human immune system no longer recognizes the virus, and the illness again gains the potential to become a pandemic. It also has the potential to be more deadly than previous variations. All the dangerous possibilities merged in 1918. The pandemic that began in the spring and produced two subsequent waves—fall 1918 and spring 1919—spread quite literally over the entire planet and, although records are at best incomplete, killed at least 40 million people.

The Influenza Pandemic of 1918 to early 1919 was a global event and cannot be accurately understood in any other context. To isolate it geographically for study is to understate its presence and impact. There was nowhere on earth that boasted even a small collection of human residents who did not suffer from influenza in 1918–1919. Although there are good local studies, there is, as yet, no satisfactory global history of the pandemic.

The death count is also less than satisfactory. The longtime common assertion of about 20 million deaths over the 46 week period of the pandemic is significantly low. That figure was usually credited to Edwin O. Jordan’s 1927 study *Epidemic Influenza*, one of the first scholarly studies of the pandemic. As more was learned, it became increasingly clear that Jordan had no solid statistics for what might today be called the Third World. The illness was everywhere—explorers at the pole isolated for six months got sick. In fact, one pathologist suggests that fully half of the human race was infected. Although it is sometimes still

seen, Jordan's estimate has been revised upward to the point that many now regard doubling it to be appropriate.

Even doubling the number may not be enough—though we will never actually know with any certainty. Unfortunately, records were not kept very consistently even in developed states. The Atlanta city fathers, for instance, were very concerned about the healthful image of their city. Furthermore the annual Southeastern Fair was held in October. The fair was both a money-maker and an important public relations event. Local businessmen were concerned about precautionary measures that closed places of amusement or required gauze masks (a common but actually worthless precaution) in public places. Neither they nor the city government's leaders wanted either the fair closed or attendance—normally drawn from all over the region—to be reduced by health concerns. They dealt with the situation by underreporting. Perhaps this was not as cynical and self-serving as it seems. In Atlanta the summer wave of the disease had been mild (almost nonexistent) and Grady Hospital—the Atlanta public facility—was closed to influenza patients during the fall wave as a result of the impact of the disease on its staff. Thus information about the local situation may have been obscured. Wishful thinking could have done the rest. On the other hand, the international horrors of the disease were known, and soldiers at Atlanta's Fort Gordon were suffering badly. By the first week in October, local civic groups had made 100,000 masks for the men at the fort. By the second week of the month, cases at the base had risen to 2,941. Although some precautionary closings were ordered, the fair was exempted, and city health officials, including Dr. J. P. Kennedy, founder of the Atlanta City Health Department, insisted there was no **epidemic** in Atlanta. By the middle of the month they had acknowledged only 2,500 cases and 81 deaths. Falling back on the **race** card, they also implied that the worst of what little problem there was could be found in the parts of the city populated by African Americans. Actually, African Americans did not suffer a disproportionate number of cases. By the end of the month, the City Council on the advice of Dr. Kennedy overruled the Board of Health and canceled the closing orders. The fair went on with historic success—setting an attendance record. The city failed to submit the required annual health report for 1918 to the state. A comparison of the actual official reports to an apology from the telephone company in which poor service is attributed to the number of sick operators seems to indicate that telephone operators were far and away the worst hit group in Atlanta. A different conclusion might be reached from one Atlantan's recollection that people “were dying like leaves falling off the trees.”

The story of Atlanta illustrates the unreliability of records. It is safe to say that the pandemic killed more Americans than World Wars I and II, Korea, and Vietnam combined, but it is much less safe to say exactly how many more—and this confusion reigned in a relatively well-developed society with, for the day, good communications and health care and little disruption as a result of the **war**. In Europe, particularly eastern Europe, the impact of the war was enormous. In many parts of the rest of the world, there was little health care and little infrastructure for meaningful reporting of mortality let alone morbidity.

Typically influenza causes high fever, body aches, and malaise with respiratory distress in only a minority of victims. It is a relatively minor disease. The first wave—there are typically three—became obvious in June 1918. It was mild, though quite infectious, and was not much noticed until it swept through Spain, when it gained the tag “Spanish Influenza.” It probably started in Central Asia with infections in swine or fowl—another

typical element of influenza—though the mildness meant that it had spread too far to be very effectively tracked before it was noticed. Other theories have abounded since 1918. As noted above, some recent scholarship suggests that the key mutation and the first outbreak were at Fort Riley, Kansas, in March 1918. It appears the disease was spread by military personnel, who did, in fact, move around the country and world that spring. There are, however, also records of scattered pockets of an unusually virulent “flu” in 1917. A 1918 article in the British medical journal *The Practitioner* went so far as to blame the Germans by attributing the disease to **corpses** rotting at the bottom of the sea poisoning seafood or causing some miasma to bubble up and poison the ether. However improbable this miasmatic theory is, it is not unusual for the era of the pandemic. Whatever the origin, the infection was clearly spread by wartime transport. The first wave caused some disruption. Absenteeism at defense plants rose and battle plans had to be adjusted. Both sides were hit at once, however, so neither in June 1918 nor later could any army take much advantage of the other’s disability. By the end of the summer, the malady seemed to be gone.

The second wave came in the mid- to late fall. It too was highly infectious (and the degree of resistance from June attacks did not seem to be as high as might be expected), but it was much more deadly. In the fall and subsequent late winter waves, the virus had a tendency to cause lesions in sufferers’ lungs, which tended to produce pneumonia. The worst cases soon showed signs of cyanosis, which almost always meant death. With the complication of pneumonia, the death rate may have reached 20 percent. Again available statistics may be inaccurate. A block study conducted by the British Ministry of Health right after the war ended showed that fewer than half of the mortal cases in England were attended by a health-care worker—even a **nurse**. Thus questions about diagnoses, symptoms, and mortality are going to remain. And how much less likely was a very sick person to see a **doctor** or nurse in Nigeria or Indochina, for instance, than even in wartime England? The third wave, early in 1919, was more like the second than the first, though it was neither as infectious nor as deadly (there appears to have been more resistance from second to third than from first to second). For most people, of course, “flu” meant 10 days of misery and then recovery, commonly with some attendant depression. The latter symptom, historian Alfred Crosby asserts, afflicted U.S. President Woodrow Wilson (1856–1924) as he tried to cope with the wily David Lloyd George (1863–1945) and Georges Clemenceau (1841–1929) at the climatic point of negotiating the Paris Peace Settlement that ended World War I.

There was another oddity about the 1918 influenza mortality. A graph of a pandemic’s mortality according to age usually looks roughly like a fishhook. There is a relatively high rate of death among the very young. This declines steadily with age through about 50 and then steadily increases, peaking among the very old. Such a graph for 1918–1919 is almost exactly turned over. It shows a relatively high death rate among the very young and then a steady increase with age peaking in the mid-30s and then decreasing with age. The very elderly were surprisingly safe. In fact, the Ministry of Health’s statistics indicate that an 80-year-old Englishman was less

A DITTY ON THE FLU (1919)

If we but knew
The cause of flu
And whence it comes and what to do,
I think that you
And we folks too
Would hardly get in such a stew
Do you?

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likely to die of influenza in 1918 than in a normal year. This pattern held throughout the world. There was some variation in the age of peak death rate, but it was always in mid-adulthood. Thus, the demographic impact of the pandemic was maximized, for the worst cases and most deaths were among those in their most productive span of years. It was complementary to the trenches, though much worse of course because the war only took about 10 million lives.

Today there is some explanation for this unusual virulence and odd age pattern of mortality. The unusual virulence of the virus caused the immune systems of youthful, strong victims to overreact. This defensive reaction caused the lungs to fill with fluid and froth, leading to death. In 1918, however, isolation of viruses was more than a decade away, and although some doctors speculated about a filter-passing organism, the disease was commonly but mistakenly blamed on Pieffer's bacillus, which was quite frequently found in those afflicted. By the time viruses could be meaningfully studied, the influenza virus had evolved to a point that the unusual symptoms were no longer found in the infected. More recently it was realized that bodies from 1918 buried in the permafrost might harbor viable examples of that era's version of the virus. In the 1980s it was felt that finding and culturing the virus was more dangerous than it was worth.

In the twenty-first century, with the ability to delineate DNA and RNA sequences, the fear of the virus has taken a backseat to the possible gains from studying it. Expeditions have been mounted to exhume bodies, isolate the virus, and study it. In 1998 scientists at the Armed Forces Institute of Pathology mapped the genetic makeup of the 1918 virus.

The people facing influenza in 1918 had little to improve their morale. Most of those infected had aches and fever that worsened, peaking in three to five days and abating in eight to ten. Patients were then urged to stay home for several extra days because of a pattern of relapses observed among those who returned to normal routines too quickly. But more dramatic cases frequently appeared. In Chicago a class of school children seemed healthy, put their heads on their desks, and were prostrate by lunch. Shoppers collapsed on the street and were dead before they reached the hospital. Fear, even terror, was the result, but there was little an individual could do.

Public health authorities took precautionary measures in many places. Authorities or owners closed gathering places—theaters, cinemas, schools, places of entertainment, and public transport systems. Masks—actually useless—were distributed. Although the disease continued to spread to every part of the planet, surely keeping people apart reduced the level of infection—if such isolation could be sustained. As in Atlanta, many local authorities did not sustain it; more commonly, people found that they had to go to work, and public transportation was their only means of doing so. Employers were not necessarily sympathetic to weeks—even unpaid weeks—off the job.

The impact of the pandemic was enormous. During the 46 weeks of its ravages, 47 percent of deaths in the United States were caused by influenza or its complications. At the Cook County Hospital in Chicago, the death rate for influenza during the pandemic was 39.8 percent. The rate for hospitalized cases in Frankfurt, Germany, was 27.3 percent. Reports from Africa indicated whole villages had been depopulated. Eskimos in Alaska also saw whole communities die. Recent estimates of deaths in India approach 20 million—long the total given for the entire planet. Although it is probable that the Black Plague of the fourteenth century killed a greater proportion of the human species, more people died in the influenza pandemic of 1918–1919 than from any other single outbreak of disease in history. **AIDS** seems virtually certain to surpass the total, but the AIDS epidemic

has taken more years to do so than there were months in the 1918–1919 pandemic. See also Contagion and Transmission; Influenza Pandemic, 1889–1890.

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FRED R. VAN HARTESVELDT

INOCULATION. See Vaccination and Inoculation.

INSECT INFESTATIONS. Since long before historical accounts recorded them, insect infestations have had a major impact on the success of agriculture, food storage, and the human psyche. In this context the term “infestation” refers to a far higher than normal number of **insects** occurring over a wide geographic area. Examples of insect species whose infestations have severely limited food and fiber production include the flightless Mormon cricket of western North America and the desert locust of Sub-Saharan Africa, the Near East, and Southwest Asia. Some insects that appear in great numbers have a more significant impact on the human psyche than upon agriculture. Periodical cicadas, often mistakenly referred to as “locusts,” emerge in eastern North America in 13- or 17-year cycles and can elicit fear and despair though they pose no threat to humans and cause little damage to native trees. Even wingless insects that also lack the ability to disperse by walking, such as bed bugs, can become significant pests. Insect species that are purposely or accidentally introduced to geographic areas to which they are not native can also reach infestation levels because they are no longer limited by their natural predators and parasites.

Desert locust (*Schistocerca gregaria*) swarms in Sub-Saharan Africa average 60 million individuals per square kilometer, often reaching as many as 10 billion individuals in a single swarm. Constituting the eighth **biblical plague** of Egypt described in Exodus 10,

such swarms can cover 75 miles (120 km) per day. These insects directly compete with humans for food, often devastating crops such as peas, beans, tomatoes, and grains, and thus causing famine in their wake. The presence of locusts has also driven human migration to areas free of these insect pests. Locusts can exist in more than one form, depending on their environment. When these insects mature in areas where they have little contact with other individuals, they become “solitarius” adults, are not very restless, and have longer lives. However, when immatures grow up in an area crowded with other locusts and when other conditions such as rainfall are present, they mature into more restless, “gregarious” adults that display aggregate behavior, even when flying. This migratory, gregarious phase has the greatest impact upon human agriculture, with the bugs often stripping all vegetation in their path. Amazingly, some swarms have been carried by winds from Africa to the Caribbean and northern South America, a distance of about 3,750 miles (6,000 km). All of the transitional stages between the solitarius and gregarious phases can be seen in nature. Phase changes can occur in other species of locusts that can also reach plague proportions in many parts of the world. Among these are the Migratory locust, the Moroccan locust, the Red locust, the Australian plague locust, the Bombay locust, the Central American locust, and the South American locust.

In the United States the Mormon cricket (*Anabrus simplex*)—not a true cricket but rather a short-winged, long-horned grasshopper—can be devastating to agricultural crops. Mormon crickets do not fly like migratory locusts but move over land in vast numbers and are known to feed on at least 250 plant species. The Mormon cricket received its name in the spring of 1848 when swarms of this insect descended upon the crops of the first Mormon settlers of the Valley of the Great Salt Lake in Utah. As the story goes, great flocks of sea gulls appeared after three days of fasting and prayer and began gorging themselves on the crickets. A prominent statue commemorating the gulls is mounted in Salt Lake City’s Temple Square.

The periodical cicadas (*Magicicada* spp.) of the eastern United States are among the longest-lived insects, living as nymphs underground for 13 or 17 years before emerging en masse to breed and overwhelming their predators in the process. The brightly colored, conspicuous, and noisy adults may emerge with as many as 1.5 million individuals per acre. Periodical cicadas occur in different broods with different distributions. Each brood contains three species, with the males of each brood producing a distinctive call. Rarely, a 13-year brood and a 17-year brood will emerge in the same year (in one area every 221 years) resulting in prodigious numbers of these insects. The mated females cut into tree branches to lay eggs, but this rarely damages native trees. Though they do not consume the foliage of plants, periodical cicadas are often called locusts because they occur in tremendous numbers. European settlers along the eastern coast of the United States saw their emergence as a bad omen and interpreted the dark “W” on their wings to mean that there would be an Indian war.

An example of an annoyance/nuisance insect that has reached infestation proportions is the bazaar fly of the Eastern Hemisphere. This fly prefers to rest on the heads of humans and returns immediately after being brushed away. Its increase in numbers and geographic range is thought to be the result of increases in the fly’s larval habitat, dog feces, which is related to human population growth in particular areas. Another fly species that can occur in great numbers and can be annoying at times in Florida is the Lovebug (*Plecia nearctica*). The common name refers to the fact that males and females remain attached for up to

three days during mating. The adult flies are a nuisance to motorists because they are attracted to highways where they splatter on the hoods and windshields of automobiles. Large numbers of lovebugs can cause overheating of liquid-cooled engines, reduce visibility, and damage automobile paint. Strangely, lovebugs were not even known to science until 1940, and it has been proposed that the ever-mounting amount of organic waste produced by the increasing human population in Florida has provided still more habitats for this fly's immature stages. The presence of wings or powerful walking legs is not essential for insects to reach infestation levels. Bed bugs possess neither, relying on humans to transport them from place to place. These human-loving, blood-feeding insects have recently reemerged as a pest in North America.

Over 200 species of insects have been introduced to the United States through **trade and travel**. Examples of insect species that have reached infestation levels since their introduction into the United States include the multicolored Asian lady beetle, the Asian tiger mosquito, the Japanese beetle, and the gypsy moth. Though a beneficial predator of aphids, adults of the multicolored Asian lady beetle (*Harmonia axyridis*) tend to aggregate in the fall on doors, windows, walls, and porches of buildings. These beetles then overwinter in wall voids from which they can emerge to invade the interior of homes in great numbers during the winter. A native of Southeast Asia, the Asian tiger mosquito (*Aedes albopictus*), was introduced to the United States in 1985 and has since spread to 26 southeastern states. It has been more successful than native container-breeding mosquitoes and is easily transported in its immature stages by the transport of discarded automobile tires. Unlike native container-breeding species, the Asian tiger mosquito aggressively bites in the daytime and can reach landing counts greater than 50 per five minute interval. The fact that this mosquito species readily utilizes human-made water-filled containers has also increased its numbers in the United States.

First discovered in the United States in 1916, Japanese beetle (*Popillia japonica*) adults are known to feed on more than 300 species of plants and are now well established in all states east of the Mississippi River except Florida. Adult Japanese beetles feed on foliage, flowers, and fruits. Leaves are typically skeletonized or left with only a tough network of veins. Japanese beetles can apparently live anywhere that there is sufficient foliage on which to feed, including the gardens of homeowners. Japanese beetles have wings and travel and feed in groups. A swarm of these beetles has been known to strip the foliage of a peach tree in as few as 15 minutes. The larvae or grubs, feeding in the soil, damage the roots of turf and pasture grasses, vegetables, nursery seedlings, and field crops. The gypsy moth (*Lymantria dispar*) is perhaps North America's most devastating forest pest. Originally introduced from France to an area near Boston, Massachusetts, in 1869, it has been spreading slowly south and west ever since. This insect gets some assistance by humans, who inadvertently transport its egg masses to previously uninfested areas. The larvae or caterpillars of the gypsy moth are known to feed on the foliage of hundreds of species of plants and can cause tree mortality (e.g., in oaks) after several successive years of defoliation. With the help of a strand of silk they produce, the larvae can "balloon" for miles to establish new infestations. Within the range of the gypsy moth, fall color enthusiasts are often disappointed because many of their favorite trees have been defoliated by this pest species.

Though many millions of dollars continue to be spent on **pesticide** research, biological control methods, and integrated pest management strategies, the infestations of insects described above will be with us for the foreseeable future.

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STEVE MURPHREE

INSECTICIDE. See Pesticides.

INSECTS, OTHER ARTHROPODS, AND EPIDEMIC DISEASE. Human beings have had to engage and interact with the world of insects from time immemorial. Insects have been held responsible for destroying food crops. They have been seen as harbingers of famine and economic disaster. In almost every part of the world, human beings have had to devote considerable energy and skill in trying to protect themselves from insects. Insects have also benefited humanity. They have often been used as sources of food and drink in certain cultures. Over time, insects have sustained a wide variety of industries: silk, wax, cochineal, shellac, and so forth.

Insects have also been considered detrimental to human life, however. They have been attributed with causing human diseases. The work of **travel** writers and natural historians has reflected such concerns for centuries. However, it was in the late nineteenth century, with the advent of medical entomology as a distinct branch of scientific knowledge, that the relationship between human diseases and insects became an area of sustained and organized academic research.

Robert Koch of Germany and **Louis Pasteur** of France, along with a host of other scientists in the nineteenth century, propounded the “**germ theory** of disease causation.” This theory suggested that living microorganisms in the blood caused an extensive range of human diseases. Following this theory, scientists eventually suggested the role of insects in transmitting diseases. It was argued that insects acted as vectors in transmitting harmful microorganisms from one **human body** to another. Henceforth, the role of insects in causing epidemic diseases has been studied in great detail. Anthrax was the first disease to have come under experimental scrutiny. These initial experiments, however, failed to affirm definitively whether insects caused the **transmission** of anthrax.

Research conducted by **Patrick Manson** in Amoy (China) and published in 1878 and 1884 confirmed that mosquitoes caused elephantiasis in humans. His works suggested that mosquitoes transmitted the filarial worm from one body to another. Manson showed that the larvae of the filarial parasite entered the body of the mosquito once it had sucked the blood of an infected person. After the mosquito died, the filarial parasite inherent in its body was released in **water**. Human beings who drank that water acquired the disease. Manson's work was eventually modified. It was later shown that filarial infection did not result from drinking infected water. Instead, it followed the bite of an infected mosquito. Despite this, his research firmly confirmed the long held hypothesis that insects play a crucial role in causing human diseases.

Following Manson's lead, many scientists set out to discover the causes behind the propagation of many epidemic diseases. Manson inspired similar research not only on human diseases but also on veterinary diseases. In the late 1860s a fever epidemic among

the cattle in Texas threatened to devastate the existing livestock economy. This “Texas cattle fever” was also referred as Spanish fever, red-water fever, and dry murrain. In 1893 Theobald Smith (1859–1934) and Fred Lucius Kilborne (1858–1936) showed that the disease was caused by **protozoa** that were spread by cattle ticks. After sucking blood from an infected animal, a tick would drop off into the grass and lay eggs from which would hatch young ticks already harboring the protozoa. Weeks after the original tick dropped from its longhorn host, its progeny were still capable of infecting other cattle. This finding was later followed by the discovery of vectors of the “Rocky Mountain spotted fever” of humans, tularaemia, and other similar diseases.

Several other forms of cattle diseases in other parts of the world were later found to be transmitted by insects. In 1895 it was shown that the fatal Nagana cattle disease in Africa was conveyed from sick to healthy animals by bloodsucking tsetse flies. This discovery paved the way for the demonstration of the cause and method of spread of the deadly human African **sleeping sickness**.

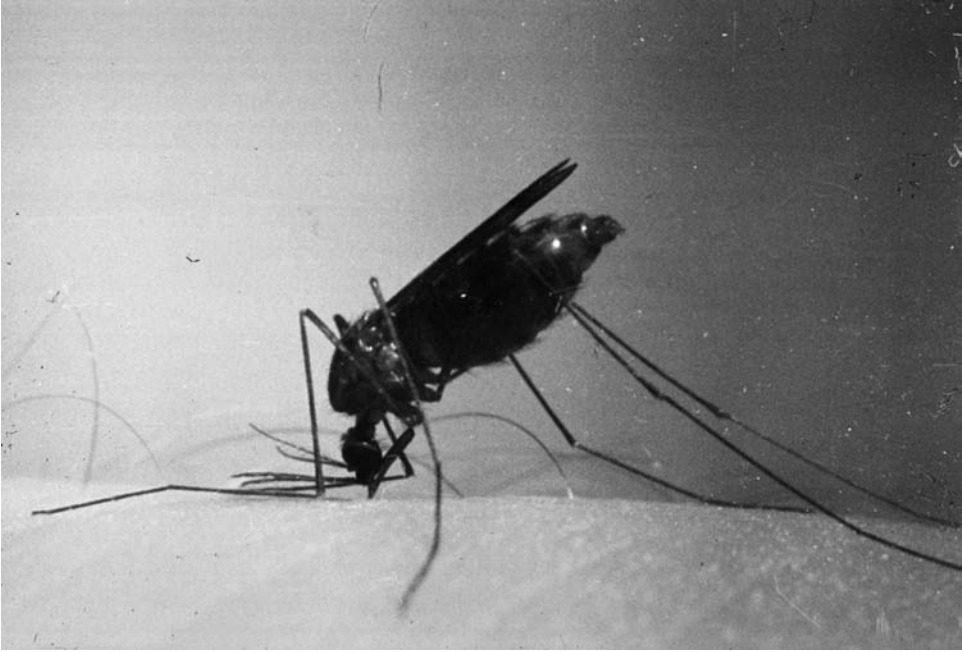
Alphonse Laveran had shown in 1880 that a parasitic protozoon caused **malaria**. Patrick Manson had hinted that mosquitoes could transmit malaria. Combining these understandings, **Ronald Ross** demonstrated how female *Anopheles* mosquitoes carried malarial parasites from one human body to another. This was soon followed by the discovery of the mode of the transmission of **yellow fever** by mosquitoes. A United States Army Commission (1900) headed by **Walter Reed**, who was assisted by James Carroll (1854–1907), Jesse Lazear (1866–1900), and Aristides Agramonte (1868–1931) supplied proof toward this discovery. Malaria and yellow fever were both considered a bane to the entire colonial world as they killed thousands of European soldiers, traders, and missionaries. Such knowledge inspired extensive projects of mosquito extermination in Africa, different parts of India, Hong Kong, the Philippine Islands, Cuba, and Panama, along with several other regions.

Dengue, or breakbone, fever is another febrile disease that was found to be caused by mosquitoes. Dengue is rarely fatal, is accompanied by rash, and can cause severe debilitating effects. The *Aedes aegypti* and *Aedes albopictus* species of mosquitoes most frequently transmit Dengue. During the World War II, an epidemic of Dengue broke out in Hawaii in 1943 and on various Pacific Islands in 1944, having an adverse effect on the military operations of the U.S. army and navy.

The sand fly fever caused by the bite of sand flies continues to be an acute and debilitating, though not fatal, disease. It is widely distributed across southern Europe, Latin America, Asia, and Africa. Attacks of large swarms of black flies classified under the species *Simulium*, apart from destroying poultry and domesticated animals, cause Onchocerciasis among **children** in various parts of tropical Africa and Latin America.

Bubonic plague is an acute infectious disease that affects both humans and rodents. Plague is primarily a disease of rodents: rats, mice, ground squirrels, and many other species are affected. The rat-flea *Xenopsylla cheopis* has been found to be the most effective vector of bubonic plague. This knowledge has been effectively employed in attempts to eradicate plague. Extermination of rats and their fleas has been an important feature of plague control. It has often been feared that bubonic plague might be carried to different parts of the world by rats through ships. As a routine practice, ships from infected ports are **fumigated** to kill the rats and their fleas.

Lice are the agents for the transmission of **typhus**. It has been shown that *Rickettsia quin-tana*, a microorganism found consistently in the stomach of infected lice, causes trench



A common malaria mosquito (*Anopheles quadrimaculatus*) in biting position. It is full of blood down to the last three segments. Courtesy of the National Library of Medicine.

fever. The housefly, in addition to being a vector of **typhoid fever**, has been incriminated along with closely related species as a vector of a number of other **animal diseases**. See also Ectoparasites; Environment, Ecology, and Epidemic Disease; Insect Infestations; Pesticides.

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ROHAN DEB-ROY

INTERNATIONAL HEALTH AGENCIES AND CONVENTIONS. Neither diseases nor the organisms that cause them recognize the political boundaries that separate human populations into nations. The natural boundaries that long isolated islands and continents—and their unique biological populations—have been crossed with increasing frequency and effectiveness. Today we live in a truly globalized society, sharing pathogens with the world. Never has international cooperation in monitoring, planning for, and confronting infectious diseases been more important. The medieval plague prompted Italian city-states to surveil their neighbors for signs of an outbreak and to

recognize each other's health passes, guaranteeing a traveler's lack of disease. Early modern maritime nations at least tacitly recognized each others' **quarantine** and isolation procedures, and **cordons sanitaires** along national borders were generally respected because no one had an interest in spreading pestilential disease. Yet the earliest multistate effort to confront **epidemic** disease began only in the mid-nineteenth century as cholera raged across European countries and their colonies.

By the 1850s Europe was rapidly undergoing **industrialization** and **urbanization** and was beginning to experience the closer ties created by such innovations as steamships, railroads, and the telegraph. Imperialism linked a lengthening list of European states to far-flung colonies, many of which served as reservoirs for infectious tropical diseases. At the same time, the medical profession in Europe was gaining increasing popular respect, raising the prospect that diseases might soon be understood and conquered. In 1830 an outbreak of epidemic **cholera** prompted the Ottoman Empire to initiate a program of international monitoring of sea and land routes between Asia and Western nations directed by the Conseil Supérieur de Santé de Constantinople (Istanbul). Two decades later, in the midst of another cholera pandemic, diplomats, **physicians**, and scientists from 12 nations participated in the First Sanitary Conference, which opened on July 23, 1851. A lack of consensus on causation led to a lack of consensus on action, but the first step had been taken. In 1859 the Second Conference convened again in Paris, but with only the diplomats present. Even so, no agreement on measures to combat cholera was ratified. The medical men rejoined the diplomats for the Third in Istanbul in 1866, and **yellow fever** was added to the agenda, but no real headway resulted. Though the agendas broadened somewhat, the same must be said for the Fourth Conference (Vienna, 1874), the Fifth (Washington, D.C., 1881; with a greater emphasis on yellow fever), and the Sixth (Rome, 1885).

During this period other developments reinforced international collaboration on matters of health and disease. The International Statistical Congresses, beginning in 1853, helped disseminate the emerging ideas and tools of the new science of **epidemiology**; the International Congress of Medicine held 11 sessions between 1867 and 1900; and the U.S. Surgeon-General began publication of the *Index Medicus*, an up-to-date international catalogue of books and articles of medical relevance. The German **Robert Koch** and Frenchman **Louis Pasteur** made their respective microbiological discoveries that confirmed modern **germ theory** of disease, while **Rudolf Virchow** in Germany and **John Snow** and **William Farr** in England paved the way for modern epidemiology.

The Seventh International Sanitary Conference, held in Rome in 1892, was a breakthrough, as it unanimously ratified the First International Sanitary Convention (agreement). Though limited to establishing quarantine protocols for ships passing into the Mediterranean through the new Suez Canal, it opened the door to a series of conventions drafted and approved by the subsequent conferences. The Eighth Conference met in Dresden, Germany, in 1893 and agreed on certain prophylactic measures and required notification during future cholera outbreaks. In 1894 the Ninth Conference convened in Paris and established guidelines for reducing the spread of cholera during the annual Islamic pilgrimage to Mecca. By 1897 **bubonic plague** had reemerged in the form of the Third Plague Pandemic and was appropriately the focus of the Tenth Conference, held in Venice. Its Fourth Convention dealt with international notification and quarantining to contain the spread of plague. Six years later, the Eleventh Conference met in Paris. Delegates agreed to work toward controlling rat populations, which had only recently been

linked to the plague; toward codifying the quarantine and other procedures established at previous conferences; and toward establishing a new organization, the Office International d'Hygiène Publique (International Office of Public Hygiene [OHIP]), which would have a largely European scope. The OHIP was founded by 12 countries—including the United States and Brazil—and met for the first time in Paris in 1908. It tackled the issue of monitoring **leprosy, tuberculosis, typhoid**, sexually transmitted diseases, and **water** quality (for cholera). Only three more conferences of this series would be held, the last in Paris in 1938.

The Eighth International Sanitary Conference, held in Washington, D.C., in 1881, laid the foundation for the First International Conference of American States, held in Washington in 1890. From this meeting emerged the International Union of American Republics, which later became the Organization of American States. Representatives at the Second International Conference of American States (Mexico City, 1901) organized the First General International Sanitary Convention of the American Republics (Washington, D.C., 1902). As a permanent executive board for executive oversight, the convention created the International Sanitary Bureau (ISB; later the Pan American Health Organization or PAHO), which remains the world's oldest international health agency. Based in Washington, the ISB was directed by the U.S. Surgeon-General and often collaborated with the **Rockefeller Foundation's** International Health Division and the U.S. Institute for Inter-American Affairs. As with the OHIP, the chief function of the ISB was to monitor and report on levels or outbreaks of infectious disease in the Western Hemisphere and to supervise its quarantine procedures.

World War I (1914–1918) not only killed millions of combatants and countless civilians in Europe but also spawned terrible outbreaks of cholera and **typhus** in its wake. More deadly than the war itself was the worldwide **influenza pandemic of 1918–1919**. The failures of international diplomacy that sparked the war led to the founding of the League of Nations (1919), and the medical emergencies to the League of Nations Health Organization (LNHO, 1923). Because the United States was not a member of the League, it could not participate in LNHO activities, so the OHIP and ISB (now the Pan American Sanitary Bureau) remained independent and active as monitors and quarantine supervisors that worked with the LNHO. Complementarily, the LNHO took a much more proactive role in supporting practical measures to prevent the outbreak and spread of disease. Aided by Rockefeller Foundation funds, the Organization disseminated the latest information, strategies, and techniques, and published a monthly report on medical situations worldwide. Unlike earlier international efforts, the LNHO covered East Asia, from an office in Singapore. It collaborated with the International Red Cross and the International Labor Office in providing public education, sending experts to trouble spots, and sponsoring committees and conferences. It sponsored research and development of treatments, public hygiene, and worldwide standardization of epidemiological matters from cause of death reporting to medical products.

The LNHO recorded many successes, but the Great Depression and weaknesses of the League of Nations helped limit the organization's effectiveness. World War II (1939–1945) severely curtailed its activities. The Allied-sponsored United Nations Relief and Rehabilitation Administration (UNRRA) emerged in 1943 amid fears of pandemics like those that followed World War I. In the wake of the war, the United Nations Conference on International Organization established a new World Health Organization (WHO) that would absorb the LNHO, OHIP, PASB, and UNRRA. On April 7, 1948,

POINTS [FOR PUBLIC HEALTH OFFICIALS] TO CONSIDER AT THE START OF AN OUTBREAK OF MEASLES (1999)

POPULATION DATA	Obtain most recent population size and age distribution.
WHAT'S BEEN DONE	List any actions already taken.
CASE REVIEW	List reports of cases in area during previous six months.
COVERAGE RATES	Obtain existing coverage data and include unofficial estimates.
SPOT MAP	Use pins or a pen to mark the location(s) of case(s) and areas targeted for immunizations on a map.
RESOURCES	Determine what resources are available at all levels for outbreak control (transportation, vaccine, cold chain materials, promotional materials, etc.). Human resources should include field staff to assist in the outbreak, including staff from other programs, district staff, medical and nursing students, interpreters, and drivers. Arrange for transport and for travel advances.
ARRIVALS	Inform appropriate health/community authorities when/where any special teams will be arriving, and ensure that specific health staff/community representatives will be present.
SUPPLIES	Organize necessary supplies: <ol style="list-style-type: none"> 1. Adequate vaccine based on estimated target population. 2. Cold chain materials: ice packs, cold boxes, vaccine carriers, thermometers, refrigeration capacity (locally available or must be brought in), possibility of purchasing ice locally. 3. Adequate supply of forms <ul style="list-style-type: none"> • Line Listings of Suspected Cases • Case Investigation Forms • Outbreak Control Summary • Mop-up Work Sheets 4. Promotional materials: pamphlets, posters, etc.

From *Measles Eradication Field Guide* (Technical Paper #41), published by the Pan American Health Organization, Pan American Sanitary Bureau, Regional Office of the World Health Organization (Washington, D.C., 1999).

the required 26 nations ratified its constitution, and it assembled for the first time in June. The International Sanitary Conventions evolved into the World Health Organization's International Health Regulations (IHR), adopted in 1969. Updated in 2005, the new IHR was implemented in 2007; 192 countries are currently party to the regulations. These require cooperating governments to inform the WHO of any reportable diseases in a timely way but do not require further action.

Since 1948 the WHO has been in the forefront as an organizer of international efforts to maintain high levels of general health, prevent the emergence or spread of disease, treat victims, and, in some cases, eradicate diseases. Controlling and eventually eradicating infectious diseases are among the highest of WHO's priorities, and success with **smallpox eradication** in 1977 set the tone for current efforts against **measles**, **TB**, **malaria**,

SOME WHO-AFFILIATED INFECTIOUS DISEASE-FIGHTING ORGANIZATIONS (2008)

FOR SPECIFIC DISEASES

International AIDS Vaccine Initiative (1996):

<http://www.iavi.org/>

Pediatric Dengue Vaccine Initiative (2003):

<http://www.pdvi.org/PdviMain.htm>

Medicines for Malaria Venture (1999):

http://www.mmv.org/rubrique.php3?id_rubrique=15

Malaria Vaccine Initiative (1999):

<http://www.malariavaccine.org/>

TB Alliance: Global Alliance for TB Drug Development

(2000): <http://www.tballiance.org/home/home.php>

Aeras: Aeras Global TB Vaccine Foundation (1997):

<http://aeras.org/>

GENERAL HEALTH OR MULTIPLE DISEASES

Drugs for Neglected Diseases Initiative (2003):

<http://www.dndi.org/>

Institute for One World Health (2000):

<http://www.oneworldhealth.org/>

Foundation for Innovative New Diagnostics (2003):

<http://www.finddiagnostics.org/>

International Partnership for Microbicides (2002):

<http://www.ipm-microbicides.org/>

and **polio**. The United Nations and WHO consider good health to be a fundamental human right and a positive goal for their activities. The WHO is thus proactive and not merely reactive to dangerous outbreaks of disease. Though headquartered in Geneva, Switzerland, WHO has six regional offices through which many of its efforts are directed. In the Western Hemisphere it is the Pan American Health Organization (Washington, D.C.; formerly the PASB). WHO also maintains offices in countries that have needs being met by the organization. Collaboration with host countries is of utmost importance, as is collaboration with non-governmental organizations, especially those that can provide technical expertise or funding. The Bill and Melinda Gates Foundation is a good example of the latter. WHO also works with other international organizations—such as the Food and Agriculture Organization (FAO), UNICEF, and

UNESCO—in areas such as nutrition, health and **personal hygiene** education, prenatal care, **children's** diseases, and **vaccinations**.

In Volume 2 of his *National Health Systems of the World*, Milton Roemer lists eight general principles that currently guide international health care efforts: 1) Multinational organizations are established by autonomous national states and may only operate in a country with its permission. 2) All who work for an international agency must be dedicated to the agency and not to their home countries. 3) An organization must respond to the needs of any country that applies for help, no matter the nature of the government (though South Africa was made a pariah because of racial segregation [apartheid]). 4) A healthy population is a key to social and economic development. 5) Within a country many parts of government and society need to collaborate to maintain good general health. 6) In a given country highest priority should be given to the problems that affect the most people, with an emphasis on primary care facilities. 7) Both preventive care and treatment must be allocated equitably throughout the society. 8) Though international concerns originated in communicable disease control, efforts must address a much wider range of diseases and disabilities. *See also* Cholera: First through Third Pandemics, 1816–1861; Colonialism and Epidemic Disease; Demographic Data Collection and Analysis, History of; Epidemiology, History of; Geopolitics, International Relations, and Epidemic Disease; Leprosy, Societal Reactions to; Measles, Efforts to Eradicate; Non-Governmental Organizations (NGOs) and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Trade, Travel, and Epidemic Disease; Yellow Fever in Latin America and the Caribbean, 1830–1940.

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JOSEPH P. BYRNE

IRISH POTATO FAMINE AND EPIDEMIC DISEASE, 1845–1850. Between 1845 and 1850, the failure of the potato crop marked the worst famine in Irish history, with over 2 million dying from starvation and accompanying disease and an equal number emigrating. The Irish famine has continued to inspire narration, interpretation, and discussion by historians because of the scope of the human tragedy and the wealth of primary source material.

The famine in Ireland was both a warning of the dangers of monoculture—in this case, the potato—and a response to a colonial legacy that had created social, economic, and political dislocation on an unprecedented scale. The colonization of Ireland by England had been born out of a fear of invasion. Consequently, by the early nineteenth century, the bulk of the Irish people had lost political autonomy and religious freedom and had suffered severe limitations on land ownership, which created an underclass that faced a precarious existence as tenants with no security. The problems were further exacerbated by rapid population growth. By the 1840s this showed signs of slowing, but with a total population estimated at 8.5 million, issues such as housing, food, employment, and well being alone were a constant concern to the authorities in both Westminster and Dublin.

For many Irish, daily subsistence meant a life of **poverty**. The staple food was the potato, a crop with advantages including two harvests a year, plants that grew in most soil, and a relatively high nutritional value. It is believed that the average adult male had a **diet** of over 13 pounds of potatoes a week, supplemented with meat and dairy products when available. Despite the occasional poor harvest, wide scale potato crop failures were unknown, and the popular image of Ireland with its rich, fertile soil meant that many outsiders refused to accept the horrific accounts of starvation once the famine had taken a fatal grip on the country. The irony of the great hunger was that there was always sufficient food being produced in Ireland, but little of it ever reached the mouths of the indigenous population because of its value as an export commodity.

In 1843 reports of a blight affecting potatoes appeared in the United States. Rapid transmission to Europe occurred in contaminated seed crops. In 1845 the blight was recorded among potato crops in southeast Britain, where it thrived in the damp, temperate climate. Farmers recognized the ominous signs of black spots on one side of the leaf, while underneath lurked the telltale white mold. When the potatoes were lifted from the ground, they were already rotten and stinking. Years later the blight was identified as *Phytophthora infestans*, a fungus that still has the potential to devastate crops.

Conservative British Prime Minister Robert Peel (1788–1850) was sufficiently concerned to direct the government to consider the blight a priority and ordered further investigation. The accepted conclusion that this was a temporary failure, however, resulted in the decision not to establish long-term government relief programs.

In Ireland, the spring potato crop of 1845 was sound; only the autumn harvest showed signs of blight. The dire reports at this time were localized, and potatoes were stored for the oncoming winter. News soon spread, however, of stored potatoes becoming rotten. Those who attempted to eat the contaminated crop were the first medical victims, struck down by severe vomiting and bowel disorders. As winter set in, reports of starvation reached the authorities, followed by inevitable accounts of fevers. By early 1846 potato crops were earnestly planted, but unlike previous crops they showed few signs of being healthy. Peel, sensing the impending disaster in Ireland, surreptitiously purchased £100,000 of American corn (maize), to be shipped directly to Cork. The clandestine nature of this purchase reflected the full extent of anti-Irish feeling found throughout Britain and the continued reluctance to set aside prejudice and provide help for the millions of innocent victims struck down by disease and starvation.

On arrival in the Irish ports, the dried corn could not be distributed until it had been made fit for human consumption by a long and complicated process. Failure to prepare it properly resulted in severe gastric disorders, with the general agreement that the corn was not so much food but Peel's "brimstone." By 1846 there was widespread failure of the potato crop throughout the United Kingdom. However, Ireland stood alone in facing the dire consequence of starvation. The fall of Peel's government and the return of the liberal Whig party initially provided a sense of optimism in Ireland. However, Lord John Russell (1792–1878) led a minority government and was still very much at the mercy of public opinion. Relief now took the form of a variety of public works that provided food in return for honest toil. This did little to feed the most vulnerable and needy.

The high incidence of death from disease as opposed to actual starvation is one of the most harrowing features of famine in general, and Ireland was spared none of the horror. As evictions of penniless tenants became common, entire families could be found sleeping in the open and scavenging for food, thereby further weakening their resistance to illness. A formidable list of diseases was recorded, with many reaching epidemic proportions. The evidence for this can be found in the 1851 *Census for Ireland* (see sidebar). The final publication covered 10 volumes, with two being specifically allocated to "Status of Disease" and "Tables of Death." The compiler was Sir William Wilde (1815–1876), a skilled Irish medical practitioner. In 1841 Wilde had been appointed Medical Commissioner to the Irish Census, though unbeknown to him, much of his time in office would be spent recording the terrible famine years and their grim aftermath. Few were better trained to make sense of this grim legacy, but Wilde himself was also aware that for each of the thousands of deaths that were recorded, many more died without any official notification of cause or even identification.

OFFICIAL BRITISH GOVERNMENT REPORT ON DISEASE DURING THE GREAT FAMINE (1856)

Concurrent with the foregoing state of famine, and the disruption of the social condition of the people, pestilence came upon the nation in the following order: Fever, Scurvy, Diarrhea and Dysentery, Cholera, Influenza, and Ophthalmia . . .

On reviewing the history of epidemic pestilence in Ireland, we are struck by the frequency with which **dysentery** has been an element of destruction, in lessening its population . . . The Census Returns have afforded a total of 93,232 deaths from dysentery, in the proportion of 75.06 females to 100 males. Of these, more than one half occurred in workhouses . . . Of 283,765 persons who died in the workhouses between 1841 and 1851, as many as 70,526 were returned as having sunk under dysentery or diarrhea . . . When we remember the masses of debilitated people that were, of necessity, congregated in the parent and auxiliary workhouses during the years of famine, we cannot wonder at the great mortality from these diseases . . .

When the famine was most severely felt, and when fever and dysentery raged with the greatest violence, Asiatic **cholera** again invaded the continent of Europe . . . and reached our shores at the end of 1848. For some wide and inscrutable reason, upon which man can only speculate, it seemed good to the Great Disposer of events [God] to mitigate considerably its fatality, compared with that of its first invasion, sixteen years before, for the returns only give as many as 35,989 deaths, in which the sexes were in the proportion of 95.57 males to 100 females.

Although **small-pox** has decreased in Ireland, both in virulence and extent, since the publication of the Census Report in 1841, there was some increase in that disease during the pestilential period of 1847, '48, and '49; yet the deaths returned to us (amounting to 35,275) in ten years) are not, considering the present state of **vaccination** in this country, of sufficient amount to warrant the assertion that small-pox influenced the great mortality of which this . . . is the analysis, although during a portion of the period it prevailed epidemically and was also very fatal in England.

An epidemic of **influenza** pervaded Great Britain in 1847 and 1848; where, although of brief duration it was of unusual fatality. The total deaths registered from influenza [in Ireland, 1841–1851] were 10,753, in the proportion of 85.5 females to 100 males.

The total deaths returned to us under the head of Starvation amounted to 21,770 . . . 70.6 females to 100 males . . . [Yet] many more must have perished from disease remotely induced by privation during the years of famine and pestilence.

From the British Government's *Census of Ireland for the Year 1851* (Dublin, 1856).

The first group to fall victim to disease was, not surprisingly, infants and children. Descriptions of marasmus, a form of severe protein deficiency affecting the very young, became common throughout Ireland. The victims are vividly portrayed in the sketches made at the time by illustrators working for the popular press. The same images also provided evidence of dropsy (currently known as edema). This was identifiable by the

painfully bloated stomachs of young victims suffering from fluid retention in response to the lack of nutrition. Today over 50 million children still suffer from marasmus and other similar conditions caused by malnutrition.

Of all the diseases that affected the Irish population at this time, **cholera** and **typhus** were undoubtedly the most virulent. Cholera decimated the urban areas that previously had avoided the worst of the famine, whereas typhus was far more widespread as a result of it being highly infectious and thriving in poverty-stricken environments such as slums and workhouses. As the displaced population sought food and shelter, people unwittingly became carriers of typhus. Among the cruelest of outbreaks was that which occurred at sea. Refugee passengers who had survived the perils of starvation and disease in Ireland often found themselves succumbing to typhus fever when confined in overcrowded ships. Thousands died as they fled in search of a better existence in the aptly named “coffin ships,” only to be cast overboard or hastily buried in the foreign soil they had believed would offer a new life.

As the famine showed no sign of abating, those with the opportunity increasingly took advantage of the chance to emigrate. The most popular options were North America and England although many countries recorded high Irish immigration at this time. The route to North America required money to purchase a single ticket, whereas the crossing to England was often free so long as passengers were prepared to act as ballast in ships returning to ports such as Liverpool. In 1847 alone, over 300,000 Irish were recorded as having entered Britain. However, they soon met with increasing hostility by both the public and the authorities. In their weakened and desperate state, they brought disease and a sense of unrest. City after city began to demand an end to the waves of immigrants, and many demanded that they be returned to Ireland. The Liverpool Poor Law Authority was the first to voice its concerns as over 90,000 homeless and often sick Irish flocked into the city, creating ghettos in urban environments that were already rife with public health concerns.

The most tragic of all emigration tales was that of Grosse Île, Canada. During the cholera epidemic in 1832, a **quarantine** station had been established on Grosse Île, a small island in the St. Lawrence River. An increasing number of Irish found themselves heading for Canada rather than the United States as the passage was cheaper, and American ports on the eastern seaboard had begun imposing restrictions on immigrants in order to avoid additional strains on local providers of social welfare and medical care. Though all passengers were supposed to be inspected for disease prior to any sea passage, few British medical officers risked carrying out this duty in Irish ports. Consequently when *The Syria* headed out for Canada in March 1847, it had on board 241 passengers, some of whom were infected with typhus. When the passengers disembarked on the island, over 200 were so ill that they had to be admitted to the small hospital. Most never recovered. On Grosse Île over 4,000 Irish immigrants died of disease within a two-month period in 1847, though many more were to perish throughout the remaining famine years. The tragedy symbolizes the dangers faced by many of the Irish diaspora who chose to flee the famine, only to face suffering and tragedy on foreign soil.

The medical officer of the station, Dr. George Douglas (director from 1836 to 1864), was utterly unprepared for the scenes he witnessed on *The Syria* and other ships that followed. Soon, any attempt to enforce disembarkation on the small island had to be abandoned. By the end of May 1847, 36 “coffin” ships lay at anchor off the island, with over 12,000 passengers waiting for permission to land. As typhus claimed its victims, bodies were brought onto the island for burial, although it soon became necessary to import soil

from the mainland to ensure that rotting **corpses** were sufficiently covered. The Canadian Legislative Assembly eventually abandoned the practice of quarantine, and Irish immigrants were soon landing directly in Quebec and other cities. Little help was forthcoming, however, and destitution along with the ravages of the Canadian winters saw many of the Irish perish within the first few months of their new lives. *See also* Capitalism and Epidemic Disease; Cholera: First through Third Pandemics, 1816–1861; Colonialism and Epidemic Disease; Contagion and Transmission; Diet, Nutrition, and Epidemic Disease; Disease, Social Construction of; Environment, Ecology, and Epidemic Disease; Human Immunity and Resistance to Disease; Malthusianism; Public Health Agencies in Britain since 1800; Race, Ethnicity, and Epidemic Disease.

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HILARY S. MORRIS

ISLAMIC DISEASE THEORY AND MEDICINE. Islamic medicine has been historically shaped by a variety of medical traditions. Although it was solidly rooted in ancient **Greco-Roman medical theories and practices**, Islamic medicine was also influenced by pre-Islamic medical beliefs and practices, prophetic medicine, and medical practices from the Indian subcontinent. In turn, Islamic medicine had a profound impact on pre-modern European medical theory and practice.

Not much is known about Islamic medicine during the first centuries of Islamic history. A massive translation movement began under the patronage of the Abbasid caliphs in the ninth century. Ancient Greek medical texts were translated first into Syriac and then into Arabic, mostly by Nestorian scholars and court physicians. Hunayn b. Ishak (d. 873) was the most accomplished translator of this period. Works of adaptations from foreign medical texts soon followed translations, and before long, Baghdad became the center of medical learning. By the late ninth century, Hellenistic and Byzantine medical theories and practices were already integrated into Islamic medical learning. The most influential works were the *materia medica* of Dioscorides, c. 40–90), writings of Rufus of Ephesus (late first century CE), and above all those of **Galen** (even more so than those of **Hippocrates**). Overall, Islamic medical learning came to be dominated by Galenic teachings of **humoral theory**, according to which disease emerged in a human body because of an imbalance of bodily humors and could be cured by restoring the balance.

As an effort to counterbalance the dominance of secular and pagan Greco-Roman medical tradition on Islamic medicine, a new genre of medical writing called "prophetic

medicine” emerged during the ninth century. These texts were mostly written by religious scholars of Islam, who gathered medical information from the Quran and *hadith* literature (which contained teachings of Muhammad). Although the authors of these texts were not opposed to medicine in principle, they wanted to give it an Islamic character. Although the genre became popular in the thirteenth and fourteenth centuries, it is hard to estimate to what extent Muslim **physicians** followed these texts.

During the tenth and eleventh centuries, there was a constant effort to organize the vast corpus of medical knowledge produced in the Islamic world. Several major medical compendia were written in this period—mainly in Arabic, but also in Persian. The works of al-Razi (**Rhazes**), al-Majusi (Haly Abbas, d. 994), and **Avicenna (Ibn Sina)** mark the apogee of Islamic medical compendia. Also, from the tenth century onwards, the Islamic world saw the emergence of **hospitals** known as **bimaristan**. The finest examples of medieval Islamic hospitals were established first in Baghdad, and then in Damascus and Cairo. The rise of hospitals prompted the development of institutional medical education, which had been informally practiced within family circles. The first medical school in the Islamic world opened in Damascus in the early thirteenth century.

Islamic medicine was exposed to influences from Indian and Chinese medical systems, mostly because of the geographic reach of Islamic Empires. As early as the ninth century, pharmaceutical substances brought to Muslim lands from India and China began to influence Islamic medicine. Muslim **pharmacists** contributed to pharmacological knowledge by integrating Indian and Chinese medicinal substances to the Hellenistic heritage of Dioscorides’ *materia medica*. Especially, during the Ilkhanid period (1256–1353), Chinese medicine began to influence Islamic medicine via the translations of Chinese medical texts into Persian.

When the **Black Death (1347–1352)** struck the Islamic world, many plague treatises were written. Compiling current knowledge about the disease, these works typically discussed the notion of **contagion** and transmissibility of plague, as well as proper conduct in times of outbreaks, on the basis of *hadith* literature. Generally written by Muslim religious scholars, medieval plague treatises held that plague was a mercy or a blessing of God, and that those who died of it attained martyrdom. Therefore, Muslims were advised not to flee but to bear the plague with patience.

Plague epidemics also triggered the practice of alternative systems of healing. People resorted to **magic** and **astrology**, as well as to pre-Islamic folkloric elements, in the search for a cure. Charms, amulets, incantations, magical squares, magic-medicinal bowls with engravings of Quranic verses and magical symbols, and talismanic shirts were all used for protection against plague. Patience, prayer, fasting, and recitations of the Quran were commonly recommended during times of epidemics.

Islamic medical literature referred to several diseases including fevers, **malaria**, **leprosy**, melancholy, eye diseases, hemorrhoids, and dietetics. Leprosy, elephantiasis, scabs, consumption, **smallpox**, **measles**, and various forms of **plague** were classified as transmissible diseases, based on the long experience of the Islamic world with them. A variety of treatises were specifically devoted to diseases such as smallpox, measles, and plague. As new diseases such as **syphilis** emerged, the topics of treatises by Muslim authors also expanded to cover these new ailments.

In the seventeenth century, Islamic medicine began to be influenced by **Paracelsianism** advocated in Europe by the followers of **Paracelsus**. This movement came to be known in the Islamic world through the translation of these works and soon became very

popular. The chemical medicine, as it was referred to, entailed the use of inorganic salts, mineral acids, and alchemical techniques for the production of its remedies. These translations also introduced to the Islamic medical literature a number of other new diseases seen in Europe, such as scurvy, chlorosis, anemia, and **sweating sickness**.

It is only in the nineteenth century that Islamic medicine underwent a substantial transformation of modernization and westernization. Many European medical texts were translated into Arabic and Persian in this period. European-style medical schools were established in Cairo and Tehran. Yet traditional elements of medicine still continued to survive and be widely practiced. In the Indian subcontinent, traditional Islamic medicine was referred to as Unani medicine and became very popular in the twentieth century, as an alternative to western medicine. *See also* Apothecary/Pharmacist; Leprosy, Societal Reactions to; Physician; Pilgrimage and Epidemic Disease; Plague in the Islamic World, 1360–1500; Plague in the Islamic World, 1500–1850; Public Health in the Islamic World, 1000–1600; Quacks, Charlatans, and Their Remedies.

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NÜKHET VARLIK

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J

JENNER, EDWARD (1749–1823). English physician Edward Jenner discovered the vaccine for **smallpox** in 1796. Discovering the vaccine to protect humans against smallpox has saved more human lives than perhaps anything else that any individual has ever done.

Edward Jenner was born May 17, 1749, in a small village, Berkley, in Gloucestershire, England. At age 14, he became an apprentice to a **surgeon**, and at age 21 he became the resident pupil of the famous surgeon John Hunter (1728–1793) in London. He returned to Berkley to practice medicine in 1773 and obtained a M.D. degree from the University of St. Andrews in 1792. He studied plants, birds, and animals, and collected fossils throughout much of his life. He also played the violin and flute, and wrote poetry.

In many rural areas of the world, it was well known that milkmaids were immune to smallpox after having cowpox. Edward Jenner heard of this at a young age, and it intrigued him for many years. After planning to use the scientific method to test his hypothesis, he waited for the right moment. On May 14, 1796, he saw a pustule on the hand of a milkmaid, Sarah Nelmes, and he took some material from this cowpox lesion and vaccinated an eight-year-old farm boy named James Phipps, after getting approval from the boy's father. Six weeks later he inoculated James with smallpox. James did not catch smallpox. Over the next several months, he carried out several more successful vaccine trials. Jenner published his findings in 1798. His success with cowpox elevated **vaccination** from **folk medicine** to scientific status and popularized it as a medical procedure. Parliament awarded Jenner £30,000 to develop and promote the vaccine. Cotton threads were dipped into vaccinal pus, or the pus was put on glass, allowed to dry, and then transported. By 1799 many people in England had been vaccinated, and the technique rapidly spread to several European countries.

EDWARD JENNER'S EARLY EXPERIMENTS WITH INOCULATION, FROM HIS "AN INQUIRY INTO THE CAUSES AND EFFECTS OF THE VARIOLAE VACCINAE, OR COW-POX" (1798)

A mare, the property of a person who keeps a dairy in the neighboring parish, began to have sore heels the latter end of the month of February, 1798, which were occasionally washed by the servant man of the farm, Thomas Virgoe . . . who in consequence became affected with sores in [his] hands, followed by inflamed lymphatic glands in the arms and axillae, shiverings succeeded by heat, lassitude, and general pains in the limbs . . .

Case XVIII.—John Baker, a child of five years old, was inoculated March 16, 1798, with matter taken from the pustule on the hand of Thomas Virgoe . . . He became ill on the sixth day with symptoms similar to those excited by cow-pox matter. On the eighth day he was free from indisposition.

Case XIX.—William Summers, a child of five years and a half old, was inoculated the same day with Baker, with matter taken from the nipples of one of the infected cows, at the farm alluded to.

Case XX.—From William Summers the disease was transferred to William Pead, a boy of eight years old, who was inoculated March 28th.

Case XXI.—April 5th: Several children and adults were inoculated from the arm of William Pead. The greater part of them sickened on the sixth day, and were well on the seventh, but in three of the number a secondary indisposition arose in consequence of an extensive erysipelatous inflammation which appeared on the inoculated arms. One of these patients was an infant of half a year old. Hannah Excell, a healthy girl of seven years old, and one of the patients above mentioned, received the infection from the insertion of the virus under the cuticle of the arm in three distinct points.

Case XXII.—From the arm of this girl matter was taken and inserted April 12th into the arms of John Macklove, one year and a half old, and Mary James, six years old.

From *The Harvard Classics: Scientific Papers*, edited by Charles W. Eliot (New York: P. F. Collier and Son, 1910).

In 1800 some vaccine material was sent to Benjamin Waterhouse (1754–1846) in the United States, and he was the first to test the smallpox vaccine in the United States. In 1967 the **World Health Organization** (WHO) started a worldwide smallpox vaccination program against the 15 million cases in 33 countries with endemic smallpox. The last case of smallpox was found in Somalia in 1977.

The University of Oxford awarded Jenner an honorary M.D. in 1813. Jenner practiced medicine in his hometown of Berkley from 1773 to his death at age 74. *See also* Scientific Revolution and Epidemic Disease; Smallpox Eradication; Smallpox in Premodern Europe.

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MARK A. BEST

JEWES. See Biblical Plagues; Black Death, Flagellants, and Jews.



Edward Jenner, M.D. Original painting by J. Northcote. Courtesy of the National Library of Medicine.

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K

KITASATO, SHIBASABURO (1852–1931). One of the first microbiologists in Japan, where he helped to open up the field of scientific medicine, Shibasaburo Kitasato's goal in life was the advancement of public health through scientific investigation. He contributed to the development of **immunology** through his early work with **diphtheria** and tetanus. He and French-Swiss bacteriologist **Alexandre Yersin** are both credited with the discovery of the microscopic bacterial organism that causes **bubonic plague**.

Kitasato was born in a village on the Japanese island of Kyushu and graduated from medical school in Tokyo. A German professor, from whom he learned that language, influenced his interest in medicine. The Japanese government sponsored his travel to Germany, which allowed him to realize his goal of working with bacteriologist **Robert Koch**. For six years, he studied **cholera**, anthrax, **typhoid fever**, **dysentery**, **tuberculosis**, and tetanus in Koch's laboratory, where he helped to establish the importance of pure cultures (a culture containing the growth or descendants of only one organism, and free of all other organisms). He and German bacteriologist **Emil von Behring** made a pioneering discovery in 1890, when they applied to diphtheria the knowledge they gained from their studies of tetanus antitoxin and showed how the blood can work to neutralize toxins.

The German government gave Kitasato the title of Professor, making him the first non-German ever to receive that honor, and when he returned home in 1892, he established his own laboratory. It was Japan's first scientific research institution, but because the Japanese government would not fund his work, he had to rely on a wealthy benefactor. When bubonic plague erupted in 1894 in Hong Kong, which was at that time a British colony, Kitasato was asked to find the cause.

Kitasato, who was assisted by a team, and Alexandre Yersin, who was working alone, were caught up in British-French political intrigue, and they met together only once. Kitasato's findings were translated into English and published in the esteemed British medical journal, *The Lancet*. Most scholars consider that he and Yersin, who had arrived

in Hong Kong at the same time, separately discovered the causal bacterium (named *Yersinia pestis* for Yersin) at virtually the same time.

In 1898 Kitasato and Kiyoshi Shiga (1871–1957), Kitasato's Japanese student, were the first to isolate the **bacterium**, named for Shiga (*Shigellosis*), which causes **dysentery**. When **pneumonic plague** broke out in Manchuria in 1911, a region on the northeast coast of China, Kitasato was sent to find ways to prevent its spread. By 1914 Kitasato's laboratory had, to his dismay, been made a branch of the Ministry of Education. He founded a private laboratory, the Kitasato Institute, a nonprofit organization that has evolved into the Kitasato University. Like von Behring, Kitasato was raised by his government to nobility in recognition of his accomplishments. *See also* Plague in China; Plague in East Asia: Third Pandemic.

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MARTHA STONE

KOCH, ROBERT (1843–1910). Robert Koch discovered the causal agents of **tuberculosis** and **cholera** and made numerous technological advances in the study of microorganisms. Born in 1843 in Clausthal in northern Germany, Koch completed a medical degree at the University of Göttingen. After serving in several inconsequential medical posts and on a tour of duty in the military during the Franco-Prussian war of 1870–1871, Koch was appointed as a district **physician** in Wollstein, a small town in Polish-speaking Prussia. Once established in Wollstein, he set up his own laboratory and launched vigorously into a study of **bacteria**.

By the middle of the nineteenth century, no diseases had been conclusively traced to bacteria. However, there was growing evidence that anthrax was bacterial in origin. Anthrax was an ideal research target partly because it had enormous economic ramifications for the European livestock industry and partly because the anthrax bacillus was gigantic in comparison to other bacteria and relatively easy to identify. As throughout his career, Koch's work on anthrax exploited his own technical innovations such as the hanging-drop method for microscopic investigations and, later, the use of photography, new staining techniques, and solid-culture media. Koch was able to trace the life cycle of the anthrax bacillus and to answer numerous questions that had clouded earlier attempts to understand the disease. He presented his research in 1876, and its significance was immediately apparent. Soon thereafter Koch accepted an appointment at the Imperial *Gesundheitsamt* (Health Office) in Berlin.

Koch's anthrax research brought him into direct competition with French microbiologist **Louis Pasteur** who, in contrast to the young and aspiring Koch, was at the crest of a long and distinguished career. At first, Pasteur praised Koch's innovations, but later, largely because of Koch's harsh and often personal attacks, their relations became hostile. Ultimately, each claimed to have provided the final proof that the anthrax bacillus caused

anthrax. Pasteur's argument rested on isolating the suspected causal organism and on inoculating pure strains into otherwise healthy animals—a procedure later codified under the name “Koch's Postulates” (which he probably adopted from his friend Edwin Klebs [1834–1913]). Once Koch adopted the Postulates, he repeatedly insisted that only by following those steps could causation be conclusively established. Ironically, although he also continued to claim that he had been the first to prove that the anthrax bacterium caused anthrax, at no point in his work on anthrax did Koch ever actually follow the Postulates. In fact, his failure to isolate and inoculate the organism was one basis for Pasteur's criticism of Koch's purported proof.

In the late nineteenth century, the disease now known as tuberculosis was the single most prominent disease in the western world. There had been repeated, but unsuccessful, attempts to show that it was bacterial in origin. Koch began studying the disease in August 1881. His work was kept absolutely secret and was conducted at a frantic pace. Relying, as usual, on technological innovations, Koch identified the causal organism and proved causation by meticulously following the Postulates. His first paper on tuberculosis, which was presented on March 24, 1882, in a meeting of the Berlin Physiological Society, was a stunning success. The younger biologist **Paul Ehrlich** described the meeting as his greatest experience in science. Within two years, Koch had also identified the causal organism for cholera. These achievements, together with Pasteur's successful anthrax and rabies inoculations, which came at about the same time, probably did more than anything else to persuade the world of the **germ theory** of disease in particular and of what has been called the etiological research program in general.

In 1891 the German government opened the Institute for Infectious Diseases and appointed Koch as the first director. Among Koch's students and colleagues at the Institute were **Emil Adolf von Behring**, who discovered **diphtheria** antitoxin; William Henry Welch (1850–1934), who was central to the rise of American bacteriology; **Shibasaburo Kitasato**, who helped develop tetanus antitoxin and identified the plague bacillus; **Gerhard Hansen**, who discovered the **leprosy**

ROBERT KOCH ON THE PREPARATION OF TUBERCULOSIS CULTURES (1882)

The simplest case in which the experiment is successful is presented, almost without exception, when an animal which has just died of tuberculosis, or a tuberculous animal which has just been killed for this purpose, is at one's disposal. First, the skin is deflected over the thorax and abdomen with instruments flamed just before use. With similarly prepared scissors and forceps, the ribs are cut in the middle, and the anterior chest wall is removed without opening the abdominal cavity, so that the lungs are to a large extent laid free. Then the instruments are again exchanged for freshly disinfected ones and single tubercles or particles of them, of the size of a millet seed, are quickly excised with scissors from the lung tissue, and immediately transferred to the surface of the solidified blood serum [coating the side of a test tube] with a platinum wire, which has been melted into a glass rod which must be flamed immediately before use. Of course, the cotton stopper [of the tube] may be removed for only a minimal time. In this manner a number of test tubes, about six to ten, are implanted with tuberculous material, because, with even the most cautious manipulation, not all test tubes remain free from accidental contamination.

Cultures that result from a growth of tubercle bacilli do not appear to the naked eye until the second week after the seeding, and ordinarily not until after the tenth day. They come into view as very small points and dry-looking scales.

From Koch's "The Etiology of Tuberculosis," translated by Berna and Max Pinner in *American Review of Tuberculosis* 25 (1932): 285–323.

bacillus; Christiaan Eijkman (1858–1930), whose work led to the discovery of vitamins; and August von Wasserman (1866–1925) and Paul Ehrlich, who made important contributions to **immunology**. All of this work brought world recognition to Koch, but there were clouds on the horizon. Probably hoping to emulate Pasteur's heralded and lucrative anthrax inoculations, in 1890 Koch had prematurely announced discovery of a substance, called tuberculin, which was expected to have prophylactic (preventive) or therapeutic significance for tuberculosis. As evidence accumulated that tuberculin was ineffective, Koch's professional credibility was tarnished. His reputation was also compromised by developments in his personal life. Around 1890 Koch fell in love with a 17-year-old actress named Hedwig Freiberg (1873–1945); he hastily divorced his wife and married Freiberg. Such behavior was incompatible with contemporary expectations, and society ostracized the couple.

Embarrassed by professional setbacks, rejected by Berlin society, and dogged by endless squabbles with competitors and former students, Koch spent more and more time away from Berlin. In 1896 he was invited to investigate *Rinderpest*, a disease that was ravaging cattle in the British colony of South Africa. He next traveled to Asia to study the **bubonic plague**. In 1898 and 1899, he visited Italy, Indonesia, and New Guinea. Between 1902 and 1907, he made several trips to Africa to investigate a range of human and animal diseases. In 1908 Koch visited America and Japan.

In 1910 Koch suffered a severe heart attack; he died a short time later. His body was cremated and the ashes deposited in a mausoleum in the Institute for Infectious Diseases in Berlin. *See also* Cholera: Fourth through Sixth Pandemics, 1862–1947; Contagion Theory of Disease, Premodern; Microscope.

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K. CODELL CARTER

L

LASSA FEVER. See Hemorrhagic Fevers; Hemorrhagic Fevers in Africa.

LATIN AMERICA, COLONIAL: DEMOGRAPHIC EFFECTS OF IMPORTED DISEASES. Epidemics of imported diseases had a significant impact on demographic patterns throughout Latin America during the colonial period. Shortly after the arrival of Europeans in the Caribbean in 1492, the transfer of diseases from the Old World to the New began. During the next three centuries, epidemics of **smallpox, measles, bubonic plague, yellow fever,** and **malaria** appeared at regular intervals. Patterns of epidemic disease varied significantly by region, influenced by such factors as geography, climate, and population density. Some diseases such as smallpox, measles, yellow fever, and malaria eventually became endemic in specific areas. The first appearance of imported diseases resulted in virgin-soil epidemics (initial outbreaks of a disease previously unknown or absent from a particular area for many generations) that often produced morbidity rates over 50 percent and mortality rates of 25 to 50 percent. In general, throughout Latin America, indigenous populations declined 75 to 90 percent in the first century following contact with Old World diseases. Although the demographic impact of imported diseases on people of African or European origin was less severe, overall, epidemic disease had a devastating impact on human populations throughout Latin America between 1492 and 1800. The combination of epidemic disease and the violence and dislocation of European conquest ultimately produced significant social, demographic, economic, and political changes among indigenous populations, facilitating European conquest and colonization of the region.

The Historical Record. The historical record regarding the demographic impact of imported diseases varies significantly by region. Because Spanish **colonialism** in much of Latin America depended on a steady supply of indigenous labor, Spanish officials attempted to document the size of native populations in particular areas. Given that the largest indigenous populations resided in central Mexico and the Andean highlands, the

most numerous and detailed records concerning epidemics of imported diseases and their demographic effects can be found in these areas. Although not as numerous, similar documents are also available for the Caribbean and Brazil, where Jesuit missionaries also recorded their observations of the demographic destruction visited upon native communities by diseases of Old World origin.

Spanish attempts to document the size of indigenous populations took a variety of forms during this early period. Some Spanish officials and settlers included estimates of the size of native populations in their written accounts. For example, Hernán Cortés (1485–1547), the conqueror of Mexico, offered estimates of the size of Aztec armies in his famous letters to the king of Spain. But the most detailed and numerous sources of demographic data during the sixteenth and seventeenth centuries derive from the efforts of royal officials to ascertain the size of indigenous populations for purposes of taxation and labor drafts. Following the military conquest of specific regions, Spanish conquerors and officials moved quickly to impose a system of tribute collection, and the first step in this process was to determine the number of Indians subject to this onerous tax. The censuses and tribute lists that resulted focused primarily on the number of adult males in a community, but in some cases they were organized by household and included the names and ages of everyone in the family. In some of the larger cities and towns of the Spanish empire, parish registers also recorded valuable information on demographic trends.

Just as the historical record varies by region, it also varies over time, with more detailed descriptions of epidemics and more complete census documents appearing during the second half of the eighteenth century. Historians and demographers have struggled with these problematic sources, especially those for the sixteenth and seventeenth centuries, for many years, and the controversy surrounding their reliability and usefulness is far from settled.

Nature of the Diseases. Before the arrival of Europeans at the end of the fifteenth century, the disease environment of the Americas resembled that of other parts of the world in many significant respects. Acute respiratory and gastrointestinal diseases posed the greatest threats to human health, just as they did among Old World populations. Archaeological and documentary evidence also indicates that epidemics of **typhus** and **influenza** probably existed in the Americas before 1492. In addition, periodic famines, accompanied by high rates of secondary infections and mortality, also claimed the lives of significant numbers of native Americans. Finally, archaeological evidence suggests that high levels of violence, often as the result of **warfare**, played an important role in reducing indigenous populations before the end of the fifteenth century. But in spite of these similarities, the native peoples of the Americas were not immunologically prepared for the advent of a number of new, virulent infections that arrived along with European colonists and African slaves beginning in the early sixteenth century.

Smallpox, measles, bubonic and **pneumonic plague**, malaria, and yellow fever, all played a role in reducing the size of native populations throughout the New World. Smallpox and measles, both viral infections with attendant skin eruptions or rashes, were among the first of these diseases to make the trans-Atlantic journey. Both infections triggered virgin-soil epidemics, with accompanying mortality rates of 25 to 50 percent. Bubonic plague and its more virulent form, pneumonic plague, were often more difficult for observers to identify because their symptoms could be confused with other illnesses. Bubonic plague is caused by a bacillus that is transmitted to humans through the bites of infected fleas; whereas pneumonic plague, also caused by the plague bacillus, is spread

directly through airborne droplets inhaled by those who come into contact with the sick. This more virulent form of the disease is characterized by high fever, headache, and sudden death, often claiming the lives of close to 100 percent of those infected.

Malaria was another imported disease that decimated American populations, both indigenous and European. Common in Europe, the disease, characterized by high fever and in some cases delirium, may have been introduced early in the sixteenth century and quickly became endemic in many areas. Although malaria is often a chronic disease, lying dormant in the human body for long periods, it can prove fatal to individuals already weakened by other infections or malnutrition.

Yellow fever was introduced from Africa as a result of the slave trade, probably during the 1640s. Symptoms of the disease, transmitted by the female *Aedes aegypti* mosquito, included sudden onset, fever, lethargy, jaundice, and sometimes the vomiting of blood. Although the disease proved especially lethal for Europeans and native Americans, Africans also succumbed, albeit in smaller numbers.

Origins and Spread. Historians have identified numerous outbreaks of disease among both European and indigenous populations in the two decades following Christopher Columbus's (1451–1506) arrival in the Caribbean. But the first clearly documented epidemic of a disease imported from the Old World began in 1518 when smallpox appeared among the native population of Hispaniola. From this seat of Spanish colonial control, the disease spread quickly to other islands and finally to the Mexican mainland in 1520, arriving in time to play a major role in Cortés's siege of the Aztec capital, Tenochtitlán. From central Mexico, smallpox made its way south into Guatemala the following year. From there the disease probably continued into other areas of Central America and eventually into the Andean highlands. Although the arrival of smallpox is less clearly documented in South America, the disease may have arrived sometime between 1524 and 1530 when an epidemic swept through the Inca Empire, claiming the lives of several members of the Inca royal family and thousands of their subjects. The first recorded epidemic of smallpox in Brazil occurred in 1562, and thereafter, the disease reappeared at regular intervals for the remainder of the colonial period. Mortality rates associated with these first outbreaks of smallpox ranged between 25 and 50 percent for native Americans.

Initial epidemics of measles were more difficult to identify because the symptoms of the disease were often confused with those of smallpox. But given the long history of these diseases among European populations, the documentary evidence suggests that both viral infections had arrived in the Americas by the 1530s. Like smallpox, epidemics of measles often resulted in mortality rates of 25 to 50 percent. In some instances, both diseases appeared simultaneously, raising mortality rates even higher.

Given the challenges of distinguishing the symptoms of bubonic and pneumonic plague from other illnesses, the arrival of plague in the Americas is difficult to pinpoint. Epidemics of an illness that triggered severe hemorrhaging from mucous membranes occurred in Mexico and Peru in the 1540s and again in Mexico in the 1570s. Some scholars have also suggested that plague may have appeared in Brazil between 1559 and 1563, as the disease was epidemic in Portugal at the time and because observers described fever and hemorrhaging as symptoms of an illness then ravaging the indigenous population.

Although the documentary record is far from conclusive, malaria may have been the first of the imported diseases to appear in the New World, possibly arriving along with Columbus's fourth expedition in 1502. Columbus recorded that he, his son, and members of his crew became seriously ill, suffering from severe fevers. Because malaria was endemic

throughout the Iberian Peninsula, many Europeans carried the plasmodium that caused the infection in their blood. Many explorers also recorded their encounters with swarms of mosquitoes, and research has revealed that the New World was home to species of the mosquito required to transmit the disease. Once introduced, malaria quickly became endemic and posed a severe threat to the health of both indigenous and European populations throughout the colonial period, especially in lowland tropical areas.

Yellow fever appears to have been the last of the Old World diseases imported to the Americas during the colonial period. Endemic to parts of Africa, the spread of this disease to other parts of the world followed the route of the African slave trade. The first documented outbreak of yellow fever occurred on the island of Barbados in 1647. From there the disease spread to other islands in the Caribbean and onto the mainland of Mexico and northern South America by the 1650s. Records indicate that epidemics of yellow fever did not reach Brazil or the Pacific coast of South America until the 1740s or even later. Both Europeans and natives proved highly susceptible to yellow fever, whereas long-term exposure to the disease among African populations conferred some measure of immunity.

The rapid and dramatic decline of native populations in response to the violence of European **colonialism** and the introduction of Old World diseases transformed the economic and political structures of indigenous societies. Migration, both forced and voluntary, altered settlement patterns and facilitated Spanish and Portuguese access to valuable natural resources. Warfare, famine, and epidemics led to declining birth rates, shrinking households, and rising rates of morbidity and mortality. Indigenous political structures changed as traditional native leaders collaborated with, or were replaced by, Spanish and Portuguese officials intent on implementing policies originating in European capitals. The responses of indigenous societies to epidemics of imported diseases and institutions of European colonialism also changed over time and included warfare and other forms of violence, messianic movements, **flight**, recourse to Spanish and Portuguese law courts, and the selective adoption and adaptation of various aspects of European culture, including Christianity.

It is interesting to note that although the history of European colonialism in Latin America has been rewritten by generations of scholars, few topics have generated the heated and often acrimonious rhetoric that surrounds the debate over the demographic history of the region on the eve of European contact. The controversy over estimating the size of New World populations began during the early sixteenth century, but the debate has been especially passionate since the 1960s. Many authors have published their calculations, some based on written records, others on mathematical formulas and computer simulations, and others on no apparent evidence at all. A review of some of the most widely cited figures reveals estimates that range from a low of 8.4 million to a high of 200 million.

Although the numbers themselves are significant, this emotional debate centers around three broad issues: First, what was the level of social, political, demographic, and economic development of New World societies before 1492? Second, to what extent did European colonialism and the introduction of Old World diseases devastate native American populations? And third, what is the nature of and appropriate use of the historical record? At the heart of this debate is a political schism between “high counters,” those who view the aftermath of 1492 as the largest genocide in human history perpetrated by Europeans against the indigenous peoples of the Americas, and “low counters,” those on the other side who argue that the native population of the New World was never large and that Europeans crossed the Atlantic to encounter a sparsely populated wilderness. The notion of the Americas as wilderness strengthens the argument that the political and economic

benefits of Western civilization outweighed the destruction occasioned by the European conquest of the Americas.

The research of the later twentieth and early twenty-first centuries has revealed much about the social, political, and economic development of native American peoples before the arrival of Europeans; but the number of people who inhabited this hemisphere at the end of the fifteenth century will probably never be known for certain. What cannot be disputed, however, is that European colonialism and the introduction of diseases from the Old World reduced native American populations by 75 to 90 percent during the first century following contact. Furthermore, although the demographic impact of imported diseases on people of African or European origin was less severe, overall, epidemic disease had a devastating impact on human populations throughout Latin America between 1492 and 1800. *See also* Demographic Data Collection and Analysis, History of; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Environment, Ecology, and Epidemic Disease; Historical Epidemiology; Human Immunity and Resistance to Disease; Insects, Other Arthropods, and Epidemic Disease; Malaria in the Americas; Measles in the Colonial Americas; Slavery and Epidemic Disease; Smallpox in Colonial Latin America; Yellow Fever in Colonial Latin America and the Caribbean.

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SUZANNE AUSTIN

LAVERAN, CHARLES LOUIS ALPHONSE (1845–1922). Alphonse Laveran was awarded the Nobel Prize for Physiology or Medicine in 1907 for his discovery of the **malaria** parasite that led to the identification of the mosquito's role in **transmission** of the disease. He was born in Paris, France, but when he was only five, his family moved to French Colonial Algeria, where his father had been transferred by the French army's medical service. Like his father and grandfather, Laveran elected to pursue a career in military medicine and completed his medical studies at the School of the Health Service of the Armies at Strasbourg in 1867. He served in the Franco-Prussian War (1870–1871) and was at the siege of Metz, where he helped care for the wounded.



Alphonse Laveran. Courtesy of the National Library of Medicine.

When the city surrendered to the Prussians, Laveran was released and returned to France. He was then sent to the military hospital at Lille where he remained until the end of the war.

By age 29, Laveran was Professor of Diseases and Epidemics of Armies at the Val-de-Grâce Hospital in Paris, and when his appointment ended in 1878, he was reassigned to Algeria. He knew that about 30 percent of army personnel suffered from malaria. Deaths from malaria were higher than those from any other cause, so he began to autopsy malaria victims and examine the blood of individuals who suffered from the disease. Laveran began his study with the black malarial pigment, an iron-containing product from infected red blood cells, found in livers, spleens, and brains of malaria victims. It was during his studies, on November 6, 1880, that he made his first observations of the living malaria parasite. While examining freshly drawn blood from his patients, he clearly saw moving parasites that could not be seen in fixed and stained preparations. At the time, Laveran still accepted the long-standing theory that malaria was some sort of toxic vapor (*mal'aria*, “bad air”) that arose in tropical swamps and was spread through the air. The connection between malarial fevers and marshes

was very old, but, as Laveran realized, there were parts of the world where marshes existed without malaria, and conversely malaria could occur where there were no marshes. For a time, Laveran also considered the possibility that the malaria “germ” was in drinking water and that it would not occur if drinking water were first boiled. However, two years before Laveran’s discovery of the malarial parasite, **Patrick Manson** had determined that the mosquito played a role in the development of another parasitic disease, and this ultimately led to the discovery of the role of the *Anopheles* mosquito in the transmission of malaria. Laveran spent his later years as a scientist studying **trypanosomiasis** and other tropical diseases caused by **protozoa**. See also Germ Theory of Disease; Insects, Other Arthropods, and Epidemic Disease; Ross, Ronald.

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RICHARD EIMAS

LAZARETTO. See Leprosarium; Pest Houses and Lazarettos.

LEEUWENHOEK, ANTONY VAN (1632–1723). Antony van Leeuwenhoek, a deeply curious man without a university education, is considered the father of bacteriology. In 1676, using a single lens **microscope** that he ground himself, he described the existence of what was later labeled by the German botanist Ferdinand Cohn (1828–1898) as **bacteria**. He believed that there was a similarity of form and function among all living things.

Leeuwenhoek was born in Delft, Holland, and prospered in the cloth trade, in which he had to use microscopes, available in Holland since the early seventeenth century, to look for flaws in material. It is possible that his interest in science was sparked by a visit to England, when he saw English scientist Robert Hooke's (1635–1703) book, *Micrographia* (1665), illustrating plants and animals seen with a compound (two lenses) microscope. Starting in 1671, Leeuwenhoek, who would not use a compound microscope, made the first of about 500 microscopes, most of them tiny, and many holding only one specimen permanently. As historian J. R. Porter puts it, his "special skill lay in polishing and mounting the lens between the metal plates, in obtaining the proper source of light, and in focusing on the object. Objects to be viewed were mounted on a small pin or specimen holder and brought into focus by adjusting two or three threaded screws, which moved the specimen in various ways in front of the lens."

Leeuwenhoek was friendly with some noted Dutch scientists, who encouraged him to share his finding with the world's oldest national scientific society, the Royal Society in England, and they translated hundreds of letters from one language to another. Leeuwenhoek used nonscientific terminology, illustrated all his letters, and described "animalcules" (the "little animals" or microorganisms) that he saw with his microscopes. He carried out experiments on bacteria, which he obtained from a variety of locations, including all his own bodily secretions. He discovered that both vinegar and hot coffee would kill bacteria and that heat would harm it. He examined bacteria that grew in sealed containers of pure rainwater infused with pepper and was the first person to see that bacteria would grow without exposure to air.

Though scientists throughout Europe were using compound microscopes to study organisms, Leeuwenhoek's work was not surpassed until the nineteenth century. Leeuwenhoek did not train any scientific apprentices, and his secrets died with him. See also Germ Theory of Disease; Scientific Revolution and Epidemic Disease.

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MARTHA STONE

LEGIONNAIRES' DISEASE. Legionnaires' Disease is a potentially fatal pneumonia caused by infection with the Gram-negative **bacterium** *Legionella pneumophila*. Mortality is highest among the elderly and individuals with compromised **immunity**. It is named for a famous outbreak among attendees at a national convention of the American Legion, an American military veterans organization, in Philadelphia during the summer of 1976. Prior to that outbreak, this organism and its association with human disease were unknown. In 1968 a similar flu-like illness with very rapid onset (2 to 48 hours after exposure) was detected among people in the Health Department Building in Pontiac, Michigan, which was later found to have been caused by *L. pneumophila*. This illness has been called Pontiac Fever; it is self-limited, resolves without treatment, and does not result in pneumonia. It is considered a less severe form of infection with *Legionella*.

The **Centers for Disease Control and Prevention** (CDC) report that the disease affects 8,000 to 18,000 individuals per year (and probably more because of underreporting). Only about 10 to 20 percent of cases are identified with outbreaks, and about 20 percent are nosocomial (hospital-acquired). The majority of cases are sporadic, not associated with clustered outbreaks. Case fatality rates have been reported between 1 and 40 percent and appear to depend on the rapidity of **diagnosis**, institution of preventive measures, and appropriate **antibiotic** treatment. No person-to-person spread has ever been noted.

The organism of Legionnaires' Disease, *L. pneumophila*, is a facultative intracellular pathogen, which means that it is able to grow within cells, but it does not have to do so. In the natural ecology of the organism, it appears that *L. pneumophila* can infect free-living amoebae in warm freshwater, especially air-conditioning cooling **water**. Its ability to grow inside of other cells explains some of its pathogenicity in humans. The organism invades and multiplies inside macrophages, especially those in the lung, eventually killing these immune defense cells. The bacteria inhibit the normal mechanisms the macrophages use for attacking bacteria—that is, they prevent fusion of the phagosomes with the lysosomes within the macrophages. In this way, *L. pneumophila* escapes the usual **immunity** provided by the macrophage system.

The nearest relative to the *Legionella* group of organisms is *Coxiella burnetii*, the pathogen responsible for Q-fever. Although *Coxiella* also invades macrophages, it appears to be able to survive within the acidic lysosomes, using a slightly different mechanism from *Legionella* for evasion of host cell destruction. Even so, the two groups of bacteria share many related genes.

Because of its intracellular location, the susceptibility of *L. pneumophila* to antibiotics in laboratory cultures is not a good guide to clinical utility. Drugs must achieve high intracellular concentrations to be effective in the infected patients. Antibiotics with good intracellular penetration include the macrolides (e.g., erythromycin), quinolones (e.g., ciprofloxacin), tetracyclines (e.g., doxycycline), and rifampin.

The outbreak from which this disease gets its name started in Bloomsburg, Pennsylvania, on July 30, 1976, with the diagnosis of pneumonia of unknown origin in three men who had attended the national convention of the American Legion in Philadelphia a few days earlier. By August 2, 1976, the Pennsylvania State Health Department realized that a new disease was occurring among other attendees at the convention. Within the week, however, investigators had provisionally ruled out most known bacteria, fungi, and **viruses** as possible causes of these pneumonia cases. Causes discussed in the scientific and popular media at that time ranged from toxic chemicals to **bioterrorism** (domestic or foreign) aimed at the veterans. By September 1976, the focus had shifted from outside

causes, such as a disease carrier, to the hotel environment itself, especially on toxins such as nickel carbonyl. For about six months, it appeared that little progress was being made, and public anxiety grew with alarmist newspaper accounts and congressional hearings. In January 1977, however, the CDC identified a previously unrecognized bacterium as being associated with the outbreak. This organism was subsequently classified as *Legionella pneumophila*. With the realization that this organism was sensitive to several known antibiotics, public anxiety abated, but not before an estimated 180 cases resulting in 29 deaths had been studied. The convention hotel was closed as well (later to reopen).

Since this initial 1976 outbreak, other outbreaks have been identified around the world: United Kingdom, 1985 and 2002; Netherlands, 1999; Spain, 2001 and 2006; Norway, 2001 and 2005; France, 2004; New Zealand, 2005; Canada, 2005; Australia, 2007; and the United States (New York), 2007. See also Disease, Social Construction of; Environment, Ecology, and Epidemic Disease.

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WILLIAM C. SUMMERS

LEPROSARIUM. Leprosaria have also been known as leper houses, leper colonies, and in the European Middle Ages lazar houses (also lazaretto, lazarette, or lazaret; after Lazarus, a biblical figure whom Christians believed was cured of his **leprosy** by Jesus). Modern leprosaria are hospitals and infirmaries that treat victims of leprosy, more properly known as Hansen's disease. Most leprosaria are residential hospitals, which is why they are also known as leper colonies. There are hundreds of leprosaria actively housing patients around the world, most notably in India, Africa, Brazil, and China. The last leprosarium in the continental United States was established in 1894 by the State of Louisiana in Carville, Louisiana. The site chosen was an abandoned plantation with a dilapidated mansion and seven old slave cabins. Known initially as the Louisiana Leper Home and staffed by Catholic nuns, the U.S. Public Health Service took over its management in 1921. Recently it was closed, but some of its research, education, and treatment functions were moved to Louisiana State University at Baton Rouge.

In the European Middle Ages leper houses were usually run by monastic houses and were thus organized in a similar fashion. The leper in effect took religious vows and removed him or herself from the community at large. Once diagnosed with leprosy (which in fact was often a misdiagnoses of other skin conditions), the medieval leper was pronounced dead and forced to enter a leprosarium. He or she was then enjoined to pray for absolution of whatever may have caused the leprosy, as all diseases in the Middle

Ages were viewed as punishments from God for sin. There were also strict laws limiting the leper's contact with the healthy; lepers were not allowed to enter most European towns during the day and usually had to ring a bell or a clapper to announce their presence, to limit physical contact with others. European experience with lepers set the pattern for isolating plague victims, and during plague outbreaks empty leprosaria often became **pest houses**.

Elsewhere in the world, and in time, other cultures also built leprosaria to isolate those afflicted with the disease. Because leprosy is a disfiguring disease, and the physically disfiguring symptoms have often been deemed too disturbing to look upon, and because the disease was generally feared as highly contagious, leper houses were created to remove the leper and protect the community. Many leprosaria were built far away from communities, to isolate the patients further. Others were built near major settlements, to ensure ease of collecting donations to support the leprosaria. Because medical science has now determined that Hansen's disease is not as contagious as once thought, and as there has been a general change in attitude toward people disfigured by disease, many leprosaria worldwide have closed, and patients have been integrated into other medical facilities or into society at large. See *also* Leprosy in the Premodern World; Leprosy in the United States; Leprosy, Societal Reactions to; Scapegoats and Epidemic Disease.

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CANDACE GREGORY-ABBOTT

LEPROSY. Leprosy is a **bacterial** infection that causes damage to skin and nerves, with resulting disfigurement and deformity. Although leprosy is now curable, and the risk to exposed individuals is extremely low, the very word leprosy continues to evoke strong emotions. The disease remains endemic in some tropical countries.

Leprosy is caused by *Mycobacterium leprae* (*M. leprae*), a slow-growing, rod-shaped bacterium. Bacteriologists classify *M. leprae* as acid-fast bacteria (AFB) because it is resistant to decolorization by acids during conventional staining. With the commonly used Fite stain, *M. leprae* appears bright red under the microscope.

Norwegian researcher **Gerhard Hansen** first identified the leprosy bacillus microscopically in 1873. *M. leprae* lives within human cells, preferring the cooler temperatures in the nerves and skin of the extremities. Scientists have never succeeded in growing cultures of *M. leprae* in nutrient broths or on agar, hampering research into the disease. *M. leprae* can be grown in nine-banded armadillos (*Dasypus novemcinctus*), the only natural nonhuman reservoirs of the disease, and in laboratory mice. Recent sequencing of the *M. leprae* genome should lead to advances in treatment and prevention.

Most people who become infected with *M. leprae* mount an immunological defense that eliminates the infection. In progressive cases, symptoms are caused not only by invasion of bacteria, but also by immune responses triggered by the bacteria. *M. leprae* is transmitted through respiratory secretions. Transmission through skin patches or sores rarely, if ever, occurs. Close contact with an infected person increases the risk of transmission. Mothers do not infect their children in the uterus, but children in crowded households are susceptible to *M. leprae*. Most victims have no known contact with the disease. Even before the introduction of antimicrobial therapy, nurses and other caregivers were rarely infected. Some individuals appear to have increased genetic susceptibility to the disease.

The incubation period of leprosy averages four to ten years. The diagnosis is usually confirmed by identification of *M. leprae* in skin scrapings or tissue samples. In untreated patients, progressive nerve damage causes loss of sensation, especially in the hands and feet. Patients are unable to feel trauma such as burns, cuts, or painful pressure leading to chronic skin ulcerations with destruction of underlying bone. In time, the tissues become contracted or deformed, and fingers and toes may be destroyed (autoamputation). Further disability results from damage to motor nerves with subsequent muscle weakness in the hands and feet. Leprosy is usually not fatal, but many victims have died from neglect, uncontrolled infections, and behavior related to their despair.

There are two major forms of leprosy as well as several intermediate or borderline forms. Tuberculoid leprosy produces pale, dry, scaling skin patches with decreased or absent feeling as a result of nerve damage. Hypertrophied (enlarged) nerves may be felt through the skin. Tuberculoid leprosy is also called paucibacillary leprosy (*pauci-*, few) because there are very few *M. leprae* present in the skin and nerves.

The more severe form of leprosy is called lepromatous leprosy. These patients develop skin thickening and nodules as well as damage to the motor and sensory peripheral nerves. The number of *M. leprae* bacteria in the body of the patient is very high (multibacillary leprosy), thus rendering untreated patients more infectious. In addition to skin and nerves, *M. leprae* may attack the eyes, nasal cartilage, and larynx causing, respectively, blindness, collapse of the nasal bridge, and hoarseness. In some patients, skin nodules on the face produce a characteristic lion-like facial expression (leonine facies).

Historically, leprosy has tended to cluster in certain geographic areas. In North America the disease was once prevalent in Louisiana and New Brunswick, Canada. Although leprosy is generally endemic rather than **epidemic**, major population dislocations under conditions of **war** or natural disaster expose more people to the disease. For example,

NAMING THE UNSPEAKABLE

Near the end of the twentieth century, victims, caregivers, and the medical community at large decided that use of the term “leper,” with its centuries-old stigmatizing power, should be abandoned in favor of “Hansen’s Disease,” a name recognizing the central role of Norwegian biologist Gerhard Hansen in leprosy research. Around the globe and across time, however, Hansen’s Disease has had many different labels. The term in Old Norse, ancestor of Hansen’s Norwegian, is directly related to the verb “to suffer.” In Mali it is “the big disease,” while Brazilians refer to it as “the spot disease.” In the southern United States some folks refer to it as “this package,” but among Cajuns in Louisiana it is “the disease you do not name.” Arabic has long had two labels: one is *djudham*, which derives from the verb to cut off or mutilate, and the other is *al-baras*, a reference to the hypopigmented white blotches on the victim’s skin.



A woman, naked to the waist, shows the lesions resulting from leprosy on her back and arms, 1979. WHO photo. Courtesy of the National Library of Medicine.

dozens of American servicemen contracted leprosy in the Philippines during the Spanish-American War. Theories explaining the sharp decline in leprosy in Europe in the fourteenth century include improved standard of living, advances in hygiene, crossover immunity from **tuberculosis**, depopulation from **bubonic plague**, and the effectiveness of isolation measures. In retrospect, isolation was probably never very effective in preventing spread of the disease. The last endemic focus of leprosy in Western Europe was in Norway, where the disease lingered into the early twentieth century.

It is not surprising that scores of ineffective drugs and treatments have been tried over the centuries in an effort to control leprosy. Chaulmoogra oil, obtained from the seeds of several species of trees, was used for hundreds of years to treat leprosy in Asia and India. Western physicians introduced injectable forms of chaulmoogra oil in the first half of the twentieth century with unpleasant side effects and questionable benefits.

In 1940, Drs. Guy Faget (1891–1947) and Frederick Johansen at the U.S. Public Health Service Hospital in Carville, Louisiana (the national leprosy hospital), discovered that new injectable drugs Promin and DDS (dapson) could help some patients, despite severe side effects.

Physicians in a number of countries soon devised effective, tolerable regimens of oral dapsone. In many patients, years of dapsone therapy eliminated *M. leprae* and reversed or improved symptoms. Outpatient treatments ended years of forced hospitalization and isolation. Within a few decades, single drug therapy with dapsone led to **drug resistance** and relapses. In some patients, therapy was complicated by severe inflammatory reactions.

Since the 1980s, the key to treatment and cure of leprosy has been multidrug therapy (MDT). Standard MDT includes dapsone, rifampin, and clofazimine, usually self-administered under medical supervision. Rifampin rapidly kills *M. leprae*. Clofazimine and dapsone slow the growth of the bacteria; clofazimine also helps prevent inflammatory reactions. **World Health Organization** regimens, designed for maximum ease of administration in medically underserved areas, range from 6 to 12 months, although treatment is usually given for longer periods in the United States. Isolation is unnecessary because patients are rendered noninfectious within a matter of weeks. Ideally, patients should be identified and treated before nerve damage leads to irreversible

ulcers, deformities, or loss of digits. Bacille Calmette-Guerin (BCG) vaccine, widely used outside the United States to prevent tuberculosis, may protect some household contacts.

In medieval Europe, leprosy was variously seen as a loathsome disease, a biblical scourge, a venereal affliction, a divine punishment, or paradoxically a symbol of divine grace. Because disease clusters occurred in households, leprosy was also considered a hereditary disorder. Today, the term “leper,” with its layers of historical meaning, is avoided because it is offensive to victims of leprosy. Some patients and advocates prefer the term Hansen’s disease.

Leprosy may have originated in antiquity, but historians are cautious in making modern diagnoses based on ancient descriptions. Biblical use of the ancient Hebrew word for scaly skin disease (*tsara-ath*) was mistranslated as “leprosy.” Prior to the introduction of effective antimicrobial therapy in the 1940s, the fundamental and almost universal response to leprosy was banishment of the victims from society to protect the community. In the prison-like setting of many government-mandated facilities for the forced isolation of leprosy victims, such as the colony established on Molokai in the Hawaiian Islands in 1865, complete neglect of hygiene and basic care resulted in foul-smelling ulcerations complicated by malnutrition and exposure. Members of religious orders and medical missionaries often assumed the onerous task of establishing and staffing hospitals or medical colonies. The best known of these was the Belgian priest Father Damien (1840–1889), who arrived at Molokai in 1873. Nineteenth-century imperialist governments frequently established isolation institutions and policies, as the Americans did in the Philippines. In every society, some victims lived secretly or remained hidden rather than face a grim future in **leprosar**. Even the best leprosy hospitals were both haven and prison for their stigmatized residents.

Since 2000 the number of new cases has decreased by about 100,000 annually, with 300,000 new cases diagnosed in 2005. Most of these cases occur in places where the disease is endemic, led by India and Brazil. Political, social, logistical, and informational barriers continue to challenge international efforts to eradicate leprosy. Fewer than 200 cases of leprosy were detected in the United States in 2005, with most occurring in immigrants from endemic areas. *See also* Diet, Nutrition, and Epidemic Disease; Leprosy in the Pre-modern World; Leprosy in the United States; Leprosy, Societal Reactions to; Scapegoats and Epidemic Disease.

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SANDRA W. MOSS

LEPROSY IN THE PREMODERN WORLD. Research in molecular evolution suggests that *Mycobacterium leprae*, the pathogen responsible for **leprosy** or Hansen's disease, probably evolved in east Africa or the Near East as a single clone that was then spread by human migrations, acquiring a very small amount of genetic diversity along the way. It probably first moved eastward to India and China and the Pacific, and then northwestward to Europe. Leprosy strains in the Americas are closely related to strains from Europe and North Africa and from West Africa, not to strains from East Asia. This indicates that leprosy was introduced to the Western Hemisphere by European settlers (especially from the Scandinavian countries, the last stronghold of the disease in Europe) and by the slave trade from West Africa. In other words, leprosy reached the Americas after Christopher Columbus (1451–1506). However leprosy was known to all the great ancient civilizations in the Old World

China, India, and the Western Pacific. Leprosy was well known in China from the middle of the first millennium BCE onward. An anecdote dating to the "Warring States" period (475–221 BCE) shows that people were frightened to approach lepers. In 1975 archeologists working on the tomb of a local official who died in 217 BCE unearthed a text on a bamboo strip describing sanctions against lepers who committed crimes. This text shows that China had a complex body of legal regulations for dealing with lepers by that time. Lepers who committed capital crimes were to be executed by drowning, an otherwise unknown method of execution that was thought to wash away ritual impurity, whereas those who committed less serious offenses were to be sent to special penal colonies for lepers. From the time of the Han dynasty onwards (206 BCE–220 CE) there are references to individuals of high social status who were thought to be suffering from the disease. Leprosy was a problem for all social classes. The philosopher Confucius (551–479 BCE) attributed leprosy to the will of heaven, but doctors sought naturalistic explanations for the disease from an early stage. The *Neijing*, a classic early Chinese work of medicine dating to the Warring States period, attributed leprosy to a factor called "feng." By the time of the *Neijing* it had already been recognized in China that many people who come into contact with leprosy cases fail to develop the disease themselves; in other words they are resistant to leprosy. Human genetic factors appear to play a very important role in determining susceptibility to leprosy. In 610 CE the doctor Chao Yuanfang (550–630) tried to explain leprosy in terms of a living pathogen that was thought to attack people. During the Song dynasty (960–1279 CE) Chen Yan (fl. c. 1174) was the first Chinese doctor to describe leprosy as an infectious disease. From China movements of peoples speaking Austronesian languages carried leprosy eastward to the Pacific Islands. Skeletons of medieval date with bone deformations typical of leprosy were excavated on Guam in the Pacific. Leprosy ("kustha") is

clearly described in the great early medical texts of India and Ceylon such as the *Susruta Samhita*. “Kustha” was an infectious disease thought to be transmitted by respiration or touch, through sexual intercourse, or through handling objects previously touched by a person with leprosy. In certain respects this analysis was extremely perceptive, because leprosy is now known to be acquired primarily by inhalation. Skeletons exhibiting symptoms of leprosy have been excavated at an Iron Age archeological site in Thailand (500 BCE–300 CE).

Ancient Near East and Egypt. There has been a considerable amount of scholarly controversy regarding the presence of leprosy in the ancient Near East. Nevertheless, the balance of probability is that it was present. One cuneiform text from ancient Mesopotamia, which mentions the destruction of fingers and toes, sounds like a description of leprosy. There is also mention of white patches or nodules on the body, possibly a distinction between tuberculoid and lepromatous leprosy, the two principal forms of the disease. There has been plenty of discussion about how to interpret the term *tsara’ath* found in the Biblical book of Leviticus. Though generally translated into English as “leprosy,” it seems preferable to interpret this word as a designation of ritual impurity in general, thought to require social exclusion, rather than as a description of a specific disease such as leprosy. However the term probably covered cases of leprosy in practice alongside sufferers from other skin diseases such as psoriasis. The Greek historian Herodotus (c. 484–425 BCE) states that social exclusion measures were taken against victims of a “white disease” in Persia in the fifth century BCE. The so-called “Phoenician disease” mentioned in a **Hippocratic** text of the fifth or fourth centuries BCE was leprosy, according to **Galen’s** commentary from the second century CE, but no detailed information about it is available. There are no clear descriptions of leprosy in ancient Egyptian medical texts, such as the papyrus Ebers, dating to the time of the Pharaohs.

Ancient Greece and Rome. The argument from the silence of the ancient Egyptian sources, which seldom describe any recognizable disease, is not conclusive. As soon as Greek migration to Egypt commenced in the late fourth century BCE, after the conquests of Alexander the Great (356–323 BCE), the Greeks started to notice the high prevalence in Egypt of leprosy, which to them was a new disease. Four skeletons, dating to the second century BCE and showing symptoms of leprosy, were excavated in the Dakhleh oasis in Egypt, possibly a colony for exiled lepers. There are no references to leprosy in the texts of the Hippocratic corpus, dating to the fourth and fifth centuries BCE, apart from the “Phoenician disease.” The physician Straton (c. 340–268 BCE) was the first Greek author to describe leprosy. Because the new disease lacked a name in Greek, Straton called it “kakochemia,” but this new term did not catch on. It was soon replaced by “elephantiasis,” which became the standard ancient Greek word for leprosy. It was also sometimes called the “sacred disease,” a euphemism also covering epilepsy. The Hippocratic word “lepra” originally had nothing to do with leprosy but was employed to translate the Hebrew *tsara’ath* into Greek and so eventually came to be associated with the new disease. The Roman encyclopedist Pliny the Elder (23–79) described leprosy as a new disease, which had only been known since the time of the doctor Asclepiades of Bithynia (late second century BCE). Similarly the medical writer Celsus (25 BCE–50 CE) regarded leprosy as a foreign disease in the first century CE. By that time the Greeks and Romans were becoming sufficiently familiar with the new disease to give good clinical descriptions of the lepromatous form, starting with Aretaeus in the first century CE, followed by Rufus of Ephesus (fl. late first c. CE) and Galen in the second century CE. Galen stated that leprosy was common

in Alexandria in Egypt, an opinion repeated by **Avicenna** in the medieval period. In the fourth century CE, the sermons of the bishops of Cappadocia (in modern Turkey), such as St. Basil (c. 330–379), demonstrate a preoccupation with the social problems created by leprosy. The slow spread of leprosy is in fact the best-documented example of the spread of a new disease into the Greco-Roman world. Leprosy spreads slowly because *Mycobacterium leprae* is a very slow-growing species of bacterium.

Medieval Europe. The spread of leprosy throughout Europe principally occurred in late antiquity and the medieval period. There were notable additions to Western knowledge about leprosy in the early medieval period. Arab physicians, such as Abul-Qasim (c. 936–1015) in Spain, and Byzantine doctors such as Paul of Aegina (c. 625–690) began to realize the importance of the neurological symptoms of tuberculoid leprosy, which is the least virulent form and had been overlooked by earlier writers. Archeological excavations of several cemeteries attached to leprosaria in Denmark and Britain have confirmed the reality of leprosy in northwestern Europe in the medieval period. The skeletal remains at Odense in Denmark show that lepers with facial symptoms were singled out for inclusion in the leprosarium, following the diagnostic criteria given by literary sources. Leprosy was not just a social construct, as has been suggested; it was a real disease in Europe at that time, although some accusations of being a leper were doubtless employed to exclude individuals from wider society. Research on ancient DNA from *Mycobacterium leprae* is also starting to make a contribution to knowledge of medieval leprosy. *See also* Ayurvedic Disease Theory and Medicine; Chinese Disease Theory and Medicine; Colonialism and Epidemic Disease; Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Greco-Roman Medical Theory and Practice; Hansen, Gerhard Armauer; Heredity and Epidemic Disease; Human Immunity and Resistance to Disease; Islamic Disease Theory and Medicine; Latin America, Colonial: Demographic Effects of Imported Diseases; Leprosy, Societal Reactions to; Paleopathology; Personal Liberties and Epidemic Disease; Religion and Epidemic Disease; Scapegoats and Epidemic Disease.

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ROBERT SALLARES

LEPROSY IN THE UNITED STATES. Leprosy, now known as **Hansen's** disease, has had a low rate of incidence in the United States. Until the period following the Civil War, American leprosy sufferers were managed locally, within their immediate communities. As the disease's symptoms take years to manifest, if they become visible at all,

some individuals were able to conceal the disease. Others lived under improvised **quarantine** in homes, hospitals, or **leprosaria**. In the late nineteenth and early twentieth centuries, however, individuals with leprosy were consolidated within a few institutions. Massachusetts briefly operated an institution for those with leprosy from 1905 until 1921, but the primary locales in which individuals were confined and treated were Carville, Louisiana, 85 miles north of New Orleans, and the Kalaupapa colony on the island of Molokai, Hawaii.

Of the 37 patients admitted to Massachusetts' Penikese Hospital over its 15-year tenure, most were immigrants and/or had no place of legal residence. Offering little in the way of therapeutic intervention, the Penikese authorities focused on regulating patients' **diets** and arranging regimens of outdoor activity thought to be beneficial. The Board of Charity of Massachusetts struggled with retaining trained staff, maintaining suitable quarters and laboratory space, and meeting the needs and desires of residents. Attuned to the facility's shortcomings, the Board repeatedly concluded that residents could not be well served. In 1913 the legislature allowed for the parole of patients not considered public health threats. After 1917, when Congress passed a law providing for the creation of a national leprosarium, Penikese had even greater difficulty obtaining appropriations, and four years later the hospital's 13 patients were transferred to Carville.

When the Louisiana Leper Home in Carville originally opened in 1894, it was the first state facility exclusively intended for the maintenance of leprosy sufferers. The state opened the home after press coverage highlighted the high incidence of leprosy in the state and exposed poor conditions within the New Orleans leprosarium. The Board of Control for the home engaged four nuns to care for the first seven patients, who moved into the slave quarters of a former plantation. When Carville was chosen to become the national leprosarium to provide "care, detention, and treatment" in 1921, the institution received a Medical Officer-in-Charge (MOC), **physicians**, and medical staff, as well as an infusion of funds for expanding and improving its facilities. Those diagnosed with leprosy in any state (except for New York, where isolation was not mandatory) could legally be apprehended and forced to reside at Carville, which was now administered by the U.S. Public Health Service (USPHS). Many who came to live in Carville, however, came of their own volition. Some came after having been reported to the health or police departments, whereas others came as a result of their own or their intimates' fears that they might spread infection. The patient census ranged between 200 and 400 individuals from the 1920s through the 1960s.

As in Massachusetts, Carville's medical staff could do little to alter the course of patients' illnesses before the development of sulfone drugs in the 1940s. The only treatment for leprosy thought to be of any value was Chaulmoogra oil, a nauseating and largely ineffective tree extract that patients could take orally or by injection. Given the lack of effective treatment, Carville's staff and administrators' primary objective was to control the movements of their charges. Beginning in 1921, patients had to adhere to rules that made their isolation more pronounced. There was no telephone designated for their use, the road to Carville was unpaved, and although small numbers of patients were permitted short vacations, they could only travel with the permission of their destinations' state health officers and had to avoid all public transportation. They also did not have the right to vote. Residents faced indefinite terms of confinement, as medical discharge was secured only by testing negative for the presence of Hansen's bacillus for 12 consecutive months.

Despite its penal features, Carville was not a sealed institution. Although the facility was surrounded by a high barbed-wire fence with a 24-hour guard, patients regularly slipped through the fence to hunt, visit Baton Rouge, or try to survive independently on the outside.

Patients cultivated a semblance of community, autonomy, and comfort that was permitted insofar as it did not interfere with Carville's priority of containing **contagion**. In the 1920s and 1930s, patients constructed cottages on the facility's grounds. A resident described Carville as "complete in its confines, with churches, shops, a theater, a morgue, the little cemetery, even a jail. Operating inside its fences are all the activities of a tiny city" (Martin, 1950, p. 75). The early Carville population was 40 percent foreign-born, two-thirds female, and less than 10 percent African American. Three quarters of patients were Catholic, a handful were Jewish, and most of the remainder were Protestant. Patient dormitories were racially segregated, but the facility's school was not.

The "tiny city" underwent a great deal of change in the 1940s, 1950s, and 1960s. During the Great Depression, patients at Carville generally did not challenge the medical-paternal order that provided for them, and they cooperated in enforcing their own seclusion. But during the Second World War and its aftermath, new therapeutics simultaneously increased patients' gratitude for the benefits they received as federal wards and, by instilling a new hope for recovery, fostered a vocal critique of the government's approach to fulfilling its mandate to care, detain, and treat.

In 1941 trials with **sulfa drugs** and sulfones were conducted at Carville, and the latter resulted in marked improvement in early cases within several months. Within two to three years, many patients were medically discharged. Equipped with these powerful new treatments, Carville's administrators continued to assert their authority over residents over the next several years, but the patient body began to organize, to resist breaches of **personal liberty**, and to demand changes. *The Star*, Carville's community newsletter, became a forum for articulating demands and a mode for circumventing the institutional hierarchy, allowing patients to communicate directly with decision-makers at the federal level and with a fascinated, and increasingly sympathetic, general public. The Surgeon-General appointed a National Advisory Committee on Leprosy to consider the recommendations made by Carville's United Patient's Committee. Ultimately, in 1947, a new MOC satisfied patients' key demands, increasing the length and frequency of holiday leave, establishing a post office branch at the complex, relaxing the terms of discharge, and hiring an occupational therapist.

In the early 1950s, patients continued to struggle to participate in setting the terms of their confinement and to assert their rights as community residents. By 1956, when residents had achieved their most complete recognition as partners in running the facility, Carville's census began to diminish, as treatment increasingly facilitated medical discharge. In the 1960s and 1970s, Carville remained an active and prolific research institute, producing pioneering investigations of techniques for rehabilitation and surgical reconstruction, as well as seminal trials of the drugs thalidomide and Rifampin. In 1981 the USPHS created a National Outreach Program for Hansen's disease, establishing 11 outpatient clinics to provide diagnosis, treatment, and ongoing care. Carville was decommissioned in the late 1990s, with some of its research programs being moved to Louisiana State University at Baton Rouge.

The other site to which the U.S. government historically confined patients with leprosy was Kalaupapa, on the Hawaiian island of Molokai. In 1909 the USPHS assumed

RULES FOR THE INMATES OF THE LOUISIANA LEPER HOME (CARVILLE, 1913)

1. PATIENTS must be in their respective rooms and places when the physician makes his visits.
2. PATIENTS must not laundry [sic], cook, bathe, nor store food and working tools in their rooms, or clothes rooms; the laundry, bathrooms, clinic and dining and ante-rooms being destined for such purposes. Living rooms and bedding must be aired daily, clothes rooms and individual clothes lockers must be aired weekly. Patients will deposit refuse bandages and dressing in receptacles designated for such, and same to be disposed of in incinerators.
3. PATIENTS will adhere to the regulations made prohibiting the men visiting the women in their enclosure and the women visiting the men in theirs. Inmates (relatives) will be allowed occasional visits in the place assigned for visitors; patients violating rules governing these visits will be denied further visits.
4. PATIENTS will be required to be in their respective rooms for the purpose of retiring at nine o'clock. Patients are prohibited the use of lamps or candles in their rooms. Lamps from halls will light rooms; book cases, desks and rolling chairs must be kept in halls. Patients are prohibited from throwing cigarette or cigar stubs upon the floor of the rooms, halls, or galleries, but same must be placed in receptacles for such or thrown upon the ground.
5. PATIENTS must assist according to their strength in the general care of the home and its inmates, and behave to one another with proper decorum. Inmates disturbing the peace by striking one another will be put in the GUARD HOUSE. Patients are prohibited the holding or keeping in their possession of FIRE ARMS. Packages intended for patients which have the appearance of containing articles prohibited to patients will be opened and inspected in the presence of one of the Sisters.
6. In order to avoid the spread of leprosy, patients are forbidden to go out of their enclosure or send out articles in their possession and prohibited trading directly with peddlers, employees, or any other persons outside the premises.
7. Guards are for the purpose of preventing patients leaving the premises without proper authority, and any guard who permits or allows a patient to violate this rule shall forfeit not less than two days' pay for same, subject to the approval of the Board.
8. A violation of any of the above rules by the patients will subject the violator to be detained in the Detention Room for a length of time commensurate with said violation, and any inmate communicating with a patient while in said Detention Room, without proper permission, will be deemed an offender and subject to be placed in said Detention Room. All reasonable complaints will be made to the Sister in charge, and same will be reported by her to the Board for its action.
9. No particular mode of religion or worship is required of any patient, but all patients are urged, for their own welfare, to attend religious services.
10. The Sisters are in charge of the Home as the representatives of this Board, and for the decorum and management of the Home they may adopt rules not herein enumerated, and not in conflict with these rules; and the rules and orders as adopted must be obeyed by the inmates and all employees.

By the order of the Board of Control Louisiana Leper Home.

J. J. Prowell, President

R. Stagg, Secretary

control over Kalaupapa, which had begun as a leper settlement in 1866. The experiences of the residents of the Hawaiian facility paralleled Carville's inhabitants' in some respects. In others, however, it reflected the facility's radically different surroundings: a politically volatile, essentially colonial, environment in which first Britain and then the United States sought to tighten an imperial grip on the territory. The vast majority of Kalaupapa's residents—an average of 135 new cases were detained each year following the 1865 Act to Prevent the Spread of Leprosy—were native Hawaiians. Hawaiians were politically and economically disenfranchised by native- and foreign-born whites and suffered severe social marginalization.

Unlike the population of Carville, which was economically and ethnically mixed, the Kalaupapa settlement was made up largely of native Hawaiians, with only a small minority of Asian immigrants and a very few *haoles* (how-leees)—that is, white foreigners and native-born whites. Because whites with the disease were allowed to leave the island, and because of systemic discrimination by whites throughout Hawaiian society, Kalaupapa's patient population was largely homogenous socially and economically.

During the 1880s and 1890s, Hawaii underwent profound political and social change as *haoles* began to assert increasing control over the island—eventually overthrowing the Hawaiian monarchy, founding a short-lived independent republic, and finally paving the way for annexation by the United States. Native Hawaiians became ever more socially, politically, and economically marginalized. At the same time, public health authorities implemented more stringent quarantine measures that disrupted the community and family structures of patients at Kalaupapa. Physicians conducted experimental procedures, often in gross violation of even the lax ethical standards of the era. Although considerable medical experimentation took place at Carville as well, patients in Louisiana were generally the beneficiaries of that research and felt invested in the process. This was not so in Kalaupapa, where medical experimentation included efforts to infect the healthy with leprosy or the already infected with other diseases such as **syphilis**.

Ultimately, discontent fueled rebellion. Some patients engaged in relatively benign displays of civil disobedience such as vandalism, whereas others took a more aggressive stance, taking up arms and engaging in gun battles with police authorities sent to enforce public health quarantine. They assassinated physicians who championed rigid isolation policies, such as removing uninfected family members from the settlement, isolating individuals, often children, at Kalaupapa without their families. Violent protest culminated in the “Leper War” between the army of the Hawaiian Republic and armed leper “rebels” who had fled from the Hawaiian Board of Health—a conflict which ended in victory for the small but determined band of resistance fighters.

American annexation of the islands in 1898 and creation of a central government with strong law enforcement and public health capabilities neutralized rebellion during the first decade of the twentieth century, but the policy of strict isolation remained in place. Those with leprosy gained more freedoms within the settlement, particularly after Hawaiians were granted American citizenship, but stigmatization of the disease outside the facility deepened. As part of an effort to make Kalaupapa more of a medical institution on par with Carville, the United States Leprosy Investigation Station was built there in 1909. But whereas patients at the settlement had largely acquiesced to experimentation during the previous decades, the research station closed in 1913 after only 9 of 900 patients would consent to serve as research subjects. Kalaupapa residents resented USPHS experiments and intrusion into their lives and became an even more insular, self-sustaining

community. Throughout the twentieth century, especially after the introduction of sulfone drugs in the 1940s, the population of Kalaupapa dwindled, but isolation laws were not abolished until 1969. During the twentieth century, the facility became, and for a small number of individuals remains, a refuge. See also Leprosy, Societal Reactions to; Medical Ethics and Epidemic Disease; Public Health Agencies, U.S. Federal.

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AVA ALKON, NICK TURSE, AND AMY FAIRCHILD

LEPROSY, SOCIETAL REACTIONS TO. "Stigma" is Greek for a distinguishing mark, and few diseases present with the range of physical marks or symptoms that **leprosy**, or **Hansen's** disease, can. From its early stages with discolored skin patches to later development of open sores, terrible body odor, and disfigurement of face and extremities, the disease has long marked its sufferer as one to be shunned by the healthy. Death was rarely swift and cure or recovery unusual, so unlike the victim of plague, smallpox, or tuberculosis, one became a leper. Historically, societies have responded to leprosy, often a label for a broad category of skin diseases, by setting those afflicted with the disease apart from the healthy—and often even from other sufferers—in ways ranging from social ostracism to physical isolation on remote islands.

Cultural explanations of how and why one is afflicted with leprosy are key to understanding the levels of stigma attached to the disease. In many cultures, as diverse as ancient China and modern Mali, Thailand, and Paraguay, traditional explanations include heredity, sorcery, diet, and accidents. In such societies, the leper may be shunned for aesthetic reasons, for begging, or for supposedly breaking a food taboo, but the stigma tends to be light, and physical banishment is rare. As the disease progresses, however, the sufferer becomes less able to work, more physically abhorrent, and often is reduced to begging for sustenance. If married, divorce is often prescribed, lest spouse and children acquire the disease.

In ancient Israel early religious (Levitical) law prescribed that priests examine those with suspicious skin patches. If found to be ritually unclean—*tsara'ath* or *zara'ath*, a term used over 20 times in the Hebrew Scriptures that included but was not limited to people with skin ailments—they were to be placed outside the camp enclosure. When these Hebrew (Old Testament) texts were translated into Greek in the third century BCE,

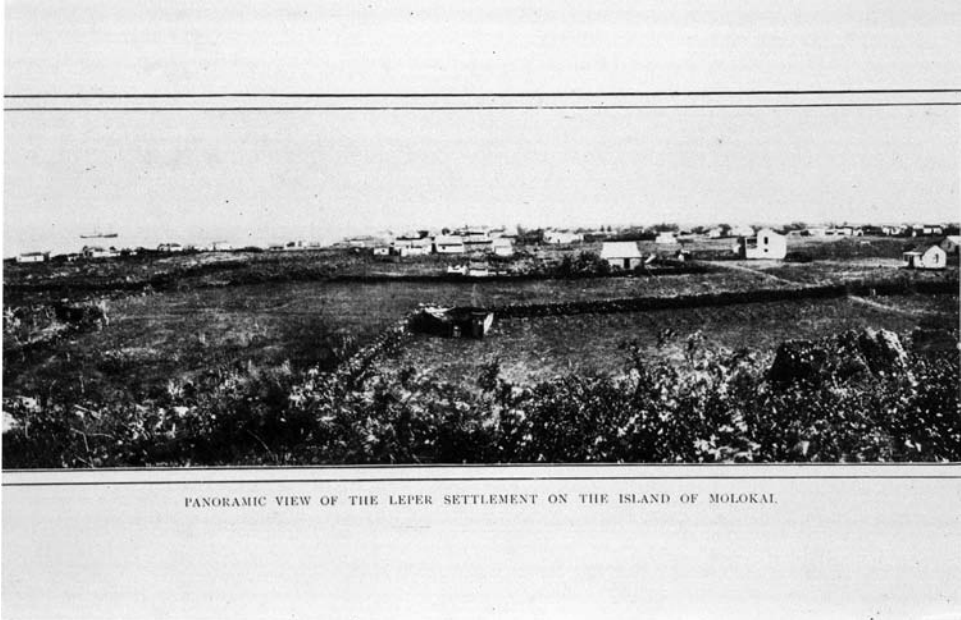
tsara'ath became *lepra*, the term for a recognized skin disease, and the leprous became a special class to be shunned, for religious no less than aesthetic reasons. When Jesus (c. 6 BCE–27 CE) healed (“cleansed”) 10 lepers, he was displaying divine power to undo ritual impurity as well as healing illness. That he sent those he healed to the priests is further recognition of the religious nature of the condition and its place in Jewish society.

Medieval Christianity retained the notion of the ritually impure leper but blended it with the charity demanded by the Gospel and exemplified by Jesus. But God inflicted leprosy, as all diseases, perhaps because of terrible personal sins. Ritual impurity evolved into sinfulness and moral failure, and the leper’s outer deformity became a sign of spiritual depravity. By contrast, early Islam, which could ignore the Old Testament in favor of the Quran and Muhammad’s (570–632) doctrines, taught that Allah imposed leprosy freely as either a blessing or a curse, with no relation to the victim’s moral status. Even so, the victim was stripped of many legal rights and reduced to the status of a minor or an insane person. Though Muhammad rejected the notion of contagion, he nevertheless urged his followers “to flee the leper as you would the lion.” Supporting the leprous was an act of charity, and this ranged from handing out alms at the mosque to donating land to support a **leprosarium**. Muslim towns and cities often had leper quarters established outside their walls, which may have contradictorily served to increase victims’ self esteem as members of a minority community while increasing stigma by isolation from the full community. In Fez, Morocco, all lepers had to reside in the quarter, though this sort of regulation seems to have been rare.

Chinese lepers were traditionally cast out of their towns and villages and collected in walled colonies whose conditions were so dreadful that many committed suicide. Indian lepers, believed to have been cursed by God, traditionally had no refuge, begging and dying in streets or alleyways, or being aided by the charitable to commit suicide by burial alive, incineration, or drowning. Believing the devil caused leprosy, premodern Russian Yakuts drove their lepers away from villages to live in solitary huts.

Though Christian saints like Francis of Assisi might embrace and even suck the pus from the wounds of lepers, high medieval Church authorities increasingly insisted on segregation and isolation of lepers from wider society. As in ancient Israel, determination of this status remained in the hands of the clergy, even after the emergence of professionalized medicine in the West. Charitable hospitals in major cities had long served as refuges for those disabled by the disease, especially in the Byzantine world. As with Jews, Muslims, and heretics, lepers fell into the category of those not well tolerated in open society, and from 1215 they had to wear distinctive clothing in the Catholic world. To the moral and aesthetic bases for segregation was added fear of physical contagion, especially with the descent of the **Black Death** from 1347. Coincidentally, the incidence of leprosy in Europe declined with the new regime of plague (perhaps as a result of improving nutrition), and many leprosaria were soon filling with plague victims, becoming **pest houses**. Keener diagnoses, left to **physicians** from the early fourteenth century, also seem to have separated out victims of related diseases, reducing the number of lepers even further.

European colonization and the **slave** trade probably brought leprosy to the New World, and with it the Christian **social construction** of the disease. Catholic clergy and religious dominated the mission fields, and native lepers were treated as had been their European cousins. In Africa Christian missionaries often encountered societies whose attitudes to lepers had been shaped by Islamic ambivalence and native tolerance. Along with colonial



PANORAMIC VIEW OF THE LEPER SETTLEMENT ON THE ISLAND OF MOLOKAI.

Panoramic view of leper settlement on Molokai. *Harper's Weekly*, August 18, 1899. Courtesy of the National Library of Medicine.

governments and Christian missionaries came the stigmatization of the leper on religious grounds.

By the early nineteenth century, many experts believed leprosy to be hereditary and noncontagious, whereas others believed in its contagious nature. British debate revived interest in medieval lepers and leprosaria, generating many myths about both. After the discovery in 1873 of the *Mycobacterium leprae* by **Gerhard Hansen**, the debate over whether leprosy was contagious tipped to the “contagionists.” Both the Royal Commission on Leprosy in India in 1891, and the First International Congress on Leprosy, held in Berlin in 1897 (presided over by **Rudolf Virchow**), adopted the contagionist position. Medical science therefore seemed to dictate segregation and isolation, and imperial governments, as well as those of free states, began imposing strict segregation measures. In 1877 Norway passed legislation restricting the movement of lepers and in 1885 required isolation in leprosaria or colonies. Sometimes brutal, sometimes welcoming, isolation prevented “contagion”, controlled vagrancy, allowed forced medical treatment and experimentation, controlled reproduction of lepers, often provided care in a communal setting and an accepting atmosphere, allowed religious proselytizing to a captive audience, and provided an alternative to life among the judgmental.

Concern for the health of white colonists and native workers in Africa and Asia began to trump vaguer notions of the lepers’ moral state, and it was voiced in popular books like H. P. Wright’s 1889 *Leprosy: An Imperial Danger*. Imperialism, racism, social Darwinism,

missionary Christianity, and the new **germ theory** interacted to provide potent support for segregation. If a germ caused leprosy, then the disease was spread by filth and sex in squalid native conditions, or so reasoned colonial physicians such as the French doctor Eduard Jeanselme (1858–1935). British Parliament considered Leprosy Acts for India in 1889 and 1896, and passed the Lepers Act in 1898. South Africa mandated isolation in 1891, and by the 1890s Kalaupapa leper colony on Hawaii's Molokai Island housed 700 residents. The Louisiana Leper Home in Carville opened in 1894 on a dilapidated plantation rented for \$750 per year; run by Sisters of Charity nuns, it became the national leper hospital in 1921.

French Catholic Father Germain-Leger Testevuide (1849–1891) opened the first leprosarium in Japan on Mount Fuji in 1888 as a refuge. Two more followed in 1892, and the state established five more in 1907. Conditions were prison-like, and because the Japanese accepted hereditary theory rather than contagion they sterilized men and aborted fetuses of pregnant women. Forced isolation of lepers returned to Japan after World War II, and by 1956 some 11,000 were housed in numerous facilities that officially closed in 1996. In 2001 the practice was declared unconstitutional, and 127 plaintiffs were awarded the equivalent of \$20 million in damages.

By the late 1980s the age of mandatory isolation was waning. Even after colonies or leprosaria are closed and patients healed, however, the problems of adjusting to the broader world lead many to remain in or near their former institutional homes. Many of China's estimated 60,000 leper colonists remain because of family abandonment and attendant shame. In a 2004 Japanese poll, only 2 percent of 4,300 current inmates desire to return home, and at Kalaupapa many remain as tour guides. At about the same time, a study of leprosy in Thai society showed that even after obvious lepers disappeared from view with effective medical treatment, the pejorative use of "leper" in daily language increased, which reinforced the psychological stigma of patients.

Since the early 1980s, a new outpatient multidrug therapy has provided a cure in two years or less with no physical deformities. In 1991 the **World Health Organization** set the goal of global elimination of Hansen's disease as a public health problem (cases reduced to 1 per 10,000 population) by 2000. Though efforts fell short, between 1985 and 2005 over 14 million cases were cured, largely thanks to donated drugs, and the number of current cases fell from 5,200,000 to 286,000 (95.5 percent). Yet stigmatization continues to keep victims from seeking effective treatment at early stages and minimizing the disease's effects. An anti-stigmatization media campaign drew 12,000 people to treatment centers in Nepal over a six-day period in 1999.

From the early 2000s, researchers have been working to develop means of quantifying leprosy-related stigma across cultures in order to understand and counteract this factor. In 2003 the generally biomedical *International Journal of Leprosy and Other Mycobacterial Diseases* committed itself to supporting social science research into the "social facets" of the disease. In a letter to the United Nations Commission on Human Rights dated January 29, 2006, Jimmy Carter (b. 1924), the Dalai Lama (b. 1935), Bishop Desmond Tutu (b. 1931), and other global activists urged "people all over the world to change their perception and foster an environment in which leprosy patients, cured persons, and their families can lead normal lives free from stigma and discrimination." See also *Leprosy in the Premodern World*; *Leprosy in the United States*; *Medical Ethics and Epidemic Disease*; *Personal Liberties and Epidemic Disease*; *Religion and Epidemic Disease*; *Scapegoats and Epidemic Disease*.

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JOSEPH P. BYRNE

LITERATURE, DISEASE IN MODERN. Literary works are rooted in the human endeavor and its challenges, so the prominence of disease among human populations ensured that **epidemics**, plagues, and other diseases would play a significant role in literature. Many of literary history's most memorable characters are those suffering from or dying with a catastrophic illness—Roderick and Madeline Usher in Edgar Allen Poe's (1809–1849) "The Fall of the House of Usher" (1839) or Benjy Compson in William Faulkner's (1897–1962) *The Sound and the Fury* (1929), for example. Additionally, some of history's greatest works of poetry are rooted in the struggle with disease or impending death, often the poet's own, as in John Milton's (1608–1674) "On His Blindness" (1652) or John Keats's (1795–1821) "La Belle Dame Sans Merci" (1819). In spite of the frequency with which plagues and illnesses appear in novels, plays, and poems, disease is significantly less common in literature than in the course of real human lives. For example, the common cold is extremely rare in literary contexts. The literary demand for conflict and economy of detail requires that diseases in literature be virulent enough to alter a character's life or the social dynamic of a story, or be worthy of the solemn reflection of a poem. As a result, disease has limited uses in literature, most often in a symbolic capacity.

The effect of disease on the social fabric of society, particularly during epidemics, has been a frequent theme of literary works. In one of the earliest such works, *The Decameron*

(1350–1353), by Giovanni Boccaccio (1313–1375), 10 young men and women are forced by the **Black Death** to leave Florence for a villa in the country, where they tell stories offering a window into Italy's changing social dynamics, such as a declining trust in the church brought on by the epidemic. Alessandro Manzoni's (1785–1873) 1825 novel *The Betrothed*, often considered one of Italy's greatest literary works, used the epidemic of **bubonic plague** that swept Milan in 1630 to convey the sort of social anarchy that an epidemic could bring to a culture during the early modern period. In Manzoni's work the plague becomes a major obstacle to his protagonists' marriage. Though outbreaks of epidemic disease declined dramatically in the Western world during the nineteenth and twentieth centuries, the complex social dynamics brought on by **industrialization** and **urbanization** made the prospect of an epidemic even more of a threat to society. Henrik Ibsen (1828–1906), in his play *An Enemy of the People* (1882), explored the potential for an epidemic to alter a society's economy and, as a result, its social relationships. In the controversial drama, a **physician** who seeks to close his town's public baths after discovering that they are the source of an epidemic among tourists is destroyed by a society determined to preserve its lucrative tourist trade. Albert Camus (1913–1960), a French writer deeply influenced by his nation's experience fighting the Nazis, examined the socially unifying power of an epidemic in his 1947 novel *The Plague*. Though true to Camus's existentialist beliefs, the novel ends with the population returning to their same selfish lifestyles once the threat has passed. By the end of the twentieth century, works of popular fiction, such as Robin Cook's (b. 1940) *Outbreak* (1987) and *Contagion* (1995), were exploring scenarios in which rapidly spreading and incurable diseases such as **Ebola** and **smallpox** become weapons of political intrigue, terrorism, or evil entrepreneurs.

Catastrophic diseases have occasionally stricken artistic and literary communities with such impact that the diseases become romanticized and mythologized in the literary works of that period, and consequently, in the public imagination. **Tuberculosis** during the Romantic Era and **Acquired Immune Deficiency Syndrome** (AIDS) near the end of the twentieth century are two of the most prominent examples. Because the diseases appeared to affect artists and writers at the peak of their careers, the mythology that developed around the diseases tended to associate them with greater creativity, a heightened emotional sensitivity, or a deeper understanding of the human condition. T. S. Eliot (1899–1965), whose 1922 poem *The Waste Land* is considered one of modernism's greatest works, was among those who believed that serious disease, in the right circumstances, could produce a flood of poetic creativity. Though humankind has been victimized throughout history by a variety of horrifying epidemics, including bubonic plague, smallpox, **cholera**, **influenza**, **polio**, and **malaria**, the frequency with which tuberculosis appears in nineteenth-century literature or AIDS appears in late-twentieth-century literature creates the impression that those diseases were far more prevalent than may actually have been the case; that they were a bigger threat to public health than were other epidemics; or, most problematic of all, that they were the price to be paid for creativity or empathy. By contrast, those epidemic and catastrophic diseases without such a mythology surrounding them, in spite of their prevalence or their threat to public health, have generally been considered in the public imagination to be merely cruel and unfortunate aspects of the human experience.

The early deaths from tuberculosis of Romantic artists as prominent as British poet John Keats and Polish composer Frédéric Chopin (1810–1849) played a major role in

the mythology that grew up around “consumption,” as tuberculosis was called at that time, and eventually led to the disease being associated with creativity throughout the nineteenth century. The effects of urbanization and the impoverishment brought on by the **Industrial Revolution** had, by the middle of the century, led to consumption becoming so common in the general population that the frequent tubercular characters in literary works, such as the kind-hearted Little Eva in Harriet Beecher Stowe’s (1811–1896) *Uncle Tom’s Cabin* (1852) or the young Paul Dombey in Charles Dickens’s (1812–1870) *Dombey and Son* (1846–1848), did not even require having their disease identified. The symptoms alone were sufficient evidence for a reader to conclude that the characters were afflicted, though both the literary and social implications were, as Dickens notes in describing Dombey, that the sufferer possessed a moral weakness of some sort. Over time, the romanticized notion of tuberculosis became so ingrained in the public imagination that it continued far into the twentieth century. Writers as renowned as Franz Kafka (1883–1924) and D. H. Lawrence (1885–1930) continued to fall victim to the disease through the period between the world wars, and major literary works of the era, such as Thomas Mann’s (1875–1955) *The Magic Mountain* and Lawrence’s *Women in Love*, offered perhaps even more idealized portrayals of the disease than works of the nineteenth century.

AIDS became the focal point of a similar public fascination after its discovery in the early 1980s. Its prevalence among artistic communities was soon echoed in a number of prominent literary works in which characters struggle with the physical and social consequences of their condition. The first book to capture a broad audience, journalist Randy Shilts’s (1951–1994) *And the Band Played On* (1987), was a chronicle of the emergence of the disease in and around San Francisco’s gay community and the frantic search by medical research teams to identify the disease and locate its source. The candor with which Shilts examined the impact of AIDS on the gay community and the subsequent search for its origins dramatically altered the public and political conversation regarding the disease. By the 1990s, many of Broadway’s most celebrated plays and musicals featured AIDS themes, including Tony Kushner’s (b. 1956) two-part drama *Angels in America* (1990), which won both the Pulitzer Prize for Drama and the Antoinette Perry (Tony) Award for best play; William Finn (b. 1952) and James Lapine’s (b. 1949) 1992 drama *Falsettos*, winner of a Tony Award for best book of a musical; Paul Rudnick’s (b. 1957) critically praised 1993 Obie (Off-Broadway) Award-winning play *Jeffrey*; and Jonathan Larson’s (1960–1996) nearly iconic musical *Rent* (1996), winner of four Tony Awards, including best musical.

Some diseases manifest symptoms that authors have found especially useful for allowing literary characters to engage in philosophical reflection, theological questioning, or heightened spiritual awareness. Ernest Hemingway’s (1899–1961) 1936 short story “The Snows of Kilimanjaro” uses the bodily decay of gangrene to inspire a man dying in the African wilderness, identified only as “Harry,” to reflect on the vast experiences of his unfulfilled and too-brief life. Similarly, in “The Death of Ivan Ilych” (1886), Leo Tolstoy (1828–1910) explored the experience of a slow and agonizing death from abdominal cancer and its power to inspire a profound self-examination on the part of its victim. Ilych, the title character, is shunned by his family and forced by the disgusting symptoms of his disease to confront the isolation and loneliness that the disease and his lifetime of selfishness have brought upon him. For both Hemingway and Tolstoy, the physical effects of their protagonists’ diseases paralleled an unexamined moral decay brought to light only by the suffering of the disease. In Peter De Vries’s (1910–1993) 1961 novel *Blood of the Lamb*,

a brother's death from pneumonia and a young daughter's death from leukemia become the impetus for De Vries's protagonist, Don Wanderlust, to confront his rationalistic self-assurance and his doubts about faith. Like Hemingway and Tolstoy, De Vries uses the specific nature of the illnesses in *Blood of the Lamb* as symbols of his protagonist's emotional struggles—*pneumonia*, from the Greek word for “spirit,” and *leukemia*, a disease that robs the blood of its life-sustaining quality. The unusual physical effects of epilepsy, with its uncontrollable seizures, suggest a heightened spiritual awareness that was utilized by Fyodor Dostoevsky (1821–1881) in his 1869 novel *The Idiot*. Dostoevsky, himself an epileptic, described the onset of the seizures experienced by his protagonist, Prince Myshkin, as a few moments of extraordinary insight into the nature of life, a doorway to spiritual apotheosis. That heightened appreciation of life (even as the protagonist may be taking his final breath) is the case with most works exploring a theological or philosophical introspection prompted by disease, though occasionally the experience of disease is portrayed as having an embittering effect on its victim, as in Joseph Conrad's (1857–1924) *Heart of Darkness* (1899) or Andre Gide's (1869–1951) *The Immoralist* (1902).

Among literary history's most memorable characters are those afflicted with mental illness. The appearance of psychological disorders—“madness”—in literature dates back to the ancient world, where in Euripides' (480 BC–406 BC) *The Bacchae* (405 BC), Dionysus, the god of wine and ecstasy, inspires a frenzied dancing, an implied temporary insanity, among the women of Thebes. In much of the literature involving a character's mental stability, the dramatic tension lies in whether the character is, in fact, mentally ill, or if instead he or she is feigning the illness, or is misdiagnosed, or is the victim of misguided social expectations. As early as William Shakespeare (1564–1616), the issue of feigned mental illness was a subject of literary intrigue. The question lies at the core of two of Shakespeare's best-known plays—*Hamlet* (1602) and *King Lear* (1606). In both cases, the illusion of insanity allows the “mad” characters—Hamlet and Edgar—to pursue surreptitious plots against the plays' powerful villains. By the nineteenth century, mentally ill characters were more often portrayed as disturbing antagonists or even villains. In Charlotte Brontë's (1816–1855) *Jane Eyre* (1847), the title character's love for Rochester is thwarted by his undisclosed marriage to a ghoulish woman he keeps locked in the attic to conceal her insanity. Yet another female character—women were portrayed as suffering from an ill-defined psychological illness much more often than were male characters—was kept locked away in an attic in Charlotte Perkins Gilman's (1860–1935) “The Yellow Wallpaper” (1892), eventually becoming delusional and experiencing hallucinations. Though only inferentially portrayed as mentally ill, Captain Ahab, the commander of the whaling ship *Pequod* in Herman Melville's (1819–1891) *Moby Dick* (1851), is afflicted by a frighteningly irrational obsession with killing one specific whale, destroying his ship and killing many of his crew in the process. Several works have utilized protagonists presumed by their society to be mentally ill to question whether such social judgments are reliable, including Fyodor Dostoevsky's *Notes from Underground* (1864) and Ken Kesey's (1935–2001) *One Flew over the Cuckoo's Nest* (1962). In both works, the protagonists manifest incidents of extraordinary mental clarity even though their insanity is largely assumed by those surrounding them.

Occasionally, authors have even invented diseases as a channel for exploring social themes. Nobel laureate José Saramago's (b. 1922) 1995 novel *Blindness* deals with the aftermath of a disease that causes instantaneous and complete blindness, leaving the victim with the sensation of seeing nothing but a milky white film. This “white darkness”

quickly strikes the entire population, with one exception who is forced to conceal her continued ability to see, leading to a dramatic social upheaval as the society tries to cope with its pandemic sightlessness. In his famous short story "The Masque of the Red Death," Edgar Allan Poe utilizes an epidemic of "red death" to explore the depth of fear and societal indifference in the face of a plague. According to the narrator, Red Death is a hemorrhagic disease causing convulsions and severe pain and leading to death within a half-hour of the onset of profuse bleeding through the pores of the skin. In Poe's story, a large group of nobles attempts to escape the disease by quarantining themselves inside a castle, only to be infected and die when a mysterious guest at a masquerade ball turns out to be the disease itself in human form. *See also* AIDS, Literature, and the Arts in the United States; Biblical Plagues; Black Death: Literature and Art; Cinema and Epidemic Disease; Disease, Social Construction of; Leprosy, Societal Reactions to; Plague Literature and Art, Early Modern European; Popular Media and Epidemic Disease: Recent Trends; Sexuality, Gender, and Epidemic Disease; Syphilis in Sixteenth-Century Europe; Tuberculosis and Romanticism.

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DEVON BOAN

LONDON, GREAT PLAGUE OF (1665–1666). The **bubonic plague** outbreak that struck London, a city of 500,000 inhabitants, and other English urban centers in 1665 and 1666 was the last such **epidemic** in the British Isles. With a death toll of over 100,000, it was the deadliest since the **Black Death** of 1349, though in percentage terms it was less severe than earlier English plagues.

Though some scholars disagree, most accept that the plague deaths were the result of the *Yersinia pestis* **bacterium** spread among humans by rat-borne fleas that found new human hosts. The high mortality rates suggest that some cases may have become contagious **pneumonic plague**, by settling in victims' lungs, and lethal **septicemic plague**, by rapidly infecting the bloodstream of others. Bills of mortality, which were published weekly and listed all local deaths by parish and cause, also show dramatic increases in the incidence of other diseases that probably flourished among the physically weakened population.

In general, the catastrophe was well documented, and historians have recourse to official sources such as the bills, parish records, and a stream of governmental directives, as well as many personal sources. Diarists such as the Royal Navy bureaucrats Samuel Pepys (1633–1703) and John Evelyn (1620–1706) privately chronicled the event, and surviving

correspondence from many other sources sheds light on personal tragedies. Plague tracts from previous outbreaks were circulated anew, while **surgeons, physicians, and apothecaries** published their own manuals of prevention and treatment, and preachers' sermons inveighed against sin and demanded the repentance that would placate the angry Deity whose responsibility for the disease was undoubted. Finally, many wrote in the wake of the plague, urging the adoption of policies and actions they believed would dampen the effects of the next epidemic. The best known of these was the novelist Daniel Defoe (1660–1731), author of *Journal of the Plague Year* (1720). Though largely fictionalized and written 55 years after the event by one who was only four years old at the time, it is the iconic description of the Great Plague.

Ironically, the English government had ample warning that plague was in the neighborhood. In the early 1660s it had swept among England's trading partners (and competitors) in the Baltic and North Sea regions and had struck Dutch cities hard in 1663 and 1664 killing 35,000 in Amsterdam. Early on, royal authorities established inspection and **quarantine** stations at the mouth of the Thames and in eastern port cities such as Great Yarmouth and restricted maritime trade with cities known to be stricken. **War** with the Dutch Republic—from March 1665—lessened the likelihood of contamination through **trade**, but victories brought Dutch prisoners to English towns, especially in East Anglia.

England suffered a few dozen scattered plague deaths in 1664, but an especially long and brutal winter raised hopes that plague would be kept at bay. Fears began to rise in London in May 1665, with 43 reported plague fatalities, but royal authorities dismissed their importance in order to prevent mass **flight** from the capital and reassure commercial and diplomatic partners. Nonetheless, theaters were closed on June 5, the Inns of Court shut their doors on June 15, and on June 21 a **cordón sanitaire** of warders appeared around the parish with the highest concentration of plague victims, St.-Giles-in-the-Fields. By mid-June, however, the bills of mortality were reporting over 100 plague deaths per week, and the flight of the frightened and wealthy began in earnest. The royal court began to abandon Westminster for Hampton Court as early as June 20, though King Charles II (1630–1685) remained until July 7.

Fear turned to horror as death counts mounted and incidences of the disease spread from poorer outlying parishes like St. Giles inward to the city itself. By late July, 86 of greater London's 130 parishes had reported a grand total of over 6,300 plague fatalities, 5,667 in July alone (of a reported total of 8,828 deaths in July). August numbers rose to 17,036 plague deaths in 113 parishes among a total of 22,413, and September fatalities spiked at a total of 30,899 with 26,230 attributed to plague, including the epidemic's worst week during which the bills reported 7,165 fatalities. They tapered off in October, and by late November fewer than 1,000 plague deaths appeared weekly. However accurate such numbers appear, both contemporaries and historians have treated them as low estimates, because parish-level reporting was inexpert, and non-Anglicans (Catholics, Quakers, Jews) were generally not counted.

Efforts to stem the deadly tide repeated past patterns: victims and family members were shut up in their houses; a few **pest houses** (with a total capacity of only 600) were opened; burials were conducted at night—at least for a time—to avoid funerary gatherings; dogs (around 40,000) and cats (perhaps 200,000) were killed as possible sources of the disease; 46 new medical publications on plague and its treatment appeared alongside dozens of reissued older works; and **quacks** confidently hawked their useless wares. Early September's terrifying numbers prompted the only attempt to cleanse the open, "miasmatic" **air** with

bonfires, an effort doused by nature after a few days. Mass graves swallowed up victims by the hundreds, the poorer folk, servants, and laborers with nowhere else to go far outnumbering the more affluent.

River ports along the Thames suffered along with London, as did East Anglian towns such as Ipswich, with some 1,700 plague deaths, and Colchester, which lost over 4,800 to plague from a total population of around 11,000. Despite cordons and flight, Cambridge, Great Yarmouth, and Norwich each lost over 15 percent of their populations, and Dover about 30 percent. Famously, the North Derbyshire parish of Eyam contracted the plague, and in June 1666 Reverend William Mompesson (1639–1709) convinced all residents of the village to accept self-sacrificing voluntary isolation lest plague spread elsewhere. In the end the village suffered 259 deaths in 76 families, or about half its population, but its neighborhood was spared the ordeal.

London regained much of its population during the winter of 1665–1666, though the following year saw an additional 2,000 succumb to the disease. All told perhaps 2 percent of England's population died of plague. The economic costs of the plague were huge and included both expenses and lost revenues. England's governing bodies and philanthropists provided as needed during the epidemic, however, and Britain's economy rebounded rapidly afterward. Wealth was redistributed through inheritance, and baptisms of newborns soared in the years that followed. Despite occurring during the **Scientific Revolution**, few if any medical insights resulted from the disaster, but reformers resolved to enhance quarantine provisions, provide pest houses in place of household isolation, and better regulate slum housing in poorer neighborhoods where the plague seemed to fester first. *See also* Apothecary/Pharmacist; Astrology and Medicine; Black Death: Modern Medical Debate; Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Diagnosis of Historical Diseases; Disinfection and Fumigation; Personal Liberties and Epidemic Disease; Plague: End of the Second Pandemic; Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Plague Literature and Art, Early Modern European; Public Health Agencies in the West before 1900; Religion and Epidemic Disease; Sydenham, Thomas; Urbanization and Epidemic Disease.

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JOSEPH P. BYRNE

LYME DISEASE. A spiral shaped **bacterium** related to that responsible for **syphilis** causes Lyme disease. Both of these related bacteria have many forms and shapes, but the corkscrew shape of the spirochete seems to predominate. Lyme is caused by the genus *Borrelia* and has many different species found around the world. It gains access to virtually the entire body in days to weeks, so fast treatment is critical. Lyme bacteria also have many ways to undermine treatment and harm humans by the use of a huge number of **antibiotic**-defeating plasmids, in addition to releasing biotoxins and slimy biofilms. Although it is found in many different ticks, the most common carrier appears to be various forms of the deer tick, a very tiny period-sized tick, which injects a painkiller, antihistamine, and anticoagulant when it bites. This is why patients often miss it. Although large mammals like deer are famous for dispersal of Lyme, it appears that smaller mammals such as chipmunks, specific mice, and other small mammals are also carriers.

Lyme disease is not a new infection; it has been found in preserved ticks from the nineteenth century. But infection rates have likely changed radically as a result of the increase of deer in some countries, together with the building of homes or other structures in areas with brush and wild fields. These factors have served only to increase the risk of infections.

Lyme is found in many countries and has been described in detail by dozens of medical papers in the last hundred years. Serious attention to Lyme disease began with Polly Murray, an artist and mother of four. Murray resides in Lyme, Connecticut, and noticed as early as the 1960s that she and her family and many local youth were sick with a special type of arthritis. In her book, *The Widening Circle*, she reports her tenacious struggle to convince **doctors** that she and her family were indeed sick, and not hypochondriacs, after having becoming infected with Lyme. In the 1960s, Lyme disease, and other tick infections like **Babesia** and **Bartonella**, were not part of routine clinical medicine. In 1971, Murray, criticized as a “doctor-chaser,” began her own systematic research, seeking out investigative medical personnel and sharing stories with fellow sufferers. Finally, she received media attention and the attention of rheumatologist Allen Steere at nearby Yale, who discovered through preliminary studies that Lyme disease was indeed the cause of much illness in Lyme, Connecticut. This attracted the attention of the medical community to this unusual infection. Doctors began to appreciate that it was not simply a psychiatric problem.

Another major milestone in the treatment of Lyme disease was the discovery that it was not a **virus** or parasite, but a bacterium. Dr. Willy Burgdorfer, working at the Rocky Mountain Laboratories, discovered that it was a bacterial spirochete. This important discovery explained why some studies using antibiotics showed some improvement with Lyme disease, and why non-bacteria-targeted treatments would probably not be effective.

Diagnosis. If a person has a bulls-eye rash, it is likely that he/she has Lyme or a related bacterial infection called “STARI.” But the bulls-eye rash is not found in most patients with Lyme. Some Lyme rashes are diagnosed as “ring worm” or are ignored. Often, bulls-eye rashes simply do not appear. However, the appearance of a bulls-eye rash is a sign to start immediate treatment, because Lyme and other possible deer tick infections may have been inserted into the human body in recent days or weeks. Often, the Lyme bacteria are already disseminated throughout the body by the time a bulls-eye rash appears.

Debates on the reliability of testing are ongoing. The most common tests are the ELISA, the Western Blot, and DNA or PCR tests. Some countries use a two-step practice: if an ELISA screening test is positive, then they run a Western Blot to confirm the positive nature

of the test. Although this is the generally accepted approach internationally, some physicians, scientists, and patients advocate that groups should report that the ELISA is unreliable and misses large numbers of obviously positive patients. Likewise, blind testing of laboratories is felt to show varying degrees of accuracy in diagnosing Lyme according to some skeptical scientists and physicians.

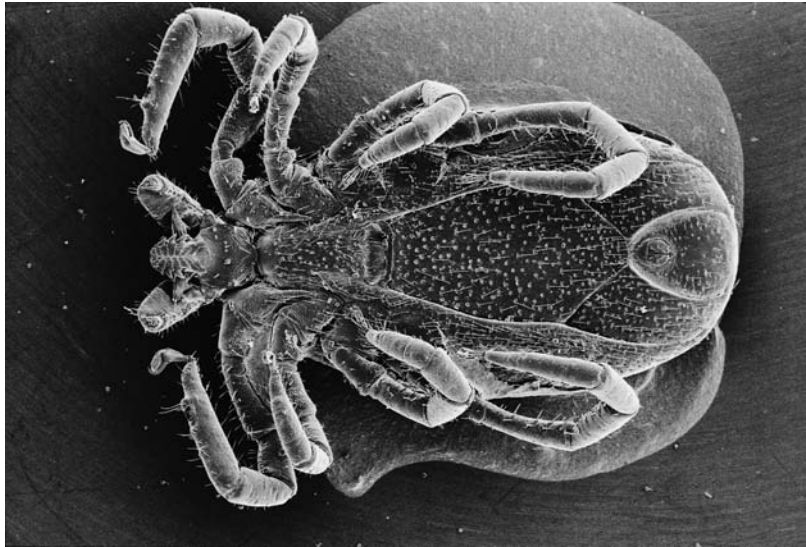
Traditional medical societies and agencies feel the Western Blot is a credible test, and yet a minority of scientists, tick infection specialty physicians, and vocal Lyme patient advocates

feel most laboratories have adjusted some of the tests in a manner that yields fewer positives. Published studies seem to show a wide variety of accuracy of tests in picking up positive Lyme, with most being over 85 percent reliable. In the context of the debate over testing accuracy, both camps agree that because Lyme primarily lives in the tissues, DNA testing of body fluids such as blood, urine, saliva, and breast milk typically will be negative.

Another way to diagnose is by ruling out other causes and determining whether the patient has had exposure to tick bites. Some individuals think nothing of routine tick bites and do not realize that they are at risk for many tick borne infections. Others have minimal risk. Those who live near deer or similar large animals, or have hobbies that take them into wild fields and brush (such as campers or hunters) are at much higher risk for Lyme than are individuals who live in cities. Also, ticks are unable to infect when the temperature is under 4.4°C (40°F). However ticks can be on logs and other items brought into a home from a cold outdoor environment, and these ticks can be active (e.g., firewood can release tiny active deer ticks as the logs thaw).

An additional way to determine if someone has Lyme disease is to rule out all the other potential causes of a patient's complaints. Like syphilis a hundred years ago, however, Lyme is felt to be the "Great Imposter" and can cause virtually any problem with the body. Therefore, looking only for arthritis, or for a specific rash or new psychiatric symptoms, will cause many infected patients to be missed.

If a medical problem has virtually all of the other possible causes ruled out, and if Lyme disease seems to be the only likely cause left, some consider a treatment trial. However,



Scanning electron microscope ventral view of adult female castor bean tick, *Ixodes ricinus*, a vector of viruses and babesiosis. It is parasitic on sheep, cattle, and wild animals. Larvae are found on many wild birds and mammals. Carries many diseases and is thought to be the main vector for transmitting Lyme disease to humans. Courtesy of David Gregory and Debbie Marshall.

many traditional physicians worry about the growth of resistant infections to unnecessary antibiotics (e.g., antibiotics used for viral sore throats) and would oppose the use of antibiotics in *possible* Lyme infection patients unless strong evidence exists.

Treatment. Treatments suggested vary depending on ideology. Most infection societies and government agencies feel a three- to four-week course of doxycycline should kill most Lyme, whereas a minority group of clinical Lyme disease experts feels that, because Lyme replicates so much more slowly than other routine bacteria, treatment should be based on patient improvement on not on a set time. Both groups agree that after four weeks some patients report still not feeling well. Yet it is not clear why this residual illness occurs. Some feel it is the result of Lyme biotoxins causing inflammation like the patented BbTox1 (a problem first suggested to exist in the 1990s by Sam Donta, M.D.). Others feel incomplete cure is the result of biofilms or bacterial slimes covering the Lyme, such that antibiotics penetrate poorly (Eva Sapi, Ph.D., and Alan McDonald, M.D.). Some feel that advanced and disseminated Lyme found deep in body tissues simply cannot be cured in four weeks, whereas others believe there is a mysterious residual bacterial debris with inflammation that takes months to be cleared from the body.

Another issue that is critical to Lyme treatment is the emerging realization that deer ticks do not carry just one infection, but many, and that it is routine for a patient with Lyme to also be infected with *Babesia*, *Bartonella*, *Anaplasma*, or *Ehrlichia*. These infections clearly make treatment of Lyme disease more difficult and some, like *Babesia*, require entirely different treatments because they are not bacteria but tiny red blood cell parasites living inside red blood cells. It is well established that these coinfections, or parallel infections, slow the speed of Lyme elimination from the body.

Avoiding Lyme disease is relatively easy. Techniques include avoiding tick endemic areas from early spring until winter, covering one's skin fully with light-colored clothing to see ticks better, and tucking long pants into socks. One should consider using the insect repellent DEET, especially on feet, ankles, and legs, and applying Permethrin to cloths. See also Personal Hygiene and Epidemic Disease.

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JAMES SCHALLER

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MAGIC AND HEALING. All societies have some belief in magic, particularly in the service of healing. Magic is the use of ritual objects, actions, or words that are believed to influence the natural world. Most magical beliefs feature a body of secret knowledge known only to the practitioner. The earliest medical beliefs were spiritual/magical in nature. Practitioners had specialized metaphysical knowledge. There are surviving magical medical texts from the earliest civilizations in all ancient languages, and magical beliefs are still incorporated into many people's medical practices.

Magic and medicine worked in two ways, in combination. One way was through the use of herbs and physical substances, such as honey or various foods. The other was through the use of ritual. For instance, an herbal healing potion might be required for a particular medical need. The herbs for that potion would have to be gathered in a ritualistic manner during times of day or seasons that were deemed magically auspicious. The herbal healing potion would then be made while incantations were recited, and further incantations might be necessary while the potion was consumed or the poultice applied.

The choice of which herb to use for healing was determined by folk wisdom based on years of observation and magical beliefs about how the physical world worked. For instance, if a plant looked like a body part, imitative magic beliefs held that it would heal wounds or cure illnesses in that part of the body. Recent studies by pharmacologists have determined that many of the magical healing cures included elements that do have healing properties. For instance, honey was used in many potions and cures, usually to make them more palatable. It was also used in poultices, because it is viscous and sticky, and the poultice would adhere better to the wound. However, it turns out that honey has natural antibacterial and antifungal properties; using honey in these cures has a real pharmacological effect.

Another type of magical healing involves prayer. Although the faithful of any **religion** do not view their use of prayer as magic, for scholars of comparative religion

and anthropology, prayer is a type of charm and ritualized behavior. Stories of miraculous cures exist in all major world religions. Sometimes the rituals become so ingrained in a culture that they persist even when the religion changes; long after England converted to Protestantism, Latin Catholic formulaic prayers were repeated over the sick and dying, in the belief that the language itself had magical healing properties. Rituals and prayer have been shown to have palliative psychological effects. Magic was used through ritual application of healing charms and medicines, and through **astrology**, which was used to predict and explain outbreaks of disease. People afraid of catching the **Black Death** sought out the protection of amulets, which they wore, and relics, which they touched as talismans in order to receive protection. A more modern example is found in Africa, where people infected with **AIDS** frequently turn to sorcerers and magicians for healing. See also Contagion Theory of Disease, Premodern; Folk Medicine; Pilgrimage and Epidemic Disease.

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CANDACE GREGORY-ABBOTT

MALARIA. The word "malaria" is derived from the Italian phrase "mal'aria" (bad air), which was regarded as the cause of the excess mortality in many marshy areas of Italy before **Alphonse Laveran's** discovery of malarial parasites in 1880. The first attested use of the Italian phrase was by Marco Cornaro (1406–1479) in a book published in Venice in 1440. Horace Walpole (1717–1797) introduced the phrase into English literature in 1740. However, the disease is much older than that. Malaria was known to all the major ancient Old World civilizations under names like tertian fever or quartan fever, which refer to its most characteristic symptoms, namely intense fevers (alternating with chills) with a periodicity of 48 or 72 hours, a response to the synchronous reproduction of generations of parasites.

Biological Agent and Its Effects. There are four species of human malaria: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*. *P. falciparum* (malignant tertian fever) is the most dangerous species, occurring principally today in Africa, India, Southeast Asia, and some parts of Oceania and South America. Its temperature requirements for reproduction in vector mosquitoes largely confine it to tropical regions, although it was common in the past in southern Europe. *P. falciparum* produces a disease that can be rapidly fatal in nonimmune individuals and can cause chronic ill-health in individuals with some immunity (acquired or inherited). Its most dangerous clinical syndrome is cerebral malaria, whereas anemia is a common manifestation in less serious cases. *P. falciparum* has a periodicity of 48 hours. However, in practice there are frequently overlapping generations of parasites producing quotidian fevers (every 24 hours) that are often hard to distinguish, both in clinical practice today and in historical literature, from other acute infectious diseases such as typhoid fever.

Plasmodium vivax also has a 48-hour periodicity but lower temperature requirements than *P. falciparum*. Consequently it had a broader geographical distribution in the past, extending across large parts of Europe and Asia as far as the northern coast of Russia. After Columbus's arrival it became widely distributed in the Americas. Today it is most frequent in India. *P. vivax* is commonly regarded as a less serious disease (benign tertian fever) than *P. falciparum*, producing chronic ill-health but rarely causing death directly. This view presumably arose because most malaria research has concentrated on the effects of *P. falciparum* in Africa. However, there are increasing reports from India of cases manifesting the severe symptoms usually associated with *P. falciparum*, but in which only *P. vivax* parasites could be detected. The modern Indian evidence is congruent with historical evidence from Europe—for example, from the marshlands of Kent and Essex in early modern England—showing extremely high mortality rates in regions where *P. vivax* was present, but *P. falciparum* could not have been endemic for climatic reasons. In these areas *P. vivax* acted synergistically with other infectious diseases such as pneumonia and tuberculosis to produce its devastating effects.

Plasmodium malariae has a periodicity of 72 hours (quartan fever). Cases of quartan fever last for considerably longer than cases of the other types of human malaria; in fact the parasites of *P. malariae* can survive inside the human host for decades. Nevertheless, the resulting disease is overall less dangerous than *P. falciparum* or *P. vivax*, although *P. malariae* can cause severe kidney problems. *Plasmodium ovale*, the fourth species of human malaria, produces a benign tertian fever. This type of malaria is rare and has little significance.

Epidemiology and Transmission. Malaria can be transmitted by any means in which contaminated blood is transferred from one person to another (blood transfusions, organ transplants, drug addicts sharing needles), but in practice it is generally transmitted by mosquitoes. Only a small proportion (certain members of the genus *Anopheles*) of all the known species of mosquito are capable of transmitting malaria efficiently. This often gave rise in the past to anophelism without malaria: localities in which there were large mosquito populations, but the wrong species of mosquito as far as the parasites are concerned. Consequently, there was no malaria. The phenomenon of anophelism without malaria helps to explain why people in the past often failed to associate malaria with mosquito bites and resorted instead to the explanation of “bad air.” Malaria frequently has a very patchy distribution in ecological terms because mosquitoes rarely fly far, often no more than a few hundred yards from their breeding sites. Consequently, it is quite possible for one village to have intense malaria while another village a couple of miles away has no malaria at all. In most parts of the world where it occurs, malaria is predominantly a disease of the countryside because mosquito populations tend to be larger in rural areas than they are in the middle of large cities. In the wet tropics malaria occurs all the year round, whereas in the dry tropics infections occur mainly in the wet season. In temperate regions such as Europe, malaria had a distinctive seasonal pattern in the past because its temperature requirements confined new cases to the summer and autumn each year. The result was that agricultural laborers were often severely affected at the time of the harvest. The epidemiology of malaria varies because the mosquito species of different regions have different habits. In Europe, for example, malaria was strongly associated with marshy regions because European mosquito species like to breed in marshes. However, in tropical Africa today, *Anopheles gambiae*, the principal vector in Africa, breeds in small (often human-made) pools and avoids marshes. As a result, draining marshes to reduce mosquito populations played an

important role in eliminating malaria from Europe, but unfortunately this technique does not work in Africa today. In Southeast Asia there are yet other mosquito species that flourish in forest environments.

Public Health Impact and Control of Malaria. Malaria had an extraordinary impact on human populations all over the world in the past, wherever it occurred, and it still does today in many areas, especially in Africa south of the Sahara. Estimates of the direct mortality caused by malaria vary widely, but it seems that at least 1 million deaths a year can be attributed to it. In addition to direct deaths, malaria frequently acts by weakening the human body's immune response to other diseases; about two-thirds of all malaria-related mortality may be explained this way. Malaria's interactions with **tuberculosis** and pneumonia in historical populations and with **HIV** today in Africa are particularly important. The age distribution of mortality varies widely. In tropical Africa, where *Anopheles gambiae* is an extremely efficient vector, transmission rates are so high that malaria is a disease of childhood. It produces very high infant mortality rates, whereas those who survive childhood have developed or inherited immunity and so do not suffer from severe clinical symptoms in adulthood. However, in Europe in the past, transmission rates were much lower, and malaria transmission was highly seasonal in nature and frequently had an epidemic rather than an endemic character. Under these epidemiological conditions, it was possible for adults, too, to be severely affected.

Where malaria has been successfully eliminated, this was achieved above all by attacking the vector mosquitoes in the marshy environments where they breed. In Italy in the early twentieth century, for example, the widespread use of the drug quinine drastically reduced direct mortality from malaria, but it did not reduce morbidity very much, nor did it prevent disease transmission. Successful elimination was achieved principally in the 1920s and 1930s, when many marshes (for instance, the notorious Pontine Marshes south of Rome) were drained by Fascist dictator Benito Mussolini (1883–1945). The elimination of malaria in many parts of the world was achieved after the end of the Second World War by the use of the **pesticide** DDT to kill mosquitoes. For a time in the 1950s and 1960s, it seemed as if malaria could be completely eradicated. Then the use of DDT was stopped because of concerns about its impact on wildlife in general. Since then the mosquitoes have started to develop resistance to other insecticides, and malaria parasites have evolved widespread drug resistance. Consequently, malaria is once again an increasing problem, especially in many parts of Africa. Unfortunately, *Anopheles gambiae* in Africa has proven to be a more difficult target than mosquito species in other parts of the world. Attempts to produce a vaccine against malaria have so far not been successful, although this may still be achieved in the future. *See also* Malaria and Modern Military History; Malaria in Africa; Malaria in Medieval and Early Modern Europe; Malaria in the Americas; Malaria in the Ancient World.

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ROBERT SALLARES

MALARIA AND MODERN MILITARY HISTORY. Throughout military history, battles have been won or lost because of the health or illness of the troops. **Malaria** is one of the diseases capable of decimating the ranks of a military force and continues to this day to be a severe and ongoing threat to military operations. Military campaigns can also have effects on local populations by forcing relocation to malarial areas and disrupting malaria prevention measures.

It is estimated that approximately half of the world's population lives in malaria-endemic areas. Many of these malarial areas are in militarily strategic locations or regions of unrest where the likelihood of military conflict is greatly increased. For every person who dies of malaria, there are 300 others infected with the disease. This large number of malaria carriers assures that there is a large reservoir of infection available to perpetuate the *Plasmodium* life cycle.

P. falciparum is the most widely spread and virulent form of malaria. This species predominates in the tropical areas of the world and is most capable of decimating a fighting force. Troops posted in a malarial region, after many years of exposure, will develop clinical **immunity** (premunition) to malaria through repeated exposure, but this premunition is rapidly lost once they leave the area where the disease is endemic. Armed forces and refugees from nonendemic areas are vulnerable in malarial areas because they have no acquired immunities to the disease.

Malaria in World War I (1914–1918). The American military, having gained experience fighting mosquito-borne diseases (malaria and **yellow fever**) during earlier conflicts, entered the First World War better prepared to deal with malaria than most other combatants. Compared to the other allied and enemy forces, they did fare somewhat better. There were only 5,000 reported cases of malaria in the American overseas forces in 1917. In the spring of 1918, there were 420,000 American troops in Europe, with 10,000 troops arriving daily. By the end of the war, America had sent almost 1.2 million troops into the conflict. During the war there were 7.5 cases of malaria per 1,000 troops per year, as reported by U.S. authorities. By comparison, in the Macedonia campaign (1916–1918), malaria disabled the French, British, and German armies for a three-year period. Close to 80 percent of the 120,000 French troops were hospitalized with malaria, and the British army, with an average strength of 124,000 troops, had 162,512 hospital admissions for the

treatment of malaria. In the same campaign, there were a total of only 23,762 British war casualties. Exact figures are not available for the German army, but it also suffered a high death (mortality) and illness (morbidity) rate from malaria during the same campaign.

The reason given for this disastrous epidemic in the Macedonia campaign was that the allied military planners had no way of knowing that the hundreds of thousands of Greek refugees, who had fled to Macedonia just prior to the landing of the British and French troops, were infected with *P. falciparum* malaria. The Allied armies, in a futile attempt to prevent or reduce a malaria outbreak, had timed their arrival in Macedonia for the end of the mosquito-breeding season, but the greatly increased availability of actively infected hosts (the refugees) provided the reservoir of infection needed for the *Anopheles* mosquitoes (the vectors) to spread malaria to the troops in epidemic proportions.

The American forces during World War I had the expertise of American military physicians such as Major **Ronald Ross** and Colonel **William Gorgas**, who had distinguished themselves in the fight against malaria during the U.S. military occupation of Cuba (1901) and the Panama Canal Action (1904–1914) and had brought their experience to the battlefields of “the War to end all Wars.” Their method of controlling malaria was to impose sanitary drives so drastic that they were referred to as “sanitary Bolshevism.” They established “mosquito brigades” to eliminate mosquito larvae from stagnant pools and marshes, and personal anti-mosquito defenses such as mosquito netting and repellants. These anti-malaria campaigns were carried out in high-risk areas in the theater of military operations and were the most effective methods available at the time. Quinine was the only effective medication during the First World War and was used in both the prevention and treatment of malaria by all of the warring armies.

Malaria in World War II (1939–1945). By the time of the outbreak of World War II, many of the hard-learned lessons about the prevention and treatment of malaria had been forgotten. Malaria caused entire divisions of soldiers to become militarily ineffective on both sides. U.S. General Douglas MacArthur (1880–1964), commander of forces in the Pacific, said in 1943, “This will be a long war, if for every division I have facing the enemy, I must count on a second division in the hospital with malaria, and a third division convalescing from this debilitating disease.”

At the outbreak of World War II, quinine was still the only effective medication for the treatment and prevention of malaria. Realizing this, in 1942 the Japanese invaded Java and seized the Dutch plantations that produced 90 percent of the world’s supply of cinchona bark from which quinine was extracted, and German forces seized the reserves of quinine stored in Amsterdam. This setback sent the Allied forces into a frenzy of activity to expand the remaining meager supply of cinchona trees, a process that could take years before the new trees matured or a viable substitute for quinine could be developed and produced.

By 1943 the United States military started using Atabrine, an unpleasant but adequate substitute for quinine that had been discovered by a German researcher prior to the war. The side effects of a bitter taste, nausea, vomiting, diarrhea, yellowing of the skin, and sometimes a temporary insanity (psychosis) were so bad that many soldiers discarded the pills and risked malaria, rather than take the medicine. In time, the side effects were overcome, and even better substitutes such as chloroquine were developed.

In the meantime, many tens of thousands of Allied troops suffered from the ravages of malaria. In some areas of the Pacific Theater, there was an American malaria rate of 4,000 cases per 1,000 troops—a figure made possible by counting each recurrence as a case.

Sixty thousand American soldiers died of malaria during the African and South Pacific campaigns. Even though the most disastrous effects of malaria occurred among the Allied forces in the South Pacific and African campaigns, the Allied campaign in Sicily, from July through September 1943, also suffered significant malarial casualties. There were 21,482 American hospital admissions for malaria compared with 17,375 admissions for war-related injuries. Most of the malaria infections were *P. vivax* and subsequently many infected allied soldiers suffered incapacitating relapses in the spring of 1944 just when they were needed most for the battles for Monte Cassino and Anzio.

For the Japanese military medical service, the greatest problem was the incidence of malaria in Burma. Even with the daily use of quinine and mosquito nets large enough to provide protection for a whole squad of soldiers, along with the use of anti-mosquito creams and sprays for those who had to leave the protection of the nets, malaria continued to be a problem in the Burma region. The overall incidence of malaria is not known, but one Japanese regiment had at least one incident of malaria for every member of the regiment.

The Italian army was taking Italcina pills for the prevention (prophylaxis) of malaria. When some Italian medical supplies, including Italcina pills, were captured in September of 1943, the pills were sent for analysis and were found to be identical to the American Atabrine. The German war machine encountered high rates of malaria in Greece and southern Ukraine and Russia after invading these areas in 1941. Medical officers distributed Atabrine and Plasmochine, but self-dosing proved impractical and ineffective. Both military and industrial labs experimented with effective insecticides and new drugs, whereas prisoner-of-war and concentration camp inmates and mental patients were subjected to often deadly experiments on proper Atabrine dosing.

Malaria in Biological Warfare. The only known attempt at biological warfare in Europe during the Second World War occurred in the autumn of 1943. The German army reversed the pumps draining the marshes just south of Anzio, and flooded the swamp area at the same time that they released millions of malaria carrying mosquitoes. The American and British forces attacked Anzio in January 1944 but avoided a massive outbreak of malaria by taking anti-malarial medication. The local Italian civilians, however, did not have access to the drugs and suffered from malaria on an epidemic scale.

Malaria in War Crimes. Following World War II, Dr. Klaus Schilling (1874–1946), a German physician and one of the world's leading experts on tropical diseases, was tried, convicted, and hanged for war crimes by the American Military Tribunal at Dachau, Germany, for conducting malaria experiments on inmates of the Dachau concentration camp. He would first infect the inmates using malaria-infected mosquitoes and then test a variety of drugs on the prisoners in an effort to find a cure for malaria. As a result of these experiments, 30 to 40 victims died from the direct result of the malaria itself and another 300 to 400 died later as a result of the debilitation brought on as a result of the malaria attacks. There were an additional unknown number of deaths as a result of overdosing with the drugs being tested.

Malaria in the Korean War (1950–1953). Malaria was endemic on the Korean peninsula prior to 1950. There are no specific figures of malaria morbidity and mortality available for the North Korean army, but it is known that the incidence of malaria increased during the conflict. In 1953, the last year of the war, South Korean Army medical records report 8,855 malaria cases, with a 35 percent decrease the following year. Foreign (United Nations) armies who participated in the war also had a significant malaria

casualty rate. American troops, who received routine anti-malarial medication in the form of weekly chloroquine tablets, reported 1,513 cases of malaria between July 1951 and November 1952. Canadian soldiers had an 11 percent incidence rate (152 cases out of 1,350 soldiers) in 1952.

Malaria in the Vietnam War (1965–1975). It was during the Vietnam War that the drug-resistant strains of malaria first emerged. In desperation American military physicians used combinations of anti-malarial medications that met with varying degrees of success. During the Vietnam War, malaria was responsible for more U.S. casualties than were combat injuries. The disease decreased the combat strength of some American units by as much as 50 percent. In 1965 the U.S. armed forces had a morbidity rate of 98 cases per 1,000 troops per year and a mortality rate of 1.7 per 1,000 troops per year.

Contemporary Conflicts. During its nine-year military occupation of Afghanistan (1979–1988), the Soviet military suffered 469,685 casualties, and of this number, 415,932 were caused by infectious diseases, primarily malaria. No reliable figures exist for the Afghani fighters. Because malaria had been eradicated in northeastern Saudi Arabia and Kuwait, which was the primary theater of operations for 697,000 American forces during Operations Desert Shield (the build-up period) and Desert Storm (the six-week war to free Kuwait from Iraq), there were only seven American cases of malaria. These cases were only among troops who had crossed into southern Iraq.

Ongoing conflicts in or near African regions plagued by malaria result not only in victims among military personnel, but also in epidemic conditions among civilians whose environments are disrupted or who are forced to relocate. The year 2003 saw a major epidemic in the war-torn area of Ethiopia that killed perhaps 100,000 people. In the Darfur region of Sudan, among 2.5 million people dislocated by war and living in squalid camps, malaria, along with pneumonia and enteric diseases, killed an estimated 200,000 to 450,000 between 2003 and 2006 alone. Access to drugs is often made impossible by combatants' hijacking of medical transport and by the sheer isolation of refugee camps.

Anti-Malaria Vaccination Quest. The ultimate defeat of malaria is expected to be the development of an effective vaccine. Unfortunately, development of a vaccine against the malaria protozoan with its myriad life stages is not a straightforward process. The U.S. military, as well as other modern military forces, has had very active vaccine development programs under way for many years. Several vaccines have been tested with mixed results, and several more advanced vaccines are in the developmental stages. See also Diet, Nutrition, and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Human Immunity and Resistance to Disease; Insects, Other Arthropods, and Epidemic Disease; Malaria in Africa; Pesticides; Typhus and War; War, the Military, and Epidemic Disease.

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THOMAS QUINN

MALARIA IN AFRICA. A series of commercial interests followed by colonial motivations has attracted Europeans into Africa since the second half of the eighteenth century. While confronting an unfamiliar landscape in an alien land, European travelers frequently suffered from various forms of fever. However, it was not until the 1840s that the name **malaria** began to be used to refer to these fevers. In those days, malaria was not recognized as a specific disease. The word malaria derived from Italian words *mal'aria*, meaning “bad air.” Malaria was believed to be a **miasma**, a poisonous form of putrid emanation that arose from decaying vegetable and animal matters. The presence of malaria was associated with marshlands and swamps. Malaria was then regarded more as a cause of diseases than as a disease itself.

“White Man’s Grave”. Africa began to be acknowledged by Europeans as a land of malaria with the failure of the Niger expedition in 1841–1842. This was a British expedition commissioned to secure the abolition of **slavery** and establish networks of trade along the river Niger in West Africa. The mission failed because most of its personnel died of fever, attributed predominantly to malaria. Throughout most of the remaining nineteenth century, malaria figured consistently in the narratives of European traders, naval personnel, missionaries, colonial **surgeons**, and military men as a major deterrent to the healthy life of Europeans in Africa. In these narratives, Africa surfaced as a typically tropical mass of land that abounded in low-lying swampy areas. It was suggested that the banks of innumerable rivers in Africa were infested with excessive vegetation that produced unhealthy miasmatic “exhalations.” Together, these impressions converged to produce the image of Africa in the popular, and to some extent in the British official, mind as the “white man’s grave” or the region of the “deadly climate.” Malaria was believed to cause different forms of periodic fever (i.e., remittent and intermittent), in addition to subjecting the body to the risks of debilitating effects of black water fever. European medical officials serving in Africa pointed out that the ill effects of malaria manifested in European bodies in different ways. Anemia, formation of sallow yellowish tint on the skin, boils, absence of blood in the lips, occasional bleeding from the gums, dyspnea on slight exertion, cardiac weakness, enlarged spleen, edema in the ankles, some loss of memory, great debility along with giddiness and frequent insomnia, Carbuncles, dysentery, hematuria, renal complications, slight bronchitis, pulmonary congestion, Brow ague or neuralgia, chronic slight jaundice, and dyspepsia were seen as diverse expressions of malaria in the body. Malaria—along with acute yellow atrophy of the liver, insolation, and **yellow fever**—was believed to inflict the greatest mortalities among European colonials and soldiers in Africa.

Dealing with Malaria. Despite the fear of malaria, Europeans continued to pursue their commercial and colonial interests in Africa. The explorations of David Livingstone (1813–1873), Richard F. Burton (1821–1890), and others opened up the vast interiors of the African continent. By the Ashanti War in 1874, different European powers had largely succeeded in dealing with the problem of malaria in Africa in different ways. The British palm oil trade in Africa, for instance, penetrated into the interior through specially devised river steamers and an ever-increasing consumption of quinine. Quinine, an extract from

the bark of the cinchona plant, began to be appreciated as the best-known cure and preventive for malarial fevers. In British garrisons posted in Africa, daily consumption of smaller doses of quinine was made a key part of the mandatory **diet** for soldiers. In the nineteenth century there was an understanding that the natives in Africa were immune to the ill effects of malaria. It was argued that the natives in Africa were so frequently exposed to malaria in their daily lives that they had adapted themselves to its onerous effects. It was suggested that the delicate bodies of the Europeans in Africa were more vulnerable to the effects of malaria. Such a belief inspired the recruitment policies of the French army. In order to reduce figures of mortality from malarial diseases among the soldiers, the French devised a strategy of recruiting from within the indigenous African populations. In missionary publicity, such as that organized by the Universities' Mission to Central Africa, and in the speeches and writings of Livingstone and Burton, one finds European susceptibility to malaria in Africa explained as an indicator of lack in vigor caused by the delicacy of civilized living.

Malaria: A Protozoan Disease. By the last decade of the nineteenth century, the meaning of the word malaria had undergone substantial transformation. The microbiological discoveries of **Louis Pasteur**, **Alphonse Laveran**, **Patrick Manson**, and Major **Ronald Ross** were received with respect among the dominant sections of the medical scientific community. Malaria began to be understood as a distinct form of fever-causing disease that was brought on by protozoan parasites in the blood. Henceforth, malaria came to be recognized as an infectious disease. Following Ronald Ross's researches, it has been proven that malarial parasites are transmitted from one body to another by female *Anopheles* mosquitoes. Therefore, with the advent of the twentieth century the history of malaria reached a new phase. Scientists and historians started to trace in historical records the presence of the fever-causing disease called malaria over the preceding centuries. In some of these writings, malaria had a very central place. It was suggested, for instance, that soldiers, merchants, or slaves coming from Africa introduced malaria into Greece in the fifth century BCE. Such writings acknowledged Africa as the ancient home of malaria. The image of Africa as a land of endemic malaria survived. Throughout the twentieth century, medical scientists and representatives of international health agencies conducting academic research on malaria frequently visited Africa. Africa was also seen as a geographical area that was perpetually in need of medical relief and philanthropy. Under the leadership of Ronald Ross, an expedition was dispatched to Sierra Leone in West Africa as early as 1899 to verify the results of his laboratory experiments pertaining to the mode of malaria **transmission**. The expedition was not merely inspired by an academic quest. In Freetown, Kissy, Wilberforce, and Lagos, Ross organized sustained assaults on the habitats of the mosquito vectors. This combination of research and relief has inspired an enduring presence of foreign medical professionals in the African continent to the present.

Malaria and the Colonial Political Economy. Studies on African locales have indicated that malaria in Africa can be explained as an effect of drought, famine, and malnutrition. In Africa, malaria has been regarded as a companion of **poverty**. **Colonialism** has often been considered a crucial factor behind the patterns of malaria in Africa. A study of malarial epidemics in Swaziland, situated between Mozambique and South Africa, in 1923, 1932, 1939, 1942, and 1946, reveals one such pattern. The subordination of economic interests of the Swazi cultivators and herdsmen to those of the South African and local European settlers reduced the ability of many Swazi to feed themselves and made them vulnerable to climatic disasters. This often turned drought into famine. Excessive rainfall and

vector (*Anopheles* mosquito) breeding often followed. Such convergences frequently resulted in massive upsurges in the incidence of malaria.

Black African society has been influenced by memories of racial discrimination and colonial oppression. Among natives, the association of the malarial elimination programs with white settlers has often bred suspicion and even contempt about the intent of such projects. In the 1930s, the South African Department of Public Health's (DPH) efforts to reduce mosquito larvae breeding areas in Zululand by pouring slicks of paraffin into streams and water supplies were interpreted as a white settler means of "poisoning" the Zulu in order to take their land and cattle. Rumors that malaria was caused by the whites, and that quinine caused sterility and abortions, spread rapidly through Zululand. Zulu people were highly suspicious of official motives for malaria control because of their previous experiences with conquest, land loss, and repression, which were rooted in the colonial context.

Malaria and Development. Measures to eliminate malaria from Africa by promoting agricultural development often failed to achieve their intended purpose. A study of the impact of agricultural development on malaria in the *lowveld* region of the former Transvaal Province of South Africa reveals how the European settler commercial farmers benefited from projects of agricultural development. Such projects often failed to address the issues of poverty, malnutrition, and malaria successfully among the poorest of the Africans. Certain studies have attributed malaria in Africa to the development projects themselves. It is likely that a fisheries project undertaken in Kenya between 1957 and 1961 necessitated the digging of pits and ponds that eventually turned into breeding places for mosquitoes. Similarly, it has been alleged that the Kariba project in Zambia, the construction of the Kalimawe dam in Tanzania, and the Keno plain rice development scheme in Kenya were followed by long periods of malarial outbreaks triggered by the changes to the **environment**.

Malaria and WHO. Although malaria continues to be a serious problem in eastern Africa, it is recognized as a hyperendemic disease throughout West Africa as well. Because biomedicine clearly understands the causes of malaria and is convinced about the proper ways to tackle it, the problem in responding to malaria is not so much medical as it is educational, bureaucratic, and financial. The **World Health Organization** (WHO) has declared malaria a target for global eradication since the 1950s. It has been reported that though malaria is a global issue, 90 percent of malaria-related deaths occur in Africa. The persistence of malaria in Africa has been explained in terms of limited resources, unfavorable ecological conditions, insufficient health coverage, extreme poverty, shortage of trained personnel, tragic misuse of resources, political instability, and disorganization of civil services. In 1998 the WHO started the "Roll Back Malaria" campaign. This campaign is not another attempt to eradicate Malaria but is a quest to halve malaria-related mortality by 2010 and again by 2015. Partners in this campaign include governments of malaria-endemic countries, donor governments, international organizations, the private sector, and several civil society bodies. In 1997 African scientists invited colleagues from other countries to a meeting in Dakar, and this led to the launch of a Multilateral Initiative on Malaria. Earlier, the regional office of WHO in Africa, the World Bank, and some nations providing development assistance led to the emergence of plans for a pan-African initiative for malaria control. This has evolved into the African Initiative on Malaria. Despite these efforts, *The Africa Malaria Report 2003* published by WHO maintained that malaria continues to be a major impediment to health in Africa south of the Sahara, where it is



A team in Togo investigating the density of mosquito larvae in streams and marshy land. WHO photo. Courtesy of the National Library of Medicine.

believed to kill very young **children** and pregnant women; it has been shown to be the cause of at least one-fifth of all deaths of young children in Africa. Initiatives to tame malaria continue to emerge. Recently, the Global Fund to Fight **AIDS, Tuberculosis, and Malaria** (GFATM) has emerged as a major source of anti-malaria grant funds. Twenty-five countries are sharing a total of \$256 million for an initial two years to invigorate malaria control activities. See also Colonialism and Epidemic Disease; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Historical Epidemiology; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria and Modern Military History; Malaria in Africa; Malaria in Medieval and Early Modern Europe; Malaria in the Americas; Smallpox, Eradication of.

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ROHAN DEB-ROY

MALARIA IN MEDIEVAL AND EARLY MODERN EUROPE. Malaria posed a continuing health hazard in medieval and early modern Europe (c. 500 C.E.–1800). Although rarely a killer except among already vulnerable victims, medieval and early modern malaria caused reoccurring fevers that often weakened people, leaving them susceptible to other diseases. Some low-lying or swampy areas, such as the region around Rome and the Po valley in Italy, southeastern England, the Loire river valley and the Gironde in France, and the Don Delta in Ukraine, were particularly susceptible to malaria during this period, although the disease was found as far north as Scandinavia. European importation of slaves from Africa to its colonies in the New World opened the way for a more deadly strain of malaria to strike Europeans, one that reached epidemic proportions in the tropical Americas although not in Europe.

Where Was Malaria Found? Malaria, one of the oldest of human diseases, is caused by four species of fever-producing protozoan parasites of the genus *Plasmodium*. *Anopheles* mosquitoes transmit all four species. Two of the four species of malarial protozoa can be found in the temperate zone of Europe: *P. malariae* and *P. vivax*. Once Europeans began to import slaves from Africa to the West Indies, they exposed themselves to the much more virulent *P. falciparum* in tropical America but not in Europe.

Fevers were commonplace in medieval and early modern Europe and were caused by numerous diseases. In early modern Europe, the term ague came to stand for all of the summer fevers to which people were prone. In many low-lying, wet areas fevers were caused by *P. malariae* or *P. vivax*, and so malarial fever came to be almost synonymous with ague. Because fevers were commonplace and no germ theory of disease existed to explain the cause of disease, malarial fevers were often lumped in with other fevers and accepted as a matter of course for people living in some areas. Nonetheless, some observers did make the connection between the incidence of fever and swampy areas. However, the connection was not between mosquitoes and fever, but between the odors generated by swampy areas and the disease—hence the term bad air (*mal'aria* in Italian) used to describe the cause of fever. The eighteenth-century Scots physician William Cullen (1710–1790), for example, thought that fevers were generally caused by exposure to putrid air or bad weather; hence, the cause for fevers was viewed as being located in the atmosphere. At least governmental responses that were directed to removing the “bad air” problem associated with swamps also helped to remove the breeding ground for the mosquitoes that carried malaria.

Plasmodium vivax causes benign tertian fevers in humans. The blood cycle in this case is of 48 hours' duration, so fevers occur every two days, peaking on the third (hence “tertian”). *P. vivax* is generally not a killer, but it produces a recurring fever that saps the strength of its victims. This malaria species may appear to cure itself, only to reappear again over two or three years. *P. vivax* settles in the liver tissue and remains there to cause

its victims periodic relapses. Although the parasite dies out in its victims, exposure conveys no immunity, so later mosquito bites cause a repeat of the cycle. A disease of the subtropics and temperate regions, it was found throughout southern Europe and as far north as southern England well into the early modern period. Many summer fevers were the product of *P. vivax*.

Plasmodium malariae was also commonplace in medieval and early modern Europe and was found throughout Europe except in the coldest climates. It produced a quartan fever that peaked every fourth day (counting the first day as day one, as did the Romans who coined the term). In this case the parasites had a 72-hour growth cycle, producing daughter parasites every third day and a high fever that followed. *P. malariae* has the ability to continue to reappear for as long as 10 years after an initial infection. This form of malaria was relatively mild and was often accepted as a normal part of life in some regions.

The Impact of Malaria. Both *P. vivax* and *P. malariae* were endemic to several regions in medieval and early modern Europe. Swampy areas provided a breeding ground for mosquitoes, and people living near low-lying areas came to expect summer fevers as a matter of course. Because humans provided a host for the malaria parasite, the disease was continually replenished ensuring a reoccurring cycle of disease. In some areas summer fevers were so common, and generally mild, that many people considered them a normal occurrence rather than a sign of illness. Some places became well known for their summer fevers, such as the region around Rome. The Pontine Marshes near Rome provided an ideal environment for malaria until they were drained in the sixteenth century. Marshy areas along the Dutch coast and in Kent and East Anglia in southern England were also noted for their summer fevers throughout the period, as were the lower reaches of the Loire valley in France. In some areas of Kent, burials often exceeded baptisms throughout the period. Malaria was endemic in some parts of England, and some of the early English colonists in the New World transmitted malaria across the Atlantic in their bloodstream so that an early outbreak in Jamestown was caused by the English colonists.

Areas infected by malaria were, nonetheless, generally less healthy than other regions because of a variety of environmental factors. Infant mortality rates were especially high in many low-lying areas, often approaching 300 per 1,000 in southeastern England, for example (the usual infant mortality rate ranged from 150 to 300 per 1,000), although not all of these deaths were directly caused by malaria. Continued malaria infections served to debilitate a population leading to other health problems. Even when death did not result from malaria attacks, the productive capacity of the population was often low because of continued weakness generated by the summer fevers.

The clearing of land for agriculture that began to expand across Europe from the central Middle Ages onward helped to expand the environment for malaria. Small pools of stagnant water were an ideal breeding ground for mosquitoes, and land clearing often produced small puddles. As Europeans expanded their agricultural reach, they occupied newly cleared land that might become the breeding ground for malaria-carrying mosquitoes. The medieval warm epoch expanded the temperate zone farther north and higher into the mountains, increasing the potential reach of malaria. The gradual cooling cycle, which reached its high point in the seventeenth century, did help to reduce the environment for malaria in northern Europe from the late seventeenth century onward.

Although European colonization of the Americas exposed them to *P. falciparum*, it also enabled them to find a remedy for the fevers caused by malaria infections. The Spanish discovered the effectiveness of the bark from the cinchona bush, a remedy that Native

Americans may have used for treating fever (this point is debated among scholars, some crediting the Jesuits in Peru with discovering the medicinal use of cinchona). The Jesuits brought cinchona to Europe from Peru in the 1630s as a specific treatment for malaria, and it was often referred to as Jesuit bark or Jesuit powder. The religious connection was so strong that some Protestants with ague (such as Oliver Cromwell [1599–1658] in England) refused to be treated with “Jesuit bark” fearing that they would be poisoned. In the nineteenth century chemists were able to isolate a gummy product from yellow cinchona bark that was effective against malaria, a substance they labeled quinine from an old Peruvian name for the bark. *See also* Colonialism and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Malaria in Africa; Malaria in the Americas; Protozoon, –zoa; Slavery and Disease.

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JOHN M. THEILMANN

MALARIA IN THE AMERICAS. Locating **malaria** in the colonial history of the Americas (from 1492) can be a difficult task. The word *malaria* hardly makes an appearance in the contemporary historical records. The fever-producing disease we now understand as malaria—caused by Plasmodium **viruses** spread by the *Anopheles* mosquito—seems to have been referred to in a variety of ways in the past. Historians have carefully searched for features of malarial fever in the records pertaining to the colonial Americas. In doing so, they have worked closely with demographers, archeologists, geologists, linguists, and medical researchers. They believe that they have been able to infer retrospectively the presence of malaria in the colonial history of the Western Hemisphere.

The Debate. There has been a long debate involving the introduction of malaria in the Americas. Some scholars have argued that malaria was present prior to the invasion by the Spanish beginning in 1492. Some have interpreted linguistic evidence to suggest that fevers rampant in the armies of Pahacutec around 1378 CE were malarial. The presence of malaria in the pre-Columbian era in the Americas has been suggested from the discovery of pictures of mosquitoes on prehistoric pottery from New Mexico. Several ancient Mayan words have been translated to mean chills, fevers, and other symptoms associated with malaria.

Caribbean Islands. The predominant view among historians, however, is that malaria was completely unknown in the Americas before the Spanish invasion. They suggest that malaria was imported first into the Caribbean islands and later into the American mainland by Spanish invaders and their African slaves after 1492. The massive movement of population, armies, explorers, slaves, cattle, and insects following the discovery of the sea route to the Americas from Europe resulted in the introduction and

spread of malaria in the New World. But malaria was only one among many diseases introduced into the Americas in the sixteenth century. Viral diseases including **influenza**, **measles**, mumps, rubella, **smallpox**, and **yellow fever**, and bacterial diseases including pneumonia, scarlet fever, pertussis, anthrax, **bubonic plague**, and **typhus** are supposed to have been imported at the same time.

Colonial North America. Spanish populations carried malaria with them as they moved beyond the Caribbean islands and across the American mainland. English colonists probably introduced the disease into the Chesapeake region at Jamestown in 1607, and French-Canadian records mention it in the later seventeenth century. A visitor to La Famine Jesuit mission in 1684 reported 150 cases. Along with smallpox, malaria was the biggest killer of northern Native Americans in the sixteenth century. Falciparum malaria and yellow fever played a major role in depopulating the warmer parts of the Americas once the European settlements began spreading. It has been estimated that mortality from malaria among the Amerindians may have been as high as 75 percent. The Indians were not the only ones to suffer the effects of malaria in the sixteenth and seventeenth centuries. Nonimmune European soldiers and sailors sent to fight colonial battles died more often from yellow fever and malaria than from battle wounds. Malaria was not always a fatal disease, of course. In some parts of northern America, as in the Mississippi Basin, it was more of an endemic debilitating condition. Some pockets in North America remained relatively free from malaria until the early eighteenth century. The first explorers and pioneers who entered the Mississippi Valley, for instance, found no malaria. In Illinois, there was almost no malaria through the whole period of French settlement up to the 1760s. Thereafter, the situation changed drastically.

Along the East Coast malaria spread with infected settlers, becoming more or less endemic from Massachusetts to Georgia. Though thriving in low-lying and warmer areas, the disease was no stranger to northern entry ports such as Philadelphia and New York City, especially in the warm, humid summer months. More than other southern regions, South Carolina proved a “graveyard” for colonists, thanks to endemic malaria. The low-lying, marshy ground and long summers that encouraged the cultivation of rice and indigo proved perfect for mosquito breeding. Malarial deaths and debilitation among the colonists and natives prompted the widespread use of immune African slave labor.

South America. As in the North, there is considerable debate involving whether malaria was native to South America or imported. Some historians have argued that malaria may have been indigenous to South America. That ancient Peruvians built their houses far from the rivers has been attributed to the probable presence of malaria. Malaria might have been one of the fevers that attacked the invading pre-Columbian Inca armies in the Upper Amazon. However, such impressions are challenged by demographic figures for this region preceding the conquest: such densities of population in that region would have been impossible under the threat of malarial fevers. Alternatively, many historians have argued that malaria was imported into South America during and after the Spanish conquest.

Many places that have since then been repeatedly devastated by malarial fevers seem to have been free from malaria at the time of conquest. Historical records suggest that the invading troops under Hernán Cortés (1485–1547) and Francisco Pizarro (1471–1541) did not complain about malaria. Guyaquil, today still heavily infested, was a health resort during the sixteenth century. As late as the seventeenth century, Spanish expeditions in the Amazon valley did not suffer from malaria. This explains why the therapeutic powers

of cinchona bark (a base for quinine) were unknown to the natives. Thus, the predominant opinion among historians is that malaria was an imported disease, and one or more strains of malarial parasites were undoubtedly imported into the Americas in the sixteenth century from endemic areas in Europe and Africa. The tropical lowlands of northern South America, the Amazon basin, and coastal Brazil are believed to have been particularly conducive to the development and propagation of mosquito-borne diseases. Studies have indicated that milder varieties of malarial parasites—for example, *Plasmodium vivax* and *Plasmodium malariae* mosquitoes—existed in several areas of Central and South America before the discovery of the New World, whereas the Spaniards and their slaves brought the fatal *Plasmodium falciparum*.

Malaria came to be referred to in South America by different names, such as *sezoes* in the eighteenth-century Brazilian interior. By the nineteenth century, malaria began to be referred to as intermittent or pernicious fever. Malarial epidemics felled huge portions of the native populations following the Spanish intrusion into Hispaniola, central Mexico, northwestern Mexico, Guatemala south of the Peten rainforest, and the central Andes. Sixteenth-century Jesuits recorded attacks of fever throughout the tropical regions. When, in the sixteenth century, Spaniards discovered that extractions from the bark of the cinchona plants provided a cure for malarial fevers, they exported it and popularized it as an anti-periodic in other parts of the world.

Malaria in the Colonial Americas and the African Slave Trade. The Indian population in the Americas died of European and African diseases, whereas the Europeans died of African diseases. The African slaves were perceived as being able to survive both. This resulted in the impression that the African slaves were immune to malaria. They were said to have survived malaria throughout their lives in their homelands. Europe was home to the milder variety of malarial parasite *Plasmodium vivax*. Thus, the malarial agents that had been transmitted by the European sailors and soldiers were seen as causing a general debilitating effect on the native Americans. In contrast, Africa has been home to the more deadly variety of malarial parasite, the *Plasmodium falciparum*. Historians have considered falciparum malaria to have been equally deadly to the Europeans and the Indians in the Americas, wherever it had been introduced to the local mosquitoes by the African slaves along the marshlands of the Atlantic and Gulf Coasts.

Malaria in the United States. By the late colonial period, malaria had receded from New England, and its incidence was falling in the Mid-Atlantic states. Westward emigration and pioneer agriculture, however, brought malaria to the Ohio and Mississippi River Valleys and beyond. Initial settlement along watercourses and the clearing of heavily forested land encouraged the *Anopheles*, and malaria soon became the dominant disease of the American Midwest. Thirty years before **Alphonse Laveran** discovered the role of *Plasmodium*, American pioneer naturalist and medical educator Daniel Drake (1785–1852) of Ohio concluded from his travel and study of regional wildlife that malaria (“autumn fever”) was a result of “animalcules” rather than miasma. He published his findings and conclusion in *A Systematic Treatise, Historical, Etiological, and Practical, on the Principal Diseases of the Interior Valley of North America* (1850–1854). Malaria’s slow decline in the Midwest from the 1860s resulted from such trends as urbanization, expansion of railroad service (which moved people away from waterways), local drainage efforts, better nutrition, and the spread of cattle raising, which provided the mosquitoes’ preferred hosts.

Malaria remained a problem in the American South, however, especially in marshy areas dedicated to labor-intensive agriculture. Civil War soldiers, whose campaigns were

generally in southern climes, suffered from malaria more often than from any other disease. In the 12 southern U.S. states between 1912 and 1915 there were still 1 million cases of malaria in a total population of 25 million people. Even so, the mechanization of agriculture and the draw of rural southerners to northern cities during World War I (1914–1918) reduced population densities, producing a dramatic reduction of 90 percent in deaths from the disease between 1910 and 1920. The application of mosquito control techniques developed during the Second World War (1939–1945) eliminated malaria from the American landscape by 1949. The **Centers for Disease Control and Prevention** (CDC) still report many annual cases in the United States (1,349 in 2005), but virtually all of them are attributed to immigration or travel by U.S. residents.

Modern Latin America. Malaria continued to plague postcolonial Latin American societies well into the twentieth century. Nineteenth-century European and Creole elites across the continent demanded and attained improvements in water supply and drainage in their enclaves, but little was done for the rural masses. At the end of World War I, the young Rockefeller Foundation took on the elimination of malaria from Caribbean and Latin American sources, in part to prevent its reintroduction into the United States via migration (a fear that remains today). Others reinforced Rockefeller's efforts during the 1930s, and after 1945 anti-malarial spraying with DDT and provision of improved drug therapy for the sick became a major task of the Pan American Sanitation Bureau (PASB; later the Pan American Health Organization). In the 1950s the **World Health Organization** (WHO), UNICEF, and the U.S. State Department aided PASB. When WHO announced its initiative for the Global Eradication of Malaria in 1956, Mexico was among the first to sign on. Others followed, but by 1967 progress was disappointing, and the scope was reduced to providing for local control measures. By 1972 the initiative was declared moribund, despite nearly \$1 billion in U.S. funding.

Malaria is still considered endemic in certain parts of Latin America. In the 1980s, a chloroquine-resistant strain of parasite, along with massive deforestations in Rondonia and other parts of the Amazon, led to significant outbreaks of malaria among miners, Indians, and settlers in the region. In the early 2000s, regional governments and other agencies increased anti-malarial budgets in a concentrated effort to reduce the incidence of the disease dramatically by 2015. Between 2002 and 2006, the region's annual budgets rose from about \$80 million to nearly \$171 million. Reported malaria deaths dropped from 348 in 2000 to 101 in 2006, though reported cases only fell from 1,146,042 to 916,467, a reduction of 20 percent. Brazil accounted for 53.5 percent of the cases in 2000 and 60 percent in 2006. But progress has not been steady, and rising global temperatures might expand the geographical range of vector mosquitoes, increasing their rate of development and reducing the extrinsic incubation time of their pathogens. *See also* Colonialism and Epidemic Disease; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Historical Epidemiology; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria and Modern Military History; Malaria in Africa; Malaria in Medieval and Early Modern Europe.

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ROHAN DEB-ROY

MALARIA IN THE ANCIENT WORLD.

China. Malaria was already one of the most widespread diseases in the Old World by the time of the earliest historical records from all the major ancient civilizations. In China a fifth-century document written by Zuo Qiuming (Spring and Autumn period, 770–476 BCE) describes how a minister developed malaria following an **insect** bite. Other sources dating to the Warring States period (476–221 BCE) describe the typical seasonal pattern of the disease in temperate to subtropical climates, its 48- (tertian) or 72-hour (quartan) periodicity in humans, and its transmission. It was already known in ancient China that malaria was transmitted by mosquito bites, long before this was discovered in Europe. Fifth-century BCE Chinese author Zhan Guo, however, attributed the disease to the entry into the human body of an evil element called "shui qi."

The Pacific and the Indian Oceans. From China malaria was carried eastward by human migrations. Unlike the Chinese civilization, many of these cultures lack written records, so historians have to rely on research into the genetic makeup of many of these societies. The strong linkage of ovalocytosis (a human genetic mutation giving resistance to cerebral malaria) to populations of speakers of Austronesian (South Pacific Islander) languages has been used as evidence for the spread of malaria by the ancestors of these populations in prehistory. They probably moved from Taiwan throughout the western Pacific to Melanesia, where the disease reaches its greatest intensity today outside Africa. Malaria, however, was unable to establish itself on some of the more remote Pacific islands because of the absence of its vectors, *Anopheles* mosquitoes. Moving in the opposite direction as well, speakers of Austronesian languages spread eastward across the Indian Ocean from Indonesia, bringing ovalocytosis to Madagascar. Malaria was also well known in India in antiquity. It is described in the great ancient **Ayurvedic** medical text *Susruta Samhita*, which dates from before 500 CE. One passage in this Sanskrit text may attribute malaria to mosquito bites, although the text is difficult to interpret.

Egypt and Mesopotamia. Egyptian papyri dating to the period of the Pharaohs do not mention the characteristic periodicity of malarial fevers. Nevertheless, the argument from silence is not decisive because hardly any diseases are clearly described in these documents. The presence of the disease from the dawn of Egyptian civilization has been confirmed by antibody tests to detect malaria antigens in tissues from desiccated bodies dating to the Predynastic Period about 3200 BCE and in later mummies as well. Greek papyri from Egypt dating to the Hellenistic and Roman periods (300 BCE–400 CE) do use the characteristic Greek terminology for malaria and describe **magic** spells that were used to try to ward off the disease. Malaria was also well known in ancient Mesopotamia. Both the symptoms of the benign tertian fevers caused by the microorganism *Plasmodium vivax* and the neurological symptoms of cerebral malaria caused by *Plasmodium falciparum* have been identified in ancient cuneiform texts from Mesopotamia.

Greece and Italy. The greatest volume of surviving evidence for malaria in antiquity relates to the world of classical Greece and Rome around the Mediterranean (800 BCE–500 CE), particularly to Rome. It is here that it is possible to appreciate most clearly the effects of the disease, its **epidemiology**, and human reactions and responses to the problems it created. The writings attributed to **Hippocrates**, those of **Galen** and other ancient medical writers, as well as those of nonmedical authors, provide abundant literary evidence. In the first century CE, the Roman author Celsus (c. 25 BCE–50 CE) clearly described and differentiated the symptoms of malignant tertian fevers, caused by *Plasmodium falciparum*; of benign tertian fevers, caused by *P. vivax*; and of quartan fevers caused by *P. malariae*. In addition, it is possible to examine human skeletal remains excavated from archaeological sites for malformations caused by inherited human genetic conditions associated with resistance to malaria, such as the anemia-causing, inherited blood disorder thalassemia, which is common in Mediterranean populations, and the sickle cell trait. Although the sickle cell trait undoubtedly first evolved in tropical Africa, the earliest direct evidence for it comes from Hellenistic burials dating to the third century BCE on the island of Failaka in the Persian Gulf, where fossilized sickle-shaped red blood cells have been directly observed under the electron microscope. This was probably the mild form of sickle cell disease found today from Arabia to India, rather than the more severe form of the disease that occurs in people from tropical Africa and in African Americans. A third avenue of research is provided by biomolecular archaeology (the study of ancient DNA and other ancient biomolecules, already alluded to above in relation to Egypt). Ancient DNA has been used to confirm an archaeologist's hypothesis that malaria was the cause of an epidemic that produced an infant cemetery in the ruins of an abandoned Roman villa at Lugnano in Umbria in central Italy in the fifth century CE.

For over 2,000 years, malaria was endemic in the countryside of central Italy around Rome. In the first century BCE, the Roman orator Cicero (106–43 BCE) records that Romulus, the legendary eighth-century founder of Rome, chose a healthy location in a pestilential region for his new city (traditional foundation date 753 BCE). The famous Seven Hills of Rome were healthy for those people, particularly the aristocracy, who lived on top of them. Though they did not make the connection, this was because mosquitoes, the vectors of malaria, only flew at the lower altitudes and around badly drained soils. In the lowlands surrounding the city of Rome in antiquity, however, malaria had as great an impact on the economy and the population as it does today in tropical Africa. Cato the Elder (234–149 BCE), one of the earliest Roman historians, indicated that building a villa in an unhealthy location in summer, the malaria season, would increase the cost of

the construction work by a quarter. The chronic ill health produced by malaria led many of the Romans to want to migrate away from their own homes. The first-century Roman historian Livy (c. 59 BCE–17 CE) stated that when the Romans invaded Campania, the region around Naples, in the fourth century BCE, in their first major excursion outside their homeland of Latium, the Roman soldiers did not want to return home after the end of the war because their farms in Latium were unhealthy, whereas Campania was healthy. This was the result of differences in the distribution of various species of mosquito, not all of which are capable of transmitting malaria. As the Romans vacated their own farms around Rome to acquire an empire, a labor shortage developed on fertile agricultural lands around the city. Malaria was most intense in low-lying areas with the best land for agriculture. The Romans solved the labor problem by importing large numbers of non-Roman slaves, who were forced to work in the fields in chain gangs, under the whip. A whole economy based on mass chattel **slavery** developed in the countryside around ancient Rome, as a response to malaria. After the collapse of the Roman Empire, malaria continued to flourish around the city of Rome until Italian dictator Benito Mussolini (1883–1945) eliminated it in the 1920s and 1930s.

Africa South of the Sahara. The historical record for Europe demonstrates what we can only assume in the case of Sub-Saharan Africa, given the scarcity of documentary evidence relating to tropical Africa before European colonization commenced. *Plasmodium falciparum*, the most dangerous of the four species of human malaria, had an extraordinary impact over a very long period of time on the development of civilization even in areas on the fringe of its geographical distribution, in southern Europe. In central Africa, where it evolved, it probably had an even greater impact in the past. Indeed, it is very likely that the presence of endemic malaria is a major reason why civilization failed to develop in antiquity in tropical Africa, where *Homo sapiens* first evolved.

Pre-Columbian New World. Whether malaria was present in the Americas before Christopher Columbus (1451–1506) is a matter of controversy, as is the presence of numerous other diseases. However, the most significant argument that is currently available is that no native American population manifests any of the human genetic mutations conferring a degree of resistance to malaria (e.g., sickle trait, thalassemia, ovalocytosis) that are so common in the Old World wherever malaria occurs today or is known to have occurred in the past. Consequently, it seems that the exposure of Amerindian populations to malaria, which occurs today in parts of Central and South America, is very recent, indicating that the disease was either not present at all or at least was not very important in the New World before Columbus. Presumably, the necessary mosquito vectors of malaria, which is a temperature-dependent disease, could not survive the passage of the ancestors of the Amerindians from Asia to North America across the Bering Strait. *See also* Chinese Disease Theory and Medicine; Diagnosis of Historical Diseases; Environment, Ecology, and Epidemic Disease; Greco-Roman Medical Theory and Practice; Human Immunity and Resistance to Disease; Malaria in Africa; Malaria in Medieval and Early Modern Europe; Malaria in the Americas; Neolithic Revolution and Epidemic Disease; Paleopathology; War, the Military, and Epidemic Disease; Water and Epidemic Diseases.

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ROBERT SALLARES

MALLON, MARY (1869–1938). Known as "Typhoid Mary," Mary Mallon is a significant figure in the history of epidemic disease because she was the first individual in the United States to be identified as a healthy carrier (a person who is contagious but has no symptoms) of **typhoid fever**. Mallon, whom the popular media of the day dubbed "The Most Dangerous Woman in America," rose to notoriety during the first decade of the twentieth century because her asymptomatic-carrier status allowed her to move freely throughout New York City and its suburbs, directly infecting 47 people (3 of whom died).

Mallon was born in 1869, in County Tyrone, Ireland. She immigrated to New York City in 1883 and worked her way through a series of menial jobs, until she eventually earned a reputation as a trustworthy and competent cook. Between 1900 and 1907, Mallon served as a cook for a number of wealthy New York–area families, infecting her employers with the typhoid bacillus (*Salmonella typhi*) through the meals she prepared.

Public health officials eventually caught up with Mallon in 1906, when an outbreak of typhoid occurred in Oyster Bay, Long Island, an affluent suburb of New York City. The outbreak attracted the attention of George Soper (1870–1948), a 37-year-old civil engineer turned public health specialist, who deduced that a local cook, Mallon, had caused the outbreak. In 1907 Soper tracked down Mallon, who was working for a family on Park Avenue (their only child eventually died of typhoid fever). Violently opposed to the idea that she could be a silent carrier, Mallon refused to cooperate with Soper. He enlisted the help of NYC Health Commissioner, Herman Biggs (1859–1923), and Dr. Sara Josephine Baker (1873–1945), an inspector from the Department of Health. Using their authority, Soper was able to take blood, urine, and stool samples, all of which tested positive for the typhoid bacillus. The emerging science of bacteriology thus proved that Mallon was in fact a healthy carrier.

Even though other healthy carriers of typhoid fever existed in New York City, Mallon was a foreign-born, Irish-Catholic, working-class woman at the peak of anti-immigrant nativism. She was automatically deemed a "threat to society" by the Department of Health. Denied her civil liberties, Mallon was forcibly isolated on North Brother Island in the East River near the Bronx. She remained a prisoner of the state until 1910.

In 1915, another typhoid outbreak occurred, this time at New York's prestigious Sloane Maternity Hospital. Twenty-five staff members contracted the disease, two of whom died. Soper determined that the cause of the outbreak was Mallon. Though she had been barred by the city authorities from ever working as a cook again, she was employed in the hospital kitchen. Once again she was isolated on North Brother Island. She remained there until her death in 1938 of pneumonia, at the age of 69. *See also* Medical Ethics and

Epidemic Disease; Public Health Agencies, U.S. Federal; Scapegoats and Epidemic Disease; Typhoid Fever in the West since 1800.

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TANFER EMIN TUNC

MALTHUSIANISM. In nature it is common for populations of **animals** and **insects** to undergo “boom and bust” cycles, in response to fluctuations in food availability. It is inherent in the process of biological evolution and natural selection that individuals, families, or groups of organisms compete with one another, up to the limits of available food and other key resources.

The word “Malthusian” refers to the view that humans, too, are subject to food supply limits acting as a final, and “bust”-generating, constraint on population growth. Malthusianism envisages that, when such food limits are reached, starvation, social disorder, and heightened mortality are the inevitable natural checks on continuing population growth. Some scholars have interpreted the written accounts of past famines and social breakdowns as illustrations of Malthusian depopulating crises. However, others have argued that the form of a crisis is shaped more by social and economic forces than by laws of biological demography.

This perennially controversial idea came from the Reverend Thomas Robert Malthus (1766–1834), an English cleric, demographer, and political economist. Malthus developed his pessimistic but highly influential views on population growth largely as a reaction to what he regarded as the undue optimism of the French political scientist and philosopher Marquis de Condorcet (1743–1794) and of his own father and associates, who included the *philosophe* Jean-Jacques Rousseau (1712–1778). Those optimistic ideas reflected the enthusiastic populist ideals behind the French Revolution. In 1798 Malthus published his famous *An Essay on the Principle of Population*, predicting that the multiplicative growth of population would outrun the usually linear increase in food supply. His “Principle of Population” stated that population, if unchecked, increases at a geometric rate (i.e., 1, 2, 4, 8, etc.), whereas the food supply grows at a much slower arithmetic rate (i.e., 1, 2, 3, 4, etc.).

This disparity, Malthus argued, must lead to a decrease in available food per person, with consequent starvation, **epidemic** disease, and worse. His phraseology was dire:

The power of population is so superior to the power of the earth to produce subsistence for man, that premature death must in some shape or other visit the human race. The vices of mankind are active and able ministers of depopulation. They are the precursors in the great army of destruction, and often finish the dreadful work themselves. But should they fail in this war of extermination, sickly seasons, epidemics, pestilence, and plague advance in terrific array, and sweep off their thousands and tens of thousands. Should success be still incomplete,

gigantic inevitable famine stalks in the rear, and with one mighty blow levels the population with the food of the world.

Writing at a time when periodic famine persisted in Europe, Malthus anticipated a food-shortage disaster during the nineteenth century. However, largely because of the gains of the second agricultural revolution in Europe and the higher food yields from cultivars brought back from Europe's adventures overseas (e.g., the potato from the Andes), this prediction did not eventuate. Further, his classically static analyses, with simple forward extrapolations of recent trends, were unsuited to the nonlinear behavior of complex social, economic, and agricultural systems.

Malthus favored moral restraint as a preemptive check on population growth. This restraint included late marriage and sexual abstinence—which he advocated particularly for the poor and working classes. The young Charles Darwin (1809–1882) was influenced by his reading about the dynamics of the Malthusian process, wherein, with limited food supplies, those who were the most politically powerful and privileged were most likely to survive. Here lay the seeds of an idea: the natural selection processes of biological evolution. *See also* Diet, Nutrition, and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Human Immunity and Resistance to Disease; Irish Potato Famine and Epidemic Disease, 1845–50; Poverty, Wealth, and Epidemic Disease; Water and Epidemic Diseases.

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ANTHONY MCMICHAEL

MANSON, PATRICK (1844–1922). A physician and expert on tropical medicine, Patrick Manson was born in Aberdeenshire, Scotland. He graduated in 1865 from Aberdeen University and in 1866 was awarded his M.D. degree. Manson spent 23 years in China and Hong Kong, where at various points he was a government health officer, had a private practice, and founded the Hong Kong School of Medicine. He eventually returned to London where he helped establish the discipline of tropical medicine.

Appointed in 1866 to the Chinese Imperial Maritime Customs as medical officer for Formosa (Taiwan), he resigned in 1871 and moved to Amoy, where he joined a missionary hospital. In this period he began to conduct research on the *filaria* worm and diseases affecting the lymphatic system. He concluded that the mosquito was an intermediary host necessary for the development of *filaria* worms, organisms responsible for causing elephantiasis. He retired to Scotland in 1889 but in 1892 moved London where he was appointed physician to the Albert Docks of the Royal Naval Hospital. There he took the opportunity to continue his research on tropical medicine. He thought that there might be a similar mosquito-parasite relationship for malaria and in 1894 published a hypothesis about the role of the mosquito in the transmission of malaria. Alphonse Laveran had also speculated about the role of the mosquito in the transmission of malaria, but it was Ronald Ross who built on the work of Manson and others to demonstrate it.



Dr. Patrick Manson. Courtesy of the National Library of Medicine.

While he was in London, Manson developed programs to control **epidemic** diseases in the British Empire. In 1894 he was appointed medical advisor to the Colonial Office, providing memoranda on public health and epidemic disease control as well as names of experts to make trips to the Empire to dispense advice to local governments. He also elicited the support of Joseph Chamberlain (1836–1914), the Colonial Secretary, for a scheme to improve research opportunities in tropical medicine and education in the discipline for physicians and public health officers. In 1898 Manson published his seminal *Tropical Diseases: A Manual of the Diseases of Warm Climates*. With support from the Colonial Office and the help of **William Simpson** and James Cantlie (1851–1946), in 1899 Manson founded the London School of Tropical Medicine, which became an important reference for the study of the control, prevention, and cure of epidemic diseases in the tropics.

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MARY P. SUTPHEN

MARBURG VIRUS. See Hemorrhagic Fevers; Hemorrhagic Fevers in Modern Africa.

MATHER, INCREASE (1639–1723) AND COTTON (1663–1728). The New England “Mather Dynasty” dominated Massachusetts religious and political life during most the seventeenth century and into the first quarter of the eighteenth. The son of Richard Mather (1596–1669), who had emigrated from England because of religious persecution for his Puritan views, Increase Mather was raised and educated in Massachusetts, preached in Congregationalist churches in England during the Puritan Commonwealth (1649–1660), and returned to New England after the restoration of the monarchy in 1660. Although his hesitation to intervene against the Salem witch trials caused some to blame him for persecution, Increase Mather held to the view that it was better for those guilty of witchcraft to go free rather than to punish the innocent, and he was skeptical of so-called “spectre (spirit) evidence.” This rather rational ethos was also evident in his promotion of a society to advance scientific knowledge and, upon his appointment as rector of Harvard College from 1686 to 1701, his encouragement of scientific study at the college. He, along with his son Cotton, also pioneered in advocacy of inoculation during a **smallpox** epidemic, an unpopular and controversial position at the time.

Like his father, Cotton Mather is chiefly known as a Congregationalist religious leader, although a speech impediment nearly discouraged him from a career as a preacher and inclined him toward the profession of medicine, a field in which he maintained an active interest. When he inoculated his own son against smallpox, nearly causing the young man to die, Cotton Mather drew the ire of his fellow citizens, including Dr. William Douglass (1691–1752), the only **physician** in Boston with a medical degree. His account of these events was published in the transactions of the Royal Society of London, which had admitted him into its membership upon the publication of his study of American natural phenomena, *Curiosa Americana* (1712–1724). As evidence of his wide-ranging interests,

Cotton Mather possessed the largest private library in colonial America. He was the author of numerous works on a variety of topics, including *Sentiments on the Small Pox Inoculated* (1721) and *An Account . . . of Inoculating the Small-Pox* (1722).

Unpublished in his lifetime was the medical manual *The Angel of Bethesda* (c. 1724). This manual discusses the general causes of illness and prescribes regimens for wellness, and it proposes an early form of **germ theory**, noting the ubiquity of microscopic organisms. It discusses specific diseases and speculates upon their causes while proposing treatments. Concerning smallpox, he attributes the cause to an “Animalculated Business” (what we would call microorganisms) and suggests a variety of treatments once the disease is contracted. As a clergyman, Cotton Mather took pains to associate disease and **epidemics** with moral and spiritual concerns, both attributing a link between sick souls and sick bodies and admonishing readers to employ the trial and suffering of illness as an occasion for repentance. *See also* Jenner, Edward; Religion and Epidemic Disease; Smallpox in Colonial North America; Vaccination and Inoculation.

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THOMAS LAWRENCE LONG

MEASLES. Measles is the English-language term for a systemic fever-producing exanthematous disease and for the **virus** that causes it. Measles is known as *la rougeole* in French, *Masern* in German, and *sarampión* in Spanish. Over the past four centuries, measles terminology has been complicated by the fact that the three major exanthematous diseases of childhood (measles, scarlet fever, and rubella) had not always been distinguished from each other. Certain terms for measles “wandered” among what we now know to be different diseases, a situation that did not resolve until the three were formally distinguished from each other in 1881. In examining the historical literature on measles published before 1900, it is advisable to review historical terminology first.

Measles Virus. Measles virus is a member of the paramyxovirus family, which includes a number of other viruses that infect a diversity of animals, with the expectation that many other related viruses remain to be identified. Within the Paramyxoviridae are the viruses that cause mumps, parainfluenza virus infection, respiratory syncytial virus infection, and metapneumovirus infection (all human diseases), as well as zoonotic henipaviruses such as Hendra virus, which has caused occasional human **epidemics**. It is believed that thousands of years ago, an ancestral virus evolved in different directions, leading to the now-diverse morbillivirus group of which measles is a member, within the larger paramyxovirus group. The morbilliviruses also include viruses of carnivores (e.g., canine distemper virus), ruminants (e.g., rinderpest virus), and cetaceans (e.g., dolphin morbillivirus). Measles disease was first purposely transmitted to humans by the virus-infected blood of ill persons in 1905; six years later, the virus was serially passaged in monkeys given respiratory secretions that contained the infectious agent. The virus was finally cultivated in tissue culture in 1954 by **John Franklin Enders** and a colleague.

A close relative of rinderpest morbillivirus, which causes a serious epizootic disease of cattle, measles virus probably arose from a common viral ancestor several thousand years ago, at some time after early human civilizations began to settle into fixed communities and to domesticate animals (c. 10,000–8,000 BCE). Thus, measles virus is undoubtedly a descendant of an animal virus that evolved to switch to a human host. It is now a uniquely human virus, although some other primate species develop disease upon experimental infection.

Measles Disease. In the absence of **vaccination**, almost all persons infected with measles virus will develop a “full blown” disease. Measles has long been regarded as a so-called “textbook disease” not only because of its unvarying clinical picture but also because of its clear epidemiologic features of extreme respiratory transmissibility, relatively fixed period of incubation time to prodromal illness (10 days) and to appearance of rash (14 days), and, in the pre-vaccine era, its propensity to infect urban infants and small children in 2- to 3-year cyclic waves.

Clinically, measles begins with nonspecific prodromal signs and symptoms: fever, malaise, and the classic “three C’s” of cough, coryza (upper respiratory inflammation and mucous development), and **conjunctivitis**. Measles also features a classical “pathognomonic sign” (a clinical finding that points to only one disease) in the appearance of Koplik spots, first described by Russian pediatrician Nil Filatov (1847–1902) but known in English by the surname of the American pediatrician who popularized the spots as a diagnostic feature (Henry Koplik, 1858–1927). Koplik spots are small bluish-white dots on a red background in the cheek mucosa, appearing about two days before the rash, and lasting a day or two after the rash appears. The rash itself is characteristically red, spotted, and raised, starting at the hairline and moving down the body over the first day or so, tending to recede in old areas of skin as it appears and develops in new areas.

Although measles has been considered a benign disease of childhood, it has long been associated with a number of severe complications whose incidences may vary widely with host and environmental factors, including severe and fatal pneumonia, corneal ulceration and blindness, acute disseminated encephalomyelitis, and subacute sclerosing panencephalitis (SSPE).

Measles History. The Persian-born **physician Rhazes** first distinguished measles from smallpox, and claimed that the same disease had been prevalent several hundred years before his time. In the early Middle Ages, reports of possible measles were further recorded, with mention of it being a childhood disease in 1224.

During the Age of Exploration, measles was one of the principal diseases, along with smallpox, to devastate New World and Pacific populations, including the loss of tens of millions of Central and South Americans in the sixteenth century, following the conquests of Hernán Cortés (1485–1547) and Francisco Pizarro (1475–1541), and of many Native Americans in what are now the United States and Canada. Medical history books contain a bewildering catalog of fatal measles epidemics that have devastated populations small and large over the past five centuries. Among these was the “virgin-soil” **measles epidemic in Fiji** of 1875. Japan apparently suffered a number of major imported measles epidemics over the past millennium, culminating in one of the most highly fatal in recorded history, appearing in 1862. Measles was so deadly in Japan that it gave rise to the folk saying: “*Hōsō* (smallpox) determines one’s looks, but *hasika* (measles) determines one’s life.” Also worthy of mention are the fatal epidemics that occurred in 1917 in the U.S. military training camps across the country, concentrated in the southern United

AN ACCOUNT OF THE MEASLES AS THEY APPEARED IN PHILADELPHIA IN THE SPRING OF 1789

This disease, like many others, had its precursor. It was either a gum-boil, or a sore on the tongue. They were very common but not universal. They occurred in some instances, several days before the fever, but in general, they made their appearance during the eruptive fever, and were a sure mark of the approaching eruption of the measles. I was first led to observe this fact, from having read Dr. Quin's accurate account of the measles in Jamaica. I shall now proceed to mention the symptoms of the measles as they appeared in the different parts of the body.

1. In the head, they produced great pain, swelling of the eye-lids, so as to obstruct the eye-sight, tooth-ache, bleeding at the nose, tinnitus aurium, and deafness; also coma for two days, and convulsions. I saw the last symptom only in one instance. It was brought on by the stoppage of a running from the ear.
2. In the throat and lungs, they produced a soreness and hoarseness, acute or dull pains in the breast and sides, and a painful or distressing cough. In one case, this cough continued for two hours without any intermission, attended by copious expectoration. In two cases I saw a constant involuntary discharge of phlegm and mucus from the mouth without any cough. One of them terminated fatally. Spitting of blood occurred in several instances. The symptoms of pneumonia vera notha [bronchial] and typhoid were very common. I saw two fatal cases from pneumonia notha, in both of which, the patients died with the trunk of the body in an erect posture. I met with two cases in which there was no cough at all till the eruption made its appearance on the fourth day, and one which was accompanied by all the usual symptoms of the cynanche trachealis humoralism [swollen upper airway].
3. In the stomach the measles produced, in many instances, sickness and vomiting. And,
4. In the bowels, griping, diarrhea, and in some instances, bloody stools. The diarrhea occurred in every stage of the disorder, but it was bloody and most painful in its decline. I attended a black girl who discharged a great many worms, but without the least relief of any of her symptoms.

There was a great variety in this disease.

From *Medical Inquires and Observations* by Dr. Benjamin Rush of Philadelphia (Philadelphia, 1796; see Google Books).

States, where recruits were more likely to have escaped childhood measles by virtue of growing up on isolated farms and in very small towns. That the rate of complication and death was so high in this healthiest segment of the population (young men prescreened for underlying physical and infectious diseases) attests to the pathogenic vigor of measles.

Measles has also figured in important advances in medicine. In 1758, three decades after smallpox inoculation had been introduced into Europe, Scots physician Francis Home (1719–1813) began inoculating subjects to prevent measles (apparently without much success). In 1846 Danish medical student (and later renowned physiologist) Peter Panum (1820–1885) conducted a measles outbreak investigation in the Faroe Islands that not only established the epidemiology and duration of protective immunity of measles, but also became a classic example of epidemiologic methods, still read by epidemiologists



Lab technicians at the Tirana Institute of Hygiene and Epidemiology in Albania inject chicken eggs with the measles virus to produce the vaccine. Courtesy of the National Library of Medicine.

more than 150 years later. Finally, it should be noted that it was chiefly the experience with severe and fatal measles pneumonia in the 1917 Army camp epidemics that led to the remarkable bacterial and pathological studies of the 1918 “Spanish influenza” by U.S. military physicians a year later, in both instances establishing as the cause of most fatalities a “one-two punch” by a respiratory virus (measles or influenza) and one or more resident pathogenic bacteria.

Measles Vaccines. Although measles immune globulin was administered early in the twentieth century, it was not until the early 1960s that measles vaccines were licensed and became widely available in the developed world. First-generation vaccines were inactivated; over several years’ time, their protective ability declined to the point where breakthrough infections occurred and resulted in an altered disease often featuring severe pneumonitis (“atypical measles”). Second-generation vaccines containing live attenuated measles viruses are now used worldwide and have been gradually reducing the burden of measles mortality in the developing world. Recent figures of the **World Health Organization** estimate 454,000 measles deaths in 2004, down 48 percent from the 871,000 annual deaths estimated five years earlier. These figures nevertheless put measles in the same category of high childhood fatality as **malaria**, general respiratory diseases, and diarrheal diseases. Given the extreme transmissibility of measles, vigorous vaccination campaigns must be ongoing in order to prevent disease in individuals and to achieve disease elimination, a goal which appears feasible though not likely to be met by 2010. A disturbing trend in

recent years has been for parents to refuse measles vaccination for their children in favor of natural exposure, sometimes at staged “measles parties” where healthy children are deliberately exposed to children with measles. This is a dangerous practice because the negligible risk of vaccination is grossly outweighed by the well-known risk of death, neurologic disease, and other morbidity caused by natural measles infection.

The Interaction of Agent, Host, and Environment. The 454,000 estimated annual measles deaths reflect the high rate with which measles complications may occur under conditions of deprivation and coinfection. It was recognized 130 years ago that acute measles fatalities were typically associated with either severe pulmonary or gastrointestinal complications. During World War I, investigators of a measles epidemic at Camp Zachary Taylor, in Louisville, Kentucky, showed that virtually 100 percent of severe and fatal measles cases were associated with streptococcal coinfection, and that bacterial pneumonia was the proximate cause of death in most of those who died. More than 75 years ago, it was recognized that measles severity was associated with vitamin A deficiency, and in more recent times it has become apparent that even low levels of vitamin A, not yet reaching clinical deficiency status, predispose individuals to more severe measles disease. Observations in Africa and elsewhere have shown that severe measles, including “hemorrhagic measles” and “black measles,” may be associated with marasmus, kwashiorkor, and underlying infections. Measles in persons with deficiencies of cell-mediated immunity can result in either severe giant cell pneumonia, often in association with multi-organ involvement, or measles inclusion body **encephalitis** (MIBE), associated with chronic replication of a defective virus. A clinically similar condition, SSPE, is now uncommon in the developing world because widespread measles vaccination has prevented early childhood infection with wild virus. SSPE is a progressive fatal neurologic disease in children with normally functioning immune systems who are infected at an early age with measles virus and like MIBE is associated with persistence of a defective virus. *See also* Children and Childhood Epidemic Diseases; Measles, Efforts to Eradicate; Measles in the Colonial Americas.

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DAVID M. MORENS

MEASLES, EFFORTS TO ERADICATE. Given the success with eradicating **smallpox**, the huge strides in eliminating **polio**, and certain epidemiological elements of **measles**, there has been a series of regional and global campaigns to eliminate and eventually eradicate measles from the world by mass immunization and close surveillance.

Measles is an acute disease that is caused by a **virus** and is highly contagious. The patient is infectious for about a week, and the disease or **vaccinations** will confer immunity on recipients. Most common among children, it can wreak havoc among nonimmune adults, as happened to indigenous peoples during periods of European colonization. Deaths are usually the result of complications from the disease. In 1954, **John Enders** and

a colleague isolated the measles virus, and a safe vaccine was ready for use in humans by the early 1960s. In the United States, the vaccination program began in earnest in 1963.

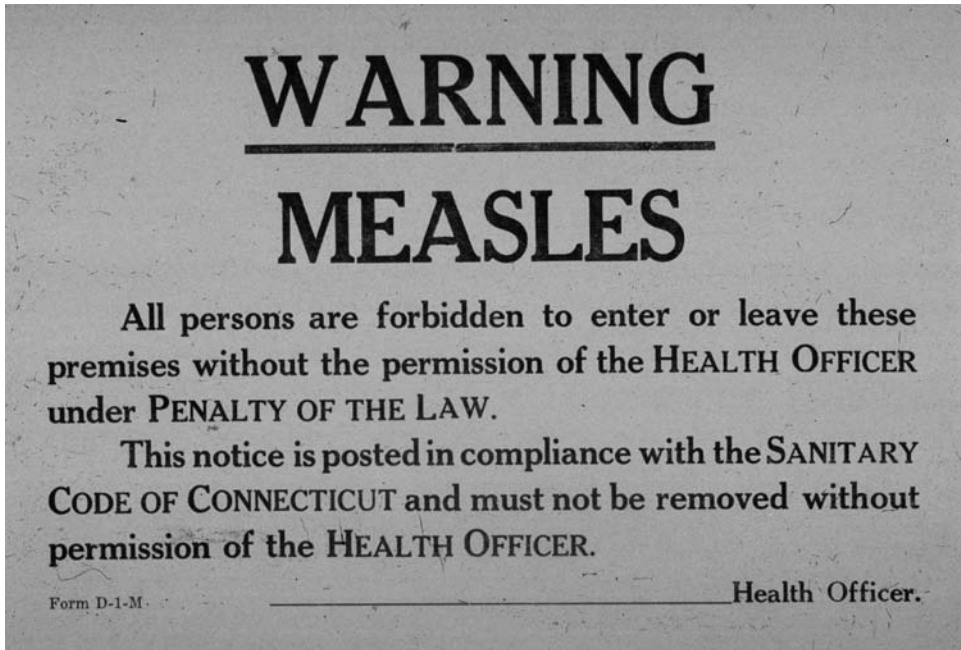
In the midst of early success, the director of the U.S. **Centers for Disease Control** (CDC) announced in 1966 its first goal of eliminating measles from the United States during the following year. Four factors made elimination of the disease seem possible: very widespread incidence of measles meant widespread immunity among older children and adults who had contracted it; measles only affects humans (though some primates can carry it), so no animal reservoir has to be considered; no one carries the disease long term, or chronically; and the herd immunity threshold, or the rate of immunity in the population below which a disease would continue to spread, was believed to be around 55 percent.

The campaign consisted of four tactics: routine infant immunization; upon entry into school, vaccination of those who had not been immunized; close surveillance of cases; and vigorous reaction to major outbreaks. In 1967 one of the two types of vaccines being used was withdrawn for having proven to provide only short periods of immunity and a tendency to predispose the recipient to atypical measles. Even so, between 1963 and 1968 reported cases in the United States fell by over 90 percent. An initiative against rubella with a new vaccine interrupted the measles program in 1969, and cases spiked from 22,000 in 1968 to over 70,000 in 1971. In the same year, the MMR (Measles, Mumps, Rubella) vaccine began to replace the more limited one for measles alone.

The campaign revealed that measles was more contagious than previously believed, and thus the herd immunity threshold was closer to 90 percent than 55; the current level of coverage was estimated to be only around 78 percent, with lowest levels in poorer inner city neighborhoods. In addition, though the surveillance system was adequate, schools were in no position to verify and immunize as required. In 1978 the CDC's goal of elimination was repeated, this time with a four-year window (by 1982). Reduction was again dramatic, with the 1978 figure of 27,000 cases falling to 1,497 in 1983, though elimination remained elusive. This time success was soured with the realization that a single dose of vaccine was insufficient, and that booster shots would be needed. All shots had to be administered after the infant was nine months old, because up to that point, the child of an immune mother retained its mother's antigens, which negated the effect of the vaccination.

In 1977 the **World Health Organization**—affiliated Pan American Health Organization (PAHO) began the Expanded Program on Immunization (EPI), which included measles coverage. With the early successes of the anti-polio campaign in the Western Hemisphere as a model, in 1987 PAHO began “catch-up” programs to immunize children between nine months and 14 years of age against measles. In 1994 PAHO set a target date of 2000 for elimination of measles from the Western Hemisphere. Between 1990 and 1995, confirmed cases of measles in Latin America and the Caribbean fell from 218,000 to 3,382. In 1995, however, Canada alone reported 2,362 cases, which prompted public health authorities there to initiate “catch-up” activities that reduced the number to 324, an 86 percent drop in one year. Meanwhile, the CDC reported a total of 55,622 U.S. cases in 1989–1991, so in 1994 the Childhood Immunization Initiative—part of the PAHO six-year initiative—established targets of 90 percent coverage and elimination of indigenous (exclusive of imported) cases by 1996. 1995 saw 309 reported cases.

The advances against measles in the Americas prompted the consideration of a global program for eradication, along the lines of the ongoing effort against polio. In July 1996 representatives of PAHO, WHO, and CDC met in Atlanta, Georgia, and decided to recommend a goal of worldwide eradication of measles within a 10- to 15-year framework.



A Measles quarantine warning. Courtesy of the National Library of Medicine.

At that time, an estimated 800,000 died of the disease annually, 500,000 in Africa, where immunization coverage was generally less than 50 percent. Globally, measles accounted for about 10 percent of mortality for children less than five years old and remained a major cause of blindness. Some efforts yielded spectacular results: in Malawi reported cases dropped from 7,000 to 2 between 1997 and 1999. But progress was never consistent: after steady reductions, in 1997 Brazil relapsed and produced some 50,000 cases, mostly around São Paulo.

As the millennium turned, and the global target date was moved back five years (to 2005), critics expressed their doubts that measles could be eradicated, but 2001 saw the launch of the Measles Initiative, signed by the WHO, UNICEF, the United Nations Foundation, the American Red Cross, and the CDC. Among the shared goals is a drop in global measles deaths of 90 percent by 2010 (from a base of 2000). Global deaths caused by measles fell by 59 percent, from about 871,000 in 1999 to about 354,000 in 2005. Africa showed the most progress, with reductions in cases and deaths estimated to be 75 percent. *See also* Children and Childhood Epidemic Diseases; Measles in the Colonial Americas; Poliomyelitis, Campaign Against; Smallpox Eradication.

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JOSEPH P. BYRNE

MEASLES EPIDEMIC IN FIJI (1875) AND EUGENICS. The 1875 Fiji measles epidemic represents a tragic landmark in epidemic history. Beyond the large number of deaths of native peoples who had never before encountered measles, the epidemic has served as a multipurpose metaphor for the terrible human and cultural losses to imported diseases during the Age of Discovery, for the still-confused epidemiological concept of "virgin-soil epidemics," and for the extent to which science could be coopted by eugenics theory during a time of great scientific change and discovery.

In the fall of 1874, its native ruler ceded the South Pacific island of Fiji to Britain as a Crown Colony, and the British government began the slow process (nine months, as it turned out) of sending out a new government from London to Fiji via Australia. In the interim, Queen Victoria (1819–1901) wished to send the ceding "Cannibal King" Cakobau ("Destroyer of Bau"; d. 1883), along with his family and a party of about 100 Fijians, to Sydney, Australia, the nearest seat of government, on a State Visit and sightseeing vacation. The voyage between Fiji and Sydney, on the *HMS Dido*, took 19 days each way. On the 13th day of the return trip back to Fiji, Cakobau's 25-year-old son developed a rash and fever. The ship surgeon diagnosed measles, then prevalent in Sydney but unknown in Fiji, and placed the son in isolation in a hastily built shack on the deck.

Against international regulations, the ship's yellow **quarantine** flag was not flying when the *Dido* sailed into port. British functionaries arriving in a small boat worsened the mistake by focusing on a seemingly more pressing problem: while in Sydney the just-married son had acquired not only measles, from which he was by then recovering, but also "a drip" (**gonorrhoea**). This discovery had to be kept from newspaper reporters: Cakobau had forsaken cannibalism and converted to Christianity, and his sons had been baptized. The possibility that Queen Victoria's first gift to Fiji might be a venereal disease in the royal household was unthinkable. During the ensuing confusion on board, no one noticed that boats were bringing impatient passengers to shore, or that most of Fiji's police force had sailed out to celebrate with the doubly infected son. And despite common knowledge about the **epidemiology** of measles in 1875, no one seems to have considered the problem of 100 Fijians potentially incubating the disease.

The problems were soon to be greatly magnified. While the king was away, the mountain cannibal chiefs had threatened to revolt against cession. The king's brother had been asked to arrange an unprecedented national meeting at which the chiefs might be persuaded to join the government. It was to be the largest gathering in Fiji's history. On January 25, 1875, 13 days (about one measles incubation period) after the *Dido*'s return, the meeting was attended by 69 chiefs, 800 others, and the same 143-man police force that had greeted the royal party's return two weeks earlier, many of them already developing fevers and rashes.

Those who attended the meeting returned to their homes throughout Fiji, seeding a deadly measles epidemic that spread like wildfire throughout the country and to all of the outlying islands, and indeed widely throughout the Pacific. In an effort to reduce fever, terrified Fijians lay down in the ocean and in streams and wrapped small children in wet grass. To stop epidemic spread, those few who remained healthy burned the homes and villages of the ill, who lay trapped inside. **Corpses** lay everywhere in the open, scavenged by dogs and wild pigs. The stench of destroyed villages was notable at a mile's distance. The king survived but his brother, the elder statesman who had arranged the fateful meeting, succumbed, and his body was thrown into a communal pit. An estimated 40,000 people, one-third of Fiji's population, died within a few weeks' time. In response, the mountain chiefs revolted, killing (and sometimes eating) British subjects, provoking an all-out war. A British military force defeated the rebels and hung their leaders.

An inquiry initiated by the angry British queen was derailed by that war, and there was never any accounting for the deadly mistakes. The term "virgin-soil epidemic" seems to have taken hold following an 1875 British parliamentary speech in which Colonial Secretary Henry Herbert Lord Carnarvon (1831–1890), seeking to understand what had happened, used the term to describe the epidemic. Twenty years later, when Queen Victoria commissioned a study of Fiji's population decrease, the measles epidemic was barely mentioned, but the cautionary tale of the quintessential "virgin-soil epidemic" remained in textbooks for another century.

"Virgin-soil epidemic" now refers simply to the reemergent introduction of an infectious disease into a completely susceptible population. However, the term came to take on a more complicated meaning during the "eugenics era," which lasted from roughly 1879 to 1933. The 1875 Fiji epidemic occurred at a time when Darwinian evolutionary theory was being imperfectly digested by scientists and the public alike. It was common supposed knowledge at the time, even among some physicians and scientists, that traits like musicality, susceptibility to **tuberculosis**, criminality, and even **poverty** were a matter of **heredity**. Eugenics theory, based on incomplete and sometimes erroneous interpretations of human genetics knowledge, sought to promote civic actions and public policies aimed at improving the human "race" by supporting procreation of the most fit and discouraging or preventing it in the least fit. In its most extreme and odious form, eugenics led to sterilization of persons with mental illnesses in the United States and to the Nazi euthanasia program, the "legal" basis of murders in the extermination camps in German-occupied territories during the years of World War II. In the United States, Great Britain, and elsewhere in Europe, eugenics theory became a refuge for "respectable" racism, and the 1875 epidemic was often cited as an argument in favor of eugenics activism.

Despite much evidence to the contrary, which continued to mount in the succeeding decades, eugenics theories led to the notion that the much higher mortality in native Fijians in 1875 was the result of "racial degeneracy," a conclusion that led directly to schemes to import Caribbean "racial groups" and force them to interbreed with Fijians. The scientific study of the current notion that populations long in isolation from infectious diseases fail to develop natural resistance to them is incomplete, and some of the evidence in favor of it is clearly erroneous or overstated. Presumably, this 130-year-old question will become better understood as genomics studies of human susceptibility and microbial evolution advance further. Other evidence suggests that incipient vitamin A deficiency, starvation, exposure to cold and wetness, lack of nursing care, and secondary bacterial pneumonias probably caused most of the 40,000 Fijian deaths. That Fijian

mortality in later measles epidemics was low suggests that “virgin-soil” theories of immune susceptibility to this infectious disease are difficult to support.

The Fijian epidemic was taught to medical students well into the 1970s (a century after it occurred), but is now gradually becoming an historical footnote of confused and uncertain meaning. Even in Fiji itself, the epidemic is only vaguely remembered. If we view it in modern terms, however, it is easy to see a different metaphor, that of the many complexities and uncertainties underlying epidemic disease emergence, which incorporates complex interactions between the microbial agent, the human host, and the **environment**. See also *Colonialism and Epidemic Disease; Disease, Social Construction of; Historical Epidemiology; Measles, Efforts to Eradicate; Race, Ethnicity, and Epidemic Disease*.

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DAVID M. MORENS

MEASLES IN THE COLONIAL AMERICAS. The effect on the Amerindian populations of the introduction of Old World diseases to the Western Hemisphere in the late fifteenth and sixteenth centuries was far more devastating than that of the **Black Death** on the Old World. **Epidemic measles** ran second only to **smallpox** as a biological agent of death, especially among the virgin native populations when first contact was made. It sporadically ravaged the Amerindians and American-born European colonists, however, long after it had become endemic.

Measles is caused by a **virus** that is easily acquired through respiration and has an incubation period of 10 to 14 days. Symptoms include coughing, a red rash, and high fever. The acute phase usually lasts about a week, though full recuperation may take months, especially if followed by a secondary disease. In societies in which it is common, measles generally becomes a childhood disease with mild effects and very low mortality for those over three years of age who receive appropriate care; lifetime **immunity** or high resistance is generally conferred. In a virgin population, however, it can spread very rapidly and kill adults, children, and even fetuses readily, especially when proper treatment is not provided, and a population is weakened by malnutrition.

Native Americans had never experienced measles before the arrival of Europeans. They did not domesticate the sheep, goats, and cattle from whose rinderpest disease measles seems to have developed, nor did the earliest migrants carry it with them through Alaska. In the early sixteenth century, measles was endemic in many Spanish cities, including Seville, from which city most voyages to the Spanish Americas originated. Measles was also widespread and endemic in other colonizing countries such as England, France, and Portugal. This meant that most colonists were immune.

Spanish America. A deadly epidemic in Hispaniola in 1518 of what many think was measles, however, spread to the Mayans of Guatemala as early as 1519 (see sidebar). A participant in Hernán Cortés’s (1485–1547) attack on Tenochtitlán (Mexico City) in 1520 wrote of the devastating impact of “the pestilence of measles and smallpox” that struck

down their foes. Pandemic measles had arrived in New Spain with colonists' **children** from the Caribbean islands by 1530. Subsequent outbreaks and its appearance in other parts of the Spanish American Empire are attributable to the continuous trans-Atlantic traffic from Spain and Africa; to the expeditions of conquistadors; to slaving expeditions and the forced movements of populations in response to local labor shortages; and to travel by native carriers, a factor that probably explains its first appearance in the Andes in the 1520s. Contemporary Spanish authors ultimately attributed the disease to God but also recognized its “stickiness,” or ability to pass from one person to another.

Named by the Nahuatl-speaking Indians in Mexico *zahuatlepiton* (awkwardly translated “little leprosy (*lepra*)” by the Spanish; smallpox was the “great *lepra*”), measles is often difficult to tease out of contemporary reports on diseases and epidemics. Descriptions are usually from untrained observers who provide minimal or even contradictory accounts, and vocabulary is fluid, often forcing the historian to conjecture about the disease described. Typically the Spanish word *serampión* indicates measles, but at times the attendant description of symptoms suggests another disease. In addition, during epidemics, measles seems often to have accompanied smallpox, **typhus**, exanthemous typhus, **diphtheria**, and mumps; and measles itself was not clearly identified clinically in Europe until the eighteenth century. Weakened by measles, the recovering victim might well fall prey to other opportunistic secondary diseases, including **encephalitis**, **influenza**, and **enteric fevers**. Colonial fatality figures are notoriously unreliable, for numerous reasons, especially when reporting mortality among Amerindian populations.

Measles may have been the disease that struck down two-thirds of the remaining Indians on Cuba in 1529. The earliest pandemic of measles occurred in New Spain between 1530 and 1534, and returned in 30-year cycles. Initially it seems that children suffered most, but in 1532 the disease was indiscriminate. By 1534 measles, dysentery, and typhoid reportedly had killed 130,000 of 150,000 natives in Culiacán alone. Further south in

EFFECTS OF EARLY MEASLES EPIDEMICS IN THE NEW WORLD (1519 AND 1532)

Mayan description of measles (?) in Guatemala, 1519:

In the course of the fifth year the pestilence began, O my children. First there was a cough, then the blood was corrupted, and the urine became yellow. The number of deaths at this time was truly terrible. The Chief Vakaki Ahmak died, and we ourselves were plunged in great darkness and deep grief, our fathers and ancestors having contracted the plague [measles], O my children.

Truly the number of deaths among the people was terrible, nor did the people escape from the pestilence.

The ancients and the fathers died alike, and the stench was such that men died of it alone. Then perished our fathers and ancestors. Half the people threw themselves into the ravines, and the dogs and foxes lived off the bodies of the men. The fear of death destroyed the old people, and the oldest son of the king at the same time as his young brother. Thus did we become poor, O my children, and thus did we survive, being but a little child—and we were all that remained.

From *Annals of the Cakchiquels*, trans by Daniel Brinton (Philadelphia: Library of Aboriginal American Literature, 1885) p. 171.

Measles in Central America, 1532:

Throughout New Spain there passed a sickness that they say is measles, which struck the Indians and swept the land, leaving it totally empty. It arrived in this province some three months ago.

From letter of *Conquistador* Pedro de Alvarado from Santiago de Guatemala; in Cook, *Born to Die*, p. 88.

Central America, measles followed influenza and smallpox from 1532 to 1534, and in Nicaragua measles followed 1531 outbreaks of bubonic and possibly pneumonic plague. As always, Indians bore the brunt, and Honduran reports lament death tolls of 50 percent and the loss of thousands of mine workers and household servants. In Guatemala a royal treasurer reported smallpox and measles in 1533, and local authorities were soon urging those using Indian labor to reduce their demands so the natives could rest and recover. Between 1558 and 1562, measles and influenza swept across Guatemala, spreading in 1563 and 1564 to central Mexico with death tolls of 50 percent in Chalco but much lower elsewhere. Guatemala suffered again in 1576–1577 from measles plus smallpox and typhus, with children most commonly struck down. From 1592 to 1597, measles, accompanied variously by smallpox, mumps and typhus, hit Mexico as far north as the Pueblo people. These victims blamed their Jesuit guests, burning down the mission and murdering a missionary in 1594.

Measles reached South America as early as the mid-1520s, probably from Guatemala. Disease fatally disrupted Inca society by killing the Inca ruler Huayna Capac around 1525 and sparking dynastic wars that weakened the Empire. A wider and deadlier pandemic spread south between 1531 and 1533 across the Andes killing perhaps a quarter of the native population. African slaves who arrived from Hispaniola may have sparked a large-scale epidemic of measles, influenza, and smallpox in Peru and Ecuador in 1558. New Granada claimed death tolls of 40,000, and with secondary influenza, Peru lost 15 to 20 percent of its native population. Such losses led to mass relocations of natives in 1570 and to the importation of ever more black slaves. This led to widespread exposure and immunization, so measles may have become endemic in parts of the north by the 1580s. Other areas were struck hard, however, between 1585 and 1592. Lima and Cuzco suffered high mortalities from measles, smallpox, and mumps. Ecuador was hit in 1586–1591, but the source is thought to have been African slaves or Francis Drake's (1540–1596) raiders in Cartagena. Moving inland, the epidemic killed 30,000 of Quito's population of 80,000 between 1587 and 1591, with 4,000 dead in three months. Children suffered most, but literally countless Indian laborers died in rural areas, and along the coast villages were extinguished or abandoned. All told, perhaps half the native population died. Because so many victims were children and young people, birth rates declined precipitously, and the population could never replace itself.

The seventeenth century opened with an epidemic outbreak of measles in New Spain accompanied by mumps and typhus in 1604. A wider pandemic with typhus, diphtheria, and scarlet fever began in the Andes in 1611. This may have spread to Guatemala in 1613, central Mexico (with smallpox) in 1615, and Nicaragua (with typhus and smallpox) in 1617. Colombia, Bolivia, Peru, and Chile suffered again in 1617–1619, with disease compounded by locust infestations and famine. High death rates resulted in entire mining operations being shut down for lack of labor. In Paraguay, Indians were collected into the Jesuit "reductions" in which diseases could spread wildly. In the 1630s, 1,000 of 7,000 died in Candelaria alone. Lima was hit by measles again in 1628 and 1634–1635, and Peru more widely in 1645 and 1648 by measles and diphtheria. A pandemic that included measles, diphtheria, typhus, and smallpox swept Colombia, Ecuador, Peru, and Bolivia between 1691 and 1695. Records suggest that between 25 and 50 percent of the Indian population died, especially children and young adults.

By the eighteenth century, pandemics should have immunized much of Spanish America's population, though the worst measles epidemic in a century occurred in

Ecuador and Colombia from 1785 to 1788. Poor crops and little labor for the harvest led to famines that weakened people's resistance. The eighteenth century also saw Spanish colonial authorities organize efforts to deal with diseases. Urban public hygiene and sanitation became priorities, at least in theory. **Physicians** were consulted and employed to treat cases and to try to determine the causes and reasons for dissemination of the diseases. In 1764 Ecuador received a medical examiner (*protomédico*), and during the virulent outbreak of 1785, he saw that **apothecaries** and physicians provided for the poor as well as the wealthy. But Quito itself had only one **hospital** for patients (another was for lepers), and this was chronically underfunded.

The English and French Colonies in North America. European contact with North America before the formal settlement of Virginia (1607) and Plymouth (1620) colonies planted infectious diseases among Amerindian populations. Florida suffered from the early 1530s, and the disease may have traveled northward through many of the Eastern Woodland tribes. Between 1592 and 1596, the Seneca Indians of Cameron Village in western New York experienced at least hundreds of casualties from measles originating in the Spanish-held American Southwest. From 1616 to 1619, an epidemic of diseases (the "great dying"), possibly including measles, destroyed perhaps 90 percent of the native population in the coastal Massachusetts region. Pilgrims discovered abandoned villages and crops before they met the local natives. English colonists in both New England and Virginia brought with them the full panoply of European diseases, and after 1619 enslaved Africans unwittingly contributed their share in the Chesapeake.

The specific impact of measles on the native population is far more difficult to ascertain for the English colonies than for the Spanish and Portuguese. The English had neither the missionaries nor government agents to keep records, nor were English-Indian relations nearly as close as were those in Latin America. Unlike the far-ranging conquistadors, English adventurers tended to remain relatively close to home. On the other hand, French fur trappers and missionaries penetrated deep inland and may have spread the disease widely.

In the seventeenth century, reports of measles outbreaks among colonists are sporadic and rare. French Jesuit missionaries north and west of the English reported "a sort of measles" and other diseases among both French and Huron Indians as early as 1634. The Hurons suffered gravely and repeatedly until 1640, losing perhaps 80 percent of their population according to the French. In the 1640s the diseases spread south and westward, leaving vast areas depopulated by death and migration. The Huron Confederation lay in ruins and the Iroquois extended their hegemony. Boston was struck first in 1657 and Connecticut during the following year, having allowed a generation of young people to be born and mature away from the measles reservoirs of Europe. Despite many cases, fatalities were few. Measles broke out widely among Canadians in 1687, reportedly after a French royal ship with at least one carrier docked on the St. Lawrence. This probably spread to the English, who suffered later the same year and in 1688. Measles struck Williamsburg, Virginia, in 1693, with an English ship being the probable source of the infection. This prompted a day of "humiliation and prayer" among the Anglican populace, a religious response usually reserved for times of plague or war.

As a result of increasingly higher levels of immigration, Boston saw the intervals between major outbreaks fall from three decades after 1657 to 11 years by the 1730s. New Englanders suffered from 1713 to 1715, with at least 150 measles-related deaths reported in Boston's bills of mortality. Though Boston seems to have been struck hardest,

adults as well as children contracted the disease in Connecticut, New York, New Jersey, and Pennsylvania. Letters from Virginia record the disease striking mostly adults in 1716 and 1717. 1729 saw another light outbreak in Boston (15 reported fatalities), and in New York City most patients were children. A decade later, Boston hosted a much more severe outbreak that may have been spread by those fleeing the city. Puritan preacher **Cotton Mather**, who lost his maid and four children, took the occasion to pen his humane and useful “A Letter about a Good Management under the Distemper of the Measles” (1739). Over the following two years, colonists in New England, New York, and New Jersey were infected as well.

In 1747 and 1748, New England, New York, Pennsylvania, and South Carolina were revisited. Patients in Charleston tended to suffer further from enteric problems, whereas those in Boston reported secondary throat “distemper.” Children in Philadelphia suffered additionally from “the flux,” whereas adults caught secondary **yellow fever**. Between 1750 and 1775, one-third of those buried in Christ Church cemetery were victims of measles. 1759 saw a mild outbreak among children in South Carolina, New York City, and Philadelphia, though Fairfield, New Jersey, experienced a severe outbreak with several attendant diseases including smallpox. Dedham, Massachusetts, on the other hand, reported 260 cases with but a single fatality. A general outbreak in the colonies occurred in 1772 and 1773, with insignificant fatalities outside the south; the *South Carolina Gazette*, however, reported “8[00] to 900” young fatalities from a population of 14,000. Among other remedies and treatments, **doctors** recommended opiates, asses’ milk, and bloodletting. The final outbreak in colonial U.S. history occurred in 1775 with broad morbidity but mild mortality, at least among whites. A study of Philadelphia’s Anglican bills of mortality (1722–1775) revealed that slaves in Philadelphia were roughly twice as likely to die of measles during epidemics as whites (crude death rates of 106 and 56 respectively), though immunity did raise a slave’s price in the market, an incentive to provide adequate care. Around 1800, measles became endemic in the United States. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Children and Childhood Epidemic Diseases; Colonialism and Epidemic Disease; Contagion and Transmission; Demographic Data Collection and Analysis, History of; Diagnosis of Historic Diseases; Disease in the Pre-Columbian Americas; Historical Epidemiology; Latin America, Colonial: Demographic Effects of Imported Diseases; Measles Epidemic in Fiji (1875) and Eugenics; Race, Ethnicity, and Epidemic Disease; Slavery and Disease; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Trade, Travel, and Epidemic Disease; War, the Military, and Epidemic Disease.

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JOSEPH P. BYRNE

MEDIA. See News Media and Epidemic Disease; Popular Media and Epidemic Disease: Recent Trends.

MEDICAL EDUCATION IN THE WEST, 1100–1500. In early medieval Europe, few healers had access to learned medical writings from Greek and Roman antiquity. Medical practitioners were trained in practical healing through apprenticeship and did not rely upon broad theoretical systems to explain the functioning of the body, the processes of disease, or the rationalization for therapeutic practices. Only a small number of monks, trained in a few prominent monastic centers, had access to the limited number of Greek medical texts available in Latin, the language of scholarship. Beginning in the eleventh century, however, western Europe received a flood of translations of previously unknown texts from Greek and Arabic into Latin. These translations provided a more intellectually sophisticated theoretical foundation for the basic **Greco-Roman** medical learning already familiar in the Latin West. Spurred in part by the influx of this new knowledge, Europe witnessed the development of universities in the thirteenth century that provided new opportunities for medical education and ultimately for the professionalization of medicine.

The school in the southern Italian town of Salerno was the earliest center of medical education to incorporate the newly translated materials in its teaching. Salerno, a crossroads of Christian, Jewish, and Arabic cultures, had gained a reputation as a place for acquiring practical medical skills and successful cures as early as the tenth century. During the twelfth century, the school began to shift from practical to theoretical medical instruction based upon a select group of the newly available medical and philosophical texts. Salernitan doctors assembled a collection of treatises known as the *Articella*, which introduced basic elements of the medical theories ascribed to **Hippocrates** and **Galen** and formed the core texts for advanced medical knowledge in the Middle Ages. Salerno's emphasis on teaching medicine through books elevated the importance of theoretical medical knowledge in relation to empirical medical knowledge gained through practical experience.

By the thirteenth century, Salerno had been eclipsed as a center for medical learning as medicine became one of the subjects available for study at the newly founded universities in Italy, France, England, and Spain. During this period, the universities most renowned as centers for medical education were those in Bologna, Montpellier, and Paris. Students at these and other universities would pursue a preliminary education in the seven liberal arts (grammar, logic, rhetoric, arithmetic, geometry, astronomy, and music), after which they could pursue a bachelor's degree in medicine. They could also continue toward a medical doctorate which would require at least 10 years of study, and which conferred the right to teach medicine anywhere in Europe.

The instruction provided at the universities was primarily based upon the study of authoritative texts. Students attended lectures where teachers would read and provide commentaries on specific passages from the books of the *Articella*, supplemented with material from **Avicenna's Canon of Medicine** and increasingly with some longer works by Galen. In addition to reading and hearing lectures on these medical authorities, students

would also be expected to engage in disputations, or formal debates, concerning textual interpretations or aimed at reconciling conflicting opinions among the authoritative texts. This style of teaching through the use of commentaries and disputations around a set of authoritative texts is often referred to as the “scholastic” method. Even in the teaching of human anatomy, in which students had the opportunity to observe public anatomical demonstrations, greater emphasis was placed on learning by reading the authoritative texts than on the careful examination of human cadavers. The importance of learning from texts did not mean that students failed to receive any practical training, however; indeed, they were often required to spend some time in medical practice or in attendance with a practicing physician before earning their degrees.

The subjects of the university medical curriculum were divided into courses in *theorica* and those in *practica*. Under *theorica*, or theoretical medicine, students learned about the philosophical basis of medicine, contemporary concepts of physiology, general pathology, and **humoral theory**. Courses in *practica* also dealt with what one might otherwise consider “theoretical” knowledge, but they emphasized material that had direct practical applications for the **diagnosis** and treatment of specific diseases. A number of *practica* manuals provided lists of diseases in order from head-to-foot, with detailed discussions as to their causes, and advice on how to diagnose and treat them. From the mid-fourteenth century, tracts (*consilia*) were also written specifically to address the disease known as the plague or pest. Together, these medical texts provided young physicians with guidance on how to recognize diseases based on a variety of signs, including the careful study of the pulse and urine, and how to prepare the appropriate medicines or dietary menus to treat them. In addition to these subjects, medical students were expected to gain some competence in astronomy, including what today is termed **astrology**, in order to understand the cosmological influences on individual health. **Epidemic** diseases were often thought to result from astrological influences, and so a proper knowledge of astronomy was deemed necessary for those seeking to recognize and treat them.

Despite the development of university medical education, the number of **physicians** trained at universities remained small throughout this period. Most medical practitioners continued to be trained through apprenticeship and received little or no theoretical education from books. The range of non-university trained healers who learned through experience included **surgeons**, **apothecaries**, midwives, and a variety of other kinds of **empirics** including those who specialized in treating eye diseases, pulling teeth, setting bones, or selling religious and magical cures. Thus, although university trained physicians became the new elites among medical practitioners in the later Middle Ages, they were only a small minority in the overall medical community. See also Air and Epidemic Diseases; Black Death (1347–1352); Corpses and Epidemic Disease; Diet, Nutrition, and Epidemic Disease; Folk Medicine; Hospitals in the West to 1900; Islamic Disease Theory and Medicine; Medical Education in the West, 1500–1900; Plague and Developments in Public Health, 1348–1600; Plague in Medieval Europe, 1360–1500; Quacks, Charlatans, and Their Remedies.

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WILLIAM H. YORK

MEDICAL EDUCATION IN THE WEST, 1500–1900. The ideal form of medical education has always been a mixture of theory, practice, and hands-on experience. Between 1500 and 1700, there were two formal and many informal methods of medical education. Those aiming to become **physicians**, the elite of the medical practitioners, attended university lectures—almost exclusively on Greco-Roman and Islamic medical texts—for several years in order to acquire the prestigious M.D., Doctorate of Medicine. From the sixteenth century, the scope of these lectures expanded to include hands-on training in anatomical dissection. Andreas Vesalius's (1514–1564) *De humani corporis fabrica* (On the Structure of the Human Body, 1543) was both a representation of and an advertisement for the value of dissection, and by the end of the seventeenth century, every prominent medical school and many hospitals provided lectures on anatomy illustrated by cadavers. Physicians' erudition, as well as the social and economic status conveyed by the M.D., led them to claim authority over all other medical practitioners, as the head had authority over all other parts of the body.

The second type of formal education was apprenticeship to a **surgeon**, a legally-contracted relationship in which the master surgeon agreed to teach the young man his craft over a period of years, in exchange for a specified fee. If physicians were the "head" of the medical profession, then surgeons were its skillful hands. Though elite surgeons in Italy might attend anatomy classes at the universities of Padua or Bologna, few surgeons elsewhere took courses or studied the scholarly literature. Instead, they honed their manual skills by serving first as their masters' servants, and gradually taking on more and more complex tasks.

There were also many informal methods of medical education, for outside of urban jurisdictions there was little government regulation of medical treatment. Medical students might travel from university to university, attending lectures by the most famous professors. Or they might learn their "business," as it was often referred to, from fathers or uncles. Women, excluded from both university and guild, learned to be midwives through formal or informal apprenticeship with an experienced midwife, often treating a range of women's and children's ailments as **empirics**.

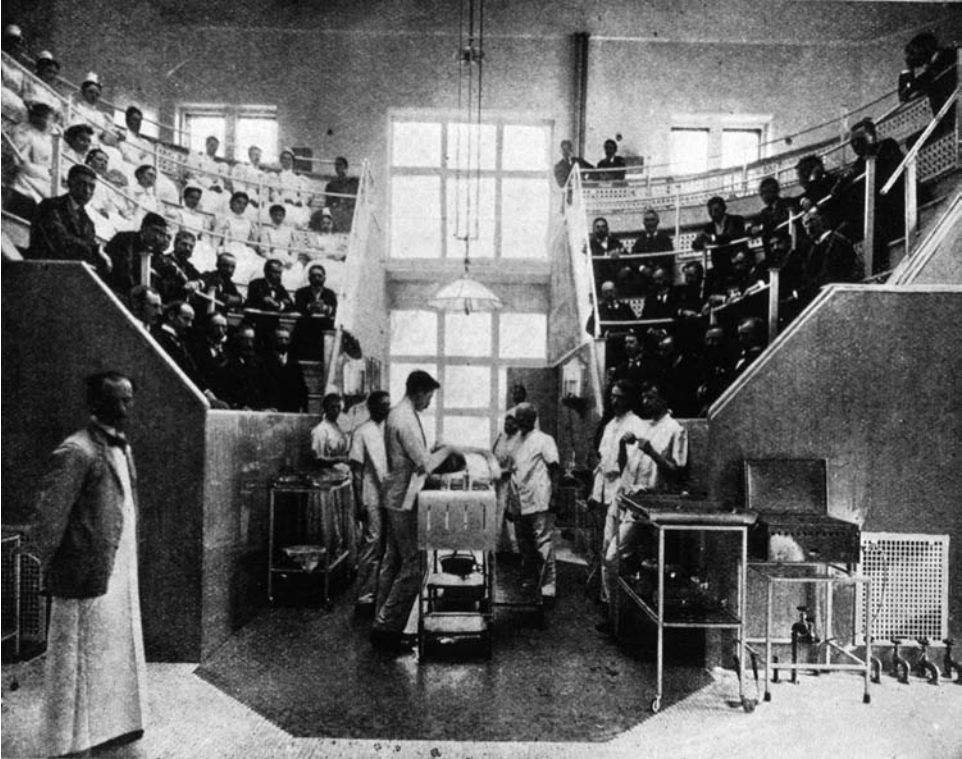
Yet when an epidemic arose, formal education mattered less than administrative ability, presence of mind, and courage in the face of certain danger. In 1630 Diacinto Gramigna was apprenticed to his father, a municipal surgeon in Prato, Italy, when the **plague** arrived. When the town's physicians left with their elite patients, Gramigna's father died, and no other surgeon would agree to work in the town's **pest house**, Prato's Town Council appointed Gramigna as surgeon. He served faithfully for the eight months that the hospital was open, even catching and recovering from the plague himself. His reward was enough money so that he could have a new suit of clothes made and burn those he had been wearing as Public Health surgeon.

By the 1700s, a new pedagogical innovation had taken hold, the introduction of clinical lectures—based upon human bodies instead of classical texts—into university medical curricula. This was a modification of traditional medical apprenticeship, and one that caught on quickly for medical students: instead of being formally bound to a master for a number of years, they could attend university lectures in which the professor used hospital patients as living case histories of specific diseases. Hermann Boerhaave (1668–1738) at the University of Leyden, Holland, gave clinical lectures using the local charity hospital, and from there the innovation was picked up by every major medical school. Other innovations followed by the early 1800s. Surgeon’s apprentices increasingly attended medical lectures, and medical schools in major cities offered courses in clinical surgery. Distinctions between medical students and surgical apprentices blurred as both groups “walked the wards” for clinical experience, attended postmortem dissection in the hospital morgue, and debated James Lind’s (1716–1794) use of lime juice for scurvy (1762) and **Edward Jenner’s** vaccination for smallpox (1798).

By the mid-nineteenth century, the best medical education lasted between three and four years and included classes in basic science—anatomy, organic and inorganic chemistry, physiology—as well as in medical practice—pathology, pharmacology, obstetrics. Clinical and surgical courses might require another year or two. New instruments, like the stethoscope, were introduced to the medical school curriculum, as was the **microscope** for examining minute structures of the **human body**. No wonder one nineteenth-century medical student wrote that “time was all too short and often we wished the twenty-four-hour day might be stretched to thirty-six” (Rosner, 1997, p. 154).

Some of the innovations brought their own risks, however. In 1861, **Ignaz Semmelweis**, working at the teaching facility of the Vienna General Hospital, attributed the high incidence of puerperal fever to the practice of medical students moving from anatomical theater to morgue to obstetrics ward without properly washing their hands. His research was later vindicated by the antiseptic principles of Joseph Lister (1827–1912), working at teaching hospitals first in Glasgow and then in Edinburgh. Modern **germ theory**, developed by **Louis Pasteur** and **Robert Koch** in the 1870s, provided for the first time a consistent, biologically based answer to the basic question of medical theory and practice: “What is the cause of disease?” It was rapidly adopted by medical schools, requiring sweeping revision of the curricula in pathology and clinical subjects. By the time of Abraham Flexner’s (1866–1959) influential report, *Medical Education in the United States and Canada* (1911), the laboratory had taken its place beside the lecture hall, anatomical theater, and hospital as an essential component of medical education.

By 1900 the medical school curriculum encompassed more subjects than ever before. Medical education was also becoming more socially diverse. Middle-class women had been calling for access to the same medical education as their brothers since the mid-nineteenth century. The world-renowned Swiss universities began admitting women on an equal footing with men from the 1860s. The *Écoles de Médecine* in Paris followed suit in the 1870s, as did many of the German universities by 1910. In Great Britain and the United States, where universities were generally treated as private institutions, women had a harder time gaining admittance. In both countries, they founded their own institutions, such as the Women’s Medical College of Philadelphia (1850) and the New Hospital for Women in London (1874). African American students in the United States faced similar obstacles and also founded their own institutions, such as Howard University in Washington, D.C., (1868). Full acceptance of diverse social groups into medical schools



Operating theater at New York's Presbyterian Hospital, 1898. Interior view of an amphitheater with an operation in progress; medical students and/or physicians and nurses are observing the surgical procedure. Courtesy of the National Library of Medicine.

remained a contentious issue throughout the twentieth century. *See also* Astrology and Medicine; Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Hospitals and Medical Education in Britain and the United States; Hospitals in the West to 1900; Humoral Theory; Medical Education in the West, 1100–1500; Plague and Developments in Public Health, 1348–1600.

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LISA ROSNER

MEDICAL EDUCATION IN THE WEST, 1900–PRESENT. See Hospitals and Medical Education in Britain and the United States.

MEDICAL ETHICS AND EPIDEMIC DISEASE. Medical ethics consists of the ethical standards that medical professionals—doctors, nurses, public health professionals, and professionals in allied health-related fields—set for themselves to govern their conduct in their relations with each other, with patients, and with the public. These standards are usually stated in professional codes of medical ethics (see sidebar). They stipulate the professional’s obligations to the public and patients with respect to care, confidentiality, dignity, protecting health, and preventing harm. They can also stipulate the extent to which health providers have a professional obligation to risk their lives or their health to treat patients afflicted by infectious disease.

Contagion Theory and Medical Ethics during Epidemics. Discussions of the medical ethics in the context of pestilence were largely absent from the medical literature until the eighteenth century. They begin to surface in conjunction with the development of medical **contagion theory**, an idea attributed to the Veronese physician **Girolamo Fracastoro**, who published a book on the subject, *On Contagion and Contagious Diseases*, in 1546. Fracastoro explained the spread of pestilence in terms of “contagion,” by which he meant transmission of diseases by minute particles in the atmosphere, on objects, and from person to person.

The introduction of contagion theory into the comparatively isolated environment of the British Isles in the early eighteenth century sheds light on why Fracastoro’s theory generated medical ethical debate. Before this period, many considered doctors useless during outbreaks of **plague in Britain**. Thomas Dekker (c. 1570–1632), a well known seventeenth-century English pamphleteer, observed that during an outbreak of **bubonic plague** in London, in 1603, “our Phisitions [physicians] . . . hid their Synodical heads . . . and I can not blame them, for their . . . drugs turned to dirt: . . . not one of them durst peepe abroad; and if anyone take upon him to play the venturous Knight, the Plague put him to his Nonplus [confounded him].” In his *Journal of the Plague Year* (1722) English novelist Daniel Defoe (1660–1731) offered a similarly bleak assessment of the efficacy of medicine during the **Great Plague of London** in 1665: “The plague defied all medicines; the very physicians were seized with it, with their preservatives in their mouths; and men went about prescribing to others and telling them what to do, ’till . . . they dropped down dead, destroyed by that very enemy they directed others to oppose.”

Attitudes changed after 1720, when the English government commissioned Richard Mead (1673–1754), a fellow of the College of Physicians, to recommend a policy for preventing an outbreak of bubonic plague, then raging in and around Marseilles, France, from reaching British shores. Mead’s report, *A Short Discourse Concerning Pestilential Contagion, and the Methods to Be Used to Prevent It* (1720), the first book of epidemiological advice produced by a medical practitioner at the request of a state, analyzed the risk of pestilence in terms of a medical theory of contagion. Heeding Mead’s advice, Parliament passed several acts in 1720 and 1721, requiring the **quarantine** of ships and the **isolation** of towns suspected of infection by means of a **cordón sanitaire**. These acts were too great an imposition on the British sense of **personal liberties** and were quickly repealed.

This vignette illustrates how the medical theory of contagion changed the relationship between physicians and pestilence. The most important change was the higher regard in which doctors were held. Unlike the seventeenth-century physicians dismissed by Dekker and Defoe, contagion theory gave the eighteenth-century physician a role—prevention.

Meade became, in effect, England's first public health commissioner, advising the government regarding how best to protect the public from contagious disease. The change also meant that Meade and other physicians were in a position to dismiss as medically irrelevant some public reactions to pestilence—penance, flagellation, scapegoating, massacres—even as they validated other traditional practices, like isolation and quarantine, as properly scientific.

Public Health Ethics. The new public health medicine embraced an ethical perspective that focused on the relationship between governmental institutions and the public. Conventional medical ethics, in contrast, had always focused on the relationship between the individual physician and the individual patient. One consequence of this difference is that, whereas conventional medical ethics can ignore politics, political considerations have infused public health medicine and ethics from their inception. Mead's recommendation of a *cordon sanitaire*, for example, whatever effects it may or may not have had in controlling a rat-borne disease transmitted by fleas, failed because the measure was unacceptable to the public. In another example of the fusion of politics with public health, Philadelphia physician, **Benjamin Rush**, a signatory to the American Declaration of Independence, preferred **environmental** (miasmatic) explanations of **yellow fever** to contagion theory in large measure because he believed that contagion theory would give governments too much power to control the lives of the governed. As the famous historian of medicine, Erwin Ackerknecht (1906–1988), observed, public health medicine has been politicized from the moment of its conception. It remains so today.

The Physician's Duty to Treat the Epidemic-Stricken. Public health medicine shares common goals with conventional medicine: preventing disease, promoting health, and healing the sick. It also shares a common moral commitment of caring for the ill. Physicians in eighteenth-century England accepted an ethical “[d]uty to come when . . . call'd whether to Rich or Poor . . . to Distant Places as well as Near, to Prisons as well as Palaces . . . in a word, to all Mankind without Exception.” The same author, however, wrote in 1715 that “tis [physicians'] Duty to consult their own Safety first . . . to visit [only] where they have Reason to believe that their Presence may be of the utmost Consequence to the Recovery of others, and not extreemly or immediately Dangerous to themselves.” Thus by offering a medical model for the spread of epidemics, contagion theory created an ethical expectation that physicians would provide medical care for the pestilence stricken, if they could do so at minimal risk to themselves.

Not surprisingly, since anti-contagionists (like Rush) believed that they faced minimal risk in providing medical care for the epidemic-stricken, they tended to provide a great deal of the medical care offered during epidemics. Rush, for example, became an exemplar of medical heroism because, while many other physicians fled, he remained in Philadelphia to tend yellow fever victims during the great epidemic of **yellow fever in North America** in 1793, which killed approximately 10 percent of the city's population. As the type of pestilence common in the nineteenth century shifted from bubonic plague to **cholera** and **typhoid**, there was a correlative decline in the risks to physicians and other caregivers. As the risks to caregivers declined, it became less acceptable for physicians to practice **flight** from epidemics, and staying to care for the epidemic stricken came to be viewed as almost obligatory. At mid-century the formal statement of medical ethics of the American Medical Association (AMA; 1847), stated that “When pestilence prevails, it is [members] duty to face the danger, and to continue their labors for the alleviation of the suffering, even at the jeopardy of their own lives.”

A commitment to caring for the epidemic stricken remained integral to medical ethics through the mid-twentieth century, even during outbreaks of highly contagious diseases, like the **influenza pandemic of 1918–1919**. When it struck the United States, William Henry Welch (1850–1934), President of the AMA (1910–1911) and founding director of the Johns Hopkins School of Hygiene and Public Health, set the standard for the nation's doctors by personally taking the lead in providing day-to-day care for influenza patients. Through 1976 the AMA's code of ethics stipulated some version of the duty to tend to the epidemic stricken, even at risk of the physician's life.

When it revised its code of ethics in 1977, however, the AMA deleted the statement that physicians were obligated to risk their lives to treat the epidemic stricken. Thus, when the **AIDS** epidemic struck the United States in the 1980s, there was no authoritative professional ethical guidance on physicians' obligation to put themselves at risk to treat AIDS patients, and some physicians refused to provide care for HIV-positive patients. Responding to this situation, the AMA issued a point of clarification: "A physician may not ethically refuse to treat a patient whose condition is within the physician's realm of competence solely because the patient is seropositive."

The AMA's statement, however, only addressed care for HIV-positive patients. It left open the question of whether physicians were obligated to treat other epidemic-stricken patients. The American College of Physicians, however, stated a broader commitment of caring for the epidemic stricken—irrespective of risk to the caregiver: "It is unethical for a physician to refuse to see a patient solely because of medical risk, or perceived risk, to the physician."

Public Health Ethics, Conventional Medical Ethics, and Confidentiality. On certain issues, public health ethics and conventional medical ethics have differed. Confidentiality, the physician's duty to protect the secrecy of a patient's medical information, is the most prominent of these. For conventional physicians to practice medicine effectively, patients need to entrust them with sensitive personal information about their lifestyles and their symptoms. This trust is facilitated because physicians promise to maintain the confidentiality of the information that patients impart to them. Through 1903 the AMA "Principles of Medical Ethics" conventional practitioners promised patients, "secrecy [is] to be Inviolable," and "no infirmity . . . observed during medical attendance, should ever be divulged by physicians." In the case of infectious diseases, however, individual patients often seek to assert confidentiality where communal protection demands publicity. Thus, public health ethics stressed the need to make information about infectious diseases public in order to prevent the spread of contagious diseases, whereas conventional medical ethics tended to stress physicians' obligations to protect patient confidentiality.

Public health ethics and conventional medical ethics remained at odds on the need to protect patient confidentiality through most of the twentieth century. When the AIDS epidemic was recognized in the 1980s, however, their positions reversed. Seeking to maximize treatment of a heavily stigmatized disease, public health medicine tended to promise HIV-positive patients complete confidentiality. In contrast, the AMA, seeking to protect physicians' health, proclaimed in its "Principles of Medical Ethics" that, "exceptions to confidentiality are appropriate when necessary to protect the public health or . . . to protect . . . health-care workers, who are endangered by persons with HIV." The AMA also holds that "when a health care provider is at risk for HIV infection because of . . . contact with potentially infected bodily fluids, it is acceptable to test the patient for HIV infection even if the patient refuses consent" (1999).

The Ethics of Vaccination. In 1721, when Richard Mead played the role of England's first public health commissioner, he not only dealt with the pestilential threat of the Plague of Marseilles but also with another pestilence: **smallpox**. Seeking to verify anecdotal evidence that **inoculation** with pus from smallpox pustules would confer **immunity**, Mead recruited Newgate prisoners to serve as research subjects. To reward their "voluntary" service, he arranged for the commutation of their sentences. When Mead had established that inoculation typically resulted in a mild immunity-conferring case of smallpox, he recommended the practice to Parliament and to the Royal Family (which dutifully followed his advice). This episode touches on two of the most ethically charged aspects of public health medicine: experimentation and **vaccination**. Vaccination requires intentionally subjecting someone to the risks associated with a vaccine in order to confer some level of immunity against a disease to which that person may, or may not, be exposed. Smallpox inoculation, for example, can result in a virulent or even fatal case of the disease itself. The point to appreciate is that, although not all vaccines are as risky as smallpox inoculations, they all entail some level of associated risk. Assessing the safety of vaccination (i.e., the levels of risk appropriate to the potential benefits of vaccination) has been controversial from Mead's day to the present.

Some individuals and families seek to minimize these risks by declining vaccination. This is a relatively safe option if 75 percent to 95 percent of the rest of the population has been vaccinated. Under these circumstances, the entire population is usually protected because of a phenomenon known as herd or community immunity. Those who decline vaccination thus have a "free ride," benefiting from the immunity conferred by the communal acceptance of the risks of vaccination without themselves undertaking any of those risks. However, free riders are at risk of contracting the disease if they become a sizeable percentage of the community. Should a large segment of the community join the "no vaccine bandwagon" and attempt to minimize their own risks by declining vaccination for themselves or their **children**, community immunity will weaken, and the unvaccinated portion of the community would be exposed to the disease. This happened in Ireland and the Netherlands in 1999–2000 when the level of communal immunity declined to well below the 95 percent internationally accepted level for controlling measles—falling to 72 percent in Ireland and to 63 percent in parts of Dublin. Reported cases of measles increased from a few hundred to 1,603 cases in Ireland and 3,292 cases in the Netherlands.

To insure that all members share the risks and benefits of vaccination fairly, some communities make vaccination mandatory for the entire population (e.g., as a condition of entering school). Mandating vaccination, however, raises issues about individuals' rights to refuse medical treatment and about the civil liberties of religious dissenters, such as Christian Scientists. Moreover, because most vaccines are administered to minor children, mandatory vaccination also raises questions about parental prerogatives to act on behalf of their minor children. Communities balance these interests in different ways. Some communities merely recommend vaccination. Some communities mandate vaccination but offer formal mechanisms for parents to decline vaccination for their minor children. Other communities consider parental refusals of vaccination for certain life-threatening diseases a form of child abuse.

The Ethics of Experimentation. As the Mead smallpox vignette illustrates, medical innovations, including the development of new vaccines, require experimentation on **human subjects**. Many subjects have been willing volunteers. As early as 1900, for example, the

American military physician **Walter Reed** used consenting volunteers to conduct experiments to confirm Carlos Finlay's (1833–1915) hypothesis that mosquitoes transmitted yellow fever. Most people, however, are reluctant to serve as human subjects for vaccines against pestilential diseases. To deal with the anticipated difficulties of recruiting volunteers for experiments on these diseases, some researchers have experimented on people without their knowledge or their consent—at times claiming that the public's good outweighed the individual's rights. Ironically, these experiments have often served the public good, not as the researcher intended, but by provoking scandals that led to major reforms in research ethics.

Scandals associated with research on pestilential diseases have led to some of the most significant reforms in modern research ethics. In the early twentieth century, for example, Germany led the world in medical research on epidemic disease. In 1898 a scandal over the surreptitious inoculation of patients with an experimental vaccine against **syphilis** led to the world's first governmental prohibition of unconsented experiments on patients. In 1911 a scandal erupted over the involuntary internment of thousands of “natives” in German East Africa. Nobel Laureate **Robert Koch** and other physicians had imprisoned unconsenting natives in a camp to test an arsenic compound's efficacy in preventing **sleeping sickness**. The compound proved dangerous and ineffective. The researchers' internment of natives provoked a scandal, which, in turn led to the first regulation protecting the rights and freedoms of colonial natives against scientific researchers.

Yet another scandal, the death of 72 children in the German city of Lübeck from **tuberculosis** as result of receiving an experimental BCG vaccine, led to the 1932 German Research Regulations. These regulations—at the time the most advanced in the world—required scientific validity, the informed voluntary consent of research subjects, prior animal experimentation, and a host of other protections for human subjects. A form of these regulations eventually found its way into international law because it became the basis of the Nuremberg Code of Research, which was formulated because of another scandal—the Nazi medical experiments that led to the 1947 Nuremberg War Crime Trials of German physicians and medical researchers. One of the accusations leveled at one trial involved research on an anti-**typhus** vaccine. Between 1942 and 1944, a German **pharmaceutical** company, *Behringwerke AG*, and the Robert Koch Institute in Berlin infected a population of 450 previously healthy concentration camp inmates with typhus to test the efficacy of experimental anti-typhus vaccines—leading to the deaths of one-third of them. The Nuremberg tribunal condemned the researchers who conducted these and other experiments, sentencing some to death and others to prison. In justifying their condemnation, the tribunal reformulated the 1932 German research ethics regulations as the Nuremberg Code of Research Ethics—making them part of international law. This code reiterated that the primary obligation of researchers was to obtain the informed voluntary consent of their subjects.

After the Second World War, the United States became the world leader in medical research. New scandals involving research on epidemic disease again generated new reforms. U.S. researchers had rejected the Nuremberg Code as “a good code of Nazis” but unnecessary for American researchers—until a headline scandal led to congressional hearings. The scandal was as follows: from 1932 to 1972, the U.S. Public Health Service had conducted a study of the natural evolution of syphilis in 399 African American men, the Tuskegee Syphilis Study, misinforming the subjects of their diagnosis, conducting

CODES OF MEDICAL ETHICS

Professions are self-regulating fields whose members are committed to using their specialized expertise in the service of some common good, such as providing health care. Until the nineteenth century, professions regulated themselves through oaths of induction like the ancient Greek Hippocratic Oath—the very word “profession” derives from the Latin term for having sworn (professed) an oath. In the nineteenth century, however, professional oaths were relegated to a ceremonial role, and the real standards governing professional conduct began to be set forth in professional codes of ethics. These codes were public statements of the specific obligations binding on everyone in a profession. Violations of professional codes of ethics can lead to censure or expulsion from professional bodies, termination of employment, and loss of licensure. Because courts typically recognize the authority of professional codes, the standards of professional conduct set out in these codes often have the force of law, and code violations can create legal liabilities, such as malpractice lawsuits.

Although professional standards for physicians get the most public attention, almost all the professionals involved in preparing for and responding to epidemics—from researchers and public health professionals, to paramedics and emergency medical technicians (EMTs), to physicians, nurses, and various allied health professionals—subscribe to formal codes of professional ethics. The National Association of Emergency Medical Technicians (NAEMT; founded in 1975), for example, has a code of ethics that commits EMTs to conserving life, alleviating suffering, promoting health, doing no harm, and encouraging the quality and equal availability of emergency medical care based on human need, with respect for human dignity, unrestricted by consideration of nationality, race, creed, color, or status. There is also an international code of nursing ethics, as well as codes from various national nursing associations. The American Public Health Association (APHA; 1872) has an elaborate code of ethics, as does the American Medical Association (AMA; 1847).

Professional standards for research on human subjects provide a good example of internationally recognized codes of professional ethics. The major research ethics codes were developed by two international professional organizations: the Council of International Organizations of Medical Science (CIOMS; founded in 1949 but issuing research ethics guidelines since 1982) of the **World Health Organization** (WHO), and the World Medical Association (WMA; founded in 1947 but issuing research ethics guidelines since 1964). Governmental and quasi-non-governmental agencies (“quangos,” such as the Medical Research Council of Britain and the U.S. National Institutes of Health) and professional societies (such as the APHA) typically align their policies and regulations with these international standards. This creates, in effect, a worldwide set of professional standards for research involving human and animal subjects, recognized and enforced by the professions and their journals and by private, governmental, and quango funding agencies.

Robert Baker

lumbar punctures (spinal taps) without informed consent, and, in some cases, denying subjects access to potentially curative antibiotics. After these hearings, the U.S. government developed a common rule for ethical research on human subjects.

The U.S. government research regulations were justified initially, and are still justified today, by a set of three basic principles. These principles were articulated in the

1979 Belmont Report. The principle of respect for persons justifies regulations mandating the informed consent of the research subject (because failure to ask people to volunteer knowingly to become research subjects shows a fundamental disrespect for them as persons). The principle of beneficence requires that experiments produce more good than harm. The principle of justice requires a fair distribution between the benefits and burdens of research, so that the affluent and well-placed do not benefit inequitably from research burdens born disproportionately by the poor and disenfranchised. The World Medical Association (WMA) adopted similar standards with the Declaration of Helsinki (1975–2002) as did the Council of International Organizations of Medical Science (CIOMS) of the World Health Organization (WHO), which has also offered guidelines for ethical research since 1982. These three codes set national and international standards for ethical research on vaccines for AIDS, **Bird flu**, **Ebola**, **SARS**, and other modern pestilences. *See also* AIDS in Africa; AIDS in America; Animal Research; Capitalism and Epidemic Disease; Disease, Social Construction of; Geopolitics, International Relations, and Epidemic Disease; International Health Agencies and Conventions; Leprosy, Societal Reactions to; Mallon, Mary; Pest Houses and Lazarettos; Popular Media and Epidemic Disease: Recent Trends; Tuberculosis in the Contemporary World; War, the Military, and Epidemic Disease.

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ROBERT BAKER

MENINGITIS. Meningitis is an inflammation of the meninges, the membranes covering the brain and spinal cord, and may have first been described by medieval **physicians**. Symptoms can be **influenza**-like, with fever, headache, and nausea common, but, depending on the cause, they can be more severe and even fatal. Meningitis can be caused by a diverse range of agents including certain drugs and cancer, but it is most commonly caused by microorganisms. Most meningitis is caused by a group of **viruses** known as enteroviruses and is often mild, not requiring treatment. Fungi also commonly cause meningitis in immunocompromised individuals, for example **HIV/AIDS** patients. Bacterial meningitis, which is endemic in most countries, is much more severe, however. It can be a rapidly progressing, life-threatening infection that primarily affects the young and has been the focus of major public health control efforts and vaccine development programs.

Biological Agents. **Bacteria** are the most clinically important and severe cause of meningitis, with just four species causing the majority of cases. *Neisseria meningitidis* (the meningococcus) causes large **epidemics** and even intercontinental pandemics; *Streptococcus pneumoniae* (the pneumococcus) is also a major cause of pneumonia; *Haemophilus influenzae*, of which serotype B causes almost all disease; and *Streptococcus agalactiae* (Group B Streptococcus or GBS) is the leading cause of meningitis in newborns.

Humans are the only known reservoir for these bacteria, which all commonly colonize the nose and throat without symptoms. GBS, which also colonizes the lower gastrointestinal tract and vagina, is transmitted from person to person by skin contact, whereas the other three species are transmitted in aerosolized respiratory droplets. **Transmission** is most efficient in closed or semi-closed communities, such as university campuses or military recruit camps, and is facilitated by factors that promote damage to the cellular lining of the nose and throat (including smoking), close contact among individuals (including overcrowded living conditions), and sharing of respiratory secretions (including coughing, sneezing, and kissing).

Importantly, disease is not part of the life cycles of these bacteria, but for largely unknown reasons, they occasionally cause systemic disease. This occurs when the bacteria invade the epithelial cells in the nose and throat and enter the bloodstream, before eventually entering the cerebrospinal fluid (the fluid between the meninges) *via* the meninges. A number of virulence factors, including polysaccharide capsules and outer membrane proteins, have been identified in each species. These also have normal roles in asymptomatic colonization including adhesion to host cells, modulation or diversion of the host immune response, and scavenging of host nutrients.

Symptoms, Morbidity, and Mortality. Different bacterial causes of meningitis cannot be easily differentiated from one another based on symptoms alone. Early in infection symptoms can resemble influenza, making **diagnosis** difficult without further testing of blood or cerebrospinal fluid. Fever, nausea, headache, and dislike of strong lights and sounds are also common symptoms. All four species commonly cause other diseases as well as meningitis, including septicemia (blood poisoning) and ear infections. Without effective clinical management and **antibiotic** treatment, bacterial meningitis can be swift, resulting in toxic shock, major organ failure, and death. Mortality rates vary from approximately 2 to 6 percent with Hib, through 10 percent for meningococci and GBS, to 25 percent in pneumococci. Neurological side effects, including brain damage, hearing damage, and learning difficulties, are common because of the infection's location, in the central nervous system. Amputations are also often necessary because of the tissue-toxicity

of bacterial surface molecules. Serious side effects in survivors are seen in approximately 20 percent of meningococcal cases, 30 percent of Hib cases, and up to 50 percent of pneumococcal and GBS cases.

Susceptibility to bacterial meningitis is strongly influenced by antibody levels, especially against the polysaccharide capsules as demonstrated by **epidemiology** studies, and a higher risk of disease exists in people with genetic antibody deficiencies. Protective antibody levels arise from passage of maternal antibody across the placenta, asymptomatic carriage of the bacteria, or antigenically cross-reactive species and **vaccination**. Genetic mutations in the host are important in determining susceptibility to all species and are thought to contribute a third of the risk of meningococcal disease.

There is very little social stigma attached to meningitis sufferers because asymptomatic bacterial carriage is common, transmission easy, and disease rare. Nevertheless, meningitis is often seen in the headlines of the regional or national press and has a huge impact on public consciousness, affecting the young, appearing at random, killing rapidly, and leaving survivors with terrible side effects.

Epidemiology. The global disease rate of bacterial meningitis was approximately 171,000 deaths per year at the turn of the twenty-first century, with the meningococcus, the pneumococcus, and Hib accounting for over 90 percent of childhood bacterial meningitis. Although carriage of all four species occurs throughout the year, disease (apart from GBS) is seasonal, with the majority of cases occurring in winter and spring in temperate regions when the rate of respiratory infections is higher.

Meningococci are carried in around 10 percent of the general population and in up to 40 percent of 15–24 year olds. They can be classified into 13 “serogroups” based on antigenic differences in their capsular polysaccharide, with 5 serogroups being responsible for more than 90 percent of disease. There are also many genetic groups of meningococci which exchange capsular types easily, but around 10 “hyperinvasive lineages” cause the majority of disease. Two disease peaks exist, the first in infants and the second in young adults, the latter thought to be caused predominantly by the increased carriage rate in this age group. Developed countries have an endemic meningococcal disease rate of 1 to 5 per 100,000 population but this is much higher in the developing world. The “Meningitis Belt” of Sub-Saharan Africa is a region with hyper-endemic levels of meningococcal disease and where large-scale epidemics occur approximately every 10 to 14 years. The worst epidemic of the twentieth century occurred in 1996, with a quarter of a million cases and 25,000 deaths. Here, the disease also displays an altered seasonality, peaking in the dry season when the dusty conditions and crowding during the cold nights exacerbate damage to the cellular lining of the nose and throat and increase transmission. The immune status of the host population is a highly important determining factor in the development of epidemics. For example, population genetic data following a 1993 epidemic in the Czech Republic showed that antigenically related meningococci had not been seen there in the three previous decades.

Pneumococci are more likely to cause pneumonia and inner ear infections than meningitis. Carriage rates vary by age, and the duration of carriage is longer in children. Virulent strains belong to 90 serotypes, based on antigenic differences in the polysaccharide capsule, and approximately 60 percent of disease is caused by just 10 serotypes. In the United States before 2000, there were approximately 60,000 annual cases of invasive pneumococcal disease and 3,300 of pneumococcal meningitis. These numbers have since fallen with the introduction of new vaccines.

Hib disease occurs worldwide, but has highest incidence in the developing world. Before Hib vaccines became available in the 1980s and 1990s, it was the leading cause of invasive bacterial disease and meningitis in children under five years of age, with 40 to 100 annual cases per 100,000 population in the United States. Carriage of Hib is low, at 0.5 to 3 percent of healthy infants and children.

GBS is carried in approximately 40 percent of pregnant women and, since the 1970s, has replaced *Escherichia coli* as the leading cause of meningitis in newborns. The disease incidence is approximately 3 in 1,000 live births, striking before or just after birth (early onset disease) or, twice as frequently, in the first few months of life (late onset disease). There is a higher risk of disease in premature babies, in prolonged labor, or when the mother is infected. There are six immunologically distinct serotypes based on the capsular polysaccharide and surface proteins, and 60 percent of infants born to colonized mothers will be colonized with the mother's serotype.

History of Research on and Control of Meningitis. Along with the descriptions by medieval Arab physicians, including Avenzoar of al-Andalus (Spain; 1091–1161) in the twelfth century, reports of “spotted fevers” go back to antiquity. It was not until the nineteenth century, though, that medical science started to understand and treat bacterial meningitis.

Meningococcal disease was first described by the Swiss physician Gaspard Vieussieux (1746–1814) in 1805 during an outbreak in Geneva, and the bacterium was first isolated by the Austrian pathologist Anton Weichselbaum (1845–1920) in 1887 in Vienna, who named it *Diplococcus intracellularis meningitidis*. *S. pneumoniae* was originally isolated by **Louis Pasteur** and pioneer American bacteriologist George Sternberg (1838–1915) independently in 1881, and the importance of the capsular polysaccharides for virulence was described in the early twentieth century. Richard Pfeiffer (1858–1945), German physician, first identified *H. influenzae* in 1892 during the **influenza pandemic** of that year. This led to *H. influenzae* being mistakenly proposed as the cause of influenza, and it was not until the 1930s, when the influenza virus was first isolated, that the bacterium was found to be a major cause of secondary infection. In the same decade the different capsular serotypes were identified, and it was found that the majority of disease was caused by serotype B (Hib).

GBS was originally known as *Streptococcus mastitidis* after it was identified as a cause of bovine mastitis (swelling of the mammary glands in cows) and was first isolated in 1887 by French veterinarian Edmond Nocard (1850–1903) (with a Charenton veterinarian named Mollereau). It was first identified in vaginal cultures by Rebecca Craighill Lancefield (1895–1981) and colleagues, who also classified the *Streptococcus* genus into groups, though it was only reported as a human pathogen by R. M. Fry in 1938. Antibiotics now play a major role in the control of this pathogen, but vaccines are being developed.

The first bacterial meningitis vaccines based on the polysaccharide capsules of meningococci, pneumococci, and Hib were introduced in the 1970s and 1980s. These were not effective in protecting infants and, since the 1990s, have been surpassed by a new generation of vaccines in which the capsular polysaccharides are conjugated (chemically linked) to immunity-boosting proteins. These have often been administered in population-scale vaccination campaigns and in infant immunization schedules, with significant impacts on disease, notably the 99 percent reduction in Hib disease to now negligible levels in the developed world. Pneumococcal vaccines are also effective and continue to change to keep pace with the disease prevalence of different serotypes. Conjugate meningococcal vaccines

against serogroups A, C, Y, and W-135 are in development, but serogroup B vaccines have so far eluded science as a result of the similarity of the serogroup B polysaccharide to molecules on human cells. To combat this, as in other diseases, a number of vaccines are being developed based on outer membrane proteins on the bacterial surface. Furthermore, as for many other infectious diseases, reverse vaccinology (genome-based vaccine design) is also yielding new vaccine candidates against bacterial meningitis.

As we enter the twenty-first century, effective antibiotics and/or vaccines are available against all four of the major bacterial causes of meningitis. However, antibiotic resistance is known in all four species, and the often high cost of vaccines has prevented their use in the developing world, where much of the disease burden lies. New genomic data and knowledge of the bacterial population structures is providing novel vaccine development strategies, which are complemented by growing global experience of how to deploy them most effectively. The effectiveness of diagnosis and early detection of symptoms continues to benefit from increased awareness campaigns, improved clinical management programs, and the use of modern molecular diagnostic tests. In the developing world, global coordination of public health and economic efforts aim to provide more funds for meningitis vaccines, though there is significant competition for funding from other serious diseases including HIV/AIDS. For now, however, bacterial meningitis is very much still with us. *See also* Children and Childhood Diseases.

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MARTIN CALLAGHAN

MIASMA THEORY. *See* Air and Epidemic Diseases.

MICROSCOPE. Archeologists have discovered magnifying lenses dating back thousands of years, but they were used for decorative, not scientific, purposes. In the early 1600s, the microscope's design evolved from the telescope, with lenses contained in a vertically mounted tube and an adjustable mirror to reflect light. The rays of light and magnifying lenses enable the observation of small objects, and thus these microscopes are called light microscopes. The microscope made its first appearance in compound form (two lenses), used most often today, near the end of the sixteenth century.

By the 1620s, microscopes began appearing in European cities, and in 1665, English scientist Robert Hooke (1635–1703) published his pioneering book *Micrographia*. It contained extremely detailed illustrations of a huge variety of microorganisms, seen through

a compound microscope that magnified about 30 to 50 times. After wondering how cork, which looked solid, could be so soft, he observed it under his microscope, and was the first to use the word “cell” to describe the small air-filled chambers he consequently saw.

Hooke was a likely influence on Dutch microscopist **Antony van Leeuwenhoek**. Using a single-lens microscope that he ground himself and which magnified up to 275 times, Leeuwenhoek made the first discovery of what are now known to be **bacteria**, along with other single-celled organisms including **protozoa**. Protozoan diseases include **sleeping sickness** and **malaria**. With the aid of the more complex microscopes that became available in the 1840s, bacteriologists **Louis Pasteur**, in France, and **Robert Koch**, in Germany, discovered the role that bacteria played in disease. Koch was one of several scientists who discovered the importance of dying techniques, which made viewing of the organisms easier.

The invention of the oil immersion lens allowed for even higher magnifications, as it allowed for oil to be placed between the organism and lens, so as to reduce the bending of light. With this high magnification, individual bacteria were able to be seen. Bacteria can be seen to have different shapes, including spherical, rod-like, or spiral, and their shape is an important way to identify them. Examples of bacterial diseases include **bubonic plague**, **cholera**, **diphtheria**, **leprosy**, **typhoid fever**, and **whooping cough**.

In the 1930s, the electron microscope was developed. The electron microscope uses a stream of electrons to coat the object, and a “picture” of the outside of the organism is then made. One disadvantage to using an electron microscope is that it kills the organism being viewed. With an electron microscope, **viruses**, submicroscopic in size, were able to be seen for the first time. Viral diseases include **measles**, **rubeola**, **rubella**, **smallpox**, **poliomyelitis**, **influenza**, and **AIDS**. The electron microscope has also provided images of all other microorganisms of unprecedented clarity and detail, revolutionizing the understanding of cellular biology. *See also* Diagnosis and Diagnostic Tools.

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MARTHA STONE

MILITARY. *See* War, the Military, and Epidemic Disease.

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Encyclopedia of Pestilence, Pandemics, and Plagues

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Encyclopedia of Pestilence, Pandemics, and Plagues

Volume 2, N–Z

Edited by
JOSEPH P. BYRNE

Foreword by
Anthony S. Fauci, M.D.



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Contents

List of Entries	vii
Guide to Related Topics	xiii
Foreword by Anthony S. Fauci, M.D.	xix
Preface	xxi
Introduction	xxiii
The Encyclopedia	1
Glossary	801
Bibliography	813
About the Editor, Advisory Board Members, and Contributors	827
Index	843

This page intentionally left blank

List of Entries

- AIDS in Africa
- AIDS in the United States
- AIDS, Literature, and the Arts in the United States
- Air and Epidemic Diseases
- Animal Diseases (Zoonoses) and Epidemic Disease
- Animal Research
- Antibiotics
- Apothecary/Pharmacist
- Armstrong, Richard
- Astrology and Medicine
- Avian Flu. See Influenza.
- Avicenna (Ibn Sina)
- Ayurvedic Disease Theory and Medicine
- Babesiosis
- Bacterium/Bacteria
- Bartonella* Diseases
- Behring, Emil von
- Biblical Plagues
- Bimaranistan/Maristan
- Biological Warfare
- Bioterrorism
- Black Death (1347–1352)
- Black Death and Late Medieval Christianity
- Black Death, Economic and Demographic Effects of
- Black Death, Flagellants, and Jews
- Black Death: Literature and Art
- Black Death: Modern Medical Debate
- Bubonic Plague
- Bubonic Plague in the United States
- Capitalism and Epidemic Disease
- Chadwick, Edwin
- Children and Childhood Epidemic Diseases
- Chinese Disease Theory and Medicine
- Cholera
- Cholera before the Pandemics
- Cholera: First through Third Pandemics, 1816–1861
- Cholera: Fourth through Sixth Pandemics, 1862–1947
- Cholera: Seventh Pandemic, 1961–Present
- Cinema and Epidemic Disease
- Colonialism and Epidemic Disease
- Conjunctivitis

- Contagion and Transmission
Contagion Theory of Disease,
Premodern
Cordon Sanitaire
Corpses and Epidemic Disease
- Demographic Data Collection and
Analysis, History of
Diagnosis and Diagnostic Tools
Diagnosis of Historical Diseases
Diet, Nutrition, and Epidemic Disease
Diphtheria
Disease in the Pre-Columbian
Americas
Disease, Social Construction of
Disinfection and Fumigation
Drug Resistance in Microorganisms
Dysentery
- Early Humans, Infectious Diseases in
Ectoparasites
Ehrlich, Paul
Empiric
Encephalitis
Encephalitis, Epidemic Outbreaks
in the Twentieth Century
Enders, John Franklin
Enteric Fevers
Environment, Ecology, and Epidemic
Disease
Epidemic and Pandemic
Epidemiology
Epidemiology, History of
Ergotism
- Farr, William
Fernel, Jean
Flight
Folk Medicine
Fracastoro, Girolamo
Frost, Wade Hampton
- Galen
Geopolitics, International Relations,
and Epidemic Disease
Germ Theory of Disease
Gonorrhoea and Chlamydia
- Gorgas, William Crawford
Greco-Roman Medical Theory
and Practice
- Haffkine, Waldemar Mordechai
Hansen, Gerhard Armauer
Hemorrhagic Fevers
Hemorrhagic Fevers in Modern Africa
Henderson, Donald Ainslie
Hepatitis
Hereditry and Epidemic Disease
Hippocrates and the Hippocratic Corpus
Historical Epidemiology
Hospitals and Medical Education in
Britain and the United States
Hospitals in the West to 1900
Hospitals since 1900
Human Body
Human Immunity and Resistance to
Disease
Human Immunodeficiency
Virus/Acquired Immune Deficiency
Syndrome (HIV/AIDS)
Human Papilloma Virus and Cervical
Cancer
Human Subjects Research
Humoral Theory
- Immunology
Industrialization and Epidemic Disease
Industrial Revolution
Influenza
Influenza Pandemic, 1889–1890
Influenza Pandemic, 1918–1919
Insect Infestations
Insects, Other Arthropods, and Epidemic
Disease
International Health Agencies and
Conventions
Irish Potato Famine and Epidemic
Disease, 1845–1850
Islamic Disease Theory and Medicine
- Jenner, Edward
Kitasato, Shibasaburo
Koch, Robert

- Latin America, Colonial: Demographic
 Effects of Imported Diseases
 Laveran, Charles Louis Alphonse
 Leeuwenhoek, Antony van
 Legionnaires' Disease
 Leprosarium
 Leprosy
 Leprosy in the Premodern World
 Leprosy in the United States
 Leprosy, Societal Reactions to
 Literature, Disease in Modern
 London, Great Plague of (1665–1666)
 Lyme Disease

 Magic and Healing
 Malaria
 Malaria and Modern Military History
 Malaria in Africa
 Malaria in Medieval and Early
 Modern Europe
 Malaria in the Americas
 Malaria in the Ancient World
 Mallon, Mary
 Malthusianism
 Manson, Patrick
 Mather, Increase and Cotton
 Measles
 Measles, Efforts to Eradicate
 Measles Epidemic in Fiji (1875)
 and Eugenics
 Measles in the Colonial Americas
 Medical Education in the West,
 1100–1500
 Medical Education in the West,
 1500–1900
 Medical Ethics and Epidemic Disease
 Meningitis
 Microscope

 Napoleonic Wars
 Neolithic Revolution and Epidemic
 Disease
 News Media and Epidemic Disease
 Nicolle, Charles Jules Henri
 Non-Governmental Organizations
 (NGOs) and Epidemic Disease
 Nurses and Nursing

 Paleopathology
 Panspermia Theory
 Paracelsianism
 Paracelsus
 Pasteur, Louis
 Penicillin
 Personal Hygiene and Epidemic Disease
 Personal Liberties and Epidemic
 Disease
 Pest Houses and Lazarettos
 Pesticides
 Pettenkofer, Max Josef von
 Pharmaceutical Industry
 Physician
 Pilgrimage and Epidemic Disease
 Plague and Developments in Public
 Health, 1348–1600
 Plague: End of the Second Pandemic
 Plague in Africa: Third Pandemic
 Plague in Britain, 1500–1647
 Plague in China
 Plague in East Asia: Third Pandemic
 Plague in Europe, 1500–1770s
 Plague in India and Oceania:
 Third Pandemic
 Plague in Medieval Europe,
 1360–1500
 Plague in San Francisco, 1900–1908
 Plague in the Contemporary World
 Plague in the Islamic World,
 1360–1500
 Plague in the Islamic World,
 1500–1850
 Plague Literature and Art, Early
 Modern European
 Plague Memorials
 Plague of Athens
 Plague of Justinian, First Pandemic
 Plagues of the Roman Empire
 Plagues of the Roman Republic
 Pneumonic and Septicemic Plague
 Pneumonic Plague in Surat, Gujarat,
 India, 1994
 Poison Libels and Epidemic Disease
 Poliomyelitis
 Poliomyelitis and American Popular
 Culture

- Poliomyelitis, Campaign Against
Popular Media and Epidemic Disease:
Recent Trends
Poverty, Wealth, and Epidemic
Disease
Protozoon, -zoa
Public Health Agencies in Britain
since 1800
Public Health Agencies, U.S. Federal
Public Health Boards in the West
before 1900
Public Health in the Islamic World,
1000–1600
Public Health Posters
- Quacks, Charlatans, and Their Remedies
Quarantine
- Race, Ethnicity, and Epidemic Disease
Reed, Walter
Relapsing Fever
Religion and Epidemic Disease
Rhazes
Ross, Ronald
Rush, Benjamin
- Sabin, Albert
St. Vitus's Dance
Salk, Jonas E.
Sanatorium
Sanitation Movement of the
Nineteenth Century
Scapegoats and Epidemic Disease
Schaudinn, Fritz Richard
Schistosomiasis
Scientific Revolution and Epidemic
Disease
Semmelweis, Ignaz
Severe Acute Respiratory Syndrome
(SARS)
Sexuality, Gender, and Epidemic
Disease
Sexual Revolution
Simond, Paul-Louis
Simpson, William John Ritchie
Slavery and Epidemic Disease
Sleeping Sickness
- Smallpox
Smallpox and the American Revolution
Smallpox Eradication
Smallpox in Canada and the United
States since 1783
Smallpox in Colonial Latin America
Smallpox in Colonial North America
Smallpox in European Non-American
Colonies
Smallpox in Premodern Europe
Smallpox in the Ancient World
Snow, John
Social Psychological Epidemics
Sulfa Drugs
Surgeon
Sweating Sickness
Sydenham, Thomas
Syphilis
Syphilis in Sixteenth-Century Europe
- Theiler, Max
Thirty Years' War
Trade, Travel, and Epidemic Disease
Tuberculosis
Tuberculosis and Romanticism
Tuberculosis in England since 1500
Tuberculosis in North America
since 1800
Tuberculosis in the Contemporary
World
Typhoid Fever in the West since 1800
Typhus
Typhus and Poverty in the Modern
World
Typhus and War
- Urbanization and Epidemic Disease
- Vaccination and Inoculation
Venereal Disease and Social Reform in
Progressive-Era America
Virchow, Rudolf
Virus
- War, the Military, and Epidemic Disease
Water and Epidemic Diseases
West Nile Fever

Whooping Cough
Wu Lien Teh

Yellow Fever
Yellow Fever Commission, U.S.
Yellow Fever in Colonial Latin America
and the Caribbean

Yellow Fever in Latin America and the
Caribbean, 1830–1940
Yellow Fever in North America to
1810
Yellow Fever in the American South,
1810–1905
Yersin, Alexandre

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Guide to Related Topics

Biological, Physiological, and Medical Theories

Air and Epidemic Diseases
Astrology and Medicine
Ayurvedic Disease Theory and Medicine
Chinese Disease Theory and Medicine
Contagion Theory of Disease
Disease in the Pre-Columbian Americas
Disease, Social Construction of
Folk Medicine
Germ Theory of Disease
Greco-Roman Medical Theories
and Practices
Humoral Theory
Islamic Disease Theory and Medicine
Magic and Healing
Malthusianism
Panspermia Theory
Paracelsianism

Biomedical Research into Disease Causes, Prevention, and Treatment

Animal Research
Antibiotics

Avicenna (Ibn Sina)
Behring, Emil von
Drug Resistance in Microorganisms
Ehrlich, Paul
Enders, John Franklin
Fernel, Jean
Fracastoro, Girolamo
Galen
Haffkine, Waldemar Mordechai
Hansen, Gerhard Armauer
Henderson, Donald Ainslie
Hippocrates and the Hippocratic Corpus
Human Subjects Research
Jenner, Edward
Kitasato, Shibasaburo
Koch, Robert
Laveran, Charles Louis Alphonse
Leeuwenhoek, Antony van
Manson, Patrick
Microscope
Nicolle, Charles Jules Henri
Paracelsus
Pasteur, Louis
Pettenkofer, Max Josef von
Poliomyelitis, Campaign Against
Reed, Walter

Rhazes
 Rush, Benjamin
 Ross, Ronald
 Sabin, Albert
 Salk, Jonas E.
 Schaudin, Fritz Richard
 Scientific Revolution and Epidemic
 Disease
 Semmelweis, Ignaz
 Simond, Paul-Louis
 Simpson, William John Ritchie
 Sydenham, Thomas
 Theiler, Max
 Wu Lien Teh
 Yellow Fever Commission, U.S.
 Yersin, Alexandre

Biological Causes of Disease

Bacterium/Bacteria
 Ectoparasites
 Insects, Other Arthropods, and
 Epidemic Disease
 Protozoon, -zoa
 Virus

Colonial Experience and Disease

Colonialism and Epidemic Disease
 Latin America, Colonial: Effects of
 Imported Diseases
 Leprosy, Societal Reactions to
 Measles in the Colonial Americas
 Slavery and Disease
 Smallpox in Colonial Latin America
 Smallpox in Colonial North America
 Smallpox in Europe's Non-American
 Colonies
 Yellow Fever in Colonial Latin America
 and the Caribbean

Cultural and Societal Effects of Epidemic Disease

AIDS, Literature, and the Arts in the
 United States

Black Death and Late Medieval
 Christianity
 Black Death, Economic and
 Demographic Effects of
 Black Death, Flagellants, and Jews
 Black Death: Literature and Art
 Cinema and Epidemic Disease
 Corpses and Epidemic Disease
 Disease, Social Construction of
 Flight
 Latin America, Colonial: Effects of
 Imported Diseases
 Leprosy, Societal Reactions to
 Literature, Disease in Modern
 Personal Liberty and Public Health
 Plague Literature and Art, Early Modern
 Plague Memorials
 Poison Libels and Epidemic Disease
 Poliomyelitis and American Popular
 Culture
 Popular Media and Epidemic Disease:
 Recent Trends
 Scapegoats and Epidemic Disease
 Tuberculosis and Romanticism
 Venereal Disease and Social Reform in
 Progressive-Era America

Diseases

Animal Diseases and Epidemics
 Babesiosis
Bartonella Diseases
 Bubonic Plague
 Cholera
 Conjunctivitis
 Diphtheria
 Disease in the Pre-Columbian Americas
 Dysentery
 Early Humans, Infectious Diseases in
 Encephalitis
 Enteric Fevers
 Ergotism
 Gonorrhea
 Hemorrhagic Fevers
 Hepatitis
 Human Immunodeficiency Virus
 (HIV)/AIDS

Human Papilloma Virus and
Cervical Cancer
Influenza
Legionnaires' Disease
Leprosy
Lyme Disease
Malaria
Measles
Meningitis
Pneumonic and Septicemic Plague
Poliomyelitis
Relapsing Fever
St. Vitus's Dance
Schistosomiasis
Severe Acute Respiratory Syndrome
(SARS)
Sleeping Sickness
Smallpox
Social Psychological Epidemics
Sweating Sickness
Syphilis
Tuberculosis
Typhus
West Nile Fever
Whooping Cough
Yellow Fever

Drugs and Pharmaceuticals

Antibiotics
Penicillin
Pharmaceutical Industry
Sulfa Drugs
Vaccination and Inoculation

Epidemics and Other Historical Disease Outbreaks

AIDS in Africa
AIDS in the United States
Armstrong, Richard
Biblical Plagues
Black Death (1347–1352)
Black Death: Modern Medical Debate
Bubonic Plague: Third Pandemic in
East Asia

Bubonic Plague: Third Pandemic in India
and Oceania
Bubonic Plague in the United States
to 2000
Cholera: First through Third Pandemics,
1816–1861
Cholera: Fourth through Sixth
Pandemics, 1863–1947
Cholera: Seventh Pandemic, 1961–Present
Diagnosis of Historical Diseases
Encephalitis, Epidemic Outbreaks in the
Twentieth Century
Gorgas, William Crawford
Hemorrhagic Fevers in Modern Africa
Historical Epidemiology
Influenza Pandemic, 1889–1890
Influenza Pandemic, 1918–1919
Insect Infestations
Irish Potato Famine and Epidemic
Diseases, 1845–1850
Leprosy in the Premodern World
Leprosy in the United States
London, Great Plague of (1665–1666)
Malaria in Africa
Mather, Increase and Cotton
Measles Epidemic in Fiji (1875)
and Eugenics
Measles in the Colonial Americas
Plague: End of the Second Pandemic
Plague in Africa: Third Pandemic
Plague in Britain (1500–1647)
Plague in China
Plague in East Asia: Third Pandemic
Plague in Europe, 1500–1770s
Plague in India and Oceania:
Third Pandemic
Plague in Medieval Europe, 1360–1500
Plague in San Francisco, 1900–1905
Plague in the Contemporary World
Plague in the Islamic World, 1360–1500
Plague in the Islamic World, 1500–1850
Plague of Athens
Plague of Justinian, First Pandemic
Plagues of the Roman Empire
Plagues of the Roman Republic
Pneumonic Plague in Surat, Gujarat,
India, 1994

Smallpox in Canada and the United States since 1783
 Smallpox in Colonial Latin America
 Smallpox in Colonial North America
 Smallpox in Europe's Non-American Colonies
 Smallpox in Premodern Europe
 Smallpox in the Ancient World
 Syphilis in Sixteenth-Century Europe
 Tuberculosis in England since 1500
 Tuberculosis in North America since 1800
 Tuberculosis in the Contemporary World
 Typhoid Fever in the West since 1800
 Yellow Fever in Colonial Latin America and the Caribbean
 Yellow Fever in Latin America and the Caribbean, 1830–Present
 Yellow Fever in North America to 1810
 Yellow Fever in the American South, 1810–1905

Epidemiology

Chadwick, Edwin
 Contagion and Transmission
 Contagion Theory of Disease
 Demographic Data Collection and Analysis, History of
 Epidemic
 Epidemiology
 Epidemiology, History of
 Farr, William
 Frost, Wade Hampton
 Historical Epidemiology
 Immunology
 Measles, Global Effort to Eradicate
 Paleopathology
 Poliomyelitis, Campaign Against
 Snow, John
 Virchow, Rudolf

Factors in Disease Outbreaks

Air and Epidemic Diseases
 Capitalism and Epidemic Disease

Children and Childhood Epidemic Diseases
 Contagion and Transmission
 Corpses and Epidemic Disease
 Diet, Nutrition, and Epidemic Disease
 Disease, Social Construction of
 Drug Resistance in Microorganisms
 Environment, Ecology, and Epidemic Disease
 Personal Hygiene and Epidemic Disease
 Geopolitics, International Relations, and Epidemic Disease
 Heredity and Epidemic Disease
 Human Immunity and Resistance to Disease
 Industrialization and Epidemic Disease
 Industrial Revolution
 Mallon, Mary
 Neolithic Revolution
 Personal Hygiene and Epidemic Disease
 Poverty, Wealth, and Epidemic Disease
 Race, Ethnicity, and Epidemic Disease
 Sexual Revolution
 Sexuality, Gender, and Epidemic Disease
 Slavery and Disease
 Trade, Travel, and Epidemic Disease
 Typhus and Poverty in the Modern World
 Urbanization and Epidemic Disease
 Water and Epidemic Diseases

Institutions

Bimaristan
 Hospitals and Medical Education in Britain and the United States
 Hospitals since 1900
 Hospitals to 1900
 Leprosarium
 Pest Houses and Lazarettos
 Sanatorium

Medical Personnel

Apothecary/Pharmacist
 Diagnosis and Diagnostic Tools

Empiric
 Medical Education in the West,
 1100–1500
 Medical Education in the West,
 1500–1900
 Hospitals and Medical Education in
 Britain and the United States
 Medical Ethics and Epidemic Disease
 Nurses and Nursing
 Physician
 Quacks, Charlatans, and Their Remedies
 Surgeon

Public Health

Cordon Sanitaire
 Demographic Data Collection and
 Analysis, History of
 Disinfection and Fumigation
 Farr, William
 Frost, Wade Hampton
 Gorgas, William Crawford
 International Health Agencies and
 Conventions
 Non-Governmental Organizations
 (NGOs) and Epidemic Disease
 Personal Liberty and Public Health
 Pesticides
 Plague and Developments in Public
 Health, 1348–1600
 Public Health Agencies in the West
 before 1900
 Public Health Agencies in Britain since
 1800
 Public Health Agencies, U.S. Federal
 Public Health in the Islamic World,
 1000–1600
 Public Health Posters
 Quarantine
 Sanitation Movement of the Nineteenth
 Century
 Smallpox Eradication
 Snow, John
 Vaccination and Inoculation
 Virchow, Rudolf

Religion

Biblical Plagues
 Black Death and Late Medieval
 Christianity
 Black Death, Flagellants, and Jews
 Islamic Disease Theory and Medicine
 Leprosy, Societal Reactions to
 Magic and Healing
 Pilgrimage and Epidemic Disease
 Religion and Epidemic Disease

Slavery

Colonialism and Epidemic Disease
 Civil War, American
 Latin America, Colonial: Effects of
 Imported Diseases
 Measles in the Colonial Americas
 Race, Ethnicity, and Epidemic Disease
 Scapegoats and Epidemic Disease
 Slavery and Disease
 Smallpox in Colonial Latin America
 Smallpox in Colonial North America
 Smallpox in Europe's Non-American
 Colonies
 Yellow Fever in Colonial Latin America
 and the Caribbean
 Yellow Fever in North America to 1810
 Yellow Fever in the American South,
 1810–1905

War

Biological Warfare
 Bioterrorism
 Colonialism and Epidemic Disease
 Malaria and Modern Military History
 Napoleonic Wars
 Smallpox and the American
 Revolution
 Thirty Years' War
 Typhus and War
 War, the Military, and Epidemic
 Disease

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NAPOLEONIC WARS. Between 1796 and 1815, the French general, and later Emperor, Napoleon Bonaparte (1769–1821) led or sent millions of French soldiers and their allies on sweeping campaigns of conquest that stretched from the Caribbean, to Moscow and Danzig on the Baltic, to the Pyramids of Egypt. As was the case with every premodern army, disease was a constant companion, and disease epidemics punctuated the two decades of turmoil. These took countless lives among Napoleon’s men, those who opposed him, and the luckless civilians encountered along the way.

Conditions of eighteenth-century **warfare** lent themselves readily to the spread of disease. Continental armies, especially those of the French Revolutionary period of the 1790s and Napoleon’s time, were enormous and drew in recruits with little concern for their general health. In barracks and camps, sanitation and **personal hygiene** were of minimal concern—though Napoleon himself emphasized both—which gave rise to many food-, water-, and parasite-borne diseases. Crowded quarters, minimal health care, unbalanced **diets**, and the stress of military regimen weakened resistance to disease, leaving diarrheal and respiratory infections virtually endemic. Finally, venereal diseases such as **syphilis** and **gonorrhea**, spread largely by prostitution and rape, also accompanied the era’s armies. Though Napoleon wished to have prostitutes banned from his camps, he was careful to have them registered and medically treated.

Exposure of an army to novel **environments** also exposed them to new pathogens. From 1794 to 1797, the British forces that garrisoned and fought the French in Haiti encountered the ravages of the tropical **yellow fever**, which had recently been imported by their colleagues from nearby Martinique. Of 20,000 troops who served, over 60 percent fell ill, and over 3,500 died, most in the swampy, filthy staging areas around Port-au-Prince in the summers of 1794 and 1795. In 1797 the command decided to abandon the island. In 1802, after François Dominique Toussaint L’Ouverture (1743–1803) took control of much of the island with his successful slave revolt, Napoleon sent 25,000 French troops to quell the

rebellion. Yellow fever struck the French this time, killing more than a hundred soldiers and sailors per day during the summer months from May to September. New arrivals were most vulnerable and died most readily, and by early 1803 some 40,000 Frenchmen of the 50,000 who served are believed to have succumbed to yellow fever and **malaria**. Toussaint held on with British help and watched the French evacuate later in 1803.

On the Continent, the typical culprit was louse-borne **typhus**. During Napoleon's successful campaign in Italy in 1796, **epidemic typhus** broke out in Mantua, spreading quickly among both French and Austrian armies, and from them to civilian populations as far south as Sicily. In 1799 Austrian and Russian troops defeated the French in the Piedmont region of northwest Italy. Typhus again broke out as the French retreated out of Italy. About a third of the French army fell to the disease, the city of Nice suffered thousands of civilian deaths, and, as the disease spread southward through Liguria, Genoa lost nearly 14,000 residents.

Meanwhile, Napoleon himself was in Egypt, battling the British for control of the eastern Mediterranean. Here his army suffered defeat at the Battle of the Pyramids and encountered endemic **bubonic plague**, which became epidemic in December 1798. The very terror of plague demoralized his men, and Napoleon went so far as to hug one of the victims to show his disbelief in its contagious nature. He stressed cleanliness in the French camps and insisted that company surgeons treat plague victims as well as they could. Blocked by the British navy, the French moved counterclockwise from Alexandria north to Jaffa in Syria, but plague hounded them. While unsuccessfully besieging Acre (Acco), Napoleon lost over 600 men per day. The shrinking French force left Jaffa, abandoning 50 plague victims after giving them opium to drink as a poison, lest they be captured and tortured by the Turks. Many vomited it up and lived to meet their captors. While his army retired to Cairo, where they lost between 30 and 40 men per day, Napoleon returned to France. The army's commanders eventually surrendered to the British, beaten as much by the plague as by the rival Empire.

Napoleon's successful campaign against the Austrians in 1805 resulted in his capture of the Habsburg capital of Vienna into whose hospitals he placed his multitude of wounded and disease ridden. As usual, typhus was the most common ailment, and it spread rapidly in the overcrowded and filthy conditions of even the grandest facility. After the Battle of Austerlitz on December 2, Napoleon used the city of Brno to house his own and his allies' 48,000 wounded. Crammed into houses, churches, monasteries, barns, and stables, the troops were soon suffering from typhus. It swept through like a scythe, leaving 12,000 soldiers and over 10,000 civilians dead. Time and again typhus plagued the day's armies: in March and April 1807 the Prussian defenders of the Baltic port city of Danzig (Gdansk) held out until typhus broke their resistance and forced the garrison to surrender to a French force that was little stronger for having suffered the disease as well.

In the summer of 1809, with Napoleon off fighting in central Europe, the British army launched its largest expeditionary force to date. Planners hoped that by taking the Dutch port of Antwerp they could crack the hold that the French had on most of western Europe. Some 40,000 incompetently led British troops landed in the Scheldt River estuary in July. Despite early successes, Antwerp proved unassailable. In late August an epidemic struck the British troops, who were campaigning in the marshy, low-lying area of Walcheren that seemed to produce the miasmas that then-current medical theory blamed for the fevers, and that in fact hosted the mosquitoes that did cause them. "Walcheren fever" has been identified as a mix of malaria, typhus, **typhoid**, and **dysentery**. Despite the campaign's failure, the army remained in place until late winter 1810, by which time

16,000 men had sickened, and 60 officers and 3,900 soldiers had died. Deaths caused by battle wounds or injuries were about 100. This disaster prompted a Parliamentary inquiry and major changes at the Army Medical Board.

The main British effort to thwart “Boney” was in Spain and Portugal, during the Peninsular Campaigns. The usual diseases dogged both sides, and even yellow fever played its part in 1810. Late in the year, after unsuccessfully testing British Gibraltar, the French laid siege to Cadiz, which was filled with refugees from the surrounding countryside. Soon the fever broke out in the city, sickening thousands and killing 2,788. Had it been during the warmer months, the effect would have been far deadlier. Including the famous victory at Waterloo in 1815, in the quarter century of wars against the French, British armed forces lost about 240,000 men. Of these, roughly 30,000 died as a result of battle and 210,000 succumbed to disease.

Napoleon’s greatest assault, and his greatest defeat, was his invasion of Russia in the summer of 1812. Perhaps as many as 600,000 French, Polish, and other allied troops marched across Russian Poland and toward Moscow. The conditions in the Russian Polish territories were dreadful, and the men contracted any number of diseases including typhus. What supply line there was was hampered by the Russians, and their practice of “scorching the earth” left little in the way of food and other necessities. One estimate has 10 percent of the French force dead or fallen along the way before the enemy was engaged. Napoleon’s victory at Borodino was won with fewer than half of the remaining French force able to fight, thanks to exhaustion and disease. After the short French occupation of Moscow in September and October, the grueling winter retreat to western Europe reduced the force tremendously. Pneumonia, typhus, trench fever (caused by louse-carried *Bartonella quintana*), and starvation all took their toll. Perhaps only 30,000 men, or 5 percent of the original force remained alive by spring. Many of these, as well as the Russian troops who pursued them (who lost around 60,000 men to disease in the process), brought typhus with them into what is now Germany, from Danzig in the north—where a Russian siege from January to May 1813 resulted in 11,400 French military and 5,592 civilian deaths from typhus—to Bavaria in the south, which wisely established **cordons sanitaires** and **quarantined** the retreating French.

Retreating ahead of his army, Napoleon returned to Paris, raised a new army of half a million men by early summer 1813, and unleashed an unsuccessful campaign in Central Europe. 105,000 of these men would die in battle, and another 219,000 of disease. After their defeat at Leipzig in October, the French left over 100,000 wounded and sick in and around the town of Freiburg, whose normal population was closer to 9,000. Typhus was rampant, and the impact on the civilian population incalculable. As a result of the French retreat from Moscow, the 1813 French offensive, and the Allies’ push back to Paris that ended in 1814, somewhere between 200,000 and 300,000 Germans lost their lives to the diseases disseminated by Europe’s armies. *See also* Colonialism and Epidemic Disease; Historical Epidemiology; Malaria in Medieval and Early Modern Europe; Plague in the Islamic World, 1500–1850; Thirty Years’ War; Typhus and War; War, the Military, and Epidemic Disease.

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JOSEPH P. BYRNE

NEOLITHIC REVOLUTION AND EPIDEMIC DISEASE. In the Paleolithic period (Old Stone Age), from approximately 30,000 to 7000 BCE, individual small groups of hunters and gatherers led a nomadic existence rather than living in larger groups with other people. This lifestyle and the absence of domesticated **animals** such as horses and cows limited the spread of disease. Most infections in this period occurred as a result of one of several distinct factors: trauma (causing osteomyelitis); zoonotic diseases, animal diseases that spread to humans; or infections acquired by eating, being injured by, or having contact with wild animals and their excreta. In addition, some diseases would have been contracted from the soil, such as anaerobic **bacteria** that penetrate the skin, and tapeworms.

The Neolithic Period (or New Stone Age) in human history occurred in Europe and the Near East from approximately 7000 to 3500 BCE. It was a revolution in both economic and social terms. Primary food sources changed from wild plants and animals, birds and fish, to cultivated plants, such as early wheat, barley, olives, the vine, and domesticated animals, such as pigs and goats. Some animals, particularly bovines, became domesticated for other uses, such as transport.

The development of agriculture fostered, and was dependent upon, the cooperation of large numbers of families who lived in close proximity to each other. There were other consequences such as population growth, craft specialization, and formation of social hierarchies created by a more predictable food supply and its control by elites. The development of agriculture also resulted in poorer, carbohydrate-rich diets and consequent undernutrition that led to less individual resistance to infection.

Disease. Disease began to play an important part in Neolithic society soon after the establishment of the earliest settlements between the eighth and third millennia BCE. Although they were scattered rather thinly and the population lived in relatively small hamlets, within a relatively short period after the start of the growing of the first food crops and the start of the domestication of animals and pastoralism, human population would have grown quite dramatically, compared to the previous hunter-gatherer communities living within the same region.

The early development of pastoralism brought with it significant dangers to the human population. Most, if not all, infectious diseases of civilization have spread to humans from the animal population. In prehistory, contacts were closest with domesticated animals, and it is therefore not surprising that many of the infectious diseases common to humans are also recognizable in animals. For example, of what we call the sporadic zoonotic diseases, **smallpox** is almost certainly connected with cowpox, and **influenza** is shared with pigs and birds; other zoonotic diseases include **measles** and mumps. These new pathogens, however, did not appear to spread at once. Some of these sporadic zoonoses transmitted from domesticated animals remained occasional and dormant until proto-**urbanization** created the conditions for them to spread and sustain crowd **transmission**. However, survivors of **epidemics** began to acquire sophisticated immune systems, and tolerance was developed to parasitic worms. However, as people moved around, it became a disaster for any newly exposed population.

The change from hunting and gathering to primitive farming was not entirely detrimental to health, as a number of factors became firmly balanced. With the beginning of farming, some stabilization of general health likely occurred, with the return of female longevity back to the norm that existed during the earlier hunter-gatherer period. This eventually created an excess of survivals over deaths in the very young, and a population increase ensued. The ending of a nomadic existence meant less stress on women during pregnancy, and postnatal adjustment and genetic adaptation of each population to endemic infections would have occurred. Most of the pathological conditions that existed in these periods would have been related to the creation of more stable communities and the formation of permanent villages. Their establishment meant that people began to live in poor conditions and in very close proximity, so that hygiene suffered and individuals were exposed to an increasing number of disease organisms.

Early forms of Neolithic social organization may have created dietary and sanitary codes, some of which might be recognizable today, that would have reduced risk of infection, but it was not just worms and other parasites that flourished in the favorable conditions created by agriculture for their spread among the human population. Protozoan, bacterial, and viral infections also had an expanded field as the human population, together with their flocks and herds, grew. However, it is only when communities become large enough, where encounters with other individuals become frequent enough, and when people lived in close proximity in poor, unhygienic conditions, that the infections brought about by these microorganisms spread. Many diseases need relatively high population densities in order to thrive and were quite insignificant to hunter-gatherer bands in early prehistory, becoming significant only with the development of permanent settlement, farming, and subsequent population nucleation. In fact, the earliest forms of settlement in small agricultural communities involved new risks of parasitic invasion. Increased contact with human excrement that accumulated in proximity to living quarters allowed for a variety of intestinal parasites to thrive.

Urban centers that first developed toward the end of the Neolithic period and then spread into the ensuing Bronze Age, made few if any arrangements for sanitation. The inhabitants would, as a rule, have used the streets and open squares and areas alongside walls for urination and defecation. The consequences of this would have been not only an increase in contagious ova, worms, and other pernicious parasites, carriers of any number of diseases, but also the contamination of supplies of public drinking **water**, such as streams, wells, and cisterns, which would thus have put public health in jeopardy. Other microorganisms would also have contaminated water supplies, particularly where a community had to rely permanently on one source. Plowing soils increased the risk of fungal disease. Stored food was often infected with **insects**, bacteria, and fungal toxins. Also, the existence of closed rural endogamous societies would have had a profound epidemiological effect, as various inherited diseases and disabilities that such inbreeding often produces would have been present.

In some parts of the Eastern Mediterranean and the Near East, for example, irrigation for farming recreated the favorable conditions for the transmission of disease parasites that prevailed in the tropical rain forests from which many of the diseases originally emerged—particularly warm shallow water, in which potential human hosts would provide a more than suitable medium for disease. Amongst them was infection by the parasitical blood fluke that pierced the skin, *Schistoma* sp., which produces **schistosomiasis** or bilharzia. Amongst the most virulent and prevalent of diseases in the period was **malaria**,

particularly infection by the *Plasmodium falciparum*, spread by the female *Anopheles* mosquito. More recent evidence points to the spread of malaria to Europe and the Near East from North Africa as early as 8000 BCE.

The Evidence. The evidence for disease in the Neolithic period, although not plentiful, can be found in the human skeletal remains from excavated cemeteries of the period. Although modern **paleopathology** can only determine incidence of chronic disease, recent work in the field of human ancient DNA (aDNA) may in the future be able to identify or infer other Neolithic disease patterns. At the same time, an understanding of the virulence and prevalence of disease may be achieved through studies of the ancient environment, through the determination of, for example, climate change and land use.

Although the understanding of changes in disease patterns brought on as the result of the Neolithic Revolution is often restricted mainly to Europe, North Africa, and the Near East, many of the societies that existed in other parts of the world such as South Asia and China would have undergone many similar experiences, and many of the diseases that emerged as a result may have become endemic and eventually become many of the pandemics that affected the ancient world in later millennia. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Early Humans, Infectious Diseases in; Environment, Ecology, and Epidemic Disease; Folk Medicine; Human Immunity and Resistance to Disease; Insect Infestations; Smallpox in the Ancient World.

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ROBERT ARNOTT

NEWS MEDIA AND EPIDEMIC DISEASE. Freedom of the press is embedded in the First Amendment to the U.S. Constitution and has since been one of the keystones of the liberal Western ideal. Americans expect their news media to be free from interference by government or other interests, to be unbiased, and to be accurate. However true this might be for major contemporary news outlets in the United States (still defined as daily newspapers and broadcast and cable television), it has hardly been the norm in other times and places. Political parties, churches, governments, and other social and political groups have traditionally published newspapers, and even in free nations like Britain the government-affiliated British Broadcasting Corporation (BBC) long had a monopoly on radio and television. Cable news television, the Internet, and talk radio have opened news reportage to a far wider field than ever before.

The news media could be said to have been born with the printing press in the mid-1450s. In most European countries censorship by the church and/or state was the norm.

In the sixteenth and seventeenth centuries, printers produced cheap handbills and broadsides (posters) warning of **bubonic plague** or providing information about it and about official actions of public note. Prayers and advertisements for patent medicines often accompanied lurid images of dancing skeletons or funeral processions. In England and some other countries, printers produced and sold weekly bills of mortality, which listed plague deaths and other fatalities by parish. The dissemination of this government data was vital in a commercial center like London, its trends dictating business as usual or upper-class flight and economic depression. Cheap almanacs, too, played a role in shaping public response to disease by predicting threatening celestial configurations or weather patterns. As commercial ventures in a crowded market, these contained advertisements and recipes for plague cures and other medicines that were often sold at the same shops where the almanacs were. In England, a markedly political press developed alongside political parties during the civil turmoil of the seventeenth century. The party in power had its newspapers defending plans, personnel, and policies, whereas the opposition sniped and criticized in the pages of its organs.

Newspapers came to America during this period, but without the political tension to sustain a reasonably free—let alone an opposition—press. Boston's *Publick Occurances*, the earliest English language newspaper in America, reported on a **smallpox** outbreak in the colonies in 1690. Fearing public panic, the Massachusetts governor forced the paper to suspend its reports. Three decades later Boston's popular religious leader **Cotton Mather** sparred with the editors of the *New England Courant* over their coverage of another outbreak of smallpox. A reasonably free press has to keep a steady balance between fact and speculation, and between the public's "right to know" and the potential for panic and social disruption.

Governments shape this balance by withholding or releasing definitive information on disease: during the early stages of plague epidemics in Marseilles, France, in 1720, and in Moscow in 1770, the respective governments downplayed or even denied reports of plague through the press, lest foreign countries suspend trade, and residents flee. Newspapers debated the merits of war and peace, of various public policies for dealing with **cholera**, of contagionism and **miasma** theory, of **germ theory**, and the merits of **vaccination**.

America's newspapers in the nineteenth century were usually tied either to political parties ("Republican" and "Democrat" are still in the names of some newspapers, whereas "Tribune" denoted the people's protector and advocate) or commercial interests. Papers shaped their coverage of **epidemics of yellow fever** and cholera with these interests in mind, often sensationalizing their reporting with lurid details and ethnic stereotyping to build circulation. William Randolph Hearst's (1863–1951) "yellow journalism" that beat the drum for war with Spain in the mid-1890s was as much about emphasizing the threat of yellow fever as it was about the early cartoon "Yellow Kid." When plague hit San Francisco in 1900, the local press followed the lead of the California governor, denying the presence of plague and openly undermining public health officials' efforts to contain the spread of the disease. At the same time, the press in New Orleans stood foursquare behind its city's claims of plague and anti-plague efforts; this support resulted in a much shorter and less deadly outbreak. The difference between reactions may lie in the older and more mature New Orleans's previous experience with yellow fever and other infectious diseases.

With the professionalization of journalism in the late nineteenth and early twentieth century, and its key role in the muckraking campaigns of the Progressive Era, journalists

tended to gravitate in favor of government reform and scientific and technological advance. In the wake of general acceptance of germ theory, popular media from magazines to movies to advertisements emphasized the threat of germs and the need to sanitize the home and workplace. **Personal hygiene** products to cleanse the body, refrigerators to preserve food safely, and window and door screens to keep insects out were the mark of the modern family. Coverage of the **influenza pandemic of 1918–1919** had its own local logic, but by and large the government received support for its efforts and thus felt justified in releasing the gruesome details. By the 1920s the *New York Times* set the national tone for what at least appeared to be the objective reporting of verified facts, a far cry from its jingoistic war-mongering of two decades earlier.

Broadcast journalism began with radio, a medium that featured news as a small though important part of its content. In totalitarian states like Nazi Germany and the USSR, the ruling party controlled the radio waves and filtered all news through its own propagandizing lens. In the United States, the large commercial networks—RCA, NBC, and CBS—controlled the dissemination of news over the airwaves. Ironically, it was a fictionalized broadcast, Orson Welles's (1915–1985) 1938 *War of the Worlds*, that demonstrated the medium's potential for creating mass hysteria. Radio brought the terrors of the London Blitz (1940) and the subsequent American involvement in World War II (1939–1945) into American living rooms. Even more intimate were the images that television delivered, beginning in the mid-1940s. Voices and faces carried more weight than mere bylines, and when reporter and gossip columnist Walter Winchell (1897–1972) decided to oppose publicly the **Salk** polio vaccine in the early 1950s, he brought a great many Americans with him. The major problem with broadcast journalism was its necessarily shallow and narrow coverage of the issues of the day. Like radio, television was essentially an entertainment medium, in which even during an hour of news, major health stories competed with local color, sports, and weather. Newspapers and magazines like *Time*, *Newsweek*, and *U.S. News and World Report* were natural media for deeper and more serious discussions of such topics as vaccine successes and failures or outbreaks of new diseases in Africa.

A new wave of important innovations has changed the landscape from the late 1980s. The founding of Cable News Network (CNN) introduced America to the 24-hour news cycle, while satellite linkups could flood the world's televisions with on-the-spot reporting as events unfolded, unmediated by editing. At the same time, the Internet established equally unmediated platforms for news and opinion with no links to “mainstream” media, and talk radio, long relegated to late-night time slots, emerged with its largely populist, libertarian, and conservative slant. Late-night talk radio has long been dominated by Art Bell (b. 1945) and his successors and their attention to news of the weird—which has included emergent and reemergent diseases and other health threats, real and imagined. For more serious students of world health issues, the Internet provides a host of resources, most reliably the reports of the **World Health Organization (WHO)** and the U.S. **Centers for Diseases Control and Prevention (CDC)**.

Emerging or reemerging diseases established themselves in Western media in 1994. **Pneumonic plague in India**, the **hantavirus** scare in America's Southwest, reports of flesh-eating **bacteria**, and magazine cover stories on infectious diseases converged with popular films featuring pestilence. **Drug-resistant** pathogens, **Ebola** fever, global warming, and the notion that a **pandemic** is only a jet airplane ride away fueled anxieties that have remained heated to this day.

In the midst of this cacophony, the traditional print media have found themselves drawn to unwarrantedly deep coverage, as was the case with the 2002–2003 **Severe Acute Respiratory Syndrome** (SARS) outbreak. Media critic Michael Fumento reported in mid-2003 that the disease to that point had killed 801 people and affected about 10 times that number worldwide. Malaria kills over 800 people every two and a half hours, he noted, and tuberculosis more than 800 people every three hours, yet neither disease received even the smallest fraction of articles the *New York Times* devoted to SARS: over 250. The Robarts Centre for Canadian Studies conducted a systematic study of U.S. and Canadian press coverage of SARS, its threat, and its effects. It revealed that the *Toronto Star* led with 556 articles over 91 days, while the *Star*, the *Globe and Mail*, the *National Post*, *New York Times*, and *USA Today* published 1,600 articles on SARS over the period, as many as 25 per day collectively. Fumento blames this “excessive” coverage in part on the hype provided by the WHO and CDC. This coverage sparked incidents of “hate speech” and property crime in Toronto, and analysts estimated that China, where SARS originated, lost some US \$50 billion in reduced trade and tourism. On the other hand, an unprecedented range of voices were recorded, from the “man in the street” to victims, health professionals, economists, businesswomen, and members of advocacy groups.

In developing countries where large portions of the population are susceptible to a range of infectious diseases, the role of the media in informing and educating the people is crucial. Here the radio, **public health posters**, and billboards are often far more important than the Internet or television, and messages need to be tailored to groups differentiated by ethnic identities, languages, **religions**, political alignments, and levels of literacy. Media campaigns urging vaccinations, condom use, or disease screening are often lost to contradictory government assurances or cultural resistance. *See also* AIDS in Africa; AIDS in America; Bioterrorism; Bubonic Plague in the United States; Cinema and Epidemic Disease; Geopolitics, International Relations, and Epidemic Disease; Hemorrhagic Fevers in Modern Africa; Measles, Efforts to Eradicate; Plague in San Francisco, 1900–1908; Poliomyelitis and American Popular Culture; Poliomyelitis, Campaign Against; Popular Media and Epidemic Disease: Recent Trends; Sexuality, Gender, and Epidemic Disease; Smallpox Eradication; Social Psychological Epidemics; Tuberculosis in the Contemporary World; War, the Military, and Epidemic Disease.

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JOSEPH P. BYRNE

NICOLLE, CHARLES JULES HENRI (1866–1936). Charles Nicolle established his place among "plague-hunters" not only with his Nobel Prize-winning demonstration of the louse transmission of **typhus**, but also with his pioneering exploration of the then-novel concept that infectious diseases—like human civilizations—were "born," "grew," and "died." "There will be new diseases," he warned. "This is a fatal fact By the time we become aware of their existence, they will already be . . . adults. They will appear as did Athena, fully armed, from Zeus's brow."

Born to a **physician** and his wife in Rouen, France, Nicolle completed medical school but followed brother Maurice to the recently created **Pasteur** Institute in Paris after growing deafness disrupted his plan to follow his father's path. In 1893 he returned to his hometown in Normandy, leading the local effort to integrate the new science of microbiology into medical practice. In 1902 he was called to direct the Pasteur Institute in Tunisia, then a French protectorate. He held this position until his death in 1936. While in Tunis, Nicolle made important discoveries about the cause, nature, and transmission of diseases from **relapsing fever** and **pandemic influenza** to trachoma and leishmaniasis. He also developed a convalescent serum for measles and a method of improving vaccine manufacture.

Nicolle is best remembered for his work on typhus—a disease long feared, but today largely controlled. By the start of the twentieth century, bacteriology had uncovered the microscopic causes and transmission routes of many diseases. It had not, however, shed much light on typhus. The disease seemed to disappear between epidemics and could not be cultivated in animals. Moreover, it rarely struck Western countries any longer, making its study difficult. Posted in North Africa, near yet outside "the West," Nicolle encountered typhus. During a particularly severe **epidemic** in 1909, he discovered animals (chimpanzees, monkeys, and later guinea pigs) capable of preserving the disease for intra-epidemic study. He used his colleagues' careful epidemiological investigations to single out the louse as the disease's probable vector. Further tests confirmed this hypothesis. In 1928 Nicolle was awarded the Nobel Prize for his typhus research.

Typhus had long been associated with **war**, **poverty**, and famine. The louse was the material link between the disease and its preferred conditions of existence. His discovery, Nicolle noted, explained typhus's disappearance in the West: cleanliness, good **diet**, and relative peace (World War I would challenge, and ultimately support, his argument) held

the disease at bay. Similarly, the continued presence of typhus in Tunisia reflected the extent to which “civilization” had yet to take hold there. Disease, Nicolle concluded, was its own civilization, existing in delicate balance with human civilization. Where humanity’s civilization fell, disease rose. Moreover, disease evolved; consequently, new disease civilizations would emerge—often in the niches humans created. Here, Nicolle set in motion the very “one microbe causes one disease” specificity that became the hallmark of bacteriology. His ideas on the enduring place of plagues in human existence helped shape future thinking on disease ecology. *See also* Bacterium/Bacteria; Influenza Pandemic, 1918–1919; Typhus and Poverty in the Modern World; Typhus and War.

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KIM PELIS

NON-GOVERNMENTAL ORGANIZATIONS (NGOs) AND EPIDEMIC DISEASE. The containment of **epidemics** is often seen as one of the primary public health responsibilities of governments. However, this role of the state becomes severely crippled during sudden natural disasters, civil strife, and **wars**. Even in times of relative stability, the disinclinations or inabilities of governments to address public health problems adequately have left entire populations more vulnerable to epidemics. Under these circumstances, the roles of non-governmental organizations (NGOs) are made more prominent. Historically, members of community bodies like parishes, guilds, and charities, as well as philanthropists and folk medical practitioners, have been the frontline in providing localized relief to the victims of epidemic outbreaks.

By the late nineteenth century, these groups had taken up geographically and functionally broader profiles. Health-based movements in the West had not only developed a greater awareness of the global dimensions of diseases, but they were also increasingly able to project their works beyond their local confines. Along with emergency relief efforts and provision of the latest curative health care, the main emphasis of these groups lay in heightening the urgency in tackling diseases that had become endemic, and therefore less noticeable than sudden epidemic outbreaks. The Rockefeller Foundation—established in 1913 from John D. Rockefeller’s (1839–1937) Standard Oil, the first generation of modern multinational corporations—embarked on a global effort to eradicate **pandemic** hookworm disease as one of its main ideals. Other NGOs with public health-related activities included the **sanitation movements** in their worldwide campaigns for sexual health against **syphilis** from the late nineteenth century until the Second World War. Like the directors of the Rockefeller Foundation, these activists were eager to present **sexually transmitted diseases** as a global pandemic that required urgent and sustained public health responses.

Globally oriented NGOs such as the International Red Cross and the Red Crescent Society and their national counterparts have also been responsible for monitoring public health situations in war zones, where they have especially monitored for any potential epidemics. Humanitarian organizations like the Médecins Sans Frontiers (Doctors without Borders) and Oxfam have been providing emergency mass **vaccination** services as well as medical assistance and temporary freshwater supplies to war-torn and disaster-stricken

areas, the populations of which are more vulnerable to epidemics like **cholera**, **measles**, and **meningitis**. The growing concerns from the late twentieth century over emerging and reemerging diseases are also increasingly reflected in the initiatives of prominent philanthropies with the global **eradication of AIDS** being the core aim of the Bill and Melinda Gates Foundation, and the improvement of effectiveness of responses to pandemics being one of the latest goals of the Rockefeller Foundation.

NGOs are also increasingly involved in supporting health communication, monitoring, and advocacy. A crucial function assumed by the non-state sector in dealing with epidemics is in the area of dissemination of information and updates on epidemiological trends. The popular media, in particular, made its mark during the **Influenza Pandemic of 1918–1919** in reporting news about the spread and public health responses to the virus. On the contrary, in light of heightened censorship as well as severe limitations of resources during the First World War, information being disseminated by official channels about the pandemic was not forthcoming. This function remains crucial in the contemporary era regarding epidemics like **Avian Flu**. Recognizing their influences, governments have even deployed print and broadcast media networks as partners against epidemics. In Southeast Asia, the newspapers and radio programs have been one of the principal portals in spreading preventive health methods against mosquito breeding during periodic outbreaks of **Dengue fever**.

Benefiting from the greater diffusion in knowledge and resources regarding medical matters, NGOs are also playing an increasing part in the field of advocacy in epidemic control and prevention. The principal agendas of these organizations are those of obtaining official recognition of the enormity and extent of the **contagion** and securing greater investment and commitment to improving access to medical treatment for victims. In this respect, AIDS has become the flagship disease for concerned groups. Being an epidemic that affects more vulnerable social and sexual minorities, health-based NGOs are also forming alliances with other interest groups and welfare organizations to amplify further the social relevance of their causes. In Kenya, these coalitions have even been institutionalized on a national basis in the Kenya Aids NGOs Consortium (KANCO), which consists of a wide network of civil society groups. The increasing recognition of AIDS as a regional and international issue is also seen in the establishment of groups like African Council of Aids Service Organization, International Council of Aids Services Organisations, as well as the Global Health Advocates (devoted to reduction of **tuberculosis**, **malaria**, and AIDS).

Although advocacy groups have frequently been either ignored or given official lip service commitments by governments, no one could dismiss the evolving watchdog function of the **World Health Organization (WHO)**. Known before 1945 as the League of Nations Health Services, one of the primary duties of WHO is to monitor the spread of infectious diseases. Its importance was heightened during the **Severe Acute Respiratory Syndrome (SARS)** pandemic in 2003. Suspicious of the attempts of national governments to downplay the severity of the spread of the disease, countries and societies relied upon WHO inspectors for the final word. In turn, the latter's official position became crucial for governments in restoring political stability and investment confidence shaken by the SARS outbreak.

Given current trends, it is likely in the near future that the presence of NGOs will prove to be crucial simultaneously at the local, regional, and global levels in dealing with epidemics. *See also* AIDS in Africa; Bioterrorism; Capitalism and Epidemic Disease;

Colonialism and Epidemic Disease; Human Papilloma Virus and Cervical Cancer; Irish Potato Famine and Epidemic Disease, 1845–1850; Malaria in Africa; Measles, Efforts to Eradicate; Medical Ethics and Epidemic Disease; Pharmaceutical Industry; Poliomyelitis and American Popular Culture; Poliomyelitis, Campaign Against; Religion and Epidemic Disease.

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LIEW KAI KHIUN

NURSES AND NURSING. Today, nursing is the largest health-care profession, and it accounts for the greatest proportion of direct care during sickness. Good nursing care is especially important during **epidemics**. A nursing tradition developed during the early years of Christianity when the Church established a benevolent function of tending the sick. At this time, deaconesses cared for the sick poor, particularly during epidemics. Another account of nursing comes during the third century when a religious group of men called the *parabolani* brotherhood cared for victims of the **Plague of Cyprian** in the Mediterranean area. The religious ethos of charity continued with the rapid outgrowth of monastic orders in the fifth and sixth centuries and extended into the Middle Ages, when **typhus** and **bubonic plague** were particularly lethal. Monasteries added hospital wards, where “to nurse” meant to give comfort and spiritual sustenance. Religious nursing orders, such as the Knights of St. Lazarus in Jerusalem who cared for victims of **leprosy**, often established specialty hospitals for the sick. Historically, men have had important roles in nursing and predominated in medieval nursing in both Western and Eastern institutions. It was not until the seventeenth century when the French priest St. Vincent de Paul (1580–1660) challenged this model that religious orders of women became more prevalent. After the Reformation, secular nurses replaced religious women as nurses in Protestant countries such as England.

The epidemic-stricken cities of the mid-nineteenth century in the United States needed hospitals and nurses immediately. During the **cholera** epidemics, however, nurses were especially hard to find. Cholera nursing was dirty and dangerous, and religious congregations of

women often filled the gap. Private and religious benevolent societies also developed a system of caring.

Times of **war** historically have been associated with epidemics such as cholera, **measles**, and **influenza**. The Crimean War was particularly influential on modern nursing when, in 1854, Englishwoman Florence Nightingale (1820–1910) and 38 nurses went to hospitals in Turkey and Crimea, where soldiers were sick from cholera and typhus. Nightingale established a record-keeping system, a series of sanitary reforms, and a nursing model that emphasized ritual, discipline, and skill that led to improvements in both military and civic hospitals. During the American Civil War, more soldiers died of disease than in battle. Lay women and religious sisters worked in military hospitals, on hospital ships, and on the battlefield. Their influence as nurses in reducing mortality was a critical event in changing public perceptions of nursing. During the Spanish American War, a third of the U.S. soldiers in army camps became ill with **malaria**, **typhoid fever**, **dysentery**, and diarrhea. Whereas male army nurses initially cared for the sick, during the Spanish American War a large cadre of female graduate nurses served. This war benefited from the nurse training school movement modeled after the Nightingale system that had begun in the United States after the Civil War.

Reform in nursing education during the early twentieth century focused on discipline and special skills. Nurses caring for victims of epidemics took temperatures, pulses, and respirations; provided skin care; used ice baths for fevers; provided comfort measures; and assisted with feeding. They bathed patients, changed linen, gave medications, and prepared and administered food for special diets. They kept the sick room clean and well ventilated and prepared **corpses**. Visiting nursing originated at the end of the nineteenth century in the United States, and typhoid fever was a common condition. Because of the potential for complications, including sudden death, care demanded the whole range of nursing knowledge, including treatment of delirium and management of emergencies such as hemorrhage. Visiting nurses were also an integral part of the public health crusade against **tuberculosis**. They provided physical care; carried out isolation procedures; and instructed patients and families about rest, sanitary measures, the control of sputum, and prevention of the spread of disease. They had to nurse across barriers of class, **race**, and language, and their work was hard and risky.

Beginning in the twentieth century, nurses were at the center of epidemic response teams. During **Walter Reed's yellow fever** experiments in Cuba, American nurse Clara Maass (1876–1901) died after she volunteered to be bitten by an infected mosquito. Through the Red Cross, nurses responded to the Armenian massacre in 1915 and led anti-typhus campaigns across Siberia in 1918. One of nurses' greatest challenges came during the **influenza pandemic of 1918–1919**. In an era before **antibiotics**, **physicians** could do little with their therapeutic regimens, but nursing care could provide hydration, warmth, good nutrition, and fever reduction. Chinese Red Cross nurses worked in army camps during World War II and played key roles in the Chinese National Health Administration's anti-epidemic units. Then, in 1948, the **World Health Organization** was established as the United Nations' public health agency. Its work includes combating epidemics, with nurses playing key roles in controlling cholera, tuberculosis, plague, and other diseases.

By 1965 nurses not only taught individuals about preventive measures, but they also screened populations for disease, participated in surveys and registrations, and performed health histories. After 1970 old and new diseases represented a continuing challenge. New strains of tuberculosis developed, and nurses carried out new infection control



Nurse with a child in a hospital, 1870. Courtesy of the National Library of Medicine.

measures while also relying on the standard therapeutic regimens of rest, nutrition, and isolation. All over the world, increasing numbers of nurses are caring for victims of **AIDS**. Through close patient monitoring, mastering new technologies, and translating research into practice, they continue to provide life-saving care. When medical care appears unable to cure AIDS, nurses remind patients and the public that they remain at the center of patient care. *See also* Hospitals and Medical Education in Britain and the United States; Hospitals in the West to 1900; Hospitals since 1900; Leprosarium; Pest Houses and Lazarettos; Religion and Epidemic Disease; Sanatorium; Typhus and War.

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BARBRA MANN WALL

P

PALEOPATHOLOGY. The term paleopathology derives from the Greek words *paleos* (ancient), *pathos* (suffering), and *logos* (study) and is defined as the scientific study of disease in ancient human and **animal** populations preserved predominantly as skeletons or mummified remains. In the present context, the focus will be on human remains and the evidence for infectious diseases as they are the primary, and often sole, source for knowledge of the health of our predecessors.

History and Scope of Paleopathology. Paleopathology as a scientific study was made more widely known by Sir Armand Ruffer (1859–1917), a British **surgeon** working in early twentieth-century Egypt, but the origins of the discipline go back to the Renaissance period of the fifteenth and sixteenth centuries. Self-trained naturalists studied skeletons of extinct animals found in caves and quarries and described the observed pathological lesions and signs of trauma. However, these studies of the strange and curious were largely seen as entertainment. Only with the nineteenth-century advances in medicine and scientific techniques for the investigation of human individuals were their diseases regarded as valuable medical science. Although these early researchers concentrated on interesting individual cases, a shift toward population-based studies was seen during the twentieth century advocated by, for example, the German pathologist **Rudolf Virchow**, and today a more multidisciplinary biocultural approach is the norm, using all available information to reconstruct past population health.

Methodology and Techniques. The **diagnosis** of a specific disease relies primarily on visual macroscopic observations of what is recognized as abnormal or pathological and is based on the knowledge of how diseases affect the human skeleton and other tissues in a modern clinical context. In recent years techniques such as ancient DNA analysis to detect a pathogen's DNA, and histology to observe changes on a microscopic level have enhanced the understanding of our ancestors' sufferings. Radiology is another useful tool, and it has been extensively, but not exclusively, used to study mummified remains, as it is

a nondestructive technique. Key to a potentially correct diagnosis is the careful description of all pathological changes seen in an individual skeleton, as well as a description of the distribution pattern of these changes within the preserved bones. It is important to consider all possible diseases that could have led to the observed changes and distribution patterns (differential diagnosis).

Limitations. Skeletal elements can only react in a limited way to disease by either forming or destroying bone, or a mixture of both. It takes several weeks for the skeletal system to respond to any pathogen infiltration. This means that any acute disease will not be visible in bone because the person died before any bone changes could occur, and the bioarcheologist is usually left with evidence for chronic disease only. In the exceptional case of soft tissue preservation in mummified remains, but also in skeletons, acute diseases such as **smallpox** or **bubonic** and **pneumonic plague** may be observable through the detection of the causative agent's own DNA. Nevertheless, this technique is destructive and cannot at present be applied to study large numbers of individuals. We are therefore largely restricted to macroscopic observations of specific chronic infectious diseases such as **tuberculosis** (TB), treponemal disease (venereal and endemic **syphilis**, bejel, and pinta) and **leprosy**, as well as the so-called nonspecific infectious responses of periostitis, osteomyelitis, and osteitis. These terms refer to the origin within a bone from which the infection derives, whether the periost (tissue covering the outer surface of bone) or a more internal bone structure such as hard cortical (surface) bone or the medullary cavity, where yellow marrow is stored. Different pathogens—for example, staphylococci or streptococci—may cause identical bone changes, hence the name nonspecific infectious disease.

Infectious Diseases and Paleopathology. Tuberculosis, also known as scrofula and phthisis, is probably one of the oldest infectious diseases affecting both humans and animals, and human skeletal evidence for TB in the Old World goes back as far as the fifth millennium before present. TB has affected humans since the beginning of animal domestication, although skeletal manifestations of the disease in archeological populations are rare. It is a disease of civilization, and the increase in TB infections worldwide has been associated with crowded living conditions, poor levels of **personal hygiene**, and **poverty**. Typical bone changes associated with TB are Pott's disease, or abnormal bending of the spinal column as a result of the destruction of vertebra, and destructive joint lesions affecting the large joints such as the hip and knee. Less diagnostic are bone changes to the visceral surface of ribs as these can also occur in nontubercular lung diseases.

However, only 3 to 5 percent of individuals suffering from TB will develop bone changes, and this might be the reason why relatively few cases of the disease have been reported in archeological populations. On the other hand, people may have died before they developed visible bone changes. New diagnostic techniques such as ancient DNA analysis can help to identify individuals with TB even in the absence of bone changes, and in the future more accurate prevalence rates can be expected.

Treponemal disease, or treponematoses, comprises a group of four syndromes: venereal syphilis, endemic syphilis (bejel), yaws, and pinta. Bone changes are absent in pinta, but prolific new bone formation on long bones can be found in the other syndromes. As a result of their similarity in appearance differentiation among the three diseases is difficult, especially in partially preserved archeological skeletons. In historical times venereal syphilis had the most devastating impact on society of the treponematoses because of its ultimately lethal course, and skeletal changes of the tertiary form

of the disease can be seen as stellate (star-shaped) scars on the skull (*caries sicca*), especially on the frontal bone. Again, similar to TB, only 5 to 15 percent of people infected with venereal syphilis will develop bone changes, and a significant proportion of archeological individuals will remain undiagnosed in the absence of any skeletal indicators. It currently remains controversial whether ancient DNA analysis can extract the pathogen's molecular structure.

Equally, the origin of venereal syphilis has been a point of controversy for decades with the Columbian theory favoring the New World as the cradle of the disease, and its dissemination into the Old World resulting from Columbus's travels. However, skeletal remains with evidence for venereal syphilis from the Old World have been dated to the pre-Columbian period. It appears that the disease was present worldwide even before its devastating effects on war-torn late fifteenth- and sixteenth-century Europe where it went hand-in-hand with deprivation, poverty, and prostitution.

Similarly to venereal syphilis, leprosy has provoked strong negative reactions in the noninfected: during the medieval period, people suffering from the disabling disease were largely confined to leprosy hospitals or **leprosaria** and stripped of their worldly possessions. Skeletal changes resulting from leprosy have only been studied since the mid-twentieth century, and the geographical source of the disease still remains somewhat unclear, but is likely to have originated from the Indian subcontinent. The currently oldest unequivocal skeletal evidence for leprosy comes from individuals found in Egypt dating to the second millennium BCE, but not until the medieval period do the numbers of skeletons with evidence for the disease increase. However, only 5 percent of individuals suffering from leprosy will show bone changes, and because the diagnosis is based largely on the distribution pattern of bone lesions, the disease might be missed in incompletely preserved archeological skeletons. Furthermore, leprosy is a disease that progresses slowly, and individuals might have died before bone changes could develop.

Nonspecific infections have been observed in skeletons worldwide, and population-based studies demonstrate an increase in chronic infectious diseases during the **Neolithic Revolution**, with the onset of agriculture and a sedentary lifestyle and subsequent increasing population numbers. For example, chronic maxillary sinusitis, visible as new bone formation on the inside of the maxillary sinuses, became more prevalent in societies with high rates of air pollution and crowded living conditions, where cross-infection could easily occur.

Although paleopathology is unable directly to diagnose acute infectious disease in skeletal remains, demographic studies may reveal periods of increased mortality. For example, mass burials discovered in the city of London and dated to the years of bubonic plague epidemics in the fourteenth century show a specific demographic profile. Here members of society were present indiscriminately, and not only the most vulnerable such as young children and elderly adults. *See also* Black Death: Modern Medical Debate; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Early Humans, Disease in; Historical Epidemiology; Syphilis in Sixteenth-Century Europe; Urbanization and Epidemic Disease.

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TINA JAKOB

PAN AMERICAN HEALTH ORGANIZATION. See International Health Agencies and Conventions.

PANDEMIC. See Epidemic.

PANSPERMIA THEORY. Panspermia is the theory that the origins of life on Earth are extraterrestrial. Proponents of panspermia believe that the seeds of life, in the form of spores, microbes, or pre-biotic compounds (life's building blocks), exist in space and, once introduced into the planet's atmosphere, developed into terrestrial life. Some modern-day advocates of the theory further contend that the bombardment of earth by organisms from space continues and is sometimes responsible for outbreaks of disease.

Panspermia, a Greek word that literally means "seeds everywhere," was coined in the fifth century BCE by the philosopher Anaxagoras (c. 500–428), who claimed that the universe was filled with *spermata* (seeds) that blossomed into life when they reached the earth. Modern proponents of the extraterrestrial origin of life, also known as exogenesis, have included Lord Kelvin (1824–1907), Svante Arrhenius (1859–1927), and Sir Francis Crick (1916–2004), co-discoverer of the DNA's double helix structure. The most active modern champions of panspermia have been two astrophysicists, Sir Fred Hoyle (1915–2001), founder of the Institute of Astronomy at Cambridge University, and his student, Dr. Chandra Wickramasinghe (b. 1939), director of Cardiff University's Centre for Astrobiology in Wales.

Concerning the great **influenza pandemic of 1918–1919**, Hoyle and Wickramasinghe noted that the outbreak seemed to have multiple points of origin and that remote regions such as small Alaskan fishing villages were struck despite their isolation. Persuaded that human contact alone could not account for the extremely rapid and unusually extensive spread of the disease around the world, they argued that the **pandemic** was caused by **viruses** that had originated in interstellar space, entered the earth's atmosphere as cometary dust, and later rained down from the stratosphere, a view almost universally dismissed by experts on the pandemic. More generally, they charted a correlation between influenza epidemics and increases in sunspot activity, hypothesizing that increased solar activity results in increased levels of cosmic dust containing flu viruses entering earth's atmosphere. The two have also attributed specific outbreaks of **Legionnaires' disease**, **polio**, and mad cow disease to extraterrestrial pathogens.

Supporters of panspermia have sought to link the development of new diseases to microbes from space, as when Dr. Hoyle proposed that **AIDS** was introduced from outer space. In 2003 Dr. Wickramasinghe and two colleagues published a letter in the prestigious British medical journal, *The Lancet*, suggesting that the corona virus responsible for

the SARS epidemic in China was extraterrestrial in origin. They cited the high altitude of the location of the initial outbreaks of the disease and the frequency of meteor showers in that region, and predicted, incorrectly, imminent independent outbreaks of SARS as more of the virus made its way from the stratosphere to the surface. Like other claims linking terrestrial disease to extraterrestrial pathogens, this proposal was rejected by the greater research community.

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TERESA LESLIE

PARACELSIANISM. Paracelsianism is a historical movement or system of ideas and practices that takes its name from texts ascribed to the sixteenth-century German doctor Theophrastus Bombastus von Hohenheim, called **Paracelsus**. Few were printed during his lifetime, but he left a wealth of unfinished manuscripts behind him as he traversed Europe. Publication of these began in earnest during the 1560s, and by the end of the century, most of his medical and philosophical treatises were in print, as were a number of spurious alchemical and magical books published under his name, making identification of Paracelsus's real voice problematic. Few of his religious treatises were published before the twentieth century, but these circulated widely as manuscripts and fed the growing desire for further reformation espoused by the Rosicrucians and pietistic religious groups inspired by Paracelsus's medical and religious ideas.

Paracelsians viewed the cosmos as having been created by the Judeo-Christian God as described in the first book of the Bible, *Genesis*, which they interpreted as a series of chemical separations of specific kinds from chaotic primeval matter. All subsequent natural causes and effects were likewise chemical, from the actions of planets on the organs of the body to the operations of drugs and diseases. The use of chemically prepared, sometimes highly toxic medicines was widely associated with Paracelsians in the sixteenth century, but soon adherents of other medical theories also began to use chemical drugs, rendering the simple association of "chemical" with "Paracelsian" problematic. In practice, even Paracelsian **physicians** were eclectic, drawing on whatever therapeutic methods they, their mentors, and their patients believed effective.

Although not oriented particularly toward epidemic diseases, Paracelsian medicine found favor against dangerous and intractable diseases such as **leprosy, epilepsy, bubonic plague**, and other "fevers," a broad classification that encompassed many infectious and acute diseases. Chemically concentrated toxic metal salts, which act quickly to provoke the desired vomiting, urination, and cleansing of the bowels were readily adopted by physicians and patients as an alternative to drawn out dosing with unconcentrated herbal remedies, depleting diets, and bloodletting.

Paracelsian philosophical, therapeutic, and religious ideas ran contrary to the basic tenets of university teaching at a fundamental level, discouraging the adoption of Paracelsian medicine in the medical schools and the guilds or colleges of physicians. As

a result, Paracelsians were most visible as itinerant healers, **surgeons**, and physicians serving as personal physicians to Europe's kings and princely courts. Consequently, they attained a visibility and cultural influence beyond their numerical strength and precipitated a hostile reaction by traditional academic physicians and theologians, who saw in Paracelsus's writings the seeds of social discord and medical malpractice. Many Paracelsians were Protestants, some with radical and pietistic sympathies that brought them into political conflict with the Catholic Church and universities. Similarly, as Protestant orthodoxies hardened, Paracelsians found themselves increasingly labeled heterodox within Lutheran and Reformed regions. The name Paracelsus remained controversial until it was rendered impotent with the passage of time and the introduction of yet newer physical, medical, and metaphysical principles in the Enlightenment. *See also* Apothecary/Pharmacist; Empiric; Humoral Theory; Medical Education in the West, 1500–1900; Scientific Revolution and Epidemic Disease.

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JOLE SHACKELFORD

PARACELSUS (THEOPHRASTUS BOMBAST VON HOHENHEIM; 1493–1541). Paracelsus, perhaps best known as an alchemist and seeker of the mythical Philosopher's Stone (which was supposed to turn lead into gold and cure all diseases), was also an early contributor to several modern sciences, including chemistry, biochemistry, pharmacology, and toxicology. Though a firm believer in **astrology** and **magic**, Paracelsus was one of the first Renaissance **physicians** to reject openly the Galenic **humoral theory** and to recognize the usefulness of chemical compounds in treating disease, thereby raising the status of alchemy and encouraging its transition into chemistry and its medical application, iatrochemistry.

Paracelsus probably took his classical nickname ("Greater than Celsus" the Roman medical writer; a common practice among Renaissance scholars) while studying medicine at the University of Ferrara around 1515. Although not a true humanist himself, Paracelsus embraced the humanist philosophy of learning directly from experience and seeking knowledge from the world around him. Whereas university-trained physicians in sixteenth-century Europe generally relied on classical authorities for their knowledge of medicine, Paracelsus rejected their texts out-of-hand, teaching his students and readers that all useful medical knowledge should be gained through the experience of treating patients and traveling.

Paracelsus's constant wanderings helped spread his reputation across Europe and the Middle East as both a miraculous healer and a conjuror of demons. Although not the most infamous alchemist of the sixteenth century—a German named Johann Faust (c. 1480–1540) claims that title—Paracelsus nonetheless made his name by discovering "occult" (hidden) knowledge previously considered off-limits. He gained much of this

knowledge by separating, isolating, and recombining chemical elements and compounds, primarily in an effort to identify remedies for specific diseases. As Paracelsus held that illness was caused by faulty alchemical processes within the body—rather than by an imbalance of Galenic humors—he reasoned that a physician could compensate with an appropriate dose of an accurately prepared chemical remedy.

One of the best diseases to which Paracelsus could apply his theory was the newly emergent **syphilis**, for which classical texts like Galen's provided neither explanation nor treatment. Aside from periodic recurrences of the **bubonic plague**, syphilis was one of the most virulent public health threats of the sixteenth century, and the disease generated many innovative cures. Paracelsus championed the use of a mercury compound (*essentia mercurialis*), despite its often lethal consequences, while denouncing as **quacks** the proponents of the ineffective but popular and less deadly guaiac, an extract of a New World tree.

In 1529 Paracelsus wrote two works in 11 volumes on the “French disease” (syphilis) in an attempt to revolutionize medical practice in the context of this terrible **epidemic**. Although these works (like the rest of his books) proved too ambitious, idiosyncratic, and combative to achieve this goal in his lifetime, Paracelsian treatment of disease through chemistry was to find many adherents in subsequent generations. *See also* Medical Education in the West, 1100–1500; Medical Education in the West, 1500–1900; Paracelsianism.

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CHRISTOPHER RYLAND

PASTEUR, LOUIS (1822–1895). The French microbiologist and chemist Louis Pasteur is, with German biologist **Robert Koch**, one of the founders of bacteriology and **immunology**. Pasteur was born in Dôle, France, and studied in Paris at the École Normale Supérieure, where he showed promise as an artist but soon turned to science. In 1849 he was appointed acting professor of chemistry at the University of Strasbourg. From 1854 to 1857 he was professor of chemistry and dean of sciences at the University of Lille, eventually returning to the École Normale Supérieure as administrator and director of scientific studies. In 1867 the Sorbonne appointed him professor of chemistry. His own microbiological research center, The Pasteur Institute, was inaugurated in Paris in 1888.

From his early work on crystals, such as those of tartaric acid, a product in the fermentation of grapes, Pasteur proceeded to examine the process of fermentation itself, a topic that would provide him with important background information and methods for his later research on contagious diseases. Yeast had been thought to be a chemical structure that served as a catalyst in the conversion of sugar into alcohol, but Pasteur discovered that yeast was organic matter, feeding on sugar and thus producing alcohol. When wine soured, it simply indicated the presence of the “wrong” kind of microorganisms. Pasteur conducted numerous experiments to prove his point, also examining the souring

of milk. In 1857 he discussed this latter problem in his famous report on lactic acid fermentation.

Pasteur's discoveries raised the question of how these microorganisms entered the fluids. There existed at the time a belief in "spontaneous generation," which meant that microorganisms could come into existence without parental organisms. Pasteur proved, however, that nothing would happen with a fermentable fluid when surrounded by sterile **air**. As soon as "regular" air was brought in contact with the substance, microorganisms began to develop. Hence, he concluded that air contains spores of microbes.

The next step for Pasteur was to examine the problem of contagious diseases that seemed to spread through direct or indirect contact. Could microorganisms possibly cause these as well? There had been **germ theories of disease** for a long time, yet they could not be proven until Pasteur's day. Pasteur was aware of these theories and in 1857 became convinced that microorganisms might also be responsible for infectious diseases. Though at first it was only a theoretical concept, in the mid-1860s Pasteur began to work on an actual problem: he was asked to examine a deadly disease of the silkworm, which threatened to ruin the silk industry in France. By the late 1860s Pasteur had identified two different silkworm diseases and the microbes that were responsible for them. Even though in the middle of his investigation Pasteur suffered a stroke that left the left half of his body permanently paralyzed, he continued to work. Indeed, already as a young student he had been convinced that it "means a great deal . . . to have will power; for deeds and work always follow the will."

But his findings did not have an immediate effect, as many physicians did not think that a link existed between the ailments of the silkworm and those of human beings. In 1876 and 1877, however, Pasteur showed that microorganisms were the cause for a disease in higher animals and human beings: anthrax. At about the same time, Robert Koch came to the same conclusion. In 1877 Pasteur published a study on anthrax, a paper that became a significant document in supporting the germ theory of disease.

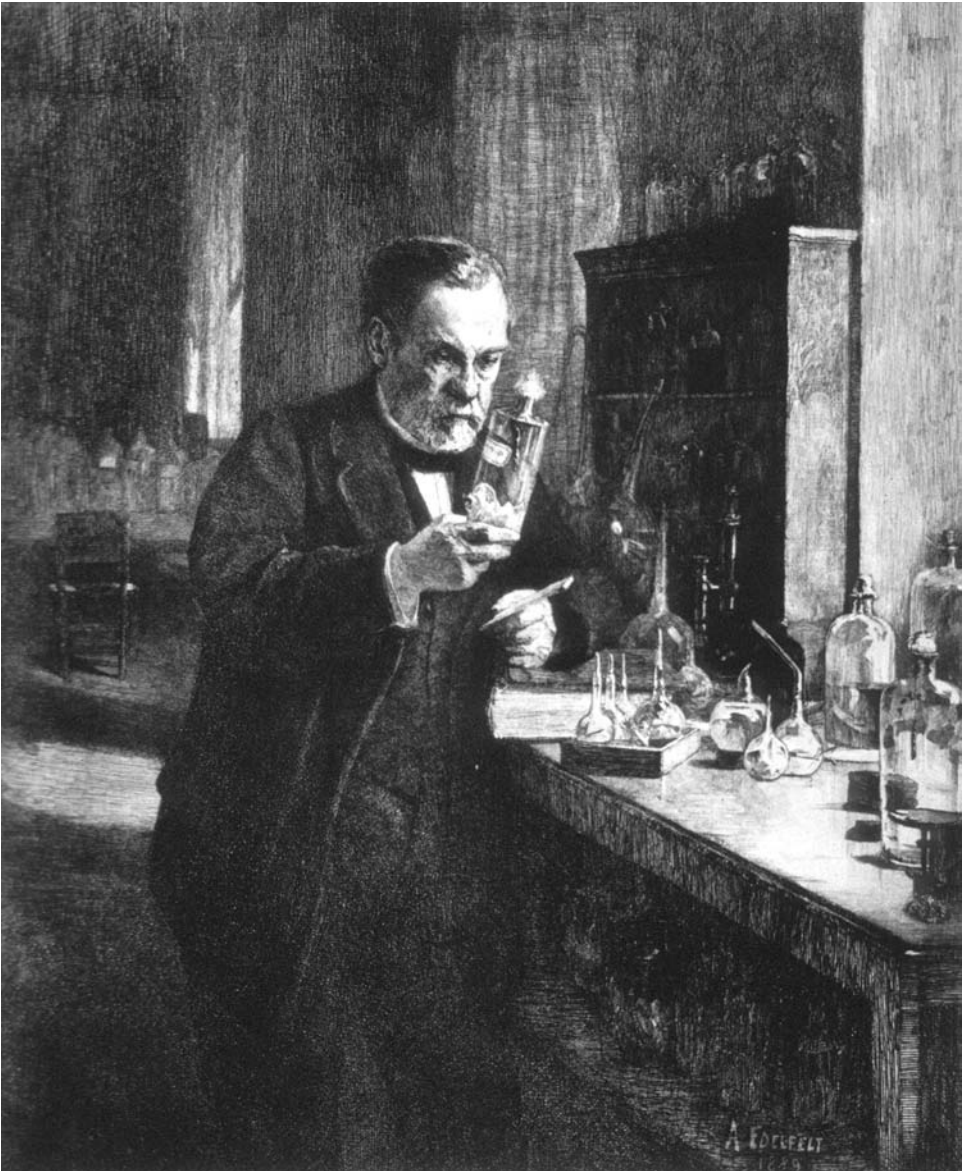
Pasteur applied the methods he had used in his experiments with fermentation to prove that anthrax **bacteria** spread the disease. These experiments showed that no matter how often an infected substance was passed from animal to animal, anthrax bacteria continued to multiply and thus remained potentially as deadly as in the blood of the first infected animal.

Once he had established these facts, Pasteur wondered what could be done to protect human beings and higher animals from those often-deadly diseases. He thus became interested in the concept of **vaccination** that had first been applied by the English physician **Edward Jenner**. Pasteur realized that a germ can change and consequently can actually be used as a vaccine. He first experimented with the problem of fowl **cholera** in chickens and found that some cultures of microorganisms did not cause the disease and instead made chickens resistant against virulent cultures in the future. Pasteur became convinced that it would be possible to produce vaccine in the laboratory. He proceeded to create a vaccine against anthrax, the effectiveness of which he demonstrated in a well-publicized demonstration in 1881. However, his anti-rabies treatment is usually cited as Pasteur's greatest triumph. In July 1885 he successfully treated the first human being, Joseph Meister, a boy suffering from rabid dog bites.

If Pasteur were alive today, he might be worried that we depend on techniques directed against microorganisms above all. Indeed, Pasteur taught that many other factors might have an effect on the course of an illness, such as the hereditary constitution of a patient,

his/her nutritional state, his/her emotional equilibrium, the season of the year, and the climate.

Even before the opening of The Pasteur Institute, Pasteur had many students who would make important contributions to microbiology. Today The Pasteur Institute is a private nonprofit foundation with about 20 establishments on five different continents. Research is focused on fighting infectious viral, bacterial, and parasitic diseases such as



Dr. Louis Pasteur. Courtesy of the National Library of Medicine.

AIDS. It has produced eight recipients of the Nobel Prize; its distinguished alumni include **Alexandre Yersin**, a French doctor of Swiss extraction who discovered the bacterium that causes **bubonic plague**, *Yersinia pestis*, which was named after him. See also Contagion Theory of Disease, Premodern; Microscope.

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ANJA BECKER

PENICILLIN. Penicillin was the first to be discovered of the important class of drugs called **antibiotics**, which are chemical substances produced by microorganisms (or sometimes now synthetically) that destroy or inhibit the growth of other microorganisms. Penicillin acts by interfering with the synthesis of cell walls in **bacteria**, causing them to rupture. Because **animal** cells are enclosed by membranes rather than walls, they are not affected by this process.

British scientist Alexander Fleming (1881–1955) discovered penicillin almost accidentally at St. Mary's Hospital in London. While investigating the staphylococci bacteria in 1928, he noticed that one of the culture plates on which he was growing the microorganism was inadvertently contaminated by a *Penicillium* mold and that no bacterial colonies were growing in the area immediately surrounding the mold. Fleming reasoned that the mold was excreting a substance that inhibited the growth of the staphylococci. He then cultured the mold on the surface of a broth in a flask and filtered off the mold. The broth, which he called "penicillin," exhibited an ability to inhibit the growth of a variety of bacteria, including some that caused serious diseases. Fleming published his results in 1929, suggesting that penicillin might prove useful as a topical antiseptic for humans that could be applied locally to wounds or infected areas. He did not propose its use as an internal therapeutic agent to combat infectious diseases in the body. Fleming and others attempted to isolate pure penicillin from the broth, but these efforts proved unsuccessful.

The introduction of penicillin as an effective therapeutic agent was accomplished at Oxford University. While researching the literature on the enzyme lysozyme, also a discovery of Fleming's, Ernst Chain (1906–1979), working in Howard Florey's (1898–1968) laboratory in 1939, read Fleming's paper on penicillin. The Oxford workers became interested in penicillin and eventually isolated it in a purer form. Toxicity tests revealed that penicillin was not harmful to experimental animals. In 1940 the Oxford group showed that mice injected with a deadly strain of streptococci bacteria survived if treated with penicillin. Clinical trials with humans in 1941 also yielded results indicating that penicillin promised effectiveness in the treatment of a number of infectious diseases.

Substantial amounts of penicillin would be needed for the extensive clinical trials required to confirm the promise of the early results and to provide adequate supplies of the drug for therapeutic use if it proved effective. In 1941 Florey tried to interest Americans in large-scale production of penicillin. Recognizing that penicillin could play a vital role

during the war, the U.S. government eventually coordinated federal research laboratories, academic institutions, and pharmaceutical companies to increase production of the drug. Penicillin production began to increase dramatically by early 1944, jumping in the United States from 21 billion units in 1943 to 1,663 billion units in 1944. The American government eventually removed all restrictions on its availability, and by March 15, 1945, penicillin was available to the consumer at the corner pharmacy.

Penicillin was a true wonder drug, much more potent against infectious diseases than any previously discovered chemical substance. In 1945, Fleming, Florey, and Chain shared the Nobel Prize in Medicine or Physiology for their discovery. The drug also opened up the door to the “era of antibiotics.” Penicillin and its variations remain important substances in today’s pharmaceutical arsenal against disease. *See also* Antibiotics; Pharmaceutical Industry.



Equipment used for making early forms of penicillin; glass flasks and leads into tops of milk-churns. Wellcome Library, London.

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JOHN PARASCANDOLA

PERSONAL HYGIENE AND EPIDEMIC DISEASE. Until the eighteenth century, hygiene, Greek for “health,” was concerned with the preservation of health and prevention of illness through personal attention to lifestyle. The theoretical basis of hygiene changed when epidemic disease ceased to be assigned to individual susceptibility or the supernatural and became associated with dirt and germs.

Classical Hygiene Transformed. In the Classical tradition, individuals could protect themselves against epidemic disease through attention to their **environment, diet,**

sleep, exercise, evacuations, sexual activity, and peace of mind. Hygiene manuals such as the *Tacuinum Sanitatis* (fourteenth/fifteenth centuries) offered advice on what constituted good **air**, food, and **water**, when to undergo purging or bloodletting, and how to recognize pestilential localities. There were debates as to whether epidemics were spread by **contagion** (physical contact) or miasma (foul air). People, where possible, tried to avoid both. Nevertheless, within this “clean living” philosophy, domestic and bodily cleanliness played little part. In Europe, public bathing declined from the Middle Ages as it became associated with prostitution, while private bathing was considered dangerous because it opened the pores to pestilential air. Clothing was brushed or sponged rather than washed, infestation with lice and parasites was common, and there were varying standards of waste disposal. When Charles II (r. 1660–1685) and his court fled from London to Oxford during the plague of 1665, for example, their excrement was left under the carpets. Other cultures’ practices contrasted with those of Europe. Dutch travelers of the seventeenth century were amazed to witness Africans of the Guinea coast washing their bodies, wiping themselves after defecating, and burning their excrement. By the nineteenth century, however, westerners perceived themselves as clean and the rest of the world as dirty. In the wake of the great **cholera** epidemics, Edward Morse (1838–1925), an American writer, saw the filth of the Orient as a menace to Europe.

The new emphasis on personal cleanliness from the eighteenth century had social as well as medical origins. French nobility, in particular, adopted cleansing rituals as a move toward civilized manners. This Old World gentrification quickly spread to the New World. In the nineteenth century, bathtubs, washbasins, and flush toilets were given their own room in wealthy homes, and cleanliness became a sign of good breeding. The unclean, namely the poor, were deemed socially unacceptable. William Buchan (1729–1805), a Scots physician, was among the first to associate the poor with dirt, disease, and danger to others. In *Domestic Medicine* (1769), he suggested that putrid fevers were caused by uncleanness amongst the inhabitants of overcrowded houses who breathed bad air and wore filthy clothes. It was insufficient, he claimed, to be clean oneself, if dirty neighbors spread infections afar. An editorial of 1777 in *The Pennsylvania Packet*, edited by Benjamin Franklin (1706–1790), warned of infectious miasmas arising from perspiration-soaked linen. In England, a Commission for Enquiring into the State of Large Towns (1844) reported that dirt and epidemic disease were inseparable. Furthermore, epidemics caused **poverty** because they killed male breadwinners.

Better Health through Cleanliness. With **germ theory** and the discovery of **bacteria** by **Louis Pasteur** and others in the later nineteenth century, dirt became the visible manifestation of the hidden agents of epidemic disease, and cleanliness the first line of defense in preventing infection. City authorities built public baths, and immigrant groups added their own, such as Russian Vapor Baths and Turkish Baths. In London, by 1912, there were over 3 million annual visits to public baths and washhouses even though many health reformers maintained that the poor “liked dirt.” Homemade soaps prepared from lye or “potash” and fat, or natural soap from plants such as soapwort (*Saponaria officinalis*), were replaced by commercial products. Pears’ soap, created in the 1790s by London barber Andrew Pears (b. 1770), was fiercely marketed in the United States by Thomas Barratt (1841–1914). In the north of England, William Lever (1851–1925) built a “hygienic” town, Port Sunlight, on the proceeds of selling Sunlight



Teacher showing students how to file their fingernails as part of the regular training in personal hygiene in Miss Kniberg's class at the Avon Avenue School, Newark, New Jersey. Courtesy of the National Library of Medicine.

soap. Lever Brothers exploited new fears of germ-spreading to promote their Lifebuoy “**disinfectant**” soap. An American advertisement for Lifebuoy urged “Daddy” to wash off “dangerous city dirt” before touching his loved ones. From 1919, all soldiers in the U.S. Army were compelled to use Lifebuoy. The work of Sir Joseph Lister (1827–1912) on antiseptics and the emphasis on **hospital** cleanliness were powerful examples for personal and domestic hygiene. The British household bleach Domestos claimed to kill all known germs. The use of dentifrice, toothbrushes, and mouthwashes such as Listerine (named after Lister) spread through western society. Toilet paper was marketed in the 1880s, and cotton underclothes largely replaced the infrequently laundered woolen and flannel garments.

From 1882, pupils in French schools were taught how to wash and use the toilet. In the United States, schools and health officials conducted crusades against diseases like **tuberculosis** by emphasizing the preventative power of personal hygiene. Children earned badges for completing health chores and took home instructions in cleanliness. After about 1910, public health campaigns in the United States switched their emphasis from public sanitation to personal hygiene, particularly in areas of high immigration. Metropolitan Insurance, for example, ran an immigrant campaign with the slogan “A bath a day keeps sickness away.” In 1927 big soap manufacturers including Lever Brothers,

Palmolive, and Colgate founded the Cleanliness Institute with headquarters in New York City. The Institute produced pamphlets such as *Better Health through Cleanliness*, aimed at health and social workers, and *The Cleanliness Journal*, which advised on presenting the cleanliness message. Twentieth-century handbooks of personal hygiene (now defined as the science of preserving and *improving* health) prioritized soap and water in the prevention of epidemic disease.

Epidemic diseases began to decline before the advent of effective vaccines and **antibiotics**, largely because of improvements in personal and public hygiene. Today, in countries with limited hygiene resources, diarrheal diseases cause 1.5 million deaths a year. In 2007 the *British Medical Journal* conducted an international survey to determine the greatest medical breakthrough of the past 160 years. Sanitation, the handmaiden of hygiene, was the undisputed winner. See also Children and Childhood Epidemic Diseases; Early Humans, Disease in; Ectoparasites; Greco-Roman Medical Theory and Practice; Insects, Other Arthropods, and Epidemic Disease; Leprosy, Societal Reactions to; Plague and Developments in Public Health, 1348–1600; Public Health Agencies in Britain since 1800; Public Health Agencies, U.S. Federal; Sanitation Movement of the Nineteenth Century; War, the Military, and Epidemic Disease.

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CAROLE REEVES

PERSONAL LIBERTIES AND EPIDEMIC DISEASE. As long as disease was seen as a product of nature (**miasma**) or the supernatural (planetary conjunctions or divine will), the individual played a minor role (perhaps angering God by sinning) in disease causation or **transmission**. Once **physicians** suspected human agency—however unwitting—societies quickly took measures to eliminate or at least reduce the threat of the individual to the social fabric. Such measures often, if not always, encroached upon personal liberties. Over time they ranged from requiring a health pass for travelers to burning a victim's goods to locking one up in a pest house or exiling one to a leper colony. A society facing an epidemic must strike a balance between traditional societal freedoms (however vague or limited) and reasonable public activities to lessen the threats posed by disease. The restrictions on the few have long been thought to safeguard the health of the many.

Loss of personal liberty is clearest when one who has, or is suspected of having, a disease is forcibly removed from the stream of everyday life. Those who suffered from **leprosy** (Hansen's Disease) were often set apart from larger society. From Ancient Israel to contemporary Japan and China, societal authorities have ostracized these disease victims. Depending on the place and time period, lepers were driven from villages, provided a life

in local **leprosar**ia and care for their disabilities, or sent across country to leper colonies, where names were changed and past identities shed. During the **Black Death** and subsequent plague **epidemics**, one of the Latin West's coping mechanisms was to isolate plague victims, often shutting them inside their own houses along with healthy family members. Though supported with food and other supplies from charity or the public coffers, no one could leave until the victim had recovered or had been dead a fixed time, and all others had a clean bill of health. The family's residence would then be scrubbed down, and goods and furnishings suspected of harboring plague would be fumigated or destroyed. Though medieval and early modern societies had a clear understanding of neither germs nor **contagion**, they acted very much as though they did.

Plague hospitals and **pest houses** were alternatives to shutting in. Though the victims were still forcibly isolated, family members were either left alone or temporarily quarantined to determine the state of their health. During epidemics such facilities were notoriously overcrowded, understaffed, and unbelievably filthy. Though many inmates in fact survived, condemnation to a pest house was tantamount to a death sentence. Even with more modern and sanitary conditions, the issues of forced institutionalization remained; the life of "Typhoid" **Mary Mallon** is an excellent case in point. Although **sanatoria** for people with **tuberculosis** had first developed as voluntary hotels for the well off, during America's Progressive Era in the early twentieth century, sanatoria were increasingly controlled by the state, and victims of TB underwent mandatory institutionalization.

From the last third of the fourteenth century, authorities in port cities and other vulnerable points along frontiers established facilities at which suspect people and cargoes would be forcibly detained for set periods of **quarantine**. Goods were often fumigated or otherwise disinfected, whereas the people were observed for signs of disease. Though developed during plague time, both the isolation hospital and quarantine became common tools in the fight against epidemic disease. Each, of course, also restricted or violated generally accepted rights to live and travel freely. Nonetheless, in the age of **cholera** pandemics during the nineteenth century, few ports administered by Western nations did not have quarantine facilities. Even returning soldiers found their voyages home delayed by mandated quarantine.

Other travel restrictions included closed city gates, **cordons sanitaires** along national borders or within cities, and mandatory health passes, which proclaimed the good health of the bearer. Again, plague prompted these measures, and they constitute some of the earliest provisions for international cooperation on public health matters. Today, nations reserve the right to deny entry to those suffering from, or believed to be suffering, from certain infectious diseases, and the questionable practice of "profiling," or giving special scrutiny to people from certain countries or with certain backgrounds, is used as a means of screening. Unrestricted access to the United States across its borders, especially that with Mexico, has long invited immigration by people who have not been screened for infectious diseases. Fears of violating immigrants' supposed human rights have hindered efforts to identify and screen these people, many of whom find themselves in the food services industries. The perceived threat of global bioterrorism has also heightened the sense of insecurity and increased levels of restrictions on passengers and cargo.

With the development of prophylactic vaccines, humankind took a huge step toward effective control of infectious diseases. Early epidemiologists understood that

for vaccines to protect a population, a certain threshold percentage (always less than 100) of that population had to receive the vaccine to induce effective “herd immunity.” Mandatory **vaccination** was the best way to insure high compliance rates, but over the past two centuries, many population groups balked at being forcibly immunized. Does accepted understanding of personal rights include that to refuse to allow infective material to be injected into one’s body? Anti-vaccination campaigns developed around state efforts to control **smallpox, polio, measles**, and in the mid-2000s, the vaccine to prevent **cervical cancer**. The state argues that public safety warrants enforced immunizations, and that after suspension of required immunizations, the diseases in question quickly rebounded dramatically. Critics usually question the effectiveness and safety of the drugs or refuse on biblical or other religious grounds or on the grounds of one’s right to one’s own person. Ironically, staunch British opposition to mass vaccinations in the 1890s led to a policy of surveillance, containment of outbreaks, and targeted vaccinations, the very model used by the **World Health Organization** in successfully eradicating smallpox in the 1960s and 1970s.

One source of opposition to mandated medical procedures is the experience with unscrupulous or **human subjects** testing. Blacks in America hold a righteous grudge against medical researchers for their roles in the infamous Tuskegee syphilis studies from the 1930s. Some Black activists have voiced concerns that **AIDS** was planted in their communities by the CIA and that drug testing was really part of the plot. The use of disease patients for uninformed drug testing is clearly unethical, but it was carried out under totalitarian regimes. Prisoners, too, though protected by international conventions, have been forced to undergo medical experiments with more or less legitimate goals. In European colonies, native sufferers from such diseases as **sleeping sickness** and leprosy became test subjects for numerous drugs and other treatments, the power differential between native and colonial doctor providing wide latitude. Historians have also looked critically at the attempts by Christian medical aid workers to convert stricken animists or Muslims under their care. In the tight confines of medical facilities where does the right to proselytize cross the patient’s right to be comforted rather than threatened with eternal torments or enticed with eternal life? On a larger scale, rights to conduct religious practices unmolested have been suspended many times in the face of public health threats. European plague laws restricted gatherings for liturgies and processions, including funerals. Colonial laws tried to regulate Indian rituals in sacred rivers and control the spread of disease during **pilgrimages**.

Finally, sexually transmitted diseases (STDs) have presented important challenges to the balance of civil rights and public health. In general, one has a right to privacy regarding his or her health, medical treatment, or medication. If one presents a threat of exposure of an infectious disease to a community, then investigators may very well ascertain past contacts in order to warn them of possible exposure. When an STD is the issue, then the contacts will have been sexual contacts, the identification and contact of whom present major issues of confidentiality. Because these might include cases of adultery, underage sexual contact, or homosexuality, officials tend to treat these with the greatest concern for privacy. Because of its association with homosexuality, AIDS advocates traditionally resisted standard reporting of the cases. Around the outbreak of AIDS in America there also swirled other controversies, not least of which was that of the gay bathhouses in cities like New York and San Francisco. These facilities played a unique role in urban homosexual community life, yet the contacts made there could be life-

threatening. Some shut down voluntarily; others were closed by order of the authorities. AIDS activists saw this not only as a violation of property rights, but also of the right of free association. Protests led to the reopening of many of these bathhouses, which many consider to be a contributing factor to the resurgence of AIDS among American homosexuals from the mid-2000s.

The history of the relationship of public health and personal freedom is riddled with examples of resistance and rebellion. History tells of inmates of pest houses in Italy, France, and Russia who rose up and fled their noxious setting, terrorizing the healthy countryside beyond. In Manila, The Philippines, in 1937 hundreds of lepers broke out of San Lázaro leprosarium and marched on the Presidential Palace for better living conditions. In the same year, 1,100 Japanese lepers in an island colony rebelled, beating their guards and going on hunger strike for better conditions.irate neighbors burned down plague hospitals, and a Russian mob rioted at the removal of religious images during the last of Moscow's plague epidemics. *See also* AIDS in Africa; AIDS in America; Black Death, Flagellants, and Jews; Colonialism and Epidemic Disease; Human Subjects Research; Irish Potato Famine and Epidemic Disease, 1845–1850; Leprosy in America; Leprosy, Societal Reactions to; Medical Ethics and Epidemic Disease; Poison Libels and Epidemic Disease; Poliomyelitis and American Popular Culture; Public Health Agencies, U.S. Federal; Race, Ethnicity, and Epidemic Disease; Religion and Epidemic Disease; Sexual Revolution; Trade, Travel, and Epidemic Disease; Tuberculosis in the Contemporary World; Venereal Disease and Social Reform in Progressive-Era America.

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JOSEPH P. BYRNE

PERTUSSIS. See Whooping Cough.

PEST HOUSES AND LAZARETTOS. Before the development of **germ theory**, the **contagion theory of disease** had a vague but powerful hold on Western notions of public health. It certainly seemed that people developed the same diseases as those with whom they had come into contact. Isolating the sick from the healthy seemed a reasonable response, especially when a plague or other widespread outbreak of disease was in the neighborhood. Long-term isolation of those suffering from Hansen's disease (**leprosy**) in monastery-like **leprosaria** or lazarettos had been practiced for centuries before the fourteenth century. The **Black Death** prompted shorter-term accommodations for those suffering through the plague (*peste* or a variation in most European languages). Rather than spending years under medical supervision, as in well-run leprosaria or later **sanatoria** for long-term respiratory disease patients, the resident of the pest house (*Pesthaus*, *pesthuis*) or lazaretto (*lazaret*, *lazzaletto*, lazar house; the term was appropriated from that for a leprosarium) was expected to die or (less likely) recover from the disease within a week or two. Unlike a **quarantine** facility, which housed for a set period of days those suspected of having a disease, the pest house warehoused the obviously sick and dying.

During late medieval and early modern plague epidemics, isolating the sick from family and neighbors could mean running them out of town, shutting them up in their own houses, or providing isolation quarters—pest houses or plague hospitals—at public expense. Besides being unbearably inhumane, chasing the sick out of town only threatened the countryside. Shutting up the sick may have been what saved Milan from the ravages of 1348, and it was systematically practiced by Duke Gian Galeazzo Visconti (1351–1402) in that city-state in the 1390s. Generally the entire family was thus enclosed with its sick members, and public funds provided food and guards until either all died or the survivors had lasted an expected period of time. Almost always an option of the wealthy and powerful, critics noted the hardships this practice placed on the less well-off family. In *Journal of the Plague Year* (1722) English novelist Daniel Defoe (c. 1660–1731) has his protagonist rail against the monstrous cruelty of shutting in, in favor of well-run and plentiful pest houses.

Hospitals were features of most European cityscapes, and in times of epidemics, they could serve to isolate and care for the stricken. In most cases, other residents were removed during the crisis. Monasteries, too, were appropriated by local governments or donated by religious orders as plague facilities, as was the case in seventeenth-century Barcelona, Spain, and Prato, Italy. Invariably, the demand for space outstripped its supply, and otherwise clean, sanitary quarters devolved into chambers of horror. Contemporary visitors recorded the sights, sounds, and smells that assaulted their senses. The emotional numbness of the caregivers and the corpse-haulers made them seem demonic to some observers, who noted that this was a foretaste of hell itself. During heavy outbreaks, in the precincts of hospitals developed shantytowns of shacks and even simple lean-tos in which the suffering were placed.

Pest houses proper eventually supplemented or replaced ad hoc arrangements as part of more or less concerted attempts at protecting public health. One of the earliest known dates to the late 1300s and was at the Venetian Adriatic colony of Ragusa (Dubrovnik), on the island of Mljet in an abandoned convent. In 1429 the Venetian government supplemented it with a purpose-built pest house at Supetar. The Venetians had their own tem-

porary structure in 1403, which they replaced with a permanent lazaretto in 1424. This also served as a maritime quarantine facility. In plague time this *Lazaretto Vecchio* (Old) quickly filled, so the *Lazaretto Nuovo* (New) appeared in 1468. Even so, in the winter of 1576 carpenters had quickly to build 1,200 huts in the Arsenal shipyard to accommodate the flood of sufferers. Like a leprosarium, a proper pest house or plague hospital might be spacious and laid out like a church; in Catholic areas an altar would be located at the crossing so all could see. Milan's San Gregorio Lazaretto, completed in 1524, consisted of a porticoed square of 288 connected 15 by 15 foot rooms around a huge open space in the center of which was a raised altar for services. The horrors of human misery met with even in such a large and well-planned facility were described by visitors and famously by Italian novelist Alessandro Manzoni (1785–1837) in *I promessi sposi* (1825–1827).

A well-planned facility would include a graveyard, quarters for personnel, and separate quarters to serve survivors who were past the acute stage and recovering (convalescing). By the seventeenth century, a typical small pest house would be provided with at least a surgeon or two, a physician when possible, and some female caregivers and male body-carriers. Their salaries were provided by the public treasury, as were food and medicines. They were usually isolated at the site and died in great numbers. To some lazaretto patients had to bring their own bedding, though charity and administrators' ingenuity usually served to provide such necessities. In some places, officials provided patients upon release a fresh suit of clothing and a small bit of cash, because their clothing and household belongings would have been incinerated in their absence.

When **bubonic plague** subsided in the eighteenth century, the pest house remained to isolate the sufferers from other acute and contagious or supposedly contagious diseases such as **smallpox**, **yellow fever**, and **cholera**. American "pest houses" were often both quarantine facilities and isolation quarters for those with infectious diseases. Philadelphia had a famous pest house at Lazaretto Station, built in response to an outbreak of yellow fever in 1799. The site served as a cargo and passenger inspection site and quarantine station, and one estimate claims that one-third of all Americans' ancestors arrived through this facility. New York City's residents established their first pest house with funds dedicated to it and a medical school that would eventually become Columbia University's School of Medicine. To deflect the stigma attached to leprosy, New Orleans's nineteenth-century leprosarium was known as "the pest house." Across North America and England, one still finds place names linked with "Pest" or "Lazaretto," and many local historians know of old or demolished buildings that once served to isolate sufferers of cholera, smallpox, or **influenza**. *See also* Disinfection and Fumigation; Hospitals in the West to 1900; Leprosy, Societal Reactions to; London, Great Plague of (1665–1666); Personal Liberties and Epidemic Disease; Plague and Developments in Public Health, 1348–1600; Plague in Europe, 1500–1770s; Plague Literature and Art, Early Modern European; Public Health Boards in the West before 1900.

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JOSEPH P. BYRNE

PESTICIDES. Pesticides are substances or mixtures of substances that are intended to kill, prevent, or repel arthropods or other pest organisms such as rodents. Humans have been using pesticides developed using herbal remedies since antiquity. For example, it is believed that ancient Egyptians used specific herbs to kill the aquatic snail hosts of human **schistosomiasis**.

Because pesticides are designed to kill or repel living organisms, there is always the risk of harm to humans, animals, and the environment. Any pesticide can be harmful if used improperly. In the United States, pesticide use is strictly regulated by the Environmental Protection Agency and various state agencies. Pesticides benefit humans by killing organisms that can transmit diseases to humans and animals or damage food or fiber crops. Pesticides such as rodenticides are beneficial because they target hosts in the life cycle of human pathogens (e.g., rats with oriental rat fleas that transmit **bubonic plague**). However, the overuse of pesticides can cause populations of target organisms to develop resistance because all individuals surviving the application of a pesticide will produce offspring that are all resistant to the pesticide and to other pesticides in the same chemical family.

Pesticides can be classified as either natural or synthetic. Natural pyrethrum, derived from finely ground chrysanthemum flowers, has been used as a pesticide for at least 2,000 years, though a synthetic version is now available. Pesticides are also classified on the basis of their chemical structure. Inorganic pesticides, which contain no carbon atoms, include arsenicals like calcium arsenate. Most of these have been removed from the market because of their high toxicity in mammals. Silicon dioxide powders that abrade the connective tissues of arthropods, causing them to dehydrate and die, are still in use. The organic pesticides, which contain carbon atoms, are mostly synthetic pesticides. The chemical structure of many modern pesticides was derived from phosphorus-containing organic compounds (organophosphates) developed from chemical warfare agents during World War I (1914–1918) such as mustard gas. Organophosphates disrupt the chemical mechanism by which nerves transfer messages to organs. Some are quite poisonous, but most do not persist in the environment. Carbamates are organic pesticides that also target the nervous system of pests. Most carbamates kill a broad range of pests and have a low toxicity for mammals. Organochlorine pesticides were commonly used in the past, but many have been removed from the market because of their detrimental effects upon human health and their persistence in the environment (e.g., DDT). Rachel Carson's 1962 book *Silent Spring* alerted the American public to the dangers associated with organochlorines. Interestingly, DDT dust is still approved for application to rodent burrows beneath buildings in the southwestern United States where bubonic plague remains endemic. Pyrethroid pesticides were developed as a synthetic version of the naturally occurring pesticide pyrethrin found in chrysanthemum seed coats. Some synthetic pyrethroids are toxic to the mammalian nervous system.

Another way that pesticides can be classified is by their target organisms. Examples include insecticides, herbicides, fungicides, rodenticides, molluscicides (target snails and slugs), acaricides (kill mites), nematicides (target small worms called nematodes), and repellents that repel pests at low concentrations and kill them at higher concentrations.

Over the past century, pesticides have played extremely important roles in controlling epidemic and epizootic diseases that have pests for vectors, including mosquito-borne malaria, yellow fever, and various encephalitis viruses; lice, tick, and flea-borne typhus;

tick-borne Lyme disease; tsetse fly-borne sleeping sickness; and kissing bug-borne Chagas' disease. Though promising new biological control methods have been introduced, pesticides will continue to play an important role in controlling pests for the foreseeable future. See also Animal Diseases (Zoonoses) and Epidemic Disease; Ectoparasites; Insect Infestations; Insects, Other Arthropods, and Epidemic Disease.

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STEVE MURPHREE

PETTENKOFER, MAX JOSEF VON (1818–1901). Max Josef von Pettenkofer was born on December 3, 1818, in the Bavarian town of Lichtenheim, the son of an impecunious peat bog farmer. With the support of his uncle, court **apothecary** to Ludwig I of Bavaria (1786–1868), Pettenkofer entered the University of Munich in 1837, specializing in science. Having excelled in his studies and taken additional courses in medical chemistry, Pettenkofer obtained a position in the Royal Mint in 1845. He researched, among other things, the separation of metals, human metabolic processes, the ventilation of buildings, and the insulating properties of fabrics.

Pettenkofer achieved fame for his work on the **epidemiology** of **cholera** and kindred intestinal diseases. He was by no means the first to apply epidemiological methods to understanding **epidemics**, but his methods were ingenious and exact. He began to study cholera in 1854 when **germ theory** was merely an adventurous speculation. During an epidemic in Bavaria, he compiled a spot-map with which to identify environmental correlates of the disease and to work out whether cholera could be passed directly from person to person. One finding particularly interested him: moist, low-lying areas were most frequently and severely hit.

Pettenkofer measured the level of soil moistness in different parts of Munich and produced graphs showing often tight correlations between high levels of groundwater and cholera morbidity. An 1873 study of an epidemic at the Royal Bavarian prison was widely considered a model for epidemiological research. Such analyses led Pettenkofer to conclude that cholera is caused by a microorganism, called "x," which was a necessary but insufficient cause of the disease. The germ caused sickness only when it produced a dangerous substance, or "z," which required it first to mature in a suitable medium, or "y." The perfect medium was moist soil containing rotting organic matter. A cholera germ could infect a new host only having spent time in damp ground. It did not spread directly from person to person, Pettenkofer concluded.

Pettenkofer's theory brought him into conflict with the leading bacteriologist **Robert Koch**. In 1883 Koch correctly claimed to have identified a specific bacillus in the stools and intestines of cholera victims in Egypt. He then went to Calcutta, India, where he claimed to have proven that this bacterium was responsible for the disease and that it spread from person to person via contaminated drinking **water**. For decades, Pettenkofer and his supporters (especially in British India) argued against Koch's position on epidemiological grounds; he and several students even ingested solutions of the putative cholera bacillus in an attempt to refute Koch's germ theory (they survived after short bouts of diarrhea).

For his opposition to Koch, history has not been kind to Pettenkofer. But in fact he made a very sound attempt at explaining an epidemiologically complex picture. Nor was he entirely incorrect: bacteria might not need to ripen in moist soil, but a correlation with high levels of groundwater is often real and important. Moreover, he helped highlight the insufficiency of Koch's near-exclusive emphasis on the germ: a later generation of scientists, including his student Elie Metchnikoff (1845–1916), would reveal that the germ is only part of the story. Perhaps most significantly, Pettenkofer's arguments about the dangers of drinking water coming into contact with foul soil led to major, life-saving sanitary improvements in Munich.

Feeling sidelined by the imperial German government and devastated by the deaths of his wife and three of his five children, on February 10, 1901, Pettenkofer tragically took his own life. *See also* Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1862–1947; Contagion and Transmission; Demographic Data Collection and Analysis, History of; Environment, Ecology, and Epidemic Disease; Sanitation Movement of the Nineteenth Century.

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JOHN WALLER

PHARMACEUTICAL INDUSTRY. For most of human history, medicines were simple preparations of plant drugs (e.g., infusions [teas], hand-rolled pills, or poultices). Healers gathered the drugs locally or bought them from traders in spices and other exotic goods. By the late Middle Ages, the profession of specialized preparers and sellers of medicines—**apothecaries**—appeared in the West from the Islamic world. Medicine making, however, remained a small-scale affair until the early 1600s. At that time a number of influences inspired change. The discoveries of New World drugs stimulated trade and new thinking concerning therapy. **Paracelsus** and his followers advocated the use of chemicals as medicines in the sixteenth century, a departure from the traditional plants prescribed by the classical Roman **Galen**. Alchemists, who originally sought the “elixir of life” and other substances of transcendental powers, turned to more mundane applications of their techniques opening up the new field of chemistry. Others working with

mining and metals added to laboratory technology. Most important of all, apothecaries picked up on the new developments and began to apply methods in the backrooms of their shops.

In the 1620s, the Society of Apothecaries of London (incorporated 1617) started to produce both galenical (plant-based) and chemical preparations. By 1703 the Society gained the monopoly of providing drugs and medicines to the Royal Navy. In France one of the first great manufacturers was Antoine Baumé (1728–1804). By 1775 his catalog included over 2,000 items and about 400 chemical preparations. In the North American colonies, wholesale druggists usually obtained their drugs from England through London import houses. When the Revolutionary War broke out, the colonists were forced to begin manufacturing medicinal chemicals and preparations to replace those from Britain. Although many of these small manufactories closed after the Treaty of Paris, a few specializing in fine chemicals continued on and formed the basis for the American chemical and pharmaceutical industries. In 1813 J. B. Trommsdorff (1770–1837), founder of the first journal dedicated to scientific pharmacy and industrial chemistry, established an early German factory for drug preparations. Well into the 1800s, however, pharmaceutical manufacturing remained largely a small to medium sized industry. With the exception of milling, machine power (steam engine) did not apply well to most aspects of medicine making, which involved precise hand operations.

A major contributor to the growth of the pharmaceutical enterprise in the eighteenth and nineteenth centuries was the making and selling of secret nostrums, the so-called “patent medicines.” A direct descendent of the panaceas and “cure-alls” of **quacks**, mountebanks, and traveling medicine peddlers, these preparations usually contained harsh laxatives or potent narcotics often in a highly alcoholic vehicle. In an age when trained **physicians** were few and costly, many common folk turned to these remedies for treatment of minor as well as serious ailments. As printing technology improved and the popular press grew, so did advertising for patent medicines, which became a staple of newspapers and magazines. These advertisements in turn helped create a larger demand for medicines that further stimulated the young pharmaceutical industry as a whole.

The development of alkaloidal chemistry in the early 1800s by pharmacists Friedrich Wilhelm Adam Sertuerner (1783–1841), Pierre Joseph Pelletier (1788–1842), Joseph Bienaimé Caventou (1795–1877), Friedrich Ferdinand Runge (1795–1867), and Pierre Jean Robiquet (1780–1840) provided an early incentive to manufacturers. Sertuerner’s discovery of how to extract morphine from opium allowed the marketing of pure constituents from plant drugs in concentrated form. Because the alkaloids were very potent, they required careful standardization, which spurred further scientific inquiries and inspired manufacturers to establish testing laboratories and boast about the purity of their products. By the middle of the nineteenth century, synthetic organic chemistry, stimulated by the making of coal-tar dyes, began to yield new drugs such as salicylic acid (1874), eventually leading to the invention of acetylsalicylic acid (aspirin) in 1898. By the end of the 1800s, manufacturers started to design complex machines that could produce end dosage forms such as sugarcoated pills and filled gelatin capsules in large quantities. Even more importantly, pharmaceutical companies in the late 1800s turned to the production of biologicals such as **diphtheria** antitoxin. The work of **Louis Pasteur**, **Emil von Behring**, and **Robert Koch** captured the imagination of the public who came to see science

as not just a tool to explore the nature of the physical universe but as a weapon against disease. By the end of the nineteenth century, the applications of discoveries in biology and chemistry by German drug manufacturers catapulted that nation into the forefront of medicine production.

The dominance of the German pharmaceutical industry continued from the 1880s until the outbreak of World War I (1914–1918). Up to that time western nations imported large quantities of drugs from Germany that were protected by patents and trademarks. However, after their entry into the war, countries opposed to Germany, like the United States, seized patents and other rights for distribution to their own national firms. In the United States, the greatest prize was the right to sell acetylsalicylic acid under the trade name Bayer Aspirin, which was acquired by Sterling Products in 1918. With the patents in hand, Great Britain, France, and the United States greatly expanded their production of drugs such as procaine, barbital, arsphenamine, and aspirin.

After World War I, Germany's leadership in chemistry helped reestablish its prominence in pharmaceutical manufacturing. In 1932 Gerhard Domagk (1895–1964) discovered the antimicrobial powers of sulfonamide, which inspired the world's pharmaceutical companies to synthesize and test hundreds of related chemicals. This effort led eventually to the discovery of a number of new drug classes (sulfonylureas and thiazide diuretics) that helped expand the international market for pharmaceuticals.

World War II (1939–1945) was a key event in the maturation of the modern pharmaceutical industry. In the United States the Office of Scientific Research and Development fostered programs to find new antimalarials, blood products, steroids, and anti-infective agents. **Penicillin**, initially discovered and tested in Britain, was produced on a massive scale in the United States for the Allies. After the war, the penicillin example drove companies for the first time to spend huge amounts of money on drug research and development. New firms that made related products (baby food, vitamins, **pesticides**) entered the pharmaceutical fields hoping to reap the expected profits.

During the 1950s, the United States became the leader in the international pharmaceutical enterprise. Laboratories poured out new drugs such as tranquilizers, antidepressants, radioactive isotopes, and antihypertensives. Emphasis remained on drugs to combat infectious disease. **Polio** vaccine, introduced in 1955, demonstrated to the public the power of pharmaceutical research and its promise for the future. Modern management methods replaced the old model of family ownership. Large capital investment came into the industry, as did vertical integration.

The reputation and future of the pharmaceutical industry came into question in the early 1960s with the thalidomide disaster. Thousands of mainly European children were born with birth defects caused by their mothers' ingestion of the drug. (The United States was spared by the efforts of the FDA's Frances Kelsey [b. 1914], who held back the drug's approval.) The regulation of drugs changed internationally because of the disaster with new stringent rules about safety and efficacy adopted in many nations. Research in the industry shifted from battling infection to tackling the maladies of the populations of wealthy nations (e.g., anxiety, high blood pressure, diabetes, and arthritis). Moreover, pharmaceutical companies began selling potent drugs (oral contraceptives and hormone replacement therapies) to prevent or treat naturally occurring conditions (pregnancy and menopause). Profits grew dramatically as the demographics of the West shifted to older populations with greater needs for medicines.

In the 1980s, firms applied the emerging tools of biotechnology to develop new drugs. The first successful product was human insulin (Humalin) produced by Lilly in 1982. The massive success of highly advertised therapies such as Tagamet (cimetidine) for stomach problems encouraged the pursuit of “blockbuster” drugs (i.e., those with sales of over \$500 million internationally). In order to market their products widely, pharmaceutical companies led the movement toward economic globalization. International mergers and acquisitions occurred at a fever pitch during the 1990s as much of the world’s medicine production came into the hands of a dozen or so major firms. Conventional drug discovery and development has slowed with fewer innovative products appearing each year. The hope for the future of the drug industry is pharmacogenomics (i.e., adapting therapies to the specific genetic make-up of the patient). If and when this advancement occurs, the nature of the pharmaceutical industry will change dramatically. *See also* Antibiotics; Capitalism and Epidemic Disease; Drug Resistance in Microorganisms; Germ Theory of Disease; Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS); Human Subjects Research; Humoral Theory; Industrial Revolution; Popular Media and Epidemic Disease: Recent Trends; Poverty, Wealth, and Epidemic Disease; Smallpox Eradication; Sulfa Drugs.

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GREGORY J. HIGBY

PHARMACIST. *See* Apothecary/Pharmacist.

PHTHISIS. *See* Tuberculosis.

PHYSICIAN. There is **paleopathological** evidence that during human prehistory, humans assisted their fellows who were injured or disabled. The bones of some prehistoric humans indicate injuries that would have totally incapacitated the individual, but nonetheless display evidence that they healed, with the person living for years following the injury. This could only have occurred with the assistance of others. In even the most primitive society, tribe, or social group, there is usually one individual who is the healer. Before the professionalization of the physician, healers over the eons have been known by many names and titles: shaman, medicine man, wise man, sorcerer, physician, doctor. For our purposes the label physician will be applied broadly at first and later in the narrower sense of one who is a formally educated and professionally accepted medical healer.

Prehistoric Physician. The earliest known depiction of a physician, “The Shaman,” can be found in the cave of Trois Frères in France dating back 17,000 to 20,000 years ago. He is depicted wearing a deer face mask and has attributes of other animals. Animal masks were probably worn to scare away the demons and evil spirits believed to be responsible for causing illness. They also served to impress the patient with the power of the physician.

Ancient Egyptian Physicians. Medicine, **magic**, and **religion** were inseparable in ancient Egypt. The oldest description of medical practices can be found in the medical papyri from ancient Egypt. The most detailed of these papyri were named after Egyptologists Georg Ebers (1837–1898) and Edwin Smith (1822–1906) and were written circa 1550 BCE. They contain medical texts believed to date back to the Old Kingdom (3300–2360 BCE) and describe hundreds of medications, incantations, and magical and religious rituals. The Ebers Papyrus deals primarily with infections and medical conditions, whereas the Smith Papyrus contains case histories of surgery and battle injuries. These were essentially the medical textbooks of the time. Modern physicians are amazed at the advanced stage of medical treatments described in these documents, including many medical treatments that remain valid to this day. Of course, the ancient Egyptian physician/priest/magician could not separate these from spiritual elements, because they were tightly interwoven into their belief system. In a sense, these early physicians had discovered the concept of holistic (mind-body-spirit) medicine. Imhotep, a physician, priest, scribe, magician, architect, and vizier (second only to Pharaoh), is the best-known Egyptian physician and might be called the “Grandfather of Modern Medicine.”

Asian Traditions. **Chinese medicine** developed independently of, but at approximately the same time as, ancient Egyptian medicine. Under the influence of Confucianism (Confucius, 551–479 BCE), medical training, testing, and practice were regularized, and physicians became members of the official bureaucracy. Herbs and acupuncture were integral elements of Chinese medical treatment, and the use of both was developed to a high degree. Further west, Mesopotamian and Persian physicians believed that when the god of death (Nergal) visited humankind, he was accompanied by the plague demon (Nasutat) who had a whole host of lesser demons that caused specific diseases such as jaundice and **tuberculosis**. Treatments and medications were recorded on clay tablets, and many of these tablets have survived into modern times. Sumerian and Persian **surgeons** were hampered by the eighteenth-century BCE Code of Hammurabi: they were well rewarded if they were successful, but if they failed the punishment was severe. For example, if the surgeon performed a successful eye operation he commanded a high fee, but if the patient lost his eye or died, the surgeon’s hands were cut off.

Among the Greeks and Romans. Greek physicians from the fifth century BCE generally followed western medicine originated by the Egyptians, but they continued to improve on medical practices. **Hippocrates**, the “Father of Modern Medicine,” combined his era’s rationalized natural philosophy with medical theory and practice. Hippocrates focused entirely on the treatment of the sick person and completely ignored the healthy one. He devised a method of **diagnostic** investigation based on observation and reason, but his followers’ medical practice relied on the rudiments of **humoral theory**.

Galen, educated in second-century CE Alexandria, Egypt, was physician to two Roman Emperors and treated wounded gladiators. He wrote over 400 essays on medicine, most of which were destroyed by fire, but his surviving works had a profound effect on medical

theory and physicians' practice in the West for some 1,500 years. His championing and development of humoral theory ended up retarding the development of medical science and practice until modern times. Unlike Hippocrates, Galen felt that a physician should first maintain the health of his patient and treat the illness if good health could not be maintained. Though he lived through the Antonine Plague, Galen wrote little that survives on infectious or epidemic diseases.

Celsus (second century CE), a famous Roman medical author, wrote *On Medicine* (*De re medica*), which is the earliest scientific medical text in Latin. Much of what is known about Roman medicine today comes from this work. Dedicated to empirical observation like Galen, Celsus described the four signs of inflammation: rubor (redness), calor (heat), dolor (pain), and tumor (swelling). These signs of inflammation are still taught in medical schools today.

One of the major factors in the fall of the Roman Empire in the West was a series of plagues and **epidemics**. To Roman physicians, the myriad symptoms were confusing, and as a consequence most forms of infectious diseases were categorized as "plague." It is believed that the diseases of **smallpox**, **bubonic plague**, **typhus**, **diphtheria**, scarlet fever, and **cholera** were all included under the diagnoses of plague. Roman physicians were ineffective when faced with these virulent diseases: their medicines and therapies were powerless. In part because of their inability to fight these plagues, the people of the late classical period (300–600 CE) lost faith in physicians and turned away from medicine and science.

Medieval and Early Modern Physicians in the West. The medieval West saw the decline of classical rationalism and scientific thinking and the rise of institutionalized religion (Islam, Roman Catholicism, Eastern Orthodoxy) with its emphasis on the supernatural rather than the natural world. Even so, the sense of charity in Christian and Muslim societies dictated that both religions support the practice of medicine. Galenic medicine all but disappeared in the Latin West, with medical ministrations left in the hands of **folk healers** and monastic *infirmarii*. The classical tradition of professional physicians remained alive in Byzantium, and Islamic cultures adopted Galenic professionalism from the Greeks and adapted it to their own traditions. Throughout the great pandemic of the **Plague of Justinian**, Byzantine and Muslim physicians displayed their inability to prevent the spread of the disease or heal its effects. This seems to have stirred especially Muslim physicians to study and advance Greco-Roman medical knowledge and practice, recording their new observations and techniques in treatises such as **Avicenna's** tenth-century *Canon*. Byzantine and Muslim physicians practiced in **hospitals** and **bimaristan**, respectively, supported by the wealthy, and availed themselves for what we might call private practice. Muslim physicians taught and studied in educational centers in cities such as Baghdad, Cairo, and Cordoba (Spain), whereas Constantinople's secular educational institutions and hospitals trained Byzantium's medical professionals.

Only in the eleventh century did the Latin West again begin producing physicians in the Greco-Roman mold. The first medical school appeared in southern Italy, at Salerno, where Catholic, Byzantine, and Muslim cultural traditions mixed. Within two centuries Church-controlled schools in many cities of western Europe were churning out physicians trained in Galenic humoral theory as transmitted through translations of Arabic texts. While many physicians exclusively served important people such as kings, nobles, and the pope, in towns physicians formed guilds to protect the integrity of their practice and limit competition. What a modern observer would call internal medicine was professionalized

in the medical schools and guilds, and with the exclusion of **empirics**, **quacks**, and even **surgeons** from their ranks. Nonetheless, physicians were helpless in the face of the **Black Death** and succeeding waves of plague; nor could they successfully treat conditions such as **leprosy**, **smallpox**, or **syphilis**, the last of which emerged in the sixteenth century. Nor, until quite late, were physicians generally allowed to serve as public health officials on urban health boards or magistracies, though well-reputed physicians were often asked for advice during times of plague or the threat of plague.

Physicians of the Nineteenth and Twentieth Centuries. Despite the **Scientific Revolution** and the Enlightenment, and the earlier challenge of the medical ideas of **Paracelsus**, Galenism continued to be the dominant medical paradigm until well into the nineteenth century. The first medical school in colonial North America was founded in 1765. At the beginning of the nineteenth century, most medical practitioners in America had never seen the inside of a medical school. They received only tutoring as an apprentice to an older and equally unqualified practitioner. With the rise of industrialization, diseases and plagues were rampant. Epidemics of **cholera**, tuberculosis, **influenza**, **typhus**, **meningitis**, and scarlet fever took many lives, and physicians were unable to fight them adequately. An epidemic of cholera broke out in Europe and caused 52,000 deaths in Britain alone before spreading to America, where it ran unchecked from 1831 until 1833. Around the middle of the nineteenth century, medical advances began to sweep across Western medicine, revolutionizing the medical care that physicians could provide. Names such as **Louis Pasteur** and **Robert Koch** (germ theory), Joseph Lister (1827–1912; sterilization), **Ignaz Semmelweis** (infection control), and Wilhelm Conrad Roentgen (1845–1923; x-ray) became household names and placed medicine on a recognizably scientific pathway. Developments in anatomy, physiology, histology, materia medica (pharmacy), biochemistry, and microbiology enhanced **medical education** and helped create a new breed of scientifically trained physicians. Increasingly, Western physicians were also given extensive training in hospitals to complement their classroom and laboratory experiences. One by one, infectious diseases came to be understood by medical researchers, themselves often physicians. Physicians could now distinguish and diagnose diseases as never before and apply appropriate treatments—or recommend public health measures—that were derived from medical research. Physicians often served as medical missionaries, bringing increasingly effective Western medicine to outposts in European colonies and establishing clinics, hospitals, and eventually training facilities.

As the twentieth century dawned, medical education and the means of successful treatment were making great strides, but with a new century came new challenges. Just as the First World War was coming to a close, the great **influenza pandemic of 1918–1919** descended. During the worldwide flu pandemic, there were an estimated 650,000 deaths related to flu in the United States alone. Physicians were ineffective in stemming the tide of this ravenous disease with their still-meager array of medications. There was, however, a small group of uniquely trained physicians who knew how to use their hands to bolster the body's immune response to fight the virus. DOs (Doctors of Osteopathy), using manipulative therapy and minimal medications, had a rate of effective treatment well above that of physicians using primarily pre-**antibiotic** pharmaceutical medications.

One of the most important developments in the medical profession was its tendency to specialization. Focused curricula and apprentice-like residencies in hospitals allowed medical students and young physicians to acquire true expertise in a wide and still

expanding range of specialties such as pediatrics, obstetrics/gynecology, cardiology, oncology, and tropical and infectious diseases. Spurring this was a growing list of new technologies for diagnosing and treating patients, and an even longer and faster growing list of pharmaceuticals. Professionalization of **nursing** (begun in the nineteenth century) and public health services helped create more stable and predictable working environments for physicians in both developed and developing regions of the world. This has proven to be especially important in areas where infectious diseases are endemic, and social disruptions such as wars and famine create conditions conducive to epidemics and detrimental to regularized health care.

Twenty-First-Century Physicians. As remarkable as the advances in medical science have been over the last 150 years, the twenty-first century promises to dwarf those achievements. Yet there is another worldwide pandemic (**Bird Flu**) looming on the horizon. Medical science has predicted the pandemic, and for the first time in the history of the world, physicians and health authorities from around the globe are amassing the forces of medical science to do battle against this impending pestilence. **Vaccines** and other medications are being stockpiled. Educational programs for the public are being developed, and worldwide communications are available. The battle against epidemic disease may never be won, but medical science and physicians continue working to improve the odds. *See also* Air and Epidemic Diseases; Apothecary/Pharmacist; Ayurvedic Disease Theory and Medicine; Colonialism and Epidemic Disease; Early Humans, Disease in; Hospitals and Medical Education in Britain and the United States; Hospitals in the West since 1900; Medical Ethics and Epidemic Disease; Non-Governmental Organizations (NGOs) and Epidemic Disease; Plague and Developments in Public Health, 1348–1600; Public Health Boards in the West before 1900; Public Health in the Islamic World, 1000–1600; Rush, Benjamin; Sydenham, Thomas.

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THOMAS QUINN WITH JOSEPH P. BYRNE

PILGRIMAGE AND EPIDEMIC DISEASE. According to the medieval English poet Geoffrey Chaucer (c. 1343–1400), in the Middle Ages spring was the season when people longed to go on pilgrimage; but as it turned out, people liked to go on pilgrimage in all seasons and in all times. Indeed, like farming and building, pilgrimage—the act of traveling to a special place for religious reasons—has developed in every society we know of, from the most primitive to the most sophisticated. Nor has modernity damped this longing. In fact, modern communication and transportation has encouraged it; every year many millions of people set out on pilgrimage to destinations all over the world, and most return.

Pilgrims are, hence, travelers and subject to the same medical issues as all travelers; because of the peculiar nature of pilgrimage, however, they also run additional risks. Although traveling is essentially *individual*, pilgrimage is more often a *mass* movement—to a fixed and predetermined place, with route and mode of travel often an integral part of the experience. It is this *mass* element, with thousands or even millions of people journeying to the same place, often at the same time of year, and staying for days or even weeks in crowded conditions, that amplifies especially the epidemic risks of traveling.

A good example comes from Islam. In the last month of the Muslim year, 2 million pilgrims from every continent travel to Mecca, Saudi Arabia. There, they spend weeks in a crowded city and then return home, often together, in packed ships and airplanes. In Varanasi, India, more than 70,000 Hindu pilgrims bathe every day in the holy Ganges River, so running a documented 66 percent risk of contracting and spreading some kind of infectious disease.

Much of the specific effect of the mass movement of pilgrimage on the spread of epidemic disease has to do with the intrinsic health and **personal hygiene** of the pilgrims themselves and with the nature of the pilgrimage sites to which they travel. Much also has to do with the kinds of diseases endemic to their place of departure, to their place of arrival, and to their modes of transportation.

For instance, the classic medieval pilgrimages to Compostella in Spain, to Rome, and to Jerusalem do not seem to have brought epidemics back to northern Europe. One reason was that the way was long, slow, and covered mainly on foot or horseback, thus excluding the most vulnerable; next, the medieval European population was relatively well fed; finally, the most common infectious diseases were not very transmissible. Thus, though

leprosy was indeed brought to Europe by returning Crusaders and pilgrims, its long latency period and relative lack of contagiousness meant that it never amounted to an epidemic. Likewise, although medieval pilgrims did die of **malaria** in Rome, its mode of transmission via mosquitoes did not allow it to flourish in the inhospitable climate (from the point of view of the mosquito) of northern Europe, and no epidemics of malaria related to pilgrimage are recorded.

On the other hand, certain microbes *do* take to a pilgrim lifestyle, especially those that are easily transmissible from person to person. **Cholera** provides a good example. Centuries ago, Indian pilgrims initially carried it with them to Mecca, where it thrived. Later, it migrated to Palestine with returning pilgrims, and there were recurrent cholera epidemics between 1831 and 1918. Similarly, the disastrous cholera epidemics of nineteenth-century England are also thought to have followed a pilgrim route. More recently, from 1984 to 1986, cholera epidemics were documented in Mecca itself, and in 1994 *Vibrio cholera* took its return journey from Mecca back to Southeast Asia, from whence it had originated.

Smallpox, too, which is easily transmitted by fomites, is another classic disease of pilgrimage. In the 1930s, an outbreak in Africa was traced to pilgrims, and the last major epidemic in Europe was carried to Yugoslavia by a pilgrim who had contracted it in Mecca. Meningococcal **meningitis**, which is not only highly contagious but also provokes a carrier rate as high as 11 percent, has been carried to America, Africa, and Asia by returning pilgrims.

Less contagious diseases such as **tuberculosis**, **Dengue**, and **poliomyelitis** have also had documented mini-epidemics traced to the gathering and then dispersal of pilgrims. Upper respiratory illnesses are particularly efficiently spread in this way. For instance, while in Mecca, 40 percent of pilgrims get some sort of viral upper respiratory illness, and pilgrims to Rome have spread **Legionnaires' disease**. Gastroenteritis is also common; in 2003 Norwalk **virus** was spread from Lourdes to nursing homes in France and Switzerland by returning Christian pilgrims.

Yet it is not the case that pilgrimage *must* lead to epidemics. For example, although millions of pilgrims visited Rome during the Jubilee Year of 2000, no epidemics occurred. Why not? Because healthy, well-fed pilgrims, with sophisticated hygiene and appropriate immunizations, are not efficient vectors. This observation suggests that the epidemic risk of pilgrimage could be limited by appropriate public health measures. Thus Saudi Arabia now requires pilgrims to Mecca to show proof of **vaccination** against **yellow fever**, meningitis, and polio. In addition, as a preventative against meningitis, each arriving pilgrim is given a prophylactic dose of ciprofloxacin. Furthermore, to minimize foodborne epidemics, pilgrims are not permitted to bring food with them from outside the country; to minimize respiratory infections, face-masks are recommended. Education on hygiene, toiletry, and spitting, and the provision of adequate housing and nutrition, has also been instituted.

With similar efforts on the part of all cities and states that belong to pilgrimage routes, it is possible to envision a reversal of the ancient linkage between pilgrimage and epidemics. Pilgrims would return home not sicker but healthier than when they left, with a new knowledge of hygiene and immunization. And instead of being a vehicle for epidemics and public illness, pilgrimage would become a vehicle for public health. *See also* Black Death, Flagellants, and Jews; Cholera: Fourth through Sixth Pandemics, 1862–1947; Cholera: Seventh Pandemic, 1961–Present; Religion and Epidemic Disease.

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VICTORIA SWEET

PILGRIMS. See Pilgrimage.

PINK EYE. See Conjunctivitis.

PLAGUE AND DEVELOPMENTS IN PUBLIC HEALTH, 1348–1600. The development of public health, defined as the implementation of specific policies aimed at controlling the outbreak or spread of disease, is generally acknowledged to have begun during the **second plague pandemic** (1348–1772). Europeans' experiences with plague in the fourteenth and fifteenth centuries led them to believe that the disease was passed from infected to healthy persons. Thus, although public health measures across Europe had traditionally included a wide range of sanitation and cleansing efforts, plague also prompted the development of new approaches that aimed to curtail contact between sick and healthy. These included the use of **quarantine**, **pest houses** and convalescent homes, and limitations on the movement of people and **trade** goods.

Fourteenth-century Western medicine was based upon **humoral theory**, which attributed disease to an internal imbalance of bodily humors. In the case of an **epidemic** like the **Black Death**, corrupt or "miasmatic" air created by filth was blamed for inducing such an imbalance, or for poisoning the body. Thus, alongside religious appeals for mercy from God, the earliest responses to plague included efforts to ward off disease through the cleaning and **disinfection** by fumigation of public spaces. Large bonfires burning aromatic herbs such as rosemary were used to purify the air, while renewed mandates on street cleaning and restrictions on dumping trash or offal aimed at reducing potential threats. The practice of trades, such as tanning, that produced noxious odors was banned or restricted to certain parts of town or times of day. As **corpses** accumulated faster than burial traditions could accommodate, concern with miasmas led to legislation dictating how the dead bodies should be collected and buried.

Italy holds a place of prominence in the history of public health, particularly in relation to plague, as municipal officials in a number of city-states, including Venice, Milan, and Florence, developed the earliest administrative bodies specifically charged with overseeing and enforcing public health measures. Over time, these officials helped create the "Italian model" of plague legislation, a variety of public health measures based on emerging notions of contagion designed to protect the healthy by removing or isolating the sick.

As early as 1348, both Venice and Florence had appointed small ad hoc groups of men to oversee health issues, thus establishing the first temporary health boards. These men were principally concerned with internal matters including sanitation and prevention of resale of clothing or bedding owned by the infected. By 1486 Venice made such boards permanent, renewed yearly. In the next century, health boards became permanent fixtures in other cities, including Florence and Milan, creating one of the hallmarks of modern public health.

Outside of Italy, city governments responded to plague outbreaks by creating temporary health committees, often by simply delegating their own members to oversee health meas-

ures. In such cases, officials were advised by medical authorities and relied heavily upon the cooperation of both medical practitioners—**physicians, surgeons, and apothecaries**—and residents to report cases of illness to the proper authorities. Whether a city relied on temporary or permanent officials to oversee public health, however, the overall approach to plague epidemics was the same.

Among the policies implemented by Italian health boards and later adopted by other municipal officials were the use of quarantines, restrictions on the movements of individuals, the revival of isolation hospitals, and the creation of convalescent homes. In 1374 both Genoa and Venice monitored ships' ports of origin and turned away any coming from infected areas. In 1377 Venice's trading colony Ragusa (Dubrovnik) instigated a maritime quarantine, requiring all arriving ships to anchor outside the harbor for 30 days so that authorities could verify that crew and cargo posed no health threat. Later expanded to 40 (*quaranta*) days, perhaps based on the Hippocratic belief that the 40th day distinguished acute diseases from chronic, this quarantine proved successful, and the practice later spread to other port cities. Similar quarantines were subsequently also used by landlocked cities, as travelers and their goods were required to remain outside the gates for up to 40 days to prove their health. This sort of preventive measure was accompanied in many areas by the use of a reactive quarantine—the restriction of infected persons and their families (and often anyone they had been in contact with) to their homes as a means of preventing further spread of disease. Authorities marked the doors of infected homes by various means (a wreath, bundle of straw, horseshoe, or other symbol) and municipal authorities often appointed individuals to act as both guards and provisioners for the shut-ins. In many cities, however, such restrictions were not absolute, as individuals were permitted outside the house either during prescribed hours (when fewer people were in the streets) or with identifying markers, such as a white stick. At the end of the period, a home would have to be cleaned and disinfected or fumigated.

The alternative to confining the infected to their homes was the use of isolation hospitals. Used first by Europeans during the Middle Ages in response to **leprosy**, these institutions, known as **pest houses** or lazarettos, gained new favor in the plague era. Whereas some areas relied upon the use of existing buildings outside city walls, others built new structures, some meant to accommodate thousands of people. At the same time, governments established convalescent homes as a means of continuing the isolation of those no longer in the acute stages of the disease, yet still not considered sufficiently healthy to be released.

In times of plague authorities also implemented further restrictions on the movements of individuals. Principally, this meant shutting some city gates and posting guards at those that remained open. These guards monitored traffic into and out of the city, questioning travelers and often requiring them to carry official papers (a sort of health passport) declaring their place of residence and testifying to their good health. Such travelers, and their goods, were often quarantined outside of city walls for a variable number of days to ensure they posed no direct threat. Beginning with the Duchy of Milan in the late fourteenth century, officials in Italian city-states expanded their control over movement by monitoring traffic not just at city gates, but also along roads, and by setting up information networks to share news of any suspected outbreaks. Here again, Italy was foremost in the creation of communication networks among separate governments (in this case the various city-states), a practice that carried over later into the rest of Europe.

Despite the existence of increasingly centralized monarchies in much of Europe, public health issues continued to be handled primarily by municipal officials. Although England

is often noted for having lagged behind Italy in adopting plague measures based on contagion theory, English monarchs were the earliest in their attempts to legislate national plague policies. The first attempt appeared in 1518, during the reign of Henry VIII (r. 1509–1547). The next set of royal orders did not appear until 1578, a lengthy interval that allowed individual cities in England to devise their own emerging programs of public health. The plague orders of 1578, set forth by the Privy Council under Elizabeth I (r. 1558–1603), provided a standard of response for the local justices of the peace, though one not always easily enforced. The English legislation included the harshest terms of shutting in, which gave confined families no chance for respite or outside contact, and which subsequently engendered strong resistance.

By the sixteenth century, popular reaction to plague restrictions varied with the strength of how tightly they were enforced. In Italy, where the health boards gained a great deal of power, efforts to control the movements of individuals by limiting or canceling festivals, processions, and other cultural traditions that brought large numbers of residents into close proximity were met with strong resistance from the people. In these city-states, public health regulations easily shifted to become social control measures, aimed particularly at the poor, at beggars, and at prostitutes. Similarly, England's strict confinement laws raised objections, especially from victims and physicians. In other areas of Europe, however, there is evidence of greater cooperation between residents and officials. In Seville, for example, though municipal officials utilized many of the same restrictions as elsewhere, they also allowed residents the opportunity to gain exemptions from restrictions under controlled circumstances. In this way, officials were often able to diffuse resentment or tensions caused by public health controls. *See also* Contagion Theory of Disease, Premodern; Cordon Sanitaire; Environment, Ecology, and Epidemic Disease; Leprosarium; Personal Liberties and Epidemic Disease; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500; Public Health Boards in the West before 1900; Public Health in the Islamic World, 1000–1600.

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KRISTY WILSON BOWERS

PLAGUE: END OF THE SECOND PANDEMIC. The **Second Plague Pandemic** began with the **Black Death** (1347–1352) and is widely believed to have initiated a cycle of recurring **epidemic** disease in Europe that lasted for the next 400 years. In both Europe and the Middle East, the recurring epidemics were frequent to the point that every year since the beginnings of the **pandemic**, plague was raging somewhere. The sudden

disappearance of plague from northwestern Europe after about 1650 is therefore extremely puzzling for historians and has led to a number of different theories based upon the nature of the disease itself, public health measures, and historical developments.

During the period between the sixteenth and mid-nineteenth centuries, a cooling period known as the Little Ice Age began. **Bubonic plague**, widely accepted as the cause of the recurring plagues of the Second Pandemic, is a bacterial disease that occurs naturally in rodents and thrives among black rat (*Rattus rattus*) populations. The inception of the Little Ice Age may have been enough to decrease the presence of the black rat in Europe, and perhaps affect its fleas (*Xenopsylla cheopis*), which transmit the plague **bacterium** from rats to humans. Supporting this theory is the relative lack of plague activity during the 1640s, which was the coldest period of the Second Pandemic. Throughout the Second Pandemic, plague was generally less active during winter months so it seems likely that cooler global temperatures could have contributed to the end of plague. However, because temperatures have always been frosty in northern Europe, which was no less plague ravaged than any other region, this theory is debatable.

If rats were the carriers of the plagues of the Second Pandemic, then the most likely culprit is the black rat because it lives in close proximity to humans, travels frequently by stowing away on ships and other transportation, and was most likely present in large numbers in Europe and the Middle East during times of plague. It has been suggested, however, that black rat populations dwindled prior to the disappearance of plague. One theory is that the brown rat (*Rattus norvegicus*) was introduced to Europe in the eighteenth century and gradually became the dominant species, edging out its less robust cousin. Because the brown rat does not live in close proximity to humans as the black rat does, the likelihood of transmission of infected fleas is less likely, thus decreasing the chance of human plague. However, since the introduction of the brown rat seems to have occurred after the disappearance of plague from Western Europe, and the two species seem to coexist quite happily, this theory has been largely discredited.

Another suggestion is that improved housing left the black rat homeless. For instance the reconstruction of London after the Great Fire (1666), which occurred a year after the ravages of the **Great Plague of London** (1665–1666), may have robbed rats of their former homes within the city, which were replaced by new, less habitable structures. This theory is weak, however, because housing improvements were not universal throughout early modern Europe, and only London was purged by fire.

On a wider scale, the rat population may have been culled by the increasing use of arsenic as rat poison in the late early modern period, as suggested by contemporary historian Kari Konkola. However, because it is quite difficult to control rats effectively by poison, and because other rat poisons had been available before arsenic, it is unclear whether such a method could explain the complete disappearance of plague.

Historian A. B. Appleby proposes that acquired immunity to bubonic plague developed among rats. In this case, infected fleas would not transmit the disease to humans, since their hosts no longer died of plague. Evidence suggests, however, that immunity in rats does not persist long, often less than a decade, which is not substantial enough to explain the plague's sudden disappearance.

A human resistance theory is plausible if the disease that caused the plagues of the second pandemic was a disease transmitted strictly person to person, allowing the gradual build-up of human resistance through recurring exposure. However, if the people of Europe were gradually building up immunity to plague, then it seems likely that the disease would

have subsided gradually but noticeably over time. Because the plague disappeared suddenly, this explanation seems unlikely.

Diseases themselves are known to change over time. For example, recently there has been great trepidation at the prospect of the Bird Flu virus mutating into a lethal human pandemic. An entirely plausible explanation for the disappearance of plague is that the germ (pathogen) itself may have evolved, in this case mutating into a less deadly form. If mutating to a less deadly version increases the chance of survival in a pathogen, then it is likely to occur, because the disease itself is dependent upon the survival of the hosts. The main problem with this theory, however, is that it is impossible to prove, and all indications are that such evolution did not occur.

More credibility has been afforded the role of human agency in the disappearance of plague. Plague **quarantine** and isolation measures evolved throughout the Second Pandemic. Isolation of the sick or suspected carriers was the basic principle, whether this meant closing off a whole town with a *cordon sanitaire* in the case of serious, uncontrollable epidemics or setting up **pest houses** within towns in which the sick could convalesce during minor or anticipated outbreaks. If plague was known to be active in another country, plague-free cities, and eventually nation-states, usually forbade entry to travelers from that region. Maritime trade and travel were similarly restricted with the implementation of quarantine stations for sailors and the closing of harbors to foreign ships, because it was noted that plague often arrived by sea. The gradual acceptance and implementation of these measures in Europe throughout the early modern period may have hindered the reintroduction of plague and consequently led to its disappearance. This is especially true along the great cordon erected by Austria along its border with the Ottoman Empire.

The gradual disappearance of plague specifically from northern Europe in the seventeenth and eighteenth centuries may also be attributed to nations such as England, France, and the Netherlands shifting their maritime commerce away from the Mediterranean basin, thereby cutting themselves off from the critical hub of the plague's reintroductions into Greater Europe. However, despite this shift, trade still continued on various levels between Northern European countries and the Mediterranean basin. The flourishing commerce between England and Turkey during the eighteenth century for example, did not spark a reintroduction of plague into northern Europe.

Generally, the disappearance of plague has also been associated with improvements in **diet**, nutrition, and sanitation in early modern Europe. Nutrition, however, does not seem to affect resistance to or contraction of bubonic plague, and several famines occurred in the latter part of the early modern period indicating that any dietary improvements were not universal. Public sanitation procedures included burning or disinfecting the possessions of the sick, habitual fumigations—because a commonly held belief was that plague was spread by noxious vapors in the air (**miasma** theory)—and in some cities, waste disposal regulations were enforced. Numerous north Italian cities, such as Florence, instituted public health boards to enforce plague-time sanitary regulations. On the whole, however, it seems unlikely that there were universal improvements in the cleanliness of cities or personal hygiene in Europe to the extent needed to end plague for good. For centuries, Islamic peoples practiced far better personal hygiene and cleanliness than Europeans, yet plague persisted much longer in the Middle East.

Responses to plague in the Middle East were limited by lucrative maritime trade and multicultural policy that encouraged human movement rather than limiting it. Additionally, Islamic belief held that human intervention was futile because God sent the plague, and it

was customary for Muslims to visit and care for their sick rather than abandon them as Europeans were prone to doing. It was not until the early nineteenth century that plague controls began to be implemented in the Middle East by the Ottoman Viceroy of Egypt, Muhammad Ali (1769–1848). Ignoring the public outcry it caused, he enforced a merciless combination of European quarantine and sanitation methods advised by foreign plague doctors and enforced by the armed forces to stamp out the disease by 1844. Egypt was free from plague for the next three generations, which seems to serve as testimony to the efficacy of these measures.

Plague's disappearance is most likely the result of a combination of the aforementioned explanations, though the validity of each theory rests primarily on uncertain factors such as the nature of the plague pathogen itself and the degree of mutation that occurred over the course of the Second Pandemic. The issue is still very much a matter of historical debate. *See also* Black Death: Modern Medical Debate; Diagnosis of Historical Diseases; Human Immunity and Resistance to Disease; Insects, Other Arthropods, and Epidemic Disease.

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KARL BIRKELBACH

PLAGUE IN AFRICA: THIRD PANDEMIC. In the mid-nineteenth century, a third **bubonic plague pandemic** began to sweep the globe, arousing terrible collective memories of the **Black Death**, the second plague pandemic that had begun 500 years earlier. By the time it ended around 1950, this new pandemic had produced a highly variable death toll. Most of the roughly 15 million lives it ended prematurely were impoverished inhabitants of India, China, Burma, and Indonesia. Perhaps the worst single outbreak was a dreadful **pneumonic plague epidemic** during 1910–1911, during which an estimated 60,000 perished. In Africa and adjacent Indian Ocean islands, worst hit were Mauritius, the French colonies of Senegal and Madagascar, and some areas of East and Central Africa.

Bubonic plague is usually a disease of wild rodents. This zoonosis now exists in a series of permanent reservoirs from its origins in the Himalayan foothills, to Indonesia, the

Rocky Mountain foothills of the southwestern United States, South Africa, and Argentina. Only accidentally does it cross over to humans. The pathogen is the bacillus *Yersinia pestis*, and the most efficient flea vector is the biting rat flea, *Xenopsylla cheopis*. For all their historical severity, bubonic plague outbreaks develop only when humans come within the range of an infected rat flea. In the Northern Hemisphere today, the odds of this happening would be astronomically small. A century ago, the risk was greater, especially for the urban poor who lived in overcrowded, unsanitary, and rat-infested housing. Also at risk were tradesmen or workers employed around bakeries, grain storage units, cargo ships, and other places where rats gravitated.

Despite breakthroughs in turn-of-the-century bacteriology and **immunology**, current plague control practices such as the burning of “infected” houses and personal effects derived in part from older European public health measures, but were also products of Orientalist and racist images of colonized subjects. Two new procedures, however, seemed more promising: rat control by means of trapping and poisoning, and mass **inoculation** with an anti-plague vaccine. These control techniques gave mixed results. Rodent kills eliminated millions annually but had little impact on the fecundity of rodents. Rat control through better building construction did succeed, especially in Western maritime cities, which might otherwise have been vulnerable to plague importation. Finding an effective and safe vaccine also proved elusive right to the present day, although effective **antibiotic** therapy has made the quest moot.

Origins and Spread. Emerging from its wild rodent reservoir in the Himalayan borderlands soon after 1855, and traveling this time not west but east, the third pandemic infected the densely populated provinces of south China before attacking Canton and then the British colonial port of Hong Kong in 1894. There it rekindled international fears, especially when it reached Macao and Fuzhou a year later, and struck Singapore and Bombay in 1896. Transported rapidly by British steam ships throughout the empire and beyond, bubonic plague took only a few years to reach every continent.

From the moment bubonic plague resurfaced in Hong Kong, international concerns arose that this old scourge would emulate **cholera** as a global menace. Though not alone, France was especially vocal in blaming lax British sanitary controls. Whereas earlier meetings of the International Sanitary Convention (founded 1851) had been preoccupied with the global cholera pandemics; the Venice Conference of 1897 was the first to deal exclusively with what the Europeans perceived as “Asiatic plague.” Delegates could not agree on binding measures, but they did erect **quarantine** and inspection barriers at the Suez Canal, facilities already in place against cholera, to guard Europe against plague. They also agreed to establish specific quarantine measures applicable to passengers and the crews of ships sailing from infected ports.

In Colonial Africa, European health officials, in an effort to mobilize the population for plague control, sometimes showed excessive enthusiasm. The British, for example, paid such generous bounties for rat-tails during and after epidemics in Malawi and Uganda that the premiums actually had an impact on the local economy. But mobilizing the entire population to control potentially infected rodents placed civilians at risk of infection. Intrusive French officials in Senegal and Madagascar attempted residential urban segregation ostensibly to control plague and generated political opposition to other, more beneficial, health measures.

Bubonic plague was rare or unknown in Sub-Saharan Africa before 1900, but it certainly had been no stranger to North Africa and Egypt. Both the **Plague of Justinian**

(first pandemic) and the second pandemic (1347 to the early nineteenth century) had wreaked havoc in the region. Plague in fact did not recede from the southern shores of the Mediterranean until after 1844. Although modernization coincided with plague's departure, commercial expansion had also introduced cholera from India. Still, when bubonic plague returned to Alexandria as part of the third pandemic in 1899, Egypt had not experienced a major epidemic of any kind for almost 20 years.

Alexandria's and Egypt's experience with the third plague pandemic was exceptionally mild in comparison with earlier experiences, and it challenged medical experts, religious and political leaders, and the general public to put forward plausible explanations. Apart from older ones based upon God's unknowable will, three basic points stood out. First, sanitary reforms had transformed the disease **environment** of Alexandria; second, the city's health officials had efficiently implemented modern plague control measures with a high degree of support from most Alexandrines; and third, Alexandria's peculiar cosmopolitan mix of foreign minorities and Egyptian nationals had somehow combined to produce cooperation rather than confrontation between the general public and health authorities assigned the task of controlling the plague epidemic.

Yet Alexandria's victory over *Y. pestis* was only partial. Although its residents had every reason to rejoice over its attenuated impact in 1899, sporadic and light outbreaks of bubonic plague returned to the city annually over the next 30 years. Worse, although Alexandria had been the only plague site in all of Egypt in 1899, soon after the disease spread to Port Suez and towns throughout the Nile Delta. From there, plague traveled far south, sparing Cairo but visiting Upper (southern) Egypt every year. There it became mildly endemic, taking roughly 10,000 lives by the time it finally burned itself out in the 1930s.

Alexandria represented perhaps the best possible result public health authorities could have hoped for from a bubonic plague epidemic at the beginning of the twentieth century. Instead of blaming victims, health officers made them as comfortable as could be expected. Egyptian health assistants were permitted to participate in plague control efforts. Isolation for patients and "suspects" was compulsory, but Muslim victims received *halal* food (that met Muslim purity requirements), and laborers were paid compensation for work days lost. Such sensitivity gave the public confidence that plague control operations served the wider interest. In too many other urban jurisdictions, interest groups worked at cross-purposes, so that political and social tensions became magnified under the plague **microscope**.

Cape Town suffered its first laboratory-confirmed case of bubonic plague in January 1901, probably imported from Argentina in a shipment of fodder for horses during the South African **War**. The vast majority of African cases and deaths occurred in the initial stages of the plague outbreak, through March 15, 1901. Thereafter, health officials forcibly evicted most Africans from the port and city center, where the infected rats and fleas were concentrated, and dispatched them to Ndabeni, a new location outside the city. The last plague case recorded for Cape Town occurred on November 9. The final tally was 389 dead among 807 reported cases.

According to local health officials, a series of factors made Cape Town vulnerable to plague. The list included wartime concentrations of troops constantly moving in and out of town; refugees pouring into an already overcrowded city; a mixed population with what observers called "filthy habits"; antiquated sewers that served as a convenient

transportation network for the extraordinary number of rats; and large quantities of forage and other stores for their food supply.

Missing from the mix was a global ecological insight into plague epidemiology, which only a few far-seeing observers were beginning to grasp. The third pandemic was gaining hold in southern Africa because the region provided an excellent natural environment for bubonic plague. *Y. pestis* thrived in a temperature range from 15 to 28 degrees Celsius with moderate humidity, and the *X. cheopis* flea multiplied fastest in a range from 20 to 28 degrees. Not only did Cape Town and most other cities of southern Africa maintain such temperatures much of the year, but *X. cheopis* proved to be commonly found in the countryside as well. Given such an attractive combination of human and natural factors, bubonic plague spread rapidly beyond Cape Town. In mid-April 1901, while plague was still gripping Cape Town, an epidemic broke out at Port Elizabeth in the eastern Cape. There, too, whites forced black Africans into a designated residential location called New Brighton, and urban Africans responded with a determined and partially successful resistance to relocation. Plague persisted on and off in Port Elizabeth until 1905, and remained in East London between 1903 and 1905. Moderate outbreaks occurred in Durban in 1902, where white panic was rampant, and in Johannesburg, where authorities burned down African slums within a few hours of discovering bubonic plague in 1904. *Y. pestis* continued its exploration of the South African hinterland, especially in southwestern Transvaal and northwestern Orange Free State, where it established a permanent reservoir among gerbils and other *veldt* rodents. Even today, the large permanent reservoir of enzootic plague poses a major threat to rural South Africans, especially those without affordable access to early diagnosis and antibiotic treatment.

Bubonic plague was the most persistent and dramatic infectious disease to strike Senegal in the twentieth century, even if chronic diseases such as **malaria** and **dysentery** killed more people. From the time it first appeared in 1914 until its final departure in 1945, scarcely a year went by without a recorded outbreak in either rural or urban areas. Recorded Senegalese deaths from plague exceeded 35,000 over 32 years, but this figure represents an unknown fraction of the real toll. Senegal may have suffered the highest case rates per 10,000 population in Africa, and worldwide second only to India.

Another scene of recurring plague is the island of Madagascar, which was heavily victimized earlier in the third pandemic but had very few cases after the late 1930s. Beginning in 1989, however, human plague again became a major health problem, especially in the capital of Antananarivo, the highlands just to the south, and at the northwestern port of Mahajanga. In 1997 alone, close to 2,000 cases were recorded, and for the decade, approximately 6,000, with case fatality rates of 20 percent. This new visitation of plague has been difficult to control for a number of suggested reasons. A permanent reservoir of *Y. pestis* persists among sylvatic rodents; three new variants of *Y. pestis* have recently emerged and may be acquiring selective advantages; most ominously, the first naturally occurring antibiotic-resistant strain of *Y. pestis* was recently isolated in Madagascar. To underscore the dangers represented in India and Madagascar, the **World Health Organization** in 1996 reclassified plague as a “reemerging” rather than a dormant disease. See also Colonialism and Epidemic Disease; International Health Agencies and Conventions; Personal Liberties and Epidemic Disease; Plague in East Asia: Third Pandemic; Plague in India and Oceania: Third Pandemic; Plague in the Contemporary World; Race, Ethnicity, and Epidemic Disease; Travel, Trade, and Epidemic Disease; Yersin, Alexandre.

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MYRON ECHENBERG

PLAGUE IN BRITAIN, 1500–1647. From 1500 to 1666, the plague was a constitutive force within British culture, affecting all aspects of lived experience from the way people prepared food to the content of their prayers and the terms of their labor. It halted trade, sent the wealthy in **flight** to the country, closed theaters, and killed thousands. Visitations were most frequent in larger cities in the southeast, with Ireland and Scotland experiencing relatively few. The worst visitations in England paralyzed portions of the nation with fear, bringing some to near standstill in 1498, 1504–1505, 1509, 1511–1521, 1523, 1535, 1543, 1563–1564, 1578, 1592–1593, 1603–1612, 1625–1626, 1636–1639, 1641, and 1643–1647. **London’s Great Plague**, England’s final plague **epidemic** and an outbreak second in impact only to the **Black Death** of 1349, struck in 1665. In every decade on average from 1500 to 1647, plague struck major ports and cities before traveling by less obvious patterns into the suburbs and then north and east into smaller towns and villages.

Some speculate that in this period the plague was not only epizootic, infecting entire rat populations, but also enzootic to the island. The fact that plague did visit London and other southeastern cities more frequently, suggests that even if it had been endemic in England, new carriers crossed the channel and increased its virulence. The primary vector was the flea, carried on rats. This has led to speculation that the rats came across the channel on ships, but it is also possible that clothing and bedding provided a suitable, temporary habitat for the fleas.

Few scholars attribute regular visitations to human-to-human transmission. The relatively slow speed at which plague spread and the fact that old and young, men and women, alike were susceptible supports the consensus that humans most often contracted the disease from fleas, not from each other. In addition, although plague visited London and other large cities more frequently than villages, it often killed a larger percentage of the population in rural communities—as many as 1 in 10 according to the historical record. This is a low number compared to the mortality rates reported from the first pandemic in the fourteenth century, but it was enough to threaten national, parish, and familial stability on a regular basis.

Records of burials in parish registers, wills proved, and London’s bills of mortality are the primary sources for determining the years in which plague caused dramatic increases in mortality rates. The number of dead listed on a weekly bill, for example, should correspond with the number of burials. These published bills are particularly useful, because from them we can establish the number of dead for a given parish each week, increases and decreases in weekly mortality rates over time, and comparative mortality rates by

region. At the time, the bills were the primary means by which people learned that plague was increasing or decreasing in virulence. The bills helped citizens determine when to close up shop and flee from the city, hunker down, or initiate thankful celebration.

Yet, there are many variables that make it difficult to rely upon these documents. Only London published bills of mortality, some parish records have not survived, and it was often the case that parish officials underreported the numbers of plague dead in order to avoid panic or intervention from the national government. Prior to the mid-sixteenth century, records of all kinds are spotty, and even in towns that paid “searchers” to enumerate the dead, the information collected never included case-specific correlation between the number that the dead person represented on the bill and the symptoms he or she had. What this means is that, if anything, the numbers we have are inaccurate because they are low. Nevertheless, the triangulation of data (wills, burials, and bills) allows us to identify useful patterns: higher rates of death from plague in poorer parishes than in wealthier ones, in late summer and early autumn than in winter, and in parishes closer to ports than in those further away, but a roughly uniform number of plague deaths with respect to victim age and gender.

Just what constituted “plague,” however, was and still is difficult to determine with absolute certainty. Men and women in Britain at the time could not have known that **bubonic plague** was caused by the plague bacillus *Yersinia pestis* that was transmitted when the rat flea (*Xenopsylla cheopis*) jumped from the black rat (*Rattus rattus*) to a human and bit. Yet, we can use their accounts of basic symptoms (fever, overly swollen lymph glands, and small skin lesions), of a two to six day incubation period, of fatality rates from 50 to 80 percent, and of the plague’s seasonal schedule, to confirm that bubonic plague was the primary contributor to deaths in these years. Although they did not have the technology we do now, people of the period were able to distinguish between bubonic plague and lesser diseases that had lower mortality rates, different symptoms, and/or longer incubation periods, such as the **sweating sickness**, **smallpox**, and **syphilis**. Although it is possible that **pneumonic plague** also contributed to high mortality rates, the symptoms, incubation rate, and mortality rate for pneumonic plague do not coincide closely enough with historical accounts of the plague in Britain to allow for consensus.

The primary source of plague was the bubonic form, and the primary vector was the rat flea, not humans. Mortality rates for people dropped when plague had run its course in the animal population and killed off the majority of the rat and flea population. One reason that 1666 marks the end of plague in Britain may be that the fire of London not only killed rats, but it also consumed many of the oldest thatched-roof buildings, which had made ideal homes for the black rat. Although there were a few reported cases of plague after 1666, there was never another major visitation in Britain.

Because they realized that a distinct threat was upon them, English monarchs and their advisory councils took action to deal with this particular scourge. King Henry VIII of England (1491–1547) had seen his own father, King Henry VII (1457–1509), grapple with the disease, and Henry VIII had spent many months in flight from the plague and away from the nation’s capital in London. During these times, his primary advisor, Thomas Cardinal Wolsey (c. 1473–1530) remained behind to ensure that government affairs remained on course. In 1518, nine years into the reign of Henry VIII, Wolsey created a set of plague orders that were based on those used on the continent; however, they were never employed nationwide or even in London. Instead, Henry VIII sent Thomas More (1478–1535) to Oxford to enforce the plague orders there. A lawyer by trade who had written *The Utopia*

(1516), who would become Lord Chancellor of England, and whom Henry VIII would execute for refusing to support his divorce from Catharine of Aragon (1485–1536), Thomas More went to Oxford to guarantee that all plague victims were quarantined within their homes so that the king could pass through the city in safety.

The success of these single-city plague orders was small compared to the nationwide standards for plague orders employed on the continent. Italian territorial states led the way, with other nations following. It would take six decades before England saw its first nationwide plague orders in place. Before this, Henry VIII's daughter Queen Elizabeth I (1533–1603) called the nation to attention through church-directed worship. In 1563, the first serious plague year of her reign, Elizabeth I and her advisory committee charged Matthew Parker, Archbishop of Canterbury (1504–1575), and Bishop Grindal (1519–1583) of London with formulating the first nationwide schedule of prayer and fasting for the prevention of disease. Prior to this, **flight** alone served to secure the nation's head. With the issue of this document, Elizabeth I broke tradition with her forebears, prescribing actions to be taken by all citizens, not only by leaders.

In 1578, the next major plague year in her reign, Elizabeth I and her council created a secular version of the nationwide prayer orders. It consisted of seventeen separate orders to the justices of the peace in all parishes in the nation. It was modeled upon continental orders similar to those followed by Thomas More to secure Oxford in 1518. These orders depended upon the shutting up of victims in their homes, collection of taxes to assist the poor, and orderly reporting by justices of the peace. These orders were thorough and flexible enough to gain them reissue in every major visitation through 1666, when they were finally revised.

When he assumed the throne after Elizabeth I's death in 1603, James I of England (1566–1625) reissued Elizabeth I's orders unchanged, but within a year, he had issued an act that increased the penalties for people who attempted to escape from sealed houses. In "An Act for the charitable relief and ordering of persons infected with the Plague," James I decreed that infected persons who attempted to escape would be forcibly returned to them, and any who ran would face death. This act was not only more severe in its pronouncements upon plague victims but it also carried more weight than Elizabeth I's orders because it was ratified by Parliament. There are no records showing that anyone was ever tried for this crime, and there were no additional changes to plague policy in the period, but writers increasingly registered their concerns regarding the inhumane practice of shutting in victims and their families.

With the printing press came the opportunity for medical practitioners, social satirists, and clergymen to hawk their written wares. The latest diagnosis and remedy for plague accompanied exclamations against bad **air**, the uncharitable nobility, and sin. The number of medical treatises printed in English in the period number nearly 200, and of these, more than four dozen were exclusively about the plague. Writers also took the opportunity to cry out in sorrow and anger over the conditions they witnessed, and they did so by publishing short pamphlets that circulated widely. One common theme was the city versus the country. As London's citizens fled in large numbers to the country, those who dwelt in the villages aimed to turn them away, for fear of infection. Flight, in fact, did more to disable economies and civil administration than the literal disease, and it damaged relationships both within cities and between city and country. In other pamphlets, authors told tales of odd and amusing behavior in plague-time in order to alleviate suffering through laughter. In sermons, the themes were never intended

to provoke mirth but rather to encourage repentance. Clergymen compared London to the biblical Sodom and Gomorrah but also to Nineveh, a city that God threatened to strike with plague but then chose to spare when the king and his subjects all prayed for forgiveness.

Records of playhouse and fair closings also illustrate the social and economic impact of plague. When plague visited London, the monarch would issue a stay against plays and order the closing of markets in order to prevent these large public gatherings from becoming sites of increased infection. Actors and vendors forced to close shop had to seek alternative forms of income. This is one reason why William Shakespeare (1564–1616) wrote his narrative poems *Venus and Adonis* and *The Rape of Lucrece*. Playhouses were closed in 1593–1594, so he turned to narrative poetry and hoped that his patrons would pay him well enough to get him to the next season. Actors and others also opted in some cases to take their shows and their wares on the road, performing and selling in neighboring towns that were not infected. Many, however, were trapped within infected regions without the means to escape. They witnessed the cessation of all commerce and the upturning of life as they knew it. In his famous *Journal of the Plague Year* (1722), Daniel Defoe's (c. 1660–1731) protagonist lives through such a crisis in 1665.

The plague left its mark on individual bodies but also on cities, nations, and their products. Some have claimed that were it not for plague we would not have Thomas More's *Utopia*, William Shakespeare's plays and poetry, or the genre of the novel, with its origins in the work of Daniel Defoe. Others, like theorist Michel Foucault (1926–1984), tell us that in the early plague orders we find the birth of the modern police state. The plague legislation from this period was certainly as far-reaching as its literature, which to this day can make us tremble with threat of "A plague o' both your houses!" (*Romeo and Juliet*). See also *Black Death: Modern Medical Debate; Demographic Data Collection and Analysis, History of; Diagnosis of Historical Diseases; Pest Houses and Lazarettos; Plague and Developments in Public Health, 1348–1600; Plague in Europe, 1500–1770s; Plague Literature and Art, Early Modern European.*

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REBECCA TOTARO

PLAGUE IN CHINA. Because European plague **epidemics** have often been described as “coming from the East,” it is assumed that China has been the source of all plague and pestilence. The historical record documenting epidemics in China is far from clear on these origins.

Traditional Chinese sources contain lists of epidemics noted in the dynastic histories and other sources that start in 243 BCE during the Qin dynasty; William McNeill (b. 1917) summarized these in the Appendix to his *Plagues and Peoples*. Based, as they are, on fragmentary and often now unavailable sources, such lists are problematic. In a careful review of historical evidence for epidemics that can be reliably considered as plague (caused by *Yersinia pestis*), Carol Benedict in *Bubonic Plague in Nineteenth Century China* presents credible historical evidence that plague existed in Yunnan Province in Southwest China as early as 1772. Its association with rats is clearly described in a poem by Shi Daonan (1765–1792) entitled “Death of Rats.” The telling line reads: “A few days following the death of the rats,/ Men pass away like falling walls.” Clearly the association of the epizootic in rats and human disease was known in China by the late eighteenth century.

The frequent local epidemics of plague in Yunnan, then Guangxi province, and finally in Guangdong province are well documented by Benedict. She shows how both the lucrative opium **trade** and the **ecology** of the indigenous host of the rat flea, the yellow-chested rat (*Rattus flavipectus*), contributed to and explained this spread.

Since the development of **germ theories** of disease in the late nineteenth century, two epidemics of plague in China have been of major significance. By 1894–1895, plague had spread outward from its initial endemic focus in Yunnan Province and had a major impact in Hong Kong, along the South China coast, and in Taiwan, soon spreading to South Africa, San Francisco, and some of the Japanese islands, becoming the third worldwide plague pandemic after the **plague of Justinian** in the sixth century and the **Black Death**, which began in the fourteenth century. The second major epidemic of plague in China occurred in the winter of 1910–1911 in the northeastern provinces of China. This epidemic took the form of **pneumonic plague**, but it did not spread beyond North China to become a dispersed pandemic. Both of these epidemics, the first in Hong Kong and the second in Manchuria, however, presented opportunities for the study of plague with the new tools and concepts of bacteriology, and both epidemics led to major advances in understanding of both the causes and spread of plague.

Plague in Hong Kong occurred at such a time and place that both bacteriology and **colonialism** were in full play. British colonial policy extended to matters of public health, both to protect the colonizers and to protect colonial investment. The Chinese resistance to Western public health measures was as much resistance to unwanted state interference in their lives as it was to the real lack of effective measures against disease in most cases. Civic activism by the British as well as the Chinese gentry was at work in Hong Kong in 1894 when the plague arrived. Medical science had just begun to unravel the role of rats and fleas in the transmission of this dread disease, though the microbe responsible for plague had not yet been identified. The proper measures to combat the plague in Hong

Kong were debated; Western medicine had to rely on accounts of plague epidemics from centuries earlier; **Chinese disease theory and medicine** relied on remedies and prophylactics not well understood by the Western authorities.

The opportunity to study an epidemic of plague in a city with a Western administrative structure and a semblance of a Western medical establishment drew two research teams to Hong Kong. The Pasteur Institute sent a skilled and experienced bacteriologist, **Alexandre Yersin**, to study the plague, and **Shibasaburo Kitasato** arrived from the Institute for Study of Infectious Diseases in Tokyo. Both soon isolated strains of **bacteria** associated with cases of the plague, but because of difference in techniques they found different organisms. Kitasato found a Gram-stain-positive organism in the blood of plague patients, whereas Yersin found a Gram-stain-negative organism in the buboes and other affected tissues of plague patients. This controversy was quietly resolved when Kitasato repeated Yersin's work and he subsequently agreed that Yersin's Gram-stain negative organism was the true cause of plague; his isolate appears to have been a spurious commensal organism. Surprisingly, to this day, this confusion over the "credit" for discovery of the plague bacillus exists in many textbooks and historical accounts.

The index case of plague in the Manchurian epidemic, as best determined by contemporary investigation, was a migrant trapper who died in Manchouli on the Chinese-Russian border in mid-October 1910. At that time, aided by the expanding railroads, Chinese hunters from the south would travel to Manchuria to trap the Siberian marmot or tarbagan (*Marmota sibirica*) for its fur. Plague was already known to be endemic among these common burrowing rodents. At the end of the trapping season, these migrant trappers would return to their homes in the south. Plague spread rapidly among the poor and crowded camps of these migrants and was carried south along the railway, initially, in this case, the Russian-controlled Chinese Eastern Railway. Plague reached Harbin on October 27, 1910; Changchun, the northern terminus of the Japanese-controlled South Manchuria Railway, on January 2, 1911; and Peking (Beijing) on January 12, 1911. When people could not get on the trains, they fled south by road and spread the disease into the countryside. Although the Russian and Japanese authorities were implementing local measures, only the central Chinese government could officially act on a broad scale. In a move to respond to both Chinese and foreign pressure, the Manchu Court through the Ministry of Foreign Affairs sent **Wu Lien Teh**, a Malaysian Chinese physician, educated at Cambridge and working for the Chinese government as Vice Dean at Peiyang Medical School, to Harbin to investigate the plague on its behalf. In late December 1910, Wu and a senior medical student named Lin arrived in Harbin. Lin was particularly valuable because Wu, as an "overseas Chinese," was not fluent in Chinese, especially the local dialects.

On his third day in Harbin, Wu managed to do a limited postmortem examination on a woman who had just died, and he observed massive infection of lung, heart, spleen, and liver with bacteria with the morphology and staining characteristics of Yersin's plague bacillus. As an astute clinician with the most up-to-date education, he made the clinical diagnosis of **pneumonic plague**, while the local Russian doctors in Harbin suspected **bubonic plague** and continued to examine patients without respiratory precautions. A senior French physician, Girard Mesny (d. 1910), sent to Harbin a little later, refused to accept Wu's evaluation and failed to take precautions. He died six days later.

Mesney's death may have been a turning point, because in January 1911 the Chinese government sent troops and police to Manchuria in an attempt to control population

movements and to enforce **quarantines**. A new plague hospital was hastily set up and the old one burned down. With the ground frozen, it was impossible to bury the dead. At one point Wu reported seeing 2,000 coffins in rows with more dead on the ground because of a shortage of coffins. Worried that rats might become infected by eating the **corpses**, Wu was able to enlist the support of some local officials, and then following the traditional Chinese approach, he wrote a memorial to the throne. Three days later he received an Imperial Edict allowing mass cremation of the dead bodies.

The rigid quarantines, cold weather, and strict isolation of the sick led to control of this epidemic, which ended in mid-March 1911. One outcome of this epidemic in which an estimated 60,000 people died, was an International Plague Conference, hosted by the Chinese government in Mukden (Shenyang) in April 1911. This conference was the first scientific conference held in China, and its proceedings became a standard reference on contemporary understanding of plague. China established the North Manchurian Plague Prevention Service under Dr. Wu in Harbin, the first official recognition of western public health by the Chinese government. Subsequent work by Wu and his colleagues on both cholera and plague in China led to the expansion of this service to become the National Quarantine Service, the first organization for public health in China up until the invasion by Japan in 1936. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Plague in East Asia: Third Pandemic; Plague in India and Oceania: Third Pandemic.

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WILLIAM C. SUMMERS

PLAGUE IN EAST ASIA: THIRD PANDEMIC. From the 1860s to 1960, plague caused by the bacillus *Yersinia pestis* swept around the world with several major **epidemics** in East Asia, most notably in China, Hong Kong, and Manchuria in the 1890s, 1910–1911, 1917, and 1920–1921. Although **bubonic plague** was the major killer during this **pandemic**, **pneumonic plague** also was present, particularly in the Manchurian epidemics. In working to combat the plague outbreak in Hong Kong in 1894, **Alexandre Yersin** and **Shibasaburo Kitasato** isolated for the first time the **bacterium** *Y. pestis* as the agent of the disease. Biovar *orientalis*, the type responsible for the third pandemic, most likely evolved from *sylvatic* (wild) biovar *antiqua* sometime in the past. Small epidemics began to be noticed in Yunnan province in southwestern China in the late eighteenth century. These early epidemics involved rural areas with low population densities, so the disease spread slowly.

Bubonic plague is a vector-borne disease with fleas serving as the vectors. Several varieties of fleas are capable of carrying *Y. pestis*, most notably *Xenopsylla cheopis*, the rat flea. Rats are the most common host for plague-carrying fleas, although other animals such as marmots and susliks often served as hosts in China and Russia. Rats are highly mobile and

often stow away on ships and other conveyances carrying grain, making it easy to spread plague over great distances.

Bubonic Plague in China. There were small epidemics in western Yunnan from the 1770s onward, but the disease remained confined to the western part of the province well into the nineteenth century. The first major modern plague epidemic in China came in 1866 when refugees from social and political unrest brought the disease to K'unming, the capital of the province of Yunnan. From there the disease spread slowly across south China reaching the seaport of Canton in 1892. This slow progress of the disease was not characteristic of earlier plague pandemics and has led to questions about the validity of the plague diagnosis for earlier epidemics. Once established in the seaports of China, it was an easy step for plague to spread to nearby Hong Kong in 1894. From the Chinese port cities, the disease spread readily worldwide, reaching first Bombay in 1896 and then Calcutta in 1898. After that few countries remained untouched as the disease spread from China to the United States in 1900. Plague-infected rats stowed away on ships leaving Chinese harbors, spreading the disease worldwide. The epidemic had turned into a pandemic by the early twentieth century. The third plague pandemic originated in China as a new biovar, and readily available transportation and international commerce made it possible for *Y. pestis* to have a worldwide reach and establish itself as endemic in several new regions such as the Americas.

Plague remained endemic in China well into the twentieth century, spreading throughout the country, though it was more common in the southwest than elsewhere. After the first major epidemic in the 1890s, the number of plague cases declined after 1920, but the disease continued to produce a steady death rate characteristic of an endemic infection.

The British authorities in Hong Kong acted quickly once the disease reached the city, setting up three plague hospitals to try to control the disease. Word of the outbreak led medical authorities elsewhere to send aid. One team, led by Dr. Shibasaburo Kitasato, arrived from Japan in early June 1894. Kitasato, trained in Germany by **Robert Koch**, set up shop at Kennedy Town hospital and quickly began to conduct autopsies to try to determine the agent of disease. Shortly thereafter Dr. Alexandre E. J. Yersin arrived from French Indochina. The idealistic Yersin had trained in **Louis Pasteur's** laboratory in Paris. Initially denied access to any corpses, he set up operations in a straw hut and eventually gained access to the bodies of some of the suspected plague victims. Both men eventually identified bacteria they claimed to be the agent of disease. Yersin's identification was the more concrete, clearly indicating it was a Gram-negative organism, and thus a likely human pathogen. Both men claimed to be the discoverers of the plague bacillus, but over time the scientific community (and Kitasato himself) recognized Yersin's work, and the bacteria *Yersinia pestis* was named in his honor in 1970 (it had previously been named *Pasteurella pestis*).

The outbreak of plague in Canton and Hong Kong illustrated the conflict between Western "scientific" medicine and **Chinese disease theory and medicine**. The **germ theory** of disease had come to be accepted in the West although not yet throughout Asia. By the late nineteenth century, the European mode for dealing with infectious disease was rigorous isolation of infected victims coupled with massive sanitation campaigns all controlled by the state. The Chinese model for dealing with infectious disease often involved care of the infected victims by their families and voluntary efforts at infection control. Europeans in Canton were critical of the performance of the local governments

in dealing with the plague epidemic. In Hong Kong the Chinese merchant elite had sponsored the charitable Donghua Hospital, which quickly worked to take charge of plague treatment in 1894. The Donghua Hospital Directorate often did not isolate plague victims from their families and often tried to assist the sick and dying to return to China. The British colonial authorities responded to the plague outbreak by isolating plague patients through forced hospitalization and rigorous efforts at enforcing sanitation. Such an approach often tore families apart as plague victims were isolated from their relatives. In the early 1890s the connection had not yet been made between fleas and the spread of the disease, and plague was still often seen as a contagious disease caused by dirty conditions. Although there is some basis in fact for relating unsanitary conditions to the spread of the plague, the British response in the 1890s was also conditioned by a presumed European superiority to all things Asian. The weight of the colonial government was brought to bear in enforcing European standards for plague treatment, arousing intense resentment by Chinese in Hong Kong and mainland China. In essence, colonialist state medicine took control from civic activism in confronting the plague.

The gradual spread of bubonic plague across China in the early stages of the pandemic led to several million deaths, but it did not cause panic or the massive mortality rates of the **Black Death**. Even in Hong Kong, where 50,000 to 100,000 people are estimated to have died in 1894, the outbreak was finally contained. The British authorities in Hong Kong often underreported the total of plague deaths, as deaths in the native population often went uncounted. Nonetheless, the death rate in Hong Kong, for example, from 1894 to 1923, was low, usually less than 5 deaths per 1,000. On the other hand, the case fatality rate (the ratio of plague deaths to plague cases) was quite high, generally exceeding 90 percent during most years of the period. Plague did not infect all of China in any one year, and so different regions of the country were often free of the disease for several years at a time.

Plague returned to southern China with another epidemic in 1917–1918. The death toll was lower than before, but several thousand people died nonetheless. The Chinese government was better prepared to confront the outbreak, so the pockets of infection were usually controlled, and the epidemic did not spread throughout the country. In essence the Chinese government had adopted the western model of **quarantine** and government control to fight the disease.

Plague Elsewhere in East Asia. The plague also spread to the Chinese island of Taiwan (Formosa), with the first case occurring in 1897. Until 1917 plague would be a regular visitor to the island. The death rate on the island was quite low, generally less than 1 per 1,000 with a case fatality rate generally in the 80–90 percent range. Here the disease was imported from the mainland and tended to be concentrated in periodic epidemics when the disease gained a foothold from a ship.

As bubonic plague spread beyond the borders of China, several other Asian countries developed epidemics or continued to experience unusually high numbers of cases. Early in the twentieth century, the disease spread to the French colony of Vietnam, where it was more concentrated in the south than the north. Even in 1910, the worst year for plague cases, the number of cases was far below that of the late 1960s, which arose from the disruptions caused by American military efforts in South Vietnam. Plague would remain endemic in Vietnam until the early 1950s when it appeared to be eradicated. Thailand, too, fell victim to the plague with 586 cases in 1917 of which 580 were fatal. The Dutch colony of Java remained free from the disease until November 1910 when a ship carrying

rice from Burma also brought rats carrying plague-infected fleas to the island. The disease spread gradually from east to west. The first wave from 1910 to 1914 affected the eastern part of the island. After a period of remission from 1915 to 1919 the plague began to spread across the rest of the island, and from 1920 to 1927 there were over 8,000 fatal cases per year, primarily in central Java. A third phase occurred from 1930 to 1934 with most of the deaths in the eastern part of the island. Nonetheless, the mortality rate throughout the period remained quite low in the Dutch colony. After 1934, plague eradication efforts by the government—mainly the destruction of older houses and the construction of brick houses that were less amenable to flea infestation—helped to bring the epidemic to a close. In both the French and Dutch colonies, a conflict existed between European and native medical practices that was similar to that which had occurred earlier in Hong Kong.

For the most part, Japan remained plague-free in the early twentieth century. Japanese officials enforced rigorous inspection standards on ships entering Japanese ports from infected Chinese ports. Even though a few cases developed, the disease never made inroads into the native rat population, so no disease reservoir developed on the islands. Japanese medical and military authorities watched with interest the course of the disease in China, and some ultimately turned to the development of plague as a biological weapon during World War II (1939–1945).

Manchuria and an Old Plague Reservoir. The third bubonic plague pandemic developed in southwestern China, but there was another plague reservoir in Mongolia and parts of Asiatic Russia. The Mongolian plague was probably the older biovar *medevalis* rather than the biovar *orientalis*. Plague was endemic in Mongolia with marmots, or tarabagons as Russians called them, serving as the primary host for *Y. Pestis*-carrying fleas.

Rural Mongolian and Manchurian folk legends long warned against coming into contact with marmots that appeared to be sick. As fur prices increased in the early twentieth century, new, less careful trappers began trapping marmots. In 1910 an epizootic occurred leading to massive deaths of marmots in Manchuria. Trappers who came into contact with the infected animals soon became infected with the plague. The initial cases appear to have been bubonic plague. However, secondary pneumonic plague infections often ensued and soon the disease had developed as primary **pneumonic plague**. Unlike bubonic plague, which tends to be a disease of summer, pneumonic plague is often a disease of winter as close human contact helps to spread the disease. Railway workers in several northern Manchurian cities who lived in close proximity to each other soon became infected in large numbers during the winter of 1910–1911 as the disease spread along the rail line south from Manzhouli to Harbin. As was generally the case with pneumonic plague, the case fatality rate approached 100 percent, so the disease burned itself out once there was no longer a susceptible population to become infected.

The Chinese government, eager to avoid foreign criticism and to prevent the Russians from exercising control of the situation, sent the young Cambridge-trained Dr. **Wu Lien Teh** to the area to take charge of fighting the disease. Thoroughly imbued with a European approach to medicine and unable to speak Chinese, Dr. Wu imposed quarantines to limit the spread of the disease and tried to provide what palliative care that he could for those infected with the plague. The combination of quarantine and the disease burning itself out led to the control of the plague, but not before 60,000 Manchurians had died. Local authorities did not always welcome Wu's efforts, as resentment against Western methods

for disease control often aroused hostility among many people, and the Western explanation for the spread of pneumonic plague confounded Chinese traditional medicine. In response to this outbreak, the Chinese government established the Manchurian Plague Prevention Service at Dr. Wu's instigation, which continued in operation until the Japanese invasion in 1931.

Manchuria was struck again by plague in 1920–1921. Like the earlier outbreak, this epidemic had a large number of primary pneumonic plague cases and originated from the Mongolian-Manchurian reservoir. The Manchurian Plague Prevention Service was able to curtail the impact of this epidemic as it had done with an epidemic in southern China in 1917–1918.

The End of the Third Pandemic. Plague continued to be recorded throughout East Asia after the mid-1920s but in declining numbers, as only small, easily contained epidemics occurred. Even the disruptions caused by World War II did not lead to a major plague outbreak. Worldwide, the aggregate number of plague cases continued to be around 5,000 annually until 1953. During the 1950s, the number of cases declined sharply, numbering slightly more than 200 in 1959. Health authorities concluded that the third pandemic was over by 1960.

Reasons for the end of the third pandemic are hard to pinpoint. During the 1950s, several forces came to bear that helped to diminish the impact of plague. Improved sanitation and **pesticides** helped to reduce rat habitat. **Antibiotic** treatment, if started early enough, was often effective in treating bubonic plague, so death rates continued to drop. However, environmental disruption increased during the 1950s, so humans came into contact more often with environments in which sylvatic plague existed. Plague continued to be endemic in parts of Mongolia and Manchuria in 1960, but elsewhere the disease appeared to be eradicated or severely limited. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Bubonic Plague in the United States; Colonialism and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Haffkine, Waldemar Mordechai; Plague in China; Plague in India and Oceania: Third Pandemic; Plague in San Francisco, 1900–1908; Plague in the Contemporary World; Simond, Paul-Louis; Trade, Travel, and Epidemic Disease.

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JOHN M. THEILMANN

PLAGUE IN EUROPE, 1500–1770s. By 1500 Europe was experiencing a period of intense change: the European “Renaissance” blossomed, and the European economy boomed as a result of **trade**. Maritime and overland commerce, which had finally recovered from the fourteenth century’s catastrophic plague outbreaks, produced wealth on an unprecedented scale, but at the same time, contact with the plague-devastated Near East made sure that the **Black Death** remained a very real part of European life. Europe suffered numerous outbreaks of the plague between 1500 and the 1770s. Although these were not as widespread as the first **epidemics** of 1347–1352, they continued to kill tens of thousands of people. Cities like Florence were ravaged in the sixteenth century; towns like Montelupo in Tuscany and much larger cities like Barcelona, Amsterdam, and London

were hit in the seventeenth; and Marseilles and Moscow were hit with plague in the eighteenth century. By relying on detailed period records left behind by bureaucrats, who inherited the Renaissance humanists’ attention to detail, and on chronicles left by an increasing number of literate artisans and middle class people, scholars are able to reconstruct the plague’s movements. Such records and accounts also help contemporary scholars to quantify mortality rates for the various epidemics that struck Europe in an attempt to understand its effects and European responses to it.

Although these records allow scholars to reconstruct the plague’s effects and movements, there is some debate over the causes of plague’s continued presence in Europe from 1500 to the 1770s. Scholars propose two theories to explain why the plague remained a part of European life for such a long time: the “plague reservoir” theory and the “trade” theory, espoused above. Those who support the “reservoir” theory argue that the plague remained ever-present in Europe, in pockets or “reservoirs” from which it spread—quite likely from one urban area, or town, to another through interregional and international contact. The “trade” theory suggests that the plague receded or even left Europe altogether after the initial epidemics of the fourteenth century only to be reintroduced

THE CITY COUNCIL OF BARCELONA, SPAIN, ON THE PLAGUE OF 1651

For many days now eight or ten carts have traveled throughout Barcelona with the sole purpose of removing corpses from houses, which are often thrown from the windows into the street and then carried off in the carts by the grave diggers, who go about playing their guitars, tambourines, and other instruments in order to forget such grave afflictions, the memory alone of which is enough to want to be done with this wretched life, which seems to be worth nothing. These grave diggers stop their carts at a street corner and cry out for everyone to bring the dead from their houses, sometimes taking two from one house, four from another, and often six from another, and after filling their carts they would take the bodies to be buried in a field near the monastery of Jesus called the “bean-field.” Apart from these [carts] some forty or fifty stretchers were used to carry those bodies which didn’t fit in the carts, and it often happened that the grave diggers would carry dead babies or other children gravely ill with the plague on their backs. The entire city is now in such a lamentable and wretched state that men cannot even remember themselves nor can they imagine the travails they suffer. . . . Priests and confessors were missing in almost all the parishes, some having died and others being absent from the city, and as a result monks administered the sacraments in the churches and especially in certain parishes. The need was so pressing that often the priest left the church with the Holy Sacrament (may it be praised) [the Eucharist or Communion] and returned only after having given last rites to fifty or sixty or more persons, and it was beyond the strength of any one person to do so much.

From *A Journal of the Plague Year: The Diary of the Barcelona Tanner Miquel Parets, 1651*, edited by James S. Amelang (New York: Oxford University Press, 1991) pp. 106–7.

through trade contact with the Near East after 1500. Both theories provide plausible explanations for the presence of the plague in towns and urban centers throughout Europe. The fact that the plague outbreaks of the sixteenth through eighteenth centuries were mostly urban provides a stark contrast to earlier epidemics which struck city and countryside alike. There is no scholarly consensus over what caused the Black Death to become an urban epidemic as opposed to a more geographically diverse plague, and scholars are especially divided over what caused it to disappear from the European continent. The examples of plague outbreaks that follow focus on the plague in urban Europe.

In the High Renaissance, Florence, Italy, was hit with plague nine times between 1509 and 1531. During those outbreaks, Florence lost several thousand inhabitants. Combining religious practice, increasingly good medical advice, and a strong centralized government, Florence, and many other Italian cities, developed a multifaceted response to the Black Death. For example, the Florentine government set up **quarantines** and built **pest houses** to sequester the sick and dying, but it also allowed Florentine citizens to conduct religious ceremonies in order to deal with the spiritual and psychological effects of the plague. Also, the Florentine government provided assurances that its authority would remain constant: a bulwark of stability in the face of nature's uncertainties. This potent concoction of religion, practical medicine, and civic strength proved to be a recipe for public order. The Florentine example of blending of civic and religious response to outbreaks of the plague is mirrored throughout Italy. Even as the Renaissance gave way to the **Scientific Revolution** and the Enlightenment, the average Italian faced the new challenges to religion brought about by intellectual and scientific advancements in a remarkably static fashion.

One might be tempted to think, anachronistically, that the dawn of the Scientific Revolution brought an end to the importance of religion in civic attempts to deal with the plague. The small Tuscan town of Montelupo provides startling evidence to the contrary. There, during a plague outbreak of 1630–1631, local officials sought to restrict religious processions in order to halt the spread of the plague. Townspeople “revolted” against authority and sound medical advice, holding their procession as planned. People from the surrounding towns declared their support by joining the Montelupese in their procession. Strangely, as historian Carlo Cipolla noted, the townspeople's devout stubbornness, contrary to reason, seems to have had no effect on the spread of the plague in Tuscany. In fact, in broader terms, by the 1660s the plague had all but disappeared from peninsular Italy.

Throughout the seventeenth and eighteenth centuries, religion remained an important part of Italian life, but outside of Italy, the strength of the church was increasingly challenged by the emergence of centralized, national governments, including those of Spain and France. However, all of these national governments, and their local representatives, still remained remarkably similar to the Italian cities in their approaches to dealing with the plague. The difference between the Italian city-states and the emerging nation-states was primarily one of scale.

As in Italy, pest houses were one of the first methods utilized by European national, regional, and local governments to deal with the plague. Those infected with the plague were sequestered with others who had the plague in an attempt to stop the disease from spreading. There, they were given medical and spiritual attention. Many of the doctors and priests who attended sick patients became infected with plague and died. Some historians claim, however, that because plague victims were isolated in pest houses, the pestilence did not spread as quickly or as virulently.

In cases in which a plague outbreak was confined to one locale or part of a city, governmental officials often set up *cordons sanitaires*, which meant that no one was allowed in or out of an infected area. This was a cruel but probably effective method of stopping the plague's spread. Finally, often on a national level, governments instituted restrictions on trade with areas known to be infected with plague. These were meant to prohibit all types of traffic between a region infected with plague and one that remained untouched by the disease. Eighteenth-century Austria, for example, set up a *cordon sanitaire* between itself and the Ottoman East, where the plague was a constant threat.

During the 1651 outbreak of the pestilence in Barcelona, tens of thousands of people died from the disease. A tanner, Miquel Parets, left a first-hand account of the plague year that details his personal loss and his anger at local officials for shunning their duties. He argued that the social and governmental elite of the city, rather than caring for the sick and seeking to prevent the spread of the plague, neglected all of their civic and religious duties, instead fleeing to the countryside to avoid death. Parets, echoing the sentiment of fourteenth-century plague chroniclers, noted that the plague destroyed the basis of Barcelona's social structure, the family. He knew this intimately, as he lost his wife and three children to the plague. Eventually, the local government set up quarantines, pest houses, and rigorous attempts to rid the city of "infected" clothing and the dead. Barcelona experienced only one more, relatively minor, plague outbreak in 1653. The initial and rather inept manner in which the plague outbreak was handled in Barcelona is characteristic of plague outbreaks throughout Europe in the seventeenth and even eighteenth centuries. Once governmental officials, in Barcelona and elsewhere, rigorously implemented plague preventatives, the outbreak nearly always ended.

The French city of Marseilles suffered a plague epidemic in 1720 and 1721 that took the lives of over 40,000 victims. Records indicate that the Marseillaise officials initially dealt with the outbreak much like their counterparts in Barcelona. However, the outbreak at Marseilles could have been dealt with more efficiently. Early on, local doctors knew that Marseilles was experiencing a virulent outbreak of plague, but governmental officials refused to act on their *diagnosis* and advice. In fact, the government even rejected local doctors' pleas to isolate plague victims and quarantine those under suspicion. When the officials finally decided to take action, it was too late; the plague had already killed thousands. But, once measures were put in place to deal with the plague, including quarantines, pesthouses, and a *cordon sanitaire*, the plague subsided and disappeared. By 1722 the last major plague outbreak in western Europe, which killed half of Marseilles's population and a sizable number of Provence's residents, was over. From there, the plague retreated to Russia where it was greeted in the Marseillaise fashion. The Tsarist government in Russia denied that the plague was affecting its chief city, Moscow, until it became obvious to Muscovites and foreigners alike that they were indeed dealing with a virulent plague outbreak.

The refusal by the Russian government to deal with the plague outbreak, let alone to provide for precautionary measures against it, led to a large number of deaths. Eventually, as with Marseilles, Muscovite governmental officials realized that they had to implement measures to stop the plague. They ordered large sections of the city to be cordoned off and burned to get rid of plague victims, their homes, and everything associated with the outbreak. The vast majority of those who died from the plague were urban (and rural) poor, and as the deaths mounted, so too did their frustration. They did not want the government to destroy their homes, nor did they want to die from plague. Riots broke out throughout

Moscow and the surrounding districts, and the Russian government responded with heavy-handed tactics. Protestors and rioters alike were mowed down with cannon balls and musket volleys. The rioters were subdued, and “slums” were burned or cleansed. It is quite likely that 50,000 to 70,000 Russians died between the years 1770 and 1772. This outbreak in Russia represented the last major occurrence of plague in Europe, ending a long and deadly relationship.

There are a number of theories that attempt to explain the disappearance of the Black Death from Europe in the 1770s. These theories are as varied as mutation of the disease into a less virulent strain or perhaps changes in climate that made Europe an unsuitable environment for the disease. Although scholars continue to debate the nature and type of disease that killed millions in Europe over a 300-year period, one contributing factor that most agree led to the plague’s disappearance seems to have been human intervention. Even though it often took governmental officials too long to respond to outbreaks of plague in their municipalities, once decisive action was taken, cases of the plague became increasingly infrequent. At first, the plague was eradicated on a local level, but by the 1770s, through intervention and prevention programs, the Black Death had disappeared from Europe. *See also* Apothecary/Pharmacist; Black Death, Economic and Demographic Effects of; Black Death: Modern Medical Debate; Bubonic Plague; Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Diagnosis of Historical Diseases; Disinfection and Fumigation; Flight; Historical Epidemiology; Hospitals in the West to 1900; Humoral Theory; London, Great Plague of (1665–1666); Medical Education in the West, 1500–1900; Paracelsianism; Plague and Developments in Public Health, 1348–1600; Plague: End of the Second Pandemic; Plague in Britain, 1500–1647; Plague in Medieval Europe, 1360–1500; Plague in the Islamic World, 1500–1850; Plague Literature and Art, Early Modern European; Plague Memorials; Pneumonic and Septicemic



Plague doctor. The hat, mask suggestive of a bird beak, goggles or glasses, and long gown identify the person as a “plague doctor” and are intended as protection. Descriptions indicate that the gown was made from heavy fabric or leather and was usually waxed. The beak contained pungent herbs or perfumes, thought to purify the air and relieve the stench. The pointer or rod was intended to keep patients at a distance. Courtesy of the National Library of Medicine.

Plague; Public Health Boards in the West before 1900; Religion and Epidemic Disease; Thirty Years' War; Urbanization and Epidemic Disease.

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WILLIAM LANDON

PLAGUE IN INDIA AND OCEANIA: THIRD PANDEMIC. In the last decade of the nineteenth century, **bubonic plague** traveled from China to Hong Kong, and thence to Bombay. From this metropolis, India's "first city," plague spread to other parts of the country within four years. By 1930, 12 million persons had succumbed to the disease.

The priority in British colonial medical policy, hitherto, had been to preserve the health of the Europeans and keep **epidemics** from spreading to their quarters in towns and cities, from the areas inhabited by Indians. Rural regions were beyond the concern of the imperial power. The British attributed epidemic diseases, which they considered endemic to India, initially to the **environment** and then to the "habits" of their subjects. When plague struck Bombay, in September 1896, the authorities knew nothing of its etiology, nor how to treat the disease. It had struck at a premier port and administrative center of British India. The fear was that Bombay, with such extensive commercial intercourse with Europe, would threaten the whole world with a revival of the frightful scourge of earlier times. It was not long before it spread by land and by sea to other parts of the province—to Ahmedabad in September, and Karachi and Poona by December—along the lines of communication. Until 1900 plague was an urban phenomenon, but as each of the more populous towns became a focus for disseminating infection into the surrounding areas, it spread from city to village and from village to village.

The colonial government consequently resorted to drastic controls to prevent its spread and empowered itself with the Epidemic Diseases Act of 1897 to enforce them. The first measure to be implemented was mass **disinfection**, on an unprecedented scale, with potassium permanganate, phenyl, lime chloride, sulfur fumigation, with the pouring of carbolic acid down drains, and even with the burning of fires to rid the air of plague germs. This was in keeping with the **miasmatic** theory of the cause of disease, then prevalent. The other steps taken included the inspection of houses in which plague victims resided, the opening up of the roofs of houses, marking them “UHH” (unfit for human habitation) and sometimes even burning them down. The afflicted were subjected to medical examination, and their clothing and bedding were destroyed. Those exposed to the infection were segregated in health camps, and the plague victims hospitalized. Restrictions were imposed on road and rail **travel** within the country, and passengers were subjected to examination at railway stations and to detention at **quarantine** camps. The British authorities also prohibited fairs and **pilgrimages**, which they saw as breeding grounds of disease. As for foreign travel, quarantine was imposed against Bombay’s port and, with the outbreak in Karachi, against all Indian ports. The Haj to Mecca by Muslim Indians was also prohibited for some time. When quarantine was lifted, all outbound vessels were inspected, their holds cleaned with lime wash, the crews medically examined, and their clothing disinfected.

This intervention was unparalleled: never before had the medical establishment wielded such power. The British ascribed the plague to the conditions in which they perceived Indians to be living: filthy, with poor ventilation, open drains, and overcrowding in the growing cities. The other causative factor, according to the British perspective, was Indian customs, prejudices, and the “native” remedies to which the people resorted. The real culprit was said to be the Indians’ poor stamina, lack of **immunity**, and **poverty**, whereas it was observed that the European was surprisingly immune. There was the usual blame game within the establishment; the sanitary commissioner of India blamed the government of Bombay for ignoring his suggestions. On the other hand, the Indians’ perception was ambivalent: some regarded plague as a judgment from God, whereas a practitioner of **ayurveda** ascribed it to the consumption of acids, salts, and bitter, in excess, and to the inhaling of damp **air**. The local **press**, publishing in the regional languages, held the municipal authorities squarely responsible, for neglecting drainage in the city of Bombay.

The anti-plague operations were more intense in the cities and towns than in the rural areas, and hence the resistance was also urban-based. The population of Bombay halved, as people fled in panic. The draconian steps met with vigorous opposition from Indians, who perceived them as culture and gender insensitive. The inspection of homes by soldiers was considered an invasion of domestic privacy, whereas the enforced segregation went against the local traditions of relatives’ caring for patients. Hospitalization was looked upon as polluting: hospitals were places where caste, religious and *purdah* observances, and food and drink prescriptions were violated. It was generally believed that people went there to die. Furthermore, it was rumored that the hearts of plague patients would be taken out to be sent to Queen Victoria (1819–1901), who had been angered by the disfigurement of her statue by protestors. The “body” was seen to have been violated with the examination of the arm pits of both men and women for the presence of buboes. In the case of the latter it was considered a dishonor that male doctors performed the examination. The extracts from contemporary newspapers show the extent of opposition,

despair, and anger. One example plaintively stated that it seemed the “body” belonged to the master (meaning the colonial power) and not to the slave. Inspections were evaded, and the infectious diseases hospital raided. This opposition is also to be seen in the background of a rising national consciousness against British rule, and thus the enforcement of measures was perceived as one more instance of the colonial state’s high-handedness and arrogance.

Yet Indian responses were not all negative and by no means uniform, even within communities. In fact, the great nationalist leader Lokamanya Tilak (1856–1920) endorsed segregation of the infected and alluded to the superstitious folly of those who regarded hospitals as chambers of death. The newspapers he was associated with, *Maratha* and *Kesari*, regularly reported the havoc caused by the enforcement of anti-plague steps in the city of Poona. It was against the manner in which the medical intervention was carried out that he protested. The plague commissioner of Poona, W. C. Rand, was so unpopular that he was assassinated. Among the Muslims in Bombay, there were contrary reactions: whereas some such as the Ismaili Khojas, led by the Aga Khan (1877–1957) were cooperative, others saw the closure of mosques and burial grounds as religious interference. Bodies of victims were sprinkled with disinfectants and cremated, contrary to the community’s burial prescription. The political leader, Badruddin Tyabji (1844–1906) explained to his fellow Muslims, at a public meeting, why these measures had been adopted. Because people had been refusing medicine, food, and drink when they did go into hospitals, caste and community hospitals were opened in the cities of Bombay province. These were for the exclusive use of these groups and were founded at Indian initiative and with Indian funding.

Within months of the outbreak, **Waldemar Haffkine**, the Russian bacteriologist assigned by the government of India to investigate the causes and to devise a method to deal with this reemergent disease, developed a prophylactic in a Bombay laboratory. Though Haffkine faced the intrigues and hostility of the British Indian Medical Service officers, who had a monopoly in the medical establishment, he persevered in perfecting the vaccine. The Aga Khan endorsed it, and his community, the Ismaili Khojas, was among the first to accept the prophylactic, both in Bombay and in Karachi. Various leading medical practitioners including Bhalchandra Krishna Bhatvadekar (1852–1922), chairman of the standing committee of the Bombay municipal corporation, propagated it in newspapers, explaining its efficacy. Medical organizations such as the Bombay Medical Union and the Grant College Medical Society endorsed the vaccine. Haffkine was made director of the Plague Research Laboratory, (PRL) in 1899, and by 1901, 8,601,123 doses of the plague vaccine had been produced and sent out to different regions of India. However, a setback to its propagation occurred, when an accident took place in 1902, at Malkowal, a village in Punjab. Nineteen vaccinated persons died of tetanus. Although this incident cost Haffkine his job, he was later exonerated when the commission of inquiry found that the contamination of the vaccine had not happened in his laboratory. The accident diminished the demand for the vaccine in the Punjab for a while, but not elsewhere. Doctors were deputed to Bombay, from both British India and the princely states, to study inoculation at the PRL.

The vigorous opposition to anti-plague measures led to a change in colonial policy, and the enforcement of controls was abandoned from the 1900s. It was then decided to promote preventive steps, with the support of the people. Inoculation was propagated by voluntary organizations involved in health care, through lectures accompa-

nied by magic lantern demonstrations (early forms of slide shows), and through the publication of pamphlets, and the harmlessness of the vaccine was explained at citizens' meetings. That inoculation was done by Indian doctors made it more acceptable, and its endorsement by leaders, such as Tilak and the other nationalist Gopal Krishna Gokhale (1866–1915), made it acceptable in the small towns and districts. Editors of regional-language newspapers were taken around the Bombay Bacteriological Laboratory, as the PRL was renamed in 1906, to see for themselves the method of the preparation of the vaccine. They then wrote papers explaining the procedures and discounting rumors. The Plague Research Commission, a body appointed by the government to determine the causes of the recurrent plague epidemics, showed in its 1908 report that the bubonic plague infection depended on the extent of the disease in the rat. Plague spread among rats and from rat to man through the rat flea *Xenopsylla cheopis*. Subsequently, rat destruction was adopted on a war footing, and the municipalities employed rat brigades.

Plague was never able to invade all of India. The most striking feature was its extremely uneven and irregular distribution: Assam and Eastern Bengal were immune. This was discovered to be the result of the plague flea, which breeds most freely and lives longest in the debris of cereals; thus, places with a link with the grain trade were affected. By the 1930s, some control had been achieved over the disease.

Plague also struck Sydney, Australia, in 1900, but there were only a total of 1,363 cases during the twentieth century, a huge contrast to India. An expert staff was trained in Sydney to search out plague rats, which were found in wharves, warehouses, shops, stables, and dilapidated cottages. The produce trade in hay, straw, chaff, and animal foodstuffs was found to be closely associated with plague rats. Plague, however, did not spread all over Sydney, thanks to the efforts of President of the Board of Health Dr. J. Ashburton Thompson (1846–1914), and investigations showed that it was confined to a very limited area. *See also* Colonialism and Epidemic Disease; Disease, Social Construction of; Flight; Plague in Africa: Third Pandemic; Plague in China; Plague in East Asia: Third Pandemic; Plague in the Contemporary World; Pneumonic Plague in Surat, Gujarat, India, 1994; Public Health Agencies in Britain since 1800; Trade, Travel, and Epidemic Disease; Vaccination and Inoculation.

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PLAGUE IN MEDIEVAL EUROPE, 1360–1500. In 1360, a decade after the **Black Death**, the second wave of the second **bubonic plague pandemic** hit Europe, and major outbreaks recurred roughly every decade to 1500. The mortality rates of the 1360 plague and subsequent outbreaks were never as high as during the 1347–1352 plague years. As in the 1347–1352 plague years, later outbreaks killed people in all age groups, but they were particularly unsettling because they included a disproportionate number of infants, children, and adolescents. This disparity caused some modern scholars to question whether the “Black Death” was actually the bubonic plague or another disease or set of diseases. Whatever the cause, Europe’s once populous countryside was nearly emptied, and city populations, too, were thinned from successive plague outbreaks, which kept Europe’s population well below pre-plague levels. This depopulation initially crippled Europe’s economy, but by 1500, it had recovered, far surpassing the pre-plague economy. Demographic and economic effects like these were accompanied by secular and religious responses to the Black Death; especially civic attempts to deal with the perceived causes of the plague and religious fervor that sought to remedy the spiritual effects of sin manifested by the plague.

The second wave of the plague appears to have killed mainly those Europeans who were born after the first outbreak of the Black Death. The traditional argument to explain the 1360 plague’s focused mortality states that the generation that survived the first wave of plague may have developed at least some temporary immunity to it. So, when the plague reappeared in 1360, the adult population was often able to fend it off, but the young population was unable to cope. Others argue that the changes to the age structure of the European population as a result of the Black Death and the resulting natalism left a greater number of children and adolescents at risk when plague epidemics recurred.

The European economy, at first ravaged by the plague, eventually benefited from the dramatic decrease in the supply of laborers. For example, after the plague struck, arable land, which was at a premium, became more accessible in rural Europe after successive waves of plague. Economic historians argue that this abundance of land, combined with advances in agricultural technology, allowed fewer Europeans to produce surpluses of grain. This, in turn, meant a better-fed and healthier population as a whole. And, in the years following the 1360 plague outbreak, in real terms, urban wages increased dramatically which meant that the population that survived the plague had access to greater wealth. The rise in urban and rural wages is explained by “demand” which outstripped the supply of labor. After a brief period of inflation, by 1400 Europe’s economy adjusted and expanded well beyond its pre-plague zenith. These direct effects of plague were accompanied by secular and religious responses to the epidemic.

In an attempt to deal with the “bad air” or “miasma” that was thought to contribute to spreading the plague, some European cities and towns focused on removing anything that produced a noxious smell, especially when plague had been reported in the neighborhood. Refuse was collected, streets were cleaned, tanners’ shops and slaughterhouses were required to remove animal byproducts from city centers to outlying regions, and human waste was dealt with more promptly. City ordinances such as these were not based upon biological or epidemiological foundations. Rather, they were based upon medieval medical concepts that today seem quaint, but cleaner cities nevertheless meant less disease.

Religion also reacted to and changed with the plague. Although religious responses varied by region, nearly all of Europe accepted the plague as God's judgment. The 1360 epidemic seemed especially biblical in nature, visiting God's judgment on the second generation—those who were born after the Black Death struck in 1347. Continued outbreaks of plague led many Europeans to believe that Christ could not be their intercessor and their judge at the same time. So, as with artistic responses to the Black Death, many Europeans turned to pre-plague traditions that they modified to make sense of and remedy the plague. The cult of the Virgin and the cult of the saints, both of which existed before the plague, provided the spiritual balm that Europeans craved. The Virgin interceded on behalf of the faithful, and the saints, especially St. Sebastian, were thought to provide spiritual and physical protection from the plague. These "cults," linked with penance and processions provided comfort to Europeans in the uncertainty brought on by the Black Death.

Between the years 1360 and 1500, the Black Death killed hundreds of thousands of Europeans. Nearly every European was touched by the plague, and nearly everyone lost a friend or relative to it. Although the Black Death certainly affected medieval Europe demographically, it also brought about new economic, civic, and religious responses, which allowed Europe to begin a long period of recovery to which the Renaissance bears witness. See also Black Death and related articles; Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Flight; Historical Epidemiology; Human Immunity and Resistance to Disease; Medical Education in the West, 1100–1500; Pest Houses and Lazarettos; Plague and Developments in Public Health, 1348–1600; Plague in China; Plague in the Islamic World, 1360–1500; Quarantine.

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WILLIAM LANDON

PLAGUE IN SAN FRANCISCO, 1900–1908. The San Francisco epidemic of **bubonic plague** comprised part of the **Third Pandemic** that had ravaged South and East Asia since the mid-nineteenth century. In 1894 **Alexandre Yersin** and **Shibasaburo Kitasato** had independently identified the *Yersinia pestis* bacterium responsible for plague's spread. In 1897 **Paul-Louis Simond** theorized the rat-to-flea-to-human transmission of plague. Many members of the United States medical community doubted this theory until later in the decade, however, and postulated other causes for its spread, including infection through contaminated dust, and racial susceptibility, particularly among Asians.

Bubonic plague arrived in Honolulu, Hawaii, in 1899, spread by ships that harbored rats infested with infected fleas. On January 2, 1900, the ship *Australia* landed at San Francisco's Angel Island **quarantine** station, bringing goods from Honolulu. After fumigation and quarantine, the *Australia* entered San Francisco's port. However, it unknowingly transported infected rats into the city.

On March 6, 1900, Wong Chut King (b. 1859) was discovered dead in the basement of a Chinatown Hotel. His death exacerbated existing prejudices toward Chinese civilians, who had long been perceived as threats to local whites. San Francisco officials responded with a total isolation of Chinatown. They repealed it, however, after three days, stating that there was no conclusive proof of plague. Joseph Kinyoun (1866–1919), a federal bacteriologist and quarantine officer for the U.S. Marine Hospital Service, forerunner of the U.S. Public Health Service, stationed at Angel Island, confirmed plague. Hoping to avoid panic and financial ruin, city officials demanded that he remain silent.

Despite official denials, plague continued to spread. On May 15, Kinyoun carried out orders from Surgeon General Walter Wyman (1848–1911) to cordon off suspected areas of Chinatown, inspect all Chinese houses, isolate suspected plague victims on Angel Island, and inoculate all Chinese residents with the **Haffkine** vaccine, a dangerous and unpopular treatment. However, Chinese community leaders challenged the orders. On May 28, Judge William Morrow ruled that the restrictions discriminated unfairly against Chinese civilians. The state of California instituted a second quarantine, but by mid-June the courts had again struck it down.

In August 1900, Kinyoun recorded the first reported cases of bubonic plague among white San Franciscans. By the end of 1900, however, there were only 22 officially documented cases, and many locals continued to deny plague.

By 1901 Kinyoun's public and discriminatory responses to plague had alienated both local leaders and the Chinese community. To settle the acrimony, Surgeon General Wyman appointed a panel of national experts to inspect San Francisco. In February 1901, this panel examined suspected cases and confirmed bubonic plague conclusively. Hoping to stifle their findings, California's Governor, Henry Gage (1852–1924), struck a deal with Surgeon General Wyman. Gage promised to work with federal officials in exchange for keeping the panel's report private.

In April 1901, Wyman replaced the maligned Kinyoun with Rupert Blue (1868–1948), another physician with the Marine Hospital Service. Blue worked more closely with Chinatown leaders and hired an interpreter and go-between to the Chinese community. Blue tried to relax suspicions among the Chinese community and rejected some of his predecessor's harsher measures. He also tested new theories that linked rats to the spread of plague. Blue's new approaches did not immediately stifle plague. Although new infections slowed in 1901, reported cases grew in summer 1902.

In October 1902, and again in January 1903, U.S. public health leaders met at national conferences and censured Governor Gage for suppressing evidence of the outbreak. At the second meeting, furious officials recommended a nationwide boycott of California unless the state ceded control over the plague campaign to federal officials. The newly elected governor, George Pardee (1857–1941), assented to these demands and allowed Blue free rein. Blue employed fumigation, rat eradication, and improvements of buildings to destroy rat breeding grounds. He also used anti-serum rather than **vaccinations**, a more expensive but much less risky form of therapy. With these measures in place, the last reported case appeared on February 19, 1904.

By fall 1904, city officials lobbied Wyman to lift federal intervention. Although Blue urged caution, Wyman withdrew him on April 4, 1905. Blue's concerns would be substantiated in 1907, when a second wave of bubonic plague struck San Francisco, just a year after the city's great earthquake. By then, however, San Franciscans were quick to call on the federal government for assistance. Blue returned to San Francisco, his com-



Tagging the morning's catch. Twelve rat-catchers attach tags to dead rats to identify where, when, and by whom they were collected. A man in the center dips a rat trap into a bucket of antiseptic solution. Photo taken between 1907 and 1909. Courtesy of the National Library of Medicine.

mitment to the theory of the rat flea vector reinforced by a 1906 confirmation of Simond's theory by the British plague commission in India. Supported by local groups like the Citizens' Health Commission, Blue's second campaign focused on exterminating rats and on early treatment. The last reported case of plague came in March 1908, bringing the final tally for both epidemics to 280 reported cases and 172 deaths.

As illustrated by city, state, and federal responses, political and economic imperatives initially took precedence over public health tactics. City and state leaders denied the existence of plague because they feared its impacts on commerce. Civic and public health officials **scapegoated** the city's Chinese community, whose members they considered racially susceptible to disease. Targeted quarantines, vaccinations, and cleanups of Chinatown resulted in significant Chinese distrust of the public health community and a failure to admit the existence of plague in other parts of the city. *See also* Bubonic Plague in the United States; Plague in China; Plague in East Asia: Third Pandemic; Plague in India and Oceania: Third Pandemic; Race, Ethnicity, and Epidemic Disease.

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JULIA F. IRWIN

PLAGUE IN THE CONTEMPORARY WORLD. After the end of the **third plague pandemic** around 1960, plague did not simply vanish, although it causes far fewer deaths in the early twenty-first century than such waterborne diseases as **cholera**. **Bubonic plague** remains endemic in central and east Asia, Africa, and North and South America with continued animal infections in areas such as Mongolia, China, the Democratic Republic of the Congo, Ecuador, and the four corners region of the American Southwest. There have continued to be episodic outbreaks since 1960, most notably in South Vietnam during the 1960s, and scattered outbreaks in diverse regions of the globe such as the Democratic Republic of the Congo, Madagascar, and Ecuador. In addition, **pneumonic plague** also remains a threat in various regions. The plague is still regarded as a major public health hazard, and the **World Health Organization (WHO)** requires immediate notification of national and international public health bodies when cases are diagnosed.

The *Yersinia pestis* **bacterium** has developed 76 strains of three biovars (biotypes), and all three biovars continue to be present in the wild. Biovar Orientalis is the most common and is endemic in North America, South America, Asia, and India, whereas biovar Medievalis is endemic in central Asia, and biovar Antiqua is endemic in Africa. Most scientists agree that biovar Orientalis has evolved from either biovar Antiqua (responsible for the **Plague of Justinian**) or biovar Medievalis (responsible for the **Black Death**), or both. There is now some indication that a fourth biovar, Microtus, may have evolved in China in the late twentieth century. Bubonic plague was introduced during the third plague pandemic into some regions where it is now endemic, such as the United States and Madagascar.

By 1959 the number of plague cases annually reported worldwide had declined to slightly more than 200, down from nearly 5,000 in 1953. **Pesticides** and rodenticides helped to produce the decline, killing both fleas and rats, the traditional hosts for the plague bacillus. Mortality rates also declined during the 1950s, reflecting the increased use of **antibiotics** and sulfa drugs as well as better patient care. Thereafter mortality rates continued to decline and hover between 4 and 10 percent. These figures are somewhat deceptive, however, because some outbreaks still produce mortality rates of 50 percent or higher. Generally the outbreaks of bubonic plague that produce high mortality rates are combined with cases of pneumonic plague, which still produces mortality rates of over 90 percent if not treated immediately. Plague vaccines continue to be developed and have proven widely effective in preventing plague outbreaks and limiting the mortality rate for those people infected.

Like many other disease-causing microorganisms, however, *Yersinia pestis* is developing resistance to antibiotics. During an outbreak of bubonic and pneumonic plague in Madagascar from 1996 to 1998, several cases displayed a resistance to treatment with chloramphenicol and ampicillin, two commonly used antibiotics. Plague in the early twenty-first century continues to display wide diversity in its ability to infect humans and in the mortality rate of those people infected. Most cases of bubonic plague have been treatable with antibiotics, as have cases of pneumonic plague, when the treatment is started almost immediately. Some cases are not always readily diagnosed, often leading to fatalities because treatment is started too late to be effective.

Another issue remains troubling. During World War II, the Japanese military began the development of biological weapons. Unit 731 went so far as to field test bubonic

plague weapons in China. After the end of the war several countries continued to develop plague as a biological weapon. The Soviet Union developed the most extensive plague arsenal, although the Russian state—along with the United States and the United Kingdom—has renounced biological warfare. Plague is more difficult to deliver than anthrax, but its potential as a weapon for a rogue state or a terrorist group cannot be discounted.

Plague during the Vietnam War. The outbreak of plague in Vietnam during the 1960s illustrates the impact of **environmental** factors on plague as well as an aggressive plague prevention campaign. *Yersinia pestis* was endemic in Southeast Asia but seemed to be under control until the Vietnam War broke out. Between 1965 and 1970, more than 25,000 cases of plague were officially reported in South Vietnam, although the actual total was many times higher. This outbreak was the first major epidemic to occur after the use of insecticides for killing fleas, which are the carrier of the *Yersinia pestis* bacteria, and antibiotics for treatment, suggesting that plague epidemics are still possible under the right set of circumstances.

As part of its strategy in the Vietnam War, the United States engaged in a major use of defoliants that helped to force the Vietnamese people off the land. South Vietnam had been a major rice exporter in 1964 but was a net importer the next year because of the damage caused by defoliation. As people moved into refugee camps, they entered surroundings that were ripe for epidemics because of overcrowding and poor sanitation. Once American troops began to withdraw in the early 1970s, the number of plague cases declined as the refugee camps were dispersed.

American troops were required to receive a series of anti-plague **vaccinations**, although cases were reported among U.S. troops, as among military support and civilian personnel, because they were not always up to date with their vaccinations. Almost all American troops infected by bubonic plague survived.

The South Vietnamese people were not so lucky. Many of the refugee camps had poor sanitation, and rats were common, although some efforts were made to apply insecticides. Plague once again infected Vietnamese cities such as Hue in 1965 even though the last reported case had been in that city in 1950. As a general rule, however, this epidemic struck rural areas more heavily than urban areas; otherwise, the mortality rate might have been higher. Although reported plague cases exceeded 5,000 late in the decade, mortality rates remained low. This was the result of both the relatively low virulence of the strain of plague in the country and the use of antibiotics in treating the disease. Charles Gregg indicates that there were between 100,000 and 250,000 plague cases in South Vietnam in the decade after 1964, probably more cases than occurred in Indochina during the Third Pandemic. In this case the environmental changes produced by war helped to lead to the outbreak of the plague epidemic in a country in which the disease was endemic.

United States. Bubonic plague first came to the United States during the third pandemic and has remained endemic in some regions of the West ever since. Plague in the United States remains a western phenomenon, with almost all cases originating west of the 100th meridian. Generally, cases in the eastern United States, such as one in Greenville, South Carolina, in 1984, have originated in the West. Prairie dogs, ground squirrels, and rabbits, rather than rats, provide the most common hosts for the fleas carrying *Yersinia pestis* in the United States. As Americans increasingly enjoyed the open

spaces of the West after 1970, they increasingly came into contact with animals infected with bubonic plague, and the number of diagnosed cases increased during the 1970s. Although disturbing, the number of U.S. cases is lower than that in Asia or Africa. WHO reported only two cases in the United States in 2002, one in 2003, and only 61 total from 1997–2003. The mortality rate in the United States ran slightly over 10 percent in the 1970s and 1980s, in part because of misdiagnoses that led to failure to treat the disease properly until it was already too late.

Plague around the World. Natural plague foci exist in several regions of the world. Since 1980 most cases of the plague have been found in 20 countries worldwide, especially in the Democratic Republic of the Congo, Madagascar, Ecuador, and Peru with scattered cases elsewhere including the United States, India, Kazakhstan, and Mongolia. In 1997, for example, WHO reported 5,519 cases (2,863 in Madagascar) with 274 fatalities. By 2003 the number had declined to 2,118 cases (181 fatalities). Although bubonic plague presents regional health hazards, secondary and primary pneumonic plague that result from an initial infection, coupled with the ease of travel, make it possible for plague to spread beyond regions where it is endemic. In 2003, 11 plague cases were diagnosed in Algeria, the first cases in 50 years. During 2006, 1,174 cases of pneumonic plague with 50 deaths occurred in the Congo, illustrating the impact of an existing plague reservoir combined with poor sanitation. There are too many natural plague reservoirs and too many different hosts for us to expect the eradication of the disease. Improved sanitation, public health facilities, and antibiotic treatment have reduced this threat. Nonetheless, severe ecological disruption in a natural focus region and the threat of bioterrorism continue to present the specter of another plague epidemic. See also Animal Diseases (Zoonoses) and Epidemic Disease; Biological Warfare; Bubonic Plague in the United States; Drug Resistance in Microorganisms; Plague in Africa: Third Pandemic; Public Health Agencies, U.S. Federal; War, the Military, and Epidemic Disease.

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JOHN M. THEILMANN

PLAGUE IN THE ISLAMIC WORLD, 1360–1500. The first fully recorded plague outbreak in the Middle East was the **pandemic** known as the **Plague of Justinian**, named after the sixth-century Byzantine emperor. For the next 200 years or so, plague recurred in the area at intervals that ranged from 9 to 13 years. Then, for reasons unknown, it disappeared, both from the Middle East and from Europe until 1347, when the **Black Death** pandemic ravaged both regions. Following this outbreak, plague continued to recur regularly in the Middle East and North Africa until its suppression

in the late nineteenth century. At one time or another, these recurrences affected most Islamic communities in southwestern Asia, North Africa, and the Iberian Peninsula. During the medieval period, 1360 to 1500, plague was recorded as far afield as Astrakhan (southeast Russia) in 1364; Astarabad (Iran, southeast of the Caspian Sea) in 1435; Herat (western Afghanistan) in 1435 and 1464; Yemen in 1438; and Tabriz (northwest Iran) in 1487.

Late medieval visitations of the plague were so idiosyncratic that neither Muslim nor Christian **physicians** and theologians could determine the etiology of the disease, and consequently no cure was found for it. **Islamic medical theory** attributed the disease to a **miasma**, whereas religious opinion regarded it as a divine mercy and martyrdom for Muslims. Viewing plague as an act of God, most Muslim physicians did not advise the avoidance of infected areas; the Prophet Muhammad (570–632) himself had denied the existence of **contagion** and enjoined his followers neither to enter nor flee an affected area. There were, however, those who disagreed: **Rhazes**, the renowned ninth-century Baghdad physician, advocated **flight**, and in Muslim Spain, Ibn al-Khatib (1313–1375), a fourteenth-century Arab physician from Granada (unjustly accused of heresy and put to death in 1375) spoke out openly against prevailing religious ideas on contagion. He recognized that plague outbreaks occurred after the arrival of people from infected areas, and noted that people who were not exposed to epidemics, such as those in prison or nomads in the desert, did not catch the disease. To prove his point, Ibn al-Khatib gave the example of a man in Sale (on the Atlantic coast of Morocco) who escaped the plague by confining himself and his household behind walls, with plenty of food and drink, and refusing to leave until the plague had disappeared.

In 1360 Islamic communities in the Middle East were still suffering from the effects of the Black Death, which had greatly reduced their numbers. However, it is the cumulative effect of later recurring epidemics that accelerated this reduction. In Upper and in Lower Egypt, plague epidemics were cited in 55 years during the 170 year period between the outbreak of the Black Death there in 1347 and the Ottoman conquest of Egypt and Syria in 1517; in Syria, outbreaks were cited in 51 years. There were apparently 20 major plague epidemics in Egypt during this period, occurring on an average of every eight to nine years; in Syria-Palestine, there were 18 major epidemics, occurring every nine-and-a-half years. Of greater demographic importance, however, is the nature of the outbreaks; **pneumonic plague** recurred regularly after the Black Death, a case of **bubonic plague**. Arabic sources clearly describe the expectoration of blood, the rapid rate of infection, and the appearance of plague in winter months.

The most virulent outbreak to occur between 1360 and 1500 was that of 1429–1430 in Egypt. This epidemic was well documented by contemporary historians because Egypt had the greatest urban concentration in the region and because the historians themselves lived there. The epidemic reached Cairo in December 1429 and spread to Upper Egypt until the middle of March 1430, when it started to decline rapidly. Two Arabic historians, al-Maqrizi (1364–1442) and Ibn Taghribirdi (fl. 1430–1450), lived through the 1429–1430 outbreak in Cairo: the latter called it the “Great Extinction” saying he had not known of anything like it in Egypt or Syria since the year 749 AH, that is, since the Black Death. Their writings not only give a vivid picture of this epidemic’s effect on Egypt, but also provide us with an idea of the consequences of plague epidemics on Islamic communities in general.

The annalist Ibn Taghribirdi, born in Cairo, describes what he himself had witnessed in the plague epidemic of the years 1429–1430 and incorporates some of al-Maqrizi's impressions about the outbreak. He records that the disease had appeared in Syria-Palestine the year before, when it struck Gaza, Jerusalem, Safad (in Galilee), and Damascus. He notes that the appearance of the epidemic in winter was unusual, because the disease normally appeared in spring. Ibn Taghribirdi relates that fasting was declared in Cairo for three days, and that people went out in a procession to the desert to pray, their voices loud in supplication to God for an end to the calamitous scourge. He comments that the death toll on that particular day was even higher than on the one before. He goes on to say that dead fish and crocodiles were found floating on lakes and on the River Nile, and that large numbers of deer and wolves were found dead in the desert between Suez and Cairo. Plague spread rapidly: at its peak, the dead in Cairo and its suburbs numbered 2,100 in one day and, in certain villages, the daily death toll was 600. The stench from decomposed bodies became intense, despite the cold weather. The author's daughter caught the disease and died on the same day, but no coffin was found for her; seven members of his brothers' families died too. He recounts an incident that he describes as a "horrific curiosity": in the confusion of burying such large numbers, a child was mistakenly taken and buried by the wrong family. Demand for coffins increased, and people resorted to carrying their dead on "planks of wood, on boxes, or in their arms". On the streets, the continuous flow of coffins was "like caravans of camels." It was difficult to bury the countless dead: grave-diggers worked through the night while relatives waited in cemeteries. Prices of shrouds rocketed, as did those of items needed by patients, such as sugar, purslane seeds, and pears, although "few received medication, while some died within the hour." Prayers over the dead were stopped in mosques; instead, they were held outside, over 40 or 50 corpses at a time. People would count each other after Friday prayers, with the absolute certainty that their number would be greatly diminished the following Friday. Everyone thought he would be the next to go; they surrendered themselves to the idea of death, repented, and made their wills. Legacies passed in quick succession from one inheritor to the next, as each new inheritor passed away. Youths started carrying prayer beads and spent most of their time praying. Because of high mortality and the preoccupation of the living with the dead, **trade** in the marketplace stopped. In the final stages of the epidemic, it was noticed that the disease struck "the elite, the notables and eminent persons while, previously, it had affected children, slaves, foreigners and servants." The disease was also thought to infect animals.

The immediate consequence of plague epidemics was urban and rural depopulation. The reduced productivity of the countryside greatly affected the prosperity of urban areas. The densely populated cities themselves, centers of trade and communication, were particularly vulnerable; here the disease spread readily and caused massive mortality.

From the middle of the fourteenth century, there was a marked decline in the population of the Middle East so that by the early fifteenth century, it had fallen by more than a third of its highest previous level. Not until the end of the nineteenth century did the population of the Middle East and North Africa return to what it had been before the Justinianic Plague of the sixth century. Furthermore, the recovery was mainly urban: the rural countryside today is less populated and less cultivated than it was fifteen centuries ago. *See also* Avicenna (Ibn Sina); Bimaristan; Plague in the Islamic World, 1500–1850; Public Health in the Islamic World, 1000–1600.

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SELMA TIBI-HARB

PLAGUE IN THE ISLAMIC WORLD, 1500–1850. Throughout the medieval and early modern periods up until the modern era, plague **epidemics** were a constant fact of life in every part of the Old World, including that dominated by Islam. At the turn of the sixteenth century, outbreaks of plague seem to have become a global phenomenon, even being carried to the New World. Because the areas infected by **bubonic plague** and its **septicemic** and **pneumonic** variations steadily expanded from the early sixteenth century onward, plague was present in at least one location in the Islamic world virtually every year between 1500 and 1850, sometimes as sporadic outbreaks affecting only a single region, and other times, as extensive episodes spread over multiple regions. From the sixteenth century onward, plagues began to break out even more frequently than before. Although major plague outbreaks occurred every 10 years on average in both the Islamic world and in Europe during the fourteenth and fifteen centuries, they began to recur every few years in the sixteenth century. By the end of the sixteenth century, plague outbreaks recurred almost every year, becoming even more of a routine/seasonal incident. After the frequent recurrences throughout the seventeenth century, plague outbreaks began to take place less regularly in the Islamic world during the eighteenth and nineteenth centuries, though with a tendency to reappear in every new generation.

During the sixteenth century, the Islamic world saw the emergence and expansion of major regional empires. The sixteenth-century Ottoman (Turkish), Safavid (Persian), and Moghul (Indian) empires added immensely to the globalization of plague pandemics in the Old World, by providing developed **trade** and communication networks through which plague could travel even more freely than before. The growth of imperial domains produced an increased level of communication, interaction, and mobility between regions brought together by conquest and subsequently bound within an administrative, military, and commercial system, which gave rise to increased, widespread, and persistent plague outbreaks.

Among these imperial bodies, the Ottoman Empire had the most important influence on the expansion of plague epidemics in the Islamic world, and this lasted into the nineteenth century. Because it consolidated at the intersection of trade routes connecting the Balkans, Caucasus and Central Asia, Asia Minor, the Arabian Peninsula, Iran, North Africa, and the eastern Mediterranean, the Ottoman Empire provided a new set of connections over which plague could spread extensively. With ongoing conquests during the sixteenth century, the size and population of the empire doubled, but new trade networks connecting the eastern Mediterranean ports and the Red Sea, as well as those of the Indian Ocean, were also integrated to the old ones. The integration of these networks had an immense impact on the spread of plague epidemics, which contributed to the disease’s globalization.

The Safavid Empire, which emerged on the eastern frontier of the Ottoman Empire in the beginning of the sixteenth century, expanded over all of Persian lands and remained in power until the eighteenth century. Having control over the Persian Gulf, the Safavids engaged in maritime trade connections with several European states and undertook a series of infrastructural provisions for the development of trade, such as building roads, bridges, and caravanserais, and providing increased security for promoting international trade. As a result, several cities thrived in the Safavid period as trade centers, especially for the silk trade. However, increased circulation of goods and people resulted in a series of epidemics in Safavid lands. The major cities of the empire were struck by repeated outbreaks of plague throughout this period.

The Moghul Empire emerged on the eastern frontier of the Safavid Empire in the early sixteenth century and expanded over the entire Indian subcontinent, remaining in power until the mid-nineteenth century. With a centralized administration, the Moghul Empire had strong commercial relations with several European countries. In addition to already established sea routes through the Red Sea and the Persian Gulf, trade connections flourished with East Africa, East Asia, and overland caravan routes westward. Given abundant international trade contacts, Moghul lands were repeatedly struck by plague outbreaks throughout this period.

Plague epidemics were particularly severe in the early modern Islamic world during the sixteenth and seventeenth centuries. There were several major outbreaks during the sixteenth century, the more important ones taking place in 1520–1522, 1534–1535, 1544–1545, 1553–1556, 1561, and 1565–1566. Yet the most terrible outbreak of the sixteenth century started in the 1570s and continued more or less until the end of the sixteenth century. Being particularly strong in Istanbul, Anatolia, the Balkans, Egypt, North Africa, and in Safavid and Moghul lands, this vast pandemic affected almost all parts of the Islamic world, as well as Europe. The seventeenth century also witnessed several major outbreaks: 1603, 1611–1613, 1620–1624, 1627, 1636–1637, 1647–1649, 1653–1656, 1659–1666, 1671–1680, 1685–1695, and from 1697 until the early years of the eighteenth century. The outbreaks of the eighteenth century were reported as mostly minor outbreaks; the major ones took place in 1713, 1719, 1728–1729, 1739–1743, 1759–1765, 1784–1786, and 1791–1792. Plague epidemics gradually disappeared during the course of the nineteenth century. The major outbreaks of the nineteenth century took place in 1812–1819 and 1835–1838. It is commonly held that the disappearance of plague epidemics in the nineteenth century in the Islamic world was the result of the adoption of quarantine measures and their implementation in the Ottoman Empire from 1838 onward. Indeed, cases of plague seemed to decrease dramatically all over Anatolia, Egypt, and the eastern Mediterranean lands of the Ottoman Empire immediately after the implementation of the new health regulations. Nevertheless, plague epidemics continued to linger for several decades in North Africa and Iraq, until the end of the nineteenth century. Although the adoption of quarantine measures certainly helped the temporary elimination of plague epidemics in the Islamic world, it is still questionable to what extent it facilitated a process of decline for the plague, which had already started in the eighteenth century and continued during the first half of the nineteenth century.

During the recurrent waves of the second pandemic, plague almost always spread to the Islamic world from western European port cities, such as Venice or Ragusa (Dubrovnik),

through commercial contact with eastern Mediterranean port cities, and proceeding from coasts to inland regions. This was especially prevalent during the late fifteenth and early sixteenth centuries, when the networks through which plague spread had not yet been well established. After the integration of Egypt, Syria, North Africa, and the western Arabian peninsula into the Ottoman realms in the sixteenth century, and especially after the gradual consolidation of new trade and communication networks into the existing ones and the subsequent globalization of plague, the spread of outbreaks followed a more complex pattern of expansion, which was not only limited to the Mediterranean basin, but also included the networks of the Black Sea region and its hinterlands, the Caucasus and Central Asia, the Red Sea, as well as those of the Indian Ocean. Alexandria, Cairo, Algiers, Aleppo, Damascus, Smyrna, Thessalonica, Istanbul, Trebizond, Erzurum, Tabriz, and several other cities in the Islamic world constantly suffered plague outbreaks, which could suggest the endemicity of plague in these lands. In fact, for the eighteenth and nineteenth centuries, it has been suggested that plague was endemic in certain parts of the Near East, especially in Persian Kurdistan, the Libyan desert, and the Asir region between Yemen and Hejaz in the Arabian peninsula, which were natural centers of the plague, from which it spread to other regions by rodents forming temporary centers for plague, in Albania-Epirus, Moldavia-Walachia, Istanbul, Anatolia, and Egypt. It is, however, hard to prove the endemicity of plague in these regions in the absence of compelling research findings.

Because of the long experience of the Islamic world with the plague, the terminology used in the sources is very clear, having been employed since the early chronicles written during the first pandemic. Islamic sources distinguish between *wabā'*, which was used to refer to epidemic disease in general, and *tā'ūn* for plague specifically. By the time of the second pandemic, both the bubonic and pneumonic forms were very accurately described in historical sources. Not only the medical sources, but also other historical sources are clear and consistent on the terminology, which suggests an established general familiarity with the disease. There are references to plague in a vast array of sources in the Islamic world, including court registers, imperial decrees, collections of legal opinion, chronicles, diplomatic correspondence, poetry, biographical dictionaries, travelogues, tombstones, and plague treatises.

The attitude of the Islamic world toward the plague has usually been portrayed as passive, a conclusion drawn largely from the Islamic plague treatises, which were generally written by legal scholars during and after the **Black Death (1347–1352)**. Islamic teaching prohibited **flight** from plague-stricken areas, and this literature sought to legitimize this prohibition by maintaining that plague was a blessing or mercy of God and a means of martyrdom for the believer. The response recommended to Muslims in times of plague was to be patient and not flee. In fact, many did flee plague outbreaks, and those who remained sought ways to protect themselves and cure the sick. Prevention was emphasized more than treatment, perhaps because no exact cure for plague was known, nor was its cause. The theories of putrefaction and **miasma** prompted specific precautionary measures. Following **Greco-Roman medical theories**, during plague outbreaks physicians recommended living at high altitudes and in places facing north. The air was to be disinfected of any putrefying matter and kept clean inside houses and in the city with vinegar, sandalwood, and rosewater, as well as through **fumigation**. Nevertheless, there was an ongoing search for remedies against plague throughout the Islamic world. Islamic plague

treatises written in this period are full of various methods of treatment (including instructions for bleeding and purging) and recipes for ointments, syrups, electuaries, unguents, plasters, fumigations, and similar remedies, as well as for foods and beverages thought to be helpful in the treatment of the disease. The common recipes were mostly made up of vegetable matter but sometimes also included animal parts and minerals. As in Europe, the use of Armenian earth, Lemnian earth, theriac, and bezoar stone was also widely recommended. In fact, Europe and the Islamic world shared a common body of medical theory and knowledge about the plague and practiced similar preventive measures and treatment methods throughout the early modern period. In addition to medicine, people resorted to **astrology**, **religion**, and **magic** in the search for a cure. Prayers, magical remedies, amulets, and similar spiritual methods of treatment acquired great importance in plague literature and daily life.

From the fifteenth century onward, plague treatises written in the Ottoman Empire reflect a new legal viewpoint on proper conduct during outbreaks. In contrast to the legal opinions expressed in the earlier literature, these works recognized a form of contagion, granted legitimacy to the need to exit a plague-infested city in search of clean air, and legally authorized such practices. The recognition of contagion also paved the way for initiatives for a public health system in the Islamic world. From the sixteenth century onward, the early modern Ottoman Empire began to adopt preliminary measures to monitor, control, and fight plague epidemics, such as using occasional **quarantines**, keeping records of death tolls, controlling the burial of the dead, and maintaining urban hygiene.

In the absence of clear statistical data and census records, it is virtually impossible to make precise demographic estimates about the Islamic world in this period. However, the effects of recurrent outbreaks were cumulative and destructive in the long run. The demographic stagnation continued in the Islamic world until the mid-nineteenth century, whereas European population growth exploded from 1500 to 1850. Nevertheless, the mortality rates for major urban plague epidemics were much lower in the Islamic world than in European cities struck during the seventeenth and eighteenth centuries. *See also* Contagion Theory of Disease, Premodern; Cordon Sanitaire; Islamic Disease Theory and Medicine; Plague in Europe, 1500–1770s; Plague in the Islamic World, 1360–1500; Public Health in the Islamic World, 1000–1600.

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NÜKHET VARLIK

PLAGUE LITERATURE AND ART, EARLY MODERN EUROPEAN. The recurrence of **bubonic plague** throughout Europe in the early modern period meant that the disease continued to stimulate the production of art and literature. Even when outbreaks became less frequent and widespread, during the latter part of the seventeenth

century, the specter of yet another **epidemic** remained vividly present. Plague literature and art refers to works that are specifically tied to the experience or anticipation of plague by their content and purpose; that is, they contain direct reference to the disease, visually or verbally, and are created for plague-related aims, whether commemorative, *ex voto*, prophetic, didactic, or prophylactic.

Some scholars have interpreted fourteenth- and fifteenth-century macabre imagery as a response to the ravages of plague by a pessimistic, fearful, and death-obsessed society. However, macabre themes in poetry and art, such as the meeting of the three living and the three dead, and the Triumph of Death, predate the **Black Death**. Along with later variations, such as the Dance of Death, Death and the maiden, and the crowned skeleton, or King Death, such themes are more plausibly interpreted as articulating long-held Christian beliefs regarding the inevitability of death, the wages of sin, and the necessity for penance. Moreover, such imagery should not be seen as purely pessimistic, but rather as hopeful and hortatory, designed to urge the readers or viewers to amend their ways while there is still time and secure their salvation.

Plague Tracts: Helpful Advice and “Warnings to Beware”. The dominant form of plague literature in this period is the **physician**-composed plague tract, circulating first in manuscript in the wake of the Black Death and pouring off the presses by the dozens by the end of the following century. Earlier texts were often republished, and new ones were continually being written. The invention of the printing press in the later fifteenth century allowed for rapid dissemination to a wide audience of literate consumers. Publication in both Latin and, ever more frequently, in all European vernaculars, meant that readership was not restricted to a learned elite but extended to artisans, merchants, householders, aristocrats, and all those concerned to find remedies for and advice on dealing with the plague.

Some tracts were written for the use and instruction of governing officials; others, which debated contentious medical issues of the day, such as whether plague was spread by miasma (poisoned **air**) or **contagion** (from person to person), seem addressed to a more specialized audience. Most, however, were intended for the general public, as readily available self-help manuals. John of Burgundy, author of one of the most popular fifteenth-century treatises, proclaimed that he wrote to ensure that “if someone lacks a physician, then each and everyone may be his own *physicus, praeservator, curator et rector*.” Another anonymous fifteenth-century writer began his tract “sorrowing for the destruction of men and devoting myself to the common good and . . . wishing health for all.” Two hundred years later, the same intentions were still generating new compositions: as a French writer advised in 1617, “The plague is a dangerous illness that brooks no delays. One doesn’t always have time or means of using physicians in good time. However, you can always use me, night or day, early and late, by means of this volume.”

The treatises usually followed a standard pattern, proceeding from an explanation of causes and signs to preventative and curative measures. Across the Catholic and Protestant divide, all writers identified the ultimate origins of epidemics in divine displeasure at human sin. Plague was both punitive and remedial, God’s means of chastising his people into virtue. Writers often took the opportunity to castigate what they saw as the sins most offensive to God. Traditional catalogues of vices (greed, sloth, immorality) were given specifically local flavor by reference to contemporary religious, social, and political grievances. For seventeenth-century

English Protestants, for example, the fault lay variously with seditious local Catholics, the conspicuous greed of governing classes, or the doctrinal rigidity of new religious groups such as the Puritans.

A key rationale for the popularity of plague tracts was the way they gave readers a sense of control over events, by providing explanations that made sense according to the beliefs of the day. Following classical and contemporary medical theories, the specific cause of plague was often identified as maleficent planetary conjunctions. Unfavorable celestial events led to poisoning and putrefaction of the local atmosphere. Such astrological interpretations did not conflict with belief in divine origins, because it was God who had set the planets in motion in the first place. Throughout the early modern period, almanacs containing, among much else, history and prognosis of plagues based on celestial movements circulated widely.

The chief reason for the popularity of the texts was hope for preservation and cure, and the longest section was thus devoted to prophylaxis. Authors recommended a regimen of **personal hygiene** and health, based on **humoral theories** and aimed at maintaining the body's correct humoral balance. Moderation in all things was the key: a calm, cheerful mind and a life of sobriety and restraint. Characteristically for the Renaissance, when many looked to the classical past for guidance on how to live in the present, in his plague treatise of 1481, the Florentine classical scholar and philosopher Marsilio Ficino (1433–1499) proposed Socrates (470–399 BCE) as a model of how to survive the plague—a Socrates, it should be said, recast in Ficino's image, as a sober, chaste, moderate, and melancholic seeker of truth.

Flight was invariably identified as the most effective form of prevention, and the classical tag “flee fast, stay long, come back late” was repeatedly quoted. Advice was also given for those forced by duty or circumstance to reside in a plague-stricken area. Because the aim was to combat the pestilential corruption of the surrounding air, precautions included isolation and the use of aromatics, fires, **fumigations**, and disinfectants. A closing section on treatment and cure of those already stricken provided medical recipes and discussed various surgical practices such as bloodletting and lancing the buboes.

Shock Tactics: Plague Narratives. Overlapping and infecting the plague tract, but also recognizably distinct by virtue of their drama and emotional affect, are descriptive accounts of particular epidemics. Vivid and terrifying narratives of the physical and social desolation wrought by plague have a long tradition in literature, reaching back to Thucydides' (460–400 BCE) famous account of the **Plague of Athens**—often repeated, translated, adapted, and versified in later centuries—and Florentine poet author Giovanni Boccaccio's (1313–1375) equally celebrated prologue to the *Decameron*, describing the horrors of the Black Death. Daniel Defoe's (1660–1731) *Journal of A Plague Year* (1722), a dramatic evocation of the Great Plague of London in 1665, is the most famous early modern example of this category.

With their shocking evocations of disaster and death, such texts are often interpreted as purely journalistic, accurate, and reliable eyewitness accounts of what actually occurred. Yet as scholars have come to recognize, they are in fact highly crafted, fictional creations, with deliberately rhetorical goals. Defoe's *Journal* is a case in point, being written many decades after the events it purports to describe, in response to news of plague in Marseilles, France. For Defoe, as for his predecessors, the ultimate aim of the brutal evo-

cation of plague's horrors is to reverse them—behind the dramatic vignettes and gruesome details is an intense desire for restoration and wholeness, for reconciliation between heaven and earth. Like preachers who include vivid anecdotes of contemporary life to bring home the moral message of their sermon, plague writers (many of whom in England were clerics) used narrative drama for emotional impact. Aesthetic horror was deliberately manufactured, drawing on well-established literary conventions, in order to move the reader's soul and set in motion what Defoe called the necessary "Work of Repentance and Humiliation." Yet the *Journal* also breaks new ground by humanizing the genre as never before, drawing on new devices of contemporary fiction to generate a more intensely personal, subjective, and hence vastly more compelling account, which explains its enduring popularity.

Plague Images: Heavenly Causes and Heavenly Cures. The same concerns at work in plague literature—to provide comprehensible explanatory models and sources of hope for prevention and cure—also motivated the creation of Catholic-inspired plague art. In the early modern period, as previously in the aftermath of the Black Death, most plague imagery was prophylactic, designed to enlist the aid of powerful heavenly protectors against the disease. Images were not created for detached aesthetic contemplation but were functioning cult objects, the focus of collective prayer and ritual in churches, chapels, and city streets, and of individual and family devotion in the home. By making images in honor of holy figures, worshippers were setting up a kind of two-way contract, characterized by mutual obligations and benefits: worshippers would honor and celebrate their holy patrons, but they expected a proper return on their investment, in the form of special favors and protection against disasters. Plague images thus provided a concrete sense of comfort and hope for those facing the continuing threat of plague, an aspect that has not always been sufficiently recognized in studies of the impact of plague on early modern populations.

Sources of Hope: A Multiplicity of Heavenly Protectors. A characteristic feature of early modern plague imagery is the multiplicity of options available for obtaining heavenly protection against the disease. Worshippers could pick and choose from a multitude of celestial defenders. Local patron saints were often the first line of supernatural defense for many communities, because they were bound to their city by special ties of affection and interest and could be relied upon to plead its cause with all the vigor and passion of a citizen on an urgent embassy to a foreign dignitary. Helpful saints like Christopher guarded against sudden death, a particularly relevant fear for plague victims, whereas others, such as Sebastian and Roch, were credited with specialist plague expertise. Often, the most popular solution was to petition a whole phalanx of saints together with the Virgin Mary, queen of heaven and powerful agent of mercy before her divine Son, who, it was widely believed, could never turn down a maternal request. Where one saint was powerful, many gathered together were virtually irresistible. This essentially confident, optimistic conviction in multiple means of accessing supernatural protection was fundamental to early modern men and women's ability to cope with the ongoing presence of plague in their midst.

Destruction and Deliverance: Changing God's Mind. Plague images usually visualized the onset of the disease as deadly arrows shot down from heaven. The arrow as a metaphor for sudden, unexpected death and disease was familiar to Western viewers from classical antiquity (Apollo the archer, god of pestilence) and, above all, from the Old

Testament. Many early modern images show an enraged deity—God the Father or Christ the Son—in the clouds hurling down wickedly barbed arrows and needle-sharp lances upon sinful humanity. Heaped piles of **corpses**, studded with the “deadly darts” like so many pincushions, vividly conveyed the sense of plague’s indiscriminate reach, cutting down young and old alike, men and women, merchant and pauper. Angels often assist God in the task of chastising humanity, kneeling on clouds to take better aim. Sometimes the plague arrows are thrown down by grinning demons, heavenly subcontractors, as it were, in the job of punishing sinners. By the seventeenth century, the arrows disappear, but the heaps of dead and dying remain, often given special poignancy by commonly recycled artistic motifs, such as the infant suckling in vain from the breast of a dead mother. Like plague narratives, these descriptive evocations of the dead and dying are less direct reportage than artistic compositions configured for maximum emotional affect.

Yet despite the carnage, the message of these plague images is not universally gloomy. No matter how angry God might be, if approached in the correct way, he could be persuaded to change his mind. As the special “friends of God,” saints could argue with the enraged deity, and even do battle with him, as one thirteenth-century Italian preacher enthusiastically declared, on behalf of their worshippers. The Virgin can sway her son to clemency or intervene directly by sheltering worshippers under her protective mantle, against which plague arrows would seek their targets in vain. And Christ himself would argue humanity’s cause, demonstratively displaying his wounds to turn aside his father’s just wrath.

Plague images brilliantly visualize this ability to change God’s mind by combining both threatening and merciful elements within the one composition. The plague arrows might have been launched, but their flight could be arrested. In a late-fifteenth-century panel by Tuscan painter Bartolomeo della Gatta (1448–1502), for example, Christ and his angels send down arrows from the heavens to devastate the town of Arezzo. But all is not lost: the plague saint Roch kneels to plead the city’s cause, and Christ, convinced, changes his mind and sends other angels to catch the arrows as they fall and break them in mid-flight. Other examples show Christ loosing arrows with one hand while blessing with the other, or an angry Christ flanked by twin angels of justice, with threateningly upraised sword, of mercy sheathing the sword as a sign of reconciliation between heaven and earth. An early sixteenth-century canvas banner paid for by governing officials of the Italian town of Perugia and designed to be carried at the head of penitential processions during epidemics, depicts the city in the grip of plague, its populace kneeling in prayer before the gathered heavenly hosts. Christ holds downward-pointing plague arrows and raises aloft the sword of justice, ready to smite, but, in the nick of time, the Virgin Mary leans forward and grasps his sword arm to prevent the downward stroke. Plague images thus constantly balance the threat of punishment with promise of deliverance.

Sebastian: The Hedgehog Saint. The most popular and frequently petitioned saintly defender against the plague was the fourth-century CE Roman martyr St. Sebastian. Scholars continue to debate why and when he was selected as a plague saint, but the key reason seems to be the potent combination of martyrdom—believed to be the most perfect imitation of Christ—and arrow symbolism in his legend. A captain in the imperial guard, Sebastian has the unusual distinction of being martyred not once but twice. The first time, he was shot through with arrows “like a hedgehog,” as his *Life* reports,

before being left for dead. Importantly, this was believed to be a real death—but the saint was resurrected by divine power, and found miraculously alive by Christians coming to collect his body for burial. The second time around, and the one that proved permanent, he was beaten to death and his corpse thrown in a sewer (from whence it was subsequently retrieved and honorably buried).

Given the longstanding conception of plague as heaven-sent arrows, Sebastian came to be venerated as a plague martyr. Moreover, he both suffered death from plague-like arrows and was resurrected through divine fiat. Because of this, he was venerated as a Christ-like savior against the plague, voluntarily accepting the arrows of disease on behalf of sinful humanity—hence the ubiquity of his presence in early modern plague art, where he is customarily represented both martyred and alive, bearing the plague arrows in his near-naked flesh, usually with no apparent ill effects. Sebastian offers himself as a literal shield between an angry God and a sinful humanity, a lightning rod deflecting to himself the plague arrows intended for his worshippers, grounding them harmlessly in his own body. The powerful combination of youthful vitality and deadly, wounding arrows reassured devotees of his unlimited protective powers against the disease.

Medical Specificity: Roch and Plague Buboes. Toward the end of the fifteenth century, the French lay pilgrim, Roch, emerged as a second universal plague saint. The rapidity with which his cult spread across Europe was the result of the coincidence of his appearance with the invention of the printing press, so much so that he has recently been dubbed the first saint of the new media. For worshippers, his appeal lay in the close alignment of his life and miracles with their own lived experience. According to his earliest biography, composed and published in 1479, Roch healed plague victims, was himself stricken with the disease, endured it patiently, and was then divinely cured. Resuming his travels, he was imprisoned as a spy, was a model prisoner, and on his deathbed was rewarded by God with the power to preserve against the plague.

Recent research has demonstrated that Roch is a problematic figure, whose existence cannot be historically documented and whose biography is replete with hagiographical *topoi*, conventional episodes common to many saintly narratives. Some scholars have even suggested he is completely fictitious, created as a saintly double of an obscure French bishop of the same name, Rachus or Rochus of Autun. Yet such debates only highlight the extent to which Roch's cult met a deeply felt need among early modern worshippers for a saint of their own time, to offer hope of cure from a disease whose symptoms were by this date long familiar.

Images of Roch stress his dual role as both healer and victim of the plague. Narrative cycles show him curing the inmates of a plague hospice, or lazaretto (see figure). At a time when many communities built plague lazarettos, and even the smallest settlement contained at least one civic hospice, this episode would have resonated directly with viewers' own experiences. Carefully particularized details of setting and costume, such as beds neatly ranged along the wall, the white nightshirts and caps of the sick, and the sober gray robes of the warden, here holding a urine specimen and attempting to dissuade the young man from what he saw as a suicidal disregard for his own safety, give these healing scenes a veracity and immediacy which speaks directly to worshippers. Naturalistic devices climax in demonstrative displays of patients' buboes. Although not clinically accurate by modern standards, the buboes are immediately recognizable and rhetorically compelling, magnetizing the gaze as dreaded signs of inevitable death imprinted on the bodies of



Giovanni Battista de Legnano, *St. Roch healing plague victims in a hospice*. Oratory of St. Roch, Santa Maria Maggiore, Piedmont, Italy, 1534. Courtesy of Louise Marshall.

otherwise healthy men, women, and children. The pathos of their bared and disfigured flesh calls upon the saint for cure and plays on contemporary fears to insist upon Roch's proven ability to heal the disease.

Yet the healer was not himself immune, and other images show Roch ostentatiously revealing the bubo on his own leg. Directed outward to contemporaries, the sight of Roch, scarred by the plague yet alive and well, must have been an emotionally charged image of promised cure. Here was tangible proof that one could survive the plague: a saint who had triumphed in his own flesh over the very disease threatening his worshippers. Moreover, like Sebastian, Roch too was venerated as a plague martyr, because, absent any opportunity of dying for the faith, the crown of martyrdom could also be won by physical suffering.

Such images create a charged dynamic between the morbidly disfigured bodies of plague victims, in image and in life, and the similarly marked body of the new saint, who welcomed the torments of the disease as a chance to imitate the sufferings of Christ, and was consequently endowed with the power to ward off such torments from his devotees.

Protestant Plague Imagery. Though Protestants of all stripes accepted divine causation of plague and the efficacy of prayer and repentance, they denied any role to intervening saints and tended to avoid fanciful depictions of divine activity. Protestant plague-inspired art tended to focus less on the plague itself than on what was considered the proper response to it: stoical preparation for a “good death” in the bosom of one’s family. Plague tracts, bills of mortality, and broadsides (cheap posters) often featured more generic symbols of death such as skulls with crossbones, flying skeletons, tombstones, and funeral processions.

Conclusion. Both literature and art fulfilled vital roles in assisting early modern men and women to cope with the ongoing threat of plague. They provided explanations for the onset of the disease in terms that made sense to their readers and viewers, allowing some sense of understanding and control over events. Vivid verbal and visual evocations of plague’s horrors were deliberately deployed to prick beholders’ consciences, warning of the dangers of continued sinning and inspiring the necessary reformation of life. Among Catholics, plague images served as concretized prayers, offered up to a range of holy intercessors to invoke their protection against the disease. Both literature and art acknowledged the inevitability of sin, and hence of divine punishment through plague, but they also remained fundamentally optimistic that possibilities of protection and cure did exist and could be mobilized to secure the desired salvation from the disease at present or at least in the next life. *See also* AIDS, Literature, and the Arts in the United States; Astrology and Medicine; Biblical Plagues; Black Death and Late Medieval Christianity; Black Death: Literature and Art; Greco-Roman Medical Theory and Practice; Literature, Disease in Modern; London, Great Plague of (1665–1666); Plague and Developments in Public Health, 1348–1600; Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Plague Memorials; Religion and Epidemic Disease.

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LOUISE MARSHALL

PLAGUE MEMORIALS. Plague memorials are commemorative monuments built for victims of plague throughout western Europe. In most cases, the erection of the monument fulfilled a vow that was made during a serious outbreak of the plague, often associated with a saint, the Virgin Mary, or the Trinity. The plague monuments also bear tangible witness to the communal impulse to honor the innumerable dead, whose resting-places were unmarked.

The first plague monuments were churches dedicated to the saints invoked during plague. Among the most important plague churches is St. Roch in Prague (1602), which was designed by Giovanni Battista Bussi for Emperor Rudolf II and is located on the grounds of Strahov monastery above Hradcany Castle. Others include the Mariensaule in Munich (1638), Rochuscapelle in Bingen (1666), and Karlskirche in Vienna (1715). In Venice, the most notable are the churches of San Giobe (1462), San Sebastiano (1506), and Santa Maria della Salute (1632). A vow from the Senate of Venice in 1576 to build a church dedicated to Christ the Redeemer resulted in the Festa del Redentore, which was celebrated on the third Sunday of July and during which the Doge publicly prayed to thank God for the end of the epidemic.

Other plague monuments include Baroque plague columns found in central and southern Europe. Influenced by the Brotherhood of the Holy Trinity (1652), the oldest of these monuments was a wooden structure built in Vienna in 1679, which represented the Trinity on a column. It was rebuilt in 1693. The new composition represented, below the Trinity figure, a cloud pyramid with angel sculptures and the praying figure of Emperor Leopold I (1640–1705).

The design of plague columns evolved to reflect Catholic ideals of the Counter-Reformation and the vision of the end of the plague as victory over sin. In addition to featuring at the base a number of plague saints, such as St. Roch, St. Sebastian, and Sts. Cosmos and Damian (as at Graz, 1679), designers emphasized the Virgin Mary. Whereas on the Leoben monument (1718) she appears halfway up the column, that at Zwettl (1727) presents Mary at the foot of the memorial. In Horn (1724), the Virgin stands on the top of the column, whereas the Trinity is grouped at its foot. In Munich (1732), the Virgin stands alone. This model is also found in Nitra, Italy (1750), and Grad (1681). The column of Olomouc in the Czech Republic (1754) contains a chapel inside. These monuments were later transformed into secular victory columns by the ostentatious display of imperial dynastic emblems. The association between columns

and the Habsburg monarchy led to the destruction of the Prague column at the end of World War I (1918).

An odd secular monument was the two horse heads in the Neumarkt of Cologne. They memorialized the miraculous healing of a woman whose husband swore he would see horses upstairs in his house before his wife could be healed, at which he turned and saw the animals leaning out of the window. More recent examples are the modern monument of Son Servera (Balears), built to commemorate the plague of 1820, and the Cattle Plague Memorial in Mucclestone (Staffordshire, England), built after the epidemic of 1865. *See also* Black Death (1347–1352); Black Death: Literature and Art; London, Great Plague of (1665–1666); Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500; Religion and Epidemic Disease.

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ADRIANO DUQUE

PLAGUE OF ATHENS. The so-called "Plague of Athens" lasted from 430 to 426 BCE in the early stages of the Peloponnesian War between Athens and Sparta in ancient Greece. It is the earliest well-described **epidemic** in European history and also one of the most controversial episodes in medical history. It illustrates very well the difficulties of retrospective diagnosis. Many different suggestions for its cause have been proposed, with no agreement whatsoever among the modern historians who have written over 200 articles about it. And so it remains, despite the availability of a lengthy contemporary description of the symptoms of the "plague" and its effects written by the Athenian historian Thucydides (c. 460–400 BCE), our main source of information on the plague. He recorded reports that the epidemic started in Ethiopia and Egypt before spreading through much of the Persian Empire and then reaching Greece. However, the only substantial information available to historians—his own account—relates solely to Athens and its port of Piraeus.

Thucydides wrote that he decided to record the symptoms so that it could be recognized should it ever recur in the future. The disease commenced with intense heat in the head; eye, throat, and tongue inflammation, with bad breath; sneezing and vomiting; upset stomach; cool skin with a rash of small blisters or ulcers; intense internal heat leading victims to throw themselves into water; sleeplessness; in the later stages ulceration of the bowels with diarrhea; gangrene of the extremities leading to loss of fingers, toes, genital organs, and eyes; and amnesia in some survivors. Modern suggestions for the cause of the disease include **typhus**, **smallpox**, **measles**, **bubonic plague**, a **hemorrhagic fever** like Ebola, **typhoid fever**, **influenza**, toxic shock syndrome, scarlet fever, anthrax, glanders, tularemia, Lassa fever, **ergotism**, and mycotoxins. The hypothesis that the epidemic was caused by a pathogen that cannot now be recognised because it has become extinct has also been proposed. Typhus and smallpox have attracted the most support, but there is no consensus. In 2006 an attempt was made to identify the pathogen in question by

analysis of ancient DNA from skeletons from a burial pit in the Kerameikos, the cemetery of Athens, dating to about 430 BCE. It was suggested that DNA sequences from one skeleton point toward typhoid fever. However these DNA sequences are far from identical to the typhoid sequence. Moreover, the typhoid hypothesis has attracted little support from medical historians who have studied the text of Thucydides. Consequently, the identity of the pathogen responsible for the Plague of Athens remains uncertain.

Thucydides also describes the social, demographic, and political effects of the Plague of Athens. It clearly weakened Athens's military effectiveness in the war's early stages, and it took the life of Athens's most highly regarded civic leader, Pericles. *See also* Diagnosis of Historical Diseases; Greco-Roman Medical Theory and Practice; Hippocrates; Historical Epidemiology; Paleopathology; Smallpox in the Ancient World; War, the Military, and Epidemic Disease.

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ROBERT SALLARES

PLAGUE OF CYPRIAN. *See* Plagues of the Roman Empire.

PLAGUE OF JUSTINIAN; FIRST PANDEMIC. This is the conventional name for a series of outbreaks of **bubonic plague** in the early middle ages, named for the Byzantine emperor Justinian I (r. 527–565) during whose rule the cycle began. Its first outbreak occurred in 541, and the **pandemic** returned in 18 waves until 750, on average every 11.6 years. It is highly probable that the pandemic originated in Africa. This was primarily a Mediterranean phenomenon: the Byzantine Empire, the Islamic world, and regions in southwestern Europe were hit more often than those in northern Europe, as the disease spread along trade routes, mostly through sea travel. As opposed to that of the late medieval **Black Death**, the identity of the **epidemic** disease as true bubonic plague has not been contested. The waves of the plague certainly caused large-scale mortality and—especially in important urban centers such as Constantinople—a sharp demographic decline, but it is still difficult to translate this into more specific demographic terms. Figures estimating the overall loss of life at 20 to 30 percent of the pre-plague population are often cited, but their accuracy and value are questionable. Certainly, labor became sparse and more expensive, more and better land was available, and manpower shortages limited military operations, whereas on a spiritual level the scourge encouraged the intensification of religious ritual and may have affected the initial spread of Islam.

There are abundant sources on the Plague of Justinian written in Greek, Syriac, Arabic, Latin, and Old Irish—mostly histories and chronicles and, to a lesser extent, narrations of saints' lives. Several sixth-century authors were eyewitnesses to the pandemic, such as the historians Procopius (d. 565), Agathias (c. 536–582), and Euagrius (c. 536–600) writing in Greek; John of Ephesus (c. 505–585), a bishop writing in Syriac; and the bishop and historian Gregory of Tours (538–593) writing in Latin. Arabic authors such as al-Madaini wrote in the late eighth and ninth centuries, as did some of the Greek and Latin authors such as Theophanes (758/60–817) and Paul the Deacon (c. 720–799), who referred to plague waves in the seventh and eighth centuries.

Several detailed descriptions of the disease enable us to identify it as bubonic plague. Procopius includes the longest account of the symptoms associated with the epidemic's first visitation in 542. Its onset was sudden and accompanied by fever. In a few days at the most, swellings developed mainly in the groin, but also inside the armpit, beside the ears, or on the thighs. Some of the infected fell into comas; others became delirious, whereas those who did not develop any of those symptoms died as a result of the mortification of the swellings. Furthermore, black pustules as large as lentils appeared in some of the patients, bringing about their death in less than one day. Others vomited blood. In those cases where the swellings became extremely large and the pus was discharged, the infected were sure to survive the disease, though sometimes with withered limbs or affected speech. Additional traits observed by other writers include patients with bloody eyes, a swelling that began in the face and spread down to the neck bringing about death, and diarrhea. John of Ephesus records the swelling in the groin, both in humans and animals. **Pneumonic plague** was probably not a prominent feature of this pandemic.

The disease was disseminated over large distances most probably through **trade** and **military** operations. Sources contemporary to the pandemic recognized this by observing that the disease spread from the ports inland. Accounts of the plague's **transmission** from human to human are contradictory: whereas some seem to affirm this, others point to the opposite, writing that **physicians** who attended plague patients were not infected by the disease.

Sources mention excessive mortality caused by the plague, often recording detailed numbers of fatalities: although these seem authoritative, they are usually rhetorical exaggerations. The closest we can come to calculating the plague-induced mortality is to do so for specific places during specific outbreaks. The total loss of life at Constantinople in 542 has been calculated at 20 percent of its population, 35 percent is suggested for Egypt in 744, and 25 percent is noted for Basrah in 749. Such figures can only illustrate the overall trends or patterns of plague-induced mortality in the period. Though the sources at our disposal focus on urban centers, there is ample evidence to suggest that mortality in the rural areas was equally high. This includes haunting images of the deserted and desolate countryside, of abandoned villages or those whose entire population had been snuffed out by disease.

As for the seasonality of the plague outbreaks, data point to an unquestionable peak in the months of April to August, with July exhibiting the highest incidence. In the Islamic world, there was a marked peak in April and a less pronounced one in August, with the period from March to August exhibiting the highest incidence of the disease throughout the year. Available data does not point toward any marked difference in the age or gender of the afflicted.

The first outbreak of the plague was the one recorded most comprehensively. Because contemporary sources place its entry point into the Byzantine Empire at Pelusium, at the

PLAGUE OUTBREAKS CONSTITUTING THE FIRST PLAGUE PANDEMIC (541–750)

1. 541: Pelusium (Egypt), Gaza, Negev, Alexandria; 542: Jerusalem and hinterland, Syria, Lycia, Constantinople, Asia Minor, North Africa, Sicily; 543: Italy, Western Balkans, Spain, Southern France; 544: Rome, Ireland; 547: Wales; 549: England, Ireland, Finland, Yemen.
2. 557–558: Amida (Syria); 558: Constantinople; 560–561: Cilicia (Asia Minor), Syria, Mesopotamia.
3. 571: Italy, Southern France; 573–574: Constantinople, Eastern Mediterranean; 576: Ireland.
4. 584: Spain, Southern France; 588: Spain, Southern France; 590: Rome, Southern France; 591–592: Western Italy, Istria, Antioch, Marseille.
5. 597: Thessalonica and hinterland; 598: Avar territory (European Turkey); 599: Constantinople, Western Asia Minor, Syria, Eastern Mediterranean; 599–600: North Africa, Italy, Southern France, Ravenna; 601: Verona.
6. 618–619: Constantinople, possibly Alexandria.
7. 626–627: Palestine; 627–628: Persia.
8. 639: Syria, Palestine, Iraq.
9. 664–666: Ireland, England; 669–670: Kufa (Iraq); 672–673: Egypt, Palestine, Kufa, Lichfield (England).
10. 680: Rome, possibly Ticinum (Pavia), Ely (England).
11. 684–687: England; 687: Syria; 689: Basrah (Iraq); 689–690: Egypt.
12. 693: Toledo, Spain; 694: Southern France; 698: Syria, Constantinople; 699–700: Iraq, Syria, Mesopotamia.
13. 704–706: Syria; 706: Iraq; 709–711: possibly Spain.
14. 713: Syria; 714–715: Egypt, possibly Crete.
15. 718–719: Iraq, Syria.
16. 724: Egypt; 725–726: Syria, Mesopotamia.
17. 732–735: Syria, Egypt, Palestine, Iraq; 735: Asia Minor.
18. 743–744: Egypt, North Africa; 744–745: Mesopotamia, Syria, Iraq; 735–746: Calabria, Sicily, possibly Rome, Continental Greece, Aegean; 747–748: Constantinople; 747–750: Iraq, Syria, Mesopotamia.

After this last visitation, the plague vanished until it resurfaced in the Second Pandemic, the Black Death.

Compiled by Dionysios Stathakopoulos

mouth of the extreme eastern branch of the Nile, scholars generally agree that the ultimate origin of the pandemic should be situated in central Africa, which remains a natural focus of sylvatic plague. From Pelusium it spread north to Alexandria, Gaza, and the Negev in 541, and the following year west across North Africa, east across the Levant, and north to Sicily, Asia Minor, and Constantinople. Plague appeared in Italy, the western Balkans, Spain, and southern France in 543, and it is mentioned in Rome and Ireland in 544. Sources record the pestilence in Wales in 547 and in 549 in England, Ireland, Finland, and Yemen. See the accompanying sidebar for information on later waves.

The immediate popular response to the plague outbreaks was often **flight**, practiced by both authorities and commoners. Imperial, civic, and religious authorities took measures

to bury the large number of dead bodies in mass graves (very few of which have so far been discovered) and to restore normality. Religious leaders instigated religious responses to the disease by organizing litanies, fasts, prayers, and processions in both the Islamic and Christian worlds. The most famous of the last of these took place in Rome in 590 under Pope Gregory the Great (c. 540–604): a sevenfold litany that allegedly brought the scourge to a halt. Although plague victims consulted physicians, they offered little or no aid as they could neither understand nor manage the disease. Instead, people turned to holy men for help. The Christian cult of St. Sebastian as plague helper began in the course of the seventh century in Italy.

The demographic crisis caused by the plague is expressly mentioned in all sources and is also corroborated by other, indirect, evidence such as the number of shipwrecks (as indicators of overall ship numbers and frequency of maritime travel), which dropped about two-thirds between the sixth and seventh centuries. Humanpower shortages were manifested in the army; agrarian depopulation was evident in the Byzantine Empire, whereas after the last wave of the plague, transfers of population to rural areas and to its capital were necessary to revitalize their economic life. A shortage of laborers increased the value of labor, whereas more and better land was available to survivors. Egyptian data on land leases indicate a marked improvement in the security and duration of leases between the first and second halves of the sixth century. This suggests a shortage of human resources and, therefore, the willingness of landowners to lease out their land under positive conditions for the lessees. Estimates of the total population decline caused by the plague are pure guesswork and should not be taken at face value; nevertheless, one may safely assume that the loss of life was considerable and certainly weakened the Byzantine Empire and the new Islamic states. On the cultural level, the plague probably sparked an “intensification of devotion.” Islam itself emerged in the midst of the pandemic, and in an unprecedented way both Christian and Muslim communities reacted with public acts of religious piety and humility such as litanies, fasts, and mass prayers. See also *Diagnosis of Historical Diseases*; *Greco-Roman Medical Theory and Practice*; *Historical Epidemiology*; *Humoral Theory*; *Islamic Disease Theory and Medicine*; *Plagues of the Roman Empire*; *Religion and Epidemic Disease*.

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DIONYSIOS STATHAKOPOULOS

PLAGUES OF THE ROMAN EMPIRE. Two major **pandemics** broke out in the Roman Empire prior to the **Plague of Justinian**: the Antonine Plague (166–190) and the Pestilence of Cyprian (251–270). In the first case the designation refers to the Roman emperor in whose reign the outbreak occurred—Marcus Aurelius Antoninus (121–180); in the second it refers to the author who recorded most of what we know about the specific visitation, Cyprian (d. 258), bishop of Carthage.

The Antonine Plague. A number of Greek and Latin sources record the pandemic. The most celebrated **physician** of Antiquity, **Galen**, who was an eyewitness, provides some information, though in a scattered and not systematic manner. The contemporary historian Cassius Dio (c. 163–229) included information on its last outbreak. Documentary evidence from Egypt, written on papyrus, is extremely important for the quantification of the disease's impact and calculation of the loss of life it caused.

Scholars have identified the Antonine Plague as **smallpox** primarily based on Galen's descriptions, which amount to scattered references to specific patients rather than a complete description of the disease in one work. He recorded symptoms such as raging fever, upset stomach and bowels, diarrhea, black stools, occasional cough and catarrh, and chiefly a black exanthem that covered the entire body, a result of putrefied blood within the fever blisters. He added that it became scabby where there was no ulceration and fell away. Galen also mentioned cases of ulcerations inside the windpipe, infecting the larynx and ultimately damaging the voice. He gave the duration of the disease as 9 to 12 days. Neither he nor any source provided information on the disease's mode of transmission or its seasonality.

The **epidemic** broke out in Mesopotamia in 165 or early 166 CE, during the Roman-Parthian war, allegedly when a pestilential spirit was released from a golden casket in the Temple of Apollo. It spread first to Parthia (in present-day Iran), then to Smyrna (165), and was then disseminated with the Roman army back to the city of Rome (166), then more widely in Italy (Aquileia attested in 168–169), in Dacia (167), and to Egypt (attested in 168–169 and 179), the Rhine, and Gaul. Emperor Marcus Aurelius died of the epidemic in 180 either in Vienna or Sirmium (in present-day Serbia). The disease broke out again in 189, striking at least Rome and Italy. The sources record countless casualties in a language evoking rhetorical exaggeration. Cassius Dio writes that during the 189 outbreak, 2,000 people died each day in Rome. Papyrological data from Egypt (chiefly tax censuses) suggest a loss of life of about 20 percent as a result of the disease; overall the Antonine Plague caused a mortality of 7 to 10 percent, with armies and urban centers being hit the hardest (perhaps at 13 to 15 percent) producing a total number of deaths around 7 to 10 million over and above the normal mortality rate. Recent scholarship suggests that there were pockets of high incidence (where mortality would reach 25–30 percent) and others of low incidence, the mortality rates of which cannot be calculated.

Plague patients certainly consulted Galen, who claimed to have managed the disease in them. The emperor Marcus Aurelius and his son were among his clients. Apart from that, there is no other evidence on the employment of physicians during the outbreaks. **Flight** from affected areas is attested as a response to the disease. Authorities took measures to ensure the proper burials of the disease's casualties, erecting statues as **plague memorials** to honor victims among the nobility and paying for the burial of common people. When Marcus Aurelius was dying of the disease he reportedly sent his son and heir Commodus (161–192) away to protect him from contracting it.

The Antonine Plague was certainly a major phenomenon because of its duration and the high mortality it induced. It was a disruptive factor in the demographic landscape and in everyday life, but it seems that the Empire recovered quickly, as data on Egypt and building programs in Italy suggest.

The Pestilence of Cyprian. A number of mostly Latin sources record the disease, most notably bishop Cyprian of Carthage, an eyewitness who devoted to it an entire oration, “On the Mortality.” Additionally, there are mentions of the disease in some of his letters. Other sources include the letters of the eyewitness bishop Dionysius of Alexandria (late third century) and works of later historians such as the author of the *Historia Augusta* (late fourth century) and Zosimus (late fifth century). Cyprian is the only author to describe its symptoms: diarrhea, continual vomiting, raging fever, bloody eyes, loss of limbs as a result of putrefaction, affected gait, and/or hearing and/or eyesight. Some modern scholars have attempted to identify this disease with **measles**, but the evidence at hand is quite meager.

An eleventh-century Greek source places the origin of the pandemic in Ethiopia, but this may merely be an imitation of Thucydides’ (460–400 BCE) account of the **Plague of Athens**. According to more securely dated information, the plague ravaged Egypt and Alexandria in 251 spreading in the same year to Rome, where it killed the emperor Hostilianus (d. 251). The disease may have been present in Italy as early as 248, but there is little evidence to allow more precise dating. In 252 it reached Carthage, flaring up again in the summer of 253, the same year in which, according to St. Jerome (c. 341–420), it ravaged Egypt and especially the great city of Alexandria; this may in fact be a reference to the outbreak in 251, but again a more precise dating is impossible. There is some evidence to suggest that there was an additional outbreak in Neokaisareia (northern Asia Minor) around 256. In 259 the disease decimated Roman troops in Syria, and in 262 it reached Italy, Greece, and Africa once again. Finally, the pestilence broke out among the troops in Sirmium in 270, killing the emperor Claudius II (c. 213–270).

The Pestilence of Cyprian occurred in a period of tensions between the Roman emperors and the emerging Christian community. The general persecution under emperor Decius (250–251) had set the tone. As a result, Christians were locally treated as **scapegoats** for any kind of natural disaster, including the pestilence. Cyprian, in a famous letter to the

BISHOP CYPRIAN OF CARTHAGE DESCRIBES THE SYMPTOMS OF THE PESTILENCE AND EXHORTS HIS FLOCK (252 CE)

This, in short, is the difference between us and others who know not God, that in misfortune they complain and murmur, while adversity does not call us away from the truth of virtue and faith, but strengthens us by its suffering. This trial, that now the bowels relaxed into a constant flux, discharge the bodily strength; that a fire originated in the marrow ferments into wounds of the fauces; that the intestines are shaken with a continual vomiting; that the eyes are on fire with the injected blood; that in some cases the feet or some parts of the limbs are taken off by the contagion of diseased putrefaction; that from the weakness arising from the maiming and loss of the body, either the gait is enfeebled, or the hearing is obstructed, or the sight darkened;—is profitable as a proof of faith. What a grandeur of spirit it is to struggle with all the powers of an unshaken mind against so many onsets of devastation and death! what sublimity to stand erect amid the desolation of the human race, and not to lie prostrate with those who have no hope in God; but rather to rejoice and to embrace the benefit of the occasion.

From Cyprian’s “On the Mortality,” in *Ante-Nicene Fathers*, Vol. 5 (Christian Literature Publishing Co., 1886).

governor of Africa, Demetrianus (third century), recorded such attitudes and countered them by writing that catastrophes in fact ensued not because Christians did not worship Roman gods, but because pagans did not worship the Christian God. Ecclesiastical authors of the period viewed the pestilence as a result of human sins and embedded it in an eschatological context. Plague is one of many signs and omens foretelling the end of the world; as such, Christians should endure it and view their suffering as a path to salvation almost equal to martyrdom. Though Roman rulers reportedly provided proper burials for all victims, Christian authors suggest that the pagan population largely abandoned the afflicted. To the contrary, Christians claimed to have not only tended their own brethren, but also to have extended their care toward anyone in need. From the pagan side, there is ample evidence to suggest a ritual response to the scourge taking the form of public religious rituals in city theaters and the consultation of oracular books. The sources are unanimous in their descriptions of mass mortality as a result of the outbreaks, but any given numbers—such as 5,000 victims in a single day—should be taken as rhetorical exaggeration. There is some evidence to suggest a disruptive effect caused by the outbreaks, but it impossible to quantify it, as the pestilence of Cyprian occurred in a period of extreme political, social, and military turmoil for the Roman Empire. *See also* Diagnosis of Historical Diseases; Greco-Roman Medical Theory and Practice; Historical Epidemiology; Plagues of the Roman Republic; Religion and Epidemic Disease.

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DIONYSIOS STATHAKOPOULOS

PLAGUES OF THE ROMAN REPUBLIC. Plagues and epidemics play a significant part in the history and literature of the Roman Republic (traditionally 509–31 BCE). References occur in a variety of sources, in which they are intertwined with **religion**, **moral-ity**, and **war**. Early Roman descriptions of plagues and epidemics (known commonly as *pestis* in Latin) rarely focus on symptoms or etiology in ways that allow for **diagnosis**. This is, in part, because of a general disregard for medical theory, but also because the famous description of the **Plague of Athens** by Thucydides (460–400 BCE) became a standard trope and served as a literary model for Roman authors.

The evidence for the occurrence and effect of plagues on early Rome is sketchy. Romans would have recorded the occurrence of plagues in the schematic annual records kept by state and religious authorities (e.g., the *annales* and *fasti*). However, nearly all official records were destroyed in about 390 BCE when Celtic Gauls sacked Rome. Moreover, Roman history did not begin to be written until near the end of the third century BCE (Quintus Fabius Pictor [b. c. 254 BCE]) and did not really start to become a subject of

Roman interest until the mid-second century BCE, when Romans such as Marcus Porcius Cato (Cato the Elder; 234–249 BCE) began to address Roman history and culture. Most of these early works remain only in citations and fragments quoted by authors of the first century BCE. Consequently, although many descriptions by later historians such as Livy (59 BCE–17 CE; *From the Founding of the City*) and Dionysus of Halicarnassus (d. c. 8 BCE; *Roman Antiquities*) have proven to be reasonably accurate of even very early Rome, reports of plagues during the early and middle Republic are based on traditions that are rarely independently verifiable or supported by first-hand evidence.

For the Romans, themselves, the story of their remarkable rise to dominance was in large measure the result of aspects of their moral and religious character as a people, and early histories of Rome record plagues in ways that highlight these features. Livy (1.31) reports that Tullus Hostilius, one of Rome's early kings (r. 673–641 BCE) and a successful military leader, brought a plague on the city and on himself because of his neglect of the gods, rendering both it and him afraid and ineffective. A similar charge of bringing a plague on Rome as a result of religious impropriety was leveled at Scipio Aemelianus (censor in 142 BCE) by one of his rivals (Lucillus Fragment 394). As in many cultures, plague signaled to the Romans that their community was in some way out of favor with the gods, and that special consultation and communal action were required. Devastating plagues circa 436–33 BCE and circa 293 BCE induced the Romans to consult the Sibylline Books (a collection of mystic and prophetic writings attributed to oracular priestesses) and to take action through dedications to Apollo the Healer in 433 BCE (Macrobius [fourth and fifth centuries BCE], *Saturnalia* 1.17.14–16; Livy 4.21–25) and by bringing the cult of the healing god Asclepius to Rome and establishing it on Tibur island about 293 BCE (Livy, 10.47; Valerius Maximus [1st century] 1.8.2; Ovid, *Metamorphoses* 15.622–744; Anonymous, *On Famous Men* 22.1–3). In both cases, these actions were said to have been immediately successful, and the stories provide us with important markers in Rome's religious development as well as insight into the archeological record.

Rome's story, however, is also one of nearly continual war, and numerous plagues and epidemic diseases played roles at different stages and at key moments in that story. Incidents often occurred (quite naturally) in situations involving siege, in which famine, poor **sanitation**, and crowded conditions contributed to both sides' vulnerability and, often, one side's defeat. As Rome battled Carthage in Sicily during the Second Punic War, a plague in 212 BCE struck both armies at the siege of Syracuse, but advantaged the besieging Romans (Livy 26.26). Returning from the east, Sulla's (138–78 BCE) successful siege of Rome in 87 BCE was aided by a devastating plague that weakened both armies but particularly Rome's defenders under Cinna (first century BCE; Plutarch, "Pompey"). Illness also began to play a role when Pompey was besieged by Julius Caesar (100–44 BCE) at Dyrrachium in 49–48 BCE (Caesar, *The Civil War* 3.48–49; Lucan, *Pharsalia* VI), shortly before the decisive battle of Pharsalus in which Caesar defeated the republican forces and took control of Rome. Besides siege, incidents of plague occur in the record with greater frequency after the second Punic War as Rome rapidly expanded its reach into new territories. This expansion created new vectors for disease and brought foreign populations into greater contact with each other through armed conflict and commerce throughout the Mediterranean basin. Significant plagues are reported in 187, 182–180, 176–175, 165, and 142 BCE (Livy 36.14, 37.1, 38.44.7, 40.19.3, 42.6; Julius Obsequens, *Book of Prodigies* 6 and 13).

In addition to accounts of historical plagues, plague became a kind of literary motif in Roman literature of the Golden Age (first century BCE through the reign of Augustus [27

BCE–14 CE]). Most authors (including Dionysus of Halicarnassus in his description of a Roman plague in 451 BCE) owe their descriptions and structure to the famous account of the Athenian plague (428–427 BCE) by the historian Thucydides (2.47–54). The Epicurean poet Lucretius (99–55 BCE), in his famous plague scene in *On the Nature of Things* (6.1138–1286), adapts this model with an Epicurean etiology of noxious particles in the air. The Augustan poet Virgil (70–19 BCE) in turn adapts Lucretius and Thucydides in his description of a plague in *Georgics* 3 that strikes animals in Noricum (somewhere between the Danube and Alps), and Ovid (43 BCE–17 CE; *Metamorphoses* 7.516–621) borrows from these accounts when he recounts how Juno struck Aegina (Greece) with a plague in retaliation for one of the god Jupiter's many affairs. In short, the extended descriptions of plagues and epidemics in Roman history and literature of the Republic are more literary than medical. See also Air and Epidemic Diseases; Disease, Social Construction of; Greco-Roman Medical Theory and Practice; Historical Epidemiology; Plagues of the Roman Empire.

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ERIC D. NELSON

PNEUMONIC AND SEPTICEMIC PLAGUE. Infection of the human body with *Yersinia pestis* is observed in two distinct forms: a blood and lymph borne infection that results in focal infection of the regional lymph nodes nearest the site of inoculation (usually a flea bite) and a pulmonary infection most often acquired by the respiratory route. The latter infection is known as the pneumonic form of plague, in contrast to the **bubonic** form of plague with its characteristic swollen lymph nodes. The causative organism, *Y. pestis*, is the same in both cases, the different pathologies being determined by the route of inoculation. When the victim's bloodstream and its defenses are overwhelmed with the bacteria so rapidly that the lymph nodes do not swell before death, the condition is said to be septicemic (blood-poisoning).

Pneumonic Plague. In spite of the distinct clinical presentation of bubonic and pneumonic plague, early writers recognized the relationship of these two manifestations of the disease, perhaps on epidemiological grounds. French **physician** Guy de Chauliac (c. 1300–1368), writing on the plague of 1349 in his *Great Surgery* (*Chirurgia Magna*, 1363) noted:

It was of two kinds: the first lasted two months, with continued fever and expectoration of blood. And they died of it in three days. The second was, all the rest of the time, also with continued fever and apostemes and carbuncles on the external parts, principally in the armpits and groin: and they died of it in five days.

It is thought that pneumonic plague accompanied many of the bubonic plague outbreaks of the **Black Death** and Second Pandemic (1347–1830s), accounting for death rates and other epidemiological factors not generally associated with plague.

The symptoms of pneumonic plague are distinctive and terrifying. The first sign of illness is stiffness, malaise, severe headache, nausea, vomiting, and general pain, with a temperature of 102 to 105°F, followed by cough with bloody sputum and acute respiratory distress. Without treatment, death from respiratory failure occurs in two to four days. In contrast, bubonic plague kills somewhat more slowly. The typical pathologic process involves coagulation necrosis in which the bacterial infection results in death of tissues with inflammation, bleeding into tissues, and then clot formation.

Because of the different mode of spread, the **epidemiology** of pneumonic plague is distinct from that of the vector (flea)-borne bubonic plague. The typical **epidemic** of pneumonic plague tends to occur in winter and early spring associated with indoor crowding and increased opportunities for person-to-person respiratory spread.

Pneumonic plague originates from cases of bubonic plague derived from the natural animal reservoirs of plague, usually flea-ridden rodents. A patient with the bubonic form of plague can develop a lung infection in the course of the bloodborne phase of the illness and may, through coughing, spitting, or other means of respiratory spread, infect others in close contact. Most often it is family members or medical personnel who are most at risk for such infection. Once the fulminant lung infection occurs, person-to-person spread becomes the rule, and a pneumonic outbreak can occur.

Prior to the introduction of **antibiotics**, there was little effective treatment for the pneumonic form of plague, and the mortality rate was close to 100 percent. Treatment with **sulfa drugs** (introduced in the late 1930s) and streptomycin (1940s) greatly diminished the mortality from pneumonic plague. Chloramphenicol and the tetracyclines further improved the treatment of plague in the 1950s and 1960s. Therapy with serum from animals inoculated with killed plague organisms was tried as early as the 1890s by French researcher **Alexandre Yersin** and his colleagues with some success at passive immunization. Active immunization of humans with various preparations of the plague bacillus, pioneered by **Waldemar Haffkine** in India, have been disappointing.

Because pneumonic plague results from human-to-human spread, simple isolation, **quarantine**, and sanitary precautions are effective in preventing or aborting outbreaks, so epidemics of pneumonic plague have not been observed since that of 1920–1921 in China, which resulted in 8,500 deaths. In 1994 there was an outbreak of **pneumonic plague in Surat, India**, and, although reported to be extensive, there appeared to have been fewer than 100 cases and 50 deaths.

Septicemic Plague. Septicemia results when the *Y. pestis* enter the bloodstream and multiply with great rapidity. This may occur before involvement of the lymphatic system leads to the characteristic swelling known as buboes (primary septicemia), or it may result from complications attending bubonic—and thus be accompanied by buboes—or pneumonic plague. The symptoms of septicemic plague are more pronounced and violent than those of bubonic, with alternating high fever and chills, vomiting, diarrhea, and abdominal pain, often followed by bleeding from nose, mouth, and anus, as well as subdermal or internal hemorrhaging with accompanying gangrene. The untreated victim goes into shock, and these cases usually result in death. Very early treatment with the antibiotics streptomycin or gentamycin should lead to full recovery. Septicemic plague cannot be spread from one person to another without the flea vector or other means of introducing the infected blood into another's bloodstream. Many historians believe that, like pneumonic plague, septicemic plague accompanied many of the outbreaks of the Second Pandemic.



Protective mask used during the pneumonic plague epidemic in Manchuria, 1910–1911. Courtesy of the National Library of Medicine.

According to the **Centers for Disease Control and Prevention (CDC)**, between 1990 and 2005, 107 cases of plague were reported in the United States; of these, 18 were primary septicemic, and 5 were primary pneumonic plague. The rapidity of death, high mortality of untreated pneumonic plague, and the relative ease of airborne distribution make *Y. pestis* of concern as a biological weapon. Because of the effectiveness of common antibiotics in treating plague, however, if a diagnosis is made promptly, the danger from weaponized plague can be mitigated. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Black Death: Modern Medical Debate; Bubonic Plague in the United States; Diagnosis of Historical Diseases; Human Body; Plague and Developments in Public Health, 1348–1600; Plague in Britain, 1500–1647; Plague in China; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500; Plague in the Contemporary World.

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WILLIAM C. SUMMERS

PNEUMONIC PLAGUE IN SURAT, GUJARAT, INDIA, 1994. **Pneumonic plague** struck Surat, in western India, in September 1994. Because the disease is highly contagious, the outbreak caused panic and, within four days, one-quarter of the population of about 1.5 million chose **flight** and abandoned the city. This exodus caused anxiety elsewhere that plague might be spread by the Surat refugees.

The reemergence of plague, after many years, was ascribed to two factors: the condition of the slums and the occurrence of two natural disasters in the area. The city's population

had tripled over the previous two decades without a simultaneous growth of infrastructure. Worsening the situation, an earthquake in the neighboring state of Maharashtra in the previous year had caused extensive damage. The disturbances and resettlement that followed brought wild rodents, which normally inhabited the forests neighboring Surat, into contact with the domestic rat population, which thrived in the **poverty**-ridden slums. Even though rats and fleas transmit **bubonic** rather than pneumonic plague, Surat's rat population is regarded as the original source of infection as the plague-infected rat population came into contact with the human population of Surat. The second disaster was the continuous monsoon rains and the flooding of the river Tapi, which had killed cattle whose rotting carcasses were scattered around the town and on which rodents fed.

Using the perspective of the political economy, Ghanshyam Shah has shown that plague was not just a biological phenomenon but the symptom of a sociopolitical disease. The local administration was corrupt and disinterested, serving only the interests of the rich and powerful at the expense of the poor and inarticulate; the municipal authorities did not ensure adequate garbage collection, water supply, or flood drainage; the private medical sector overprescribed modern medicines, and the public sector was inefficient and inadequate. Analysis of the social and demographic data of the victims showed that 80 percent were male blue-collar migrant workers, between the ages of 16 and 35, with little or no education, living and working in squalid conditions.

The outbreak was quickly diagnosed, and it did not have the impact originally feared. The fatality rate was 35 percent of the diagnosed cases, with around 80 people dying between September 18 and October 7, 1994. The most effective response came from the people who cleaned the streets and from junior doctors who worked tirelessly in public hospitals. Doctors of the New Civil Hospital rapidly administered antimicrobial therapy in the form of tetracycline and chloramphenicol, and the death rate dropped dramatically.

Under the dynamic leadership of the municipal commissioner, S. R. Rao, various public health and sanitation measures were undertaken in the post-plague period, making Surat among the cleanest cities in India. The corrective steps implemented included the decentralization of public health administration, the widening of roads, the demolition of illegal structures, and the instituting of sanitary improvements, including the installation of toilets and arrangements for garbage collection. The lesson Surat gave is that there is space within the system for remedial measures. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Antibiotics; Contagion and Transmission; Environment, Ecology, and Epidemic Disease; Plague in India and Oceania: Third Pandemic; Plague in the Contemporary World; Urbanization and Epidemic Disease.

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POISON LIBELS AND EPIDEMIC DISEASE. Even the mere mention of poison or **epidemic** disease evokes a sense of mystery and danger. As both phenomena share associations with the hidden and the unknown, it is no surprise that people who have faced the frightening prospect of a mysterious illness have relied on the equally enigmatic but more concrete notion of poison as a direct causal agent. This has given rise to the phenomenon of the “poison libel,” in which people who are trying to explain the origin and propagation of an epidemic disease have blamed individuals, or even entire social or religious groups, for deliberately using “poison” to spread disease.

Tracing the origin of disease to people spreading a poison reveals the natural tendency to relate an unknown and uncontrollable phenomenon, like epidemic disease, to one with a more obvious cause and effect, such as deliberate poisoning. Perhaps the most infamous poison libel comes from the time of the so-called **Black Death** in the mid-fourteenth century, when Jews were accused of poisoning the wells in order to spread plague to Christians. As a result, hundreds of Jews were either exiled or tried and executed (though the trials were hardly fair), and there are reports of mass suicides of Jewish communities to avoid the mistreatment that often followed the accusations. Similarly, the recurring episodes of **bubonic plague** and other epidemic diseases throughout sixteenth-century Italy encouraged many suggestions of plague-spreading conspiracies, in which nefarious individuals were thought to have smeared some kind of poison on the walls of a town to infect its inhabitants.

Just as libels usually offer little justification for their claims, the evidence offered in trials of plague-spreaders or well-poisoners was often flimsy at best and nonexistent at worst. It usually amounted to little more than a report of loitering or “suspicious” activity. Although many of the accused confessed to the charges of spreading poison and thus further fueled the possibility of its legitimacy, most confessed only under duress or threat of torture. Court documents lack any specificity in terms of what kind of poison was actually used, usually describing it as a powder or grease. The vagaries of the testimony, however, did not make poison spreading any less acceptable as a viable explanation. The seriousness in which the accusations were both made and acted upon demonstrates the urgency with which people tried to understand and control the disease at hand.

The notion that poison could be smeared on walls to cause epidemic disease sounds almost ludicrous to modern ears, yet the historical examples of “poison libels” must be understood in conjunction with the long-standing medical framework that linked poison and disease. The root of the association can be traced back to the earliest Western medical literature in which the cause of disease was linked to the concept of “**miasma**” or “bad air.” The idea was that there was something foul, putrid, or even poisonous about the air itself that could bring illness, by virtue of its poisonous nature, to those who breathed it. Nor was direct contact required for someone to be poisoned. The belief that poison could act at a distance was virtually common knowledge, an idea embodied in the legend of the fabled basilisk—an animal reputedly able to poison through all five senses, including hearing and vision.

The relationship between poison and disease was considerably strengthened during the Black Death. At the outbreak of the plague, physicians struggled to understand its astonishing mortality, and in particular how it came to and moved across the whole of Europe. In response, doctors such as Gentile da Foligno (d. 1348) described this pestilential disease as some kind of poison in the environment, perhaps emanating from rotting corpses or putrid swamps, or as a result of a poisonous exhalation from the ground after an earth-

quake. This poison could move around the environment and eventually find its way inside the human body, poisoning it. By association, the general notion of poison was imbued with the power to spread disease, and towns under a self-imposed isolation to prohibit the arrival of plague considered the spread of external poisons a very real threat indeed. Upon entering the city walls, travelers who were carrying any kind of ointment or potion were occasionally directed to consume them to prove to officials that they were not disease-causing poisons. The role of poison in disease was not merely a function of the plague, but in fact remained a much-discussed medical topic throughout sixteenth-century works on poison, such as those by Italian physicians Girolamo Cardano (1501–1576) and Girolamo Mercuriale (1530–1606).

Not only were poison libels an effort to identify a more tangible cause of a disease, but they were also, in many cases, an effort to associate a dangerous evil, such as poison, with marginal and often misunderstood social groups, who were themselves considered evil in some respects. Just as with the accusations against medieval Jews, whose different religious beliefs elicited scorn from the mainstream Christian majority, it was thought that those people spreading plague or poison were somehow in league with the devil. Associations with evil were especially common with respect to those people who were thought to practice some form of black magic and who could harness occult natural powers to bring ill-health to their targets. In this way, poison libels overlap to some extent with witch-hunts, though witchcraft (which could be used for good as well as evil) and poison conspiracies must not be thought of as the same thing. The way that poison libels target misunderstood social groups is also similar to the notion of “blood libels,” accusations of using human blood in religious ceremonies. These, too, have historically been leveled against Jews, but they continue to be applied today, as case in the case of modern practitioners of Voodoo, who are often viewed as a peripheral community with bizarre and satanic rituals.

The general notion of poison as a cause of disease has persisted into the modern era as well. Because the line between medicine and poison can be very fine indeed, radically new drugs

REPORT OF JEWISH “CONFESSIONS” TO POISONING WATER SOURCES IN SAVOY DURING THE BLACK DEATH (1348)

On 19 September Balavigny confessed, without being put to the question [tortured], that three weeks after Pentecost Mussus the Jew of Villeneuve told him that he had put poison in the public drinking fountain of his own town, namely in the custom-house there, and that afterwards he did not drink its water, but only drank from the lake. He also confessed that Mussus had told him that he had likewise placed poison in the public drinking fountain at Chillon, namely in the custom-house under some stones. The spring was then investigated and some poison found. Some of it was given to a Jew, who died, thereby proving that it was poison. He said further that rabbis had instructed him and other Jews not to drink water for nine days after poison had been put in it, and he said that as soon as he had put poison in the spring he immediately warned other Jews.

He confesses further that a good two months earlier he had been at Évian and, while talking the matter with a Jew called Jacob, had asked him, among other things, whether he had a letter and poison like the others; to which Jacob replied that he had. Afterward he asked him whether he had obeyed the instructions, to which Jacob replied that he had not placed the poison himself but had given it to Savetus the Jew who had put it into the spring *de Morer* at Évian. He urged on Balavigny the wisdom of dealing with the instructions in the same way.

From the *Strassburg Urkundenbuch*; translated by Rosemary Horrox in her *The Black Death* (New York: Manchester University Press, 1994), p. 213.

or medical techniques have kindled fears of poison in the minds of wary medical consumers. Some early opponents of **vaccination**, for example, argued that it was tantamount to administering a poison and would be more harmful than the disease itself. Nor does the sentiment behind poison libels necessarily need to involve poison explicitly, but rather the more general notion that one group uses disease to control another. This is perhaps most clear when proponents of underrepresented groups accuse a real or perceived oppressor of “poisoning” them. The frighteningly fast spread of **Human Immunodeficiency Virus** in the late twentieth century brought suggestions that it was in fact a government-produced disease deliberately spread among the disproportionately affected minority groups, such as African Americans, homosexuals, and drug users. More recently, in 2003, skepticism of medical treatment led northern states of Nigeria to halt a Western-led effort to eradicate **poliomyelitis** after rumors circulated that the so-called vaccine was actually the AIDS virus.

The typical modern medical definition of poison that focuses on specific measurable variables, such as toxicity, somewhat obscures the complex and multilayered concept of poison as it has been employed throughout history. In the case of poison libels, poison has functioned in two major ways. First, it is a specific, discrete cause of disease that has made intuitive sense to those looking for an explanation. Second, poison has functioned as a convenient and medically acceptable way to assign direct human agency as a cause of disease. Although the relationship between poison and disease is no longer as medically rigorous as it once was, the sentiment of infection and corruption persists in the popular imagination and continues to influence the meaning of poison: we still speak of harmful ideas or ideologies spreading like poison and corrupting unsuspecting minds. Of course, poison libels are more about trying to make sense of the unknown than they are about poison, with the result being that they have at times constituted something of a “mob mentality” fueled by fear and ignorance. At the same time, these episodes richly provide both historical and contemporary insight for what they reveal about the confluence of both medical and social uncertainties. *See also* AIDS in America; Black Death, Flagellants, and Jews; Personal Liberties and Epidemic Disease; Poliomyelitis and American Popular Culture; Religion and Epidemic Disease; Scapegoats and Epidemic Disease; Vaccination and Inoculation.

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FREDERICK W. GIBBS

POLIO. See Poliomyelitis.

POLIOMYELITIS. Poliomyelitis (polio) was once the source of seasonal terror for parents. Beginning in the early twentieth century, polio was **epidemic** in developed nations, including the United States, during warm summer months. The fear of contracting the disease dictated many a family's summertime activities.

Biological Agent and Its Effects. The infective agent for poliomyelitis is a single-stranded DNA **virus** in the picornavirus family, closely related to enterovirus and coxsackievirus. A virus cannot reproduce itself unless it enters a living human cell. Poliovirus has a natural affinity to human nervous system tissue, being specifically attracted to a type of nerve cell in the spinal cord and brainstem called an anterior horn cell. This cell, also known as the motor neuron, has as its function the control of muscular activity in the body. Infection of the motor neuron causes destruction of the cell, leading to weakness in the muscles controlled by that nerve cell. There are three major types of poliovirus and many variations within each type.

The virulence of the various types of poliovirus found across the world differs quite substantially. Type I was most common and most likely to cause limb paralysis in epidemics. Type II was milder and most likely to cause mild or asymptomatic cases. Type III was very rare but caused a severe form of polio termed bulbar polio. This form of the disease weakened the muscles that controlled the diaphragm. Weakness in these muscles caused respiratory failure and death.

There was known to be a broad spectrum of disease severity during any epidemic polio outbreak. Most who contracted the virus had either no symptoms at all or only very mild flu-like symptoms that resolved completely without specific treatment. About 10 percent of people experienced a minor illness consisting of fever, headache, and sore throat. Only 1 percent developed major illness characterized by viral **meningitis** and severe muscle aching lasting 5 to 10 days. One-third of the major illness cases developed the paralytic form of polio. Typically, these patients had a rapidly progressive weakness in one or more limbs. The severity of weakness was unpredictable and extremely variable from one patient to the next. The weakness could be temporary or permanent. Approximately 5 percent of patients with paralytic polio died of respiratory failure as a result of muscle weakness, despite devices such as the "iron lung" and the rocking bed. These contraptions assisted breathing for patients whose respiratory muscles were weakened by polio.

Transmission and Epidemiology. Polio is spread through oral-fecal contact with the virus. This mode of transmission is typically exacerbated by poor sanitary conditions. Prior to routine **vaccination**, virtually everyone had been infected by poliovirus by adulthood, usually in early childhood. The majority of adults in countries with advanced sanitation infrastructure at the onset of the twentieth century had **immunity** to poliovirus. **Children** had a lower rate of immunity. In unsanitary conditions, however, children are more uniformly infected very early in life and are more likely to experience mild disease. It has been proposed that the late-nineteenth-century invention of modern plumbing and sewage containment led to the shift toward epidemic polio by preventing widespread infantile exposure to mild poliovirus. Once someone has been infected with poliovirus, lifelong immunity develops that prevents future reinfection. The prevention of common infantile polio subsequently allowed children to be infected with the more virulent strains later in life.

Epidemic polio, infantile paralysis, began in the early twentieth century. Historically, polio had been sporadic, but it had existed since ancient history. Paralytic poliomyelitis became epidemic in the United States and Europe during the early twentieth century.

Outbreaks of a few hundred or thousand cases were reported in Sweden in 1905 and in New York City in 1907 and 1916. Subsequently, the incidence gradually increased annually. There was an average of 5,000 to 10,000 reported cases per year in the United States until 1944. After 1944 there was a more dramatic yearly increase in incidence, peaking in 1954 with over 60,000 cases.

The introduction of the inactivated, “killed,” polio vaccine (IPV) in 1955 led to an abrupt and precipitous decline in new polio cases. Within five years after introduction of IPV, the incidence of polio had declined 90 percent. The subsequent introduction of the oral, live, attenuated “Sabin” vaccine resulted in similar declines in Europe and Russia. Despite the development of effective vaccination, paralytic polio caused by naturally occurring, wild-type virus continues to affect Sub-Saharan Africa and the Indian subcontinent. In the past 25 years, over 90 percent of new cases have been in just four countries: India, Nigeria, Pakistan, and Afghanistan. Recent outbreaks in the 1990s around Nigeria and neighboring countries were the result of poor acceptance of vaccination efforts by the local populace. The **World Health Organization** leads an extensive vaccination campaign, but multiple conspiracy theories abounded in Nigeria regarding contamination of the oral Sabin vaccine, prompting widespread refusal of treatment. Vaccination rates below 50 percent resulted in outbreaks of polio affecting several hundred people a year, until the government was able to convince the population of the safety of the vaccines.

In the United States and Europe, polio has virtually been eradicated. Fewer than 10 cases per year have occurred in the United States. One minor outbreak occurred in a small, isolated religious community where childhood immunizations had been shunned.

Nearly all cases in the developed world are now traceable back to the live attenuated strain of poliovirus in the oral Sabin vaccine. It is estimated that one in 750,000 primary vaccines develop vaccine-related polio, although these cases are generally milder than wild-type polio. These cases are the result of mutation of the live attenuated vaccine back to a virulent form of virus. The oral Sabin vaccine has been commonly used for mass vaccination in the developing world. As wild-type polio approaches eradication in the whole world in the twenty-first century, widespread vaccination programs are beginning to transition exclusively to the killed Salk vaccine to eliminate all cases of polio.

Major Outbreaks with Public Health Responses. The early twentieth-century public health response to polio focused on patient isolation. Historical reports suggest that public health officials and **physicians** patrolled neighborhoods where new cases were reported. The home was inspected for adherence to published hygiene and **quarantine** regulations. Patients, usually children, were often separated from the family and sent to **sanatoria** to recuperate away from unaffected children. There was a basic lack of understanding about the disease that made public health interventions ineffective and terrifying for the populace. The draconian measures employed did not halt or slow the seasonal outbreaks of disease. Specialized polio wards and hospitals were developed to care for the large number of acute and convalescing patients.

History of Research and Control of the Disease. It was known as early as 1908 that polio was caused by a virus. In 1931 Sir Frank Macfarlane Burnet (1899–1985) discovered that more than one type of poliovirus existed, and that infection with one type did not prevent later infection with another type. Scientists described three types of polio in 1949 and discovered in 1952 that the poliovirus circulated in the bloodstream. The biologist **John Enders** reported in 1954 that he was able to grow poliovirus on non-nervous system tissue.



A nurse and two corpsmen of the U.S. Army attend to a poliomyelitis patient in an iron lung. Courtesy of the National Library of Medicine.

He used **antibiotics** to prevent **bacteria** from contaminating the viral cultures, thus producing pure virus for use in research. For their work Enders, Thomas Weller (1915–), and Frederick Robbins (1916–2003) received the Nobel Prize in 1954.

Early attempts to create a vaccine against polio were unfortunate failures. In 1954 two separate versions of a vaccine were widely tested. Both a killed and an attenuated live vaccine made on monkey nervous system tissue were developed. Neither addressed all three types of poliovirus. Both were unsuccessful and resulted in many healthy children contracting paralytic or fatal polio. In 1954 **Jonas Salk** was ready to test a killed virus vaccine (IPV) for effectiveness in inducing immunity to polio. When the results of the trial on nearly 2 million children were presented in 1955, it appeared that the vaccine was about 68 percent effective in preventing polio Type I, 100 percent effective against Type II, and 92 percent effective against Type III. This was an historical moment in medicine. The Salk vaccine is given as two injections spaced one month apart. A booster is needed every five years to maintain immunity. Because it is inactivated, the vaccine is safe for those with weak immune systems.

Albert Sabin developed a live attenuated poliovirus vaccine. This vaccine was also proven effective in a large trial conducted in Russia in 1956. Oral Sabin vaccine is given in three doses in the first two years of life, and a booster is given when the child starts

school. The advantage of a live, attenuated vaccine is its long-lasting immunity. A disadvantage is that it cannot be used for patients with weakened immune systems, because it can cause active polio in these patients. Both Salk and Sabin vaccines are effective and have their advantages and disadvantages. The Sabin vaccine is nearly uniformly used in the United States at this time.

There is no medication to treat the poliovirus once active infection occurs. **Antibiotics** are ineffective against viruses, and no available antiviral medicine has any effect on the poliovirus. The focus of treatment is support for the afflicted patient through the illness and recuperation. Physical therapy is paramount. Long-term support of children in iron lungs confined children for long stretches of time. Modern ventilators now support respiratory failure if required. *See also* Animal Research; Environment, Ecology, and Epidemic Disease; Human Subjects Research; Medical Ethics and Epidemic Disease; Non-Governmental Organizations (NGOs) and Epidemic Disease; Personal Hygiene and Epidemic Disease; Poliomyelitis and American Popular Culture; Poliomyelitis, Campaign Against.

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LARA J. KUNSCHNER

POLIOMYELITIS AND AMERICAN POPULAR CULTURE. Although people had suffered from **poliomyelitis** for thousands of years, few cases were reported in the United States until the latter half of the nineteenth century, and even then the isolated cases were rare. This changed, however, in the summer of 1916 when the first major polio **epidemic** hit the United States. By most accounts, the epidemic began in Brooklyn, New York, when a small number of children reported being unable to move their arms or legs. Terrified parents rushed their children to neighborhood and family doctors, who were initially baffled by the various symptoms. As the weeks passed, the number of cases continued to rise. Health professionals finally came to realize that they had an epidemic of infantile paralysis, or polio, on their hands, but they could offer no sufficient explanation for the outbreak, treat its symptoms, or prevent its spread. Polio eventually killed and cripp-

pled thousands of Americans and changed the national culture forever, as it became one of the world's most feared diseases.

Cultural Impact of Polio in the United States. One immediate effect of the polio epidemic of 1916 was to shake the confidence of Americans who had come to believe that they lived in an enlightened period that included the gradual reduction of some infectious diseases, the spread of new and more effective techniques of sanitation, and the extension of life expectancy. The polio epidemic challenged their optimism and their confidence in science and technology as the medical profession seemed appallingly ignorant about the disease and impotent in the face of the growing human suffering it caused. As a result, the scientific community too often turned its attention to a frequent **scapegoat** in such situations, blaming the disease on the rapidly increasing numbers of foreign immigrants, as well as the dirty and often unhealthy slums in which they lived. This reaction drew directly on the new emphasis on public sanitation and **personal hygiene**, and scientists often explained the spread of polio to the upper classes as resulting from either direct contact with the poor or with family pets that had been similarly contaminated.

Ironically, targeting the poor turned out to be a significant mistake, as the disease was likely a byproduct of modern sanitation methods themselves. As public sewers were closed, infants found themselves less exposed to mild strains of polio, resulting in a loss of immunity in children and adults. Ultimately, then, polio struck people of all races and socioeconomic positions, whether urban or suburban, clean or dirty, rich or poor—although the young suffered the most. By December 1916, the polio epidemic had spread from New York to 27 states in the East, and eventually into the Midwest. Over 27,000 cases were reported in a seven-month period, and of those a full 6,000 perished, with most of the rest left paralyzed or deformed. To make it worse, following the initial epidemic in 1916, Americans experienced a terrifying recurrence of the disease each summer with parents every year fearing the beaches, swimming pools, water fountains, and fire hydrants that might spread the disease to their children.

Perhaps the greatest immediate effect of the polio epidemics on most Americans could be found in their experiences with the traditional public health measures used to combat the disease. The typical response was a combination of compulsory isolation, **quarantine**, and sanitation. Health officials often set timetables for exposure and determined whether patients could remain at home or had to be forcefully hospitalized by the "Sanitary Squads." In New York City thousands tried to flee the city by car, train, or ferry but were barred from leaving by quarantine guards who demanded written proof that the travelers were polio-free. At the same time, public health doctors monitored large groups of children in city parks, schools, and movie theaters, and theaters, schools, and amusement parks could be closed at the slightest hint of an outbreak. Many American children avoided these measures when their parents continued the isolation and quarantine policies on their own and without governmental insistence, because medical science seemed incapable of understanding and removing the polio threat. Sadly, none of these efforts accomplished much, and every spring American parents waited in dread for the summer months to arrive.

During the 50 years that polio terrorized millions of Americans, and even in the years following the development of effective and affordable vaccines, many critics argued that the threat of the disease had been consistently overstated. Other diseases and conditions were certainly more deadly, but attention had often been diverted from these to polio,

leaving other problems under-addressed by government and medicine alike. Polio epidemics in the United States indeed killed thousands, and many rightly feared the disease for that reason alone. Still, many others were terrified of polio because it seemed to target the young as its most common victims, and because it typically left these children crippled, deformed, and isolated. Once the illness had been contracted, its victims were afforded no substantial medical treatment beyond physical therapy designed to assist their fight for survival. For example, in the 1940s, “rocking tables” were introduced to help patients avoid the buildup of fluids in the lungs, and, if the patient could not breathe, he or she would be confined to an “iron lung,” which provided noninvasive assistance until the patient could once again breathe without help. Although these devices were helpful and saved the lives of many polio victims, they were also very expensive and cumbersome, and they became a visual representation of the horror of the disease. Even when not confined to an iron lung, patients often suffered for life, hobbling on crutches or being confined to a wheelchair, and the legions of victims continued to increase for decades until the 1950s, when there were more than 20,000 new polio patients each year.

Addressing the Polio Threat in America. In 1921 Franklin D. Roosevelt (1882–1945) contracted polio, suffering total paralysis from the waist down. As President, in 1938 Roosevelt helped found the National Foundation for Infantile Paralysis (known later as the March of Dimes) that raised millions of dollars for the rehabilitation of those who suffered from paralytic polio and later invested heavily in funding the research that led to effective polio vaccines. Exploiting the concerns and fears of ordinary Americans, the March of Dimes successfully initiated a new approach to fundraising when it sought small donations (only one dime at a time) from millions of individuals. The polio threat also led to a massive celebrity fundraising effort with endorsements and support offered by such cinema stars as Betty Grable (1916–1973), Humphrey Bogart (1899–1957), Jack Benny (1894–1974), and Veronica Lake (1922–1973) who raised public attention and massive contributions for the work of the March of Dimes. Even Mickey Mouse (b. 1928) raised money in movie theaters by singing “Hi Ho, Hi Ho, we’ll lick that polio,” before ushers passed around collection buckets to the patrons.

Finally, in 1946 the March of Dimes introduced another fundraising innovation, the “poster child.” Rather than using photos of pathetic and pitiable children, the organization portrayed the child victims as happy, fresh-faced, and full of promise—except for that wheelchair or leg brace. These measures were successful, and by 1955, the March of Dimes had raised over \$25 million for polio research, funding the efforts of both **Jonas Salk** and **Albert Sabin**, the 1954–1955 field trials of the vaccines, and later the provision of **vaccinations** free of charge for thousands of children. Once the Sabin and Salk vaccines were shown to be effective, the disease rapidly decreased in importance throughout most of the industrialized world, and the social impact of that success has been incalculable as few today fear the crutches, wheelchairs, and iron lungs of the recent past.

Only when millions of American school children stood in line waiting their turn to be vaccinated did the disease that had gripped several generations of Americans finally pass from the nightmares of parents and children alike. At the same time, the eradication of this last of the dreaded childhood diseases reinvigorated the faith of many Americans in the ability of medical science to find solutions to seemingly insolvable problems, and scientists once again earned the public’s respect, admiration, and trust. Discovered during the height of the Cold War, the vaccines also inspired countless Americans, as the con-

quest of polio affirmed American technological and scientific prowess. See also *Children and Childhood Epidemic Diseases; Poliomyelitis, Campaign Against*.

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BART DREDGE

POLIOMYELITIS, CAMPAIGN AGAINST. It was not until the late nineteenth and early twentieth centuries that noticeable outbreaks of polio (**poliomyelitis**) began occurring. These were concentrated in areas, particularly the United States, where improved sanitation was reducing the incidence of other infectious diseases. Although the cause of this pattern is not certain, perhaps improvements in sanitation reduced infections of infants with less virulent forms of the disease, leaving them without the resistance that accompanies exposure.

Initial research blundered into blind alleys. A major change began with a tragedy. Franklin Roosevelt (1882–1945), a rising star in the Democratic Party, came down with adult-onset polio in 1921, almost completely losing the use of his legs. His political career seemed ruined, and he began a vain struggle to regain his physical mobility. One of his initiatives was to buy Warm Springs, a threadbare spa and resort in Georgia. He intended to turn Warm Springs into a combination vacation site and polio rehabilitation center. This plan failed because vacationers did not want to mix with patients who had been crippled by polio and who, some thought, were possibly still infectious. With the help of Basil O'Connor (1892–1972), his law partner, Roosevelt turned Warm Springs into a rehabilitation center and started the National Foundation for Infantile Paralysis (NFIP). The NFIP revolutionized philanthropic activities with the March of Dimes program that sought small contributions from everyday people.

The NFIP treated polio as horrible but conquerable. It was criticized for overstating the threat of a relatively rare disease, but its funds meant that no American victim of polio went without aid. When the idea of mixing racial groups at Warm Springs was resisted, the Foundation built a facility for African American patients at Tuskegee, Alabama. Patients received help with the cost of medical care, physical rehabilitation, and, when necessary, iron lungs and long-term maintenance. Through World War II the provision of care was the NFIP's greatest success, and research remained somewhat haphazard, distracted by the differing approaches of scientists. After the war, O'Connor determined to give the research effort more focus. The disease affirmed his decision by striking ever more children: 25,000 in 1946 rising to 58,000 in 1952. It was the fastest growing infectious disease, but the chances of dying or even being crippled remained quite small. The real

impact was psychological and driven by Foundation public relations. From 1951 to 1955, the NFIP raised the then-enormous sum of \$250 million, much of which flowed into research.

The search for a vaccine followed two paths: live **virus** and killed virus. Advocates for the former, led by **Albert Sabin** of the University of Cincinnati, argued that dependable, long-term immunity could best be established by exposure to a weakened but living strain of the virus. Unfortunately, a weakened virus might regain strength as it passed through the human system, and it would take some years to perfect. Development of a killed virus vaccine was less creative scientifically but quicker. **Jonas E. Salk** at the University of Pittsburgh spearheaded this work. Less well known than Sabin, Salk started with the tedious task of identifying the types of the virus—there turned out to be three—and then got funding from the NFIP for vaccine research. By 1951 Salk was ready to test his vaccine, though the Foundation's Immunization Committee favored the live virus version. The tests were conducted privately with only a few of Foundation's leaders involved. Although the trials of Salk's vaccine were positive, Sabin and the Immunization Committee remained dubious about long-term acquired resistance. Nonetheless, O'Connor reported to the NFIP trustees that a breakthrough had occurred. O'Connor was determined to move ahead rapidly with the Salk vaccine. A new committee was created to get around bickering in the Immunization Committee, and large-scale field tests were planned for 1954. Some committee resignations resulted from the decision, as did much debate over test protocols. Should all possible children receive the vaccine, with their results compared to the unvaccinated? Or should some be given a placebo to allow for comparison within a particular group? The former meant that more children would get the possible protection, whereas the latter was more scientifically sound. In the end they followed popular opinion and used a combination of the two methods. Opinion was polarized because Sabin openly attacked the Salk virus, and influential gossip columnist Walter Winchell (1897–1972) called it deadly. Test results turned out quite positive, though the vaccine did not produce immunity in all recipients.

Not surprisingly, the nation was ecstatic. Popular demand clamored for **vaccination**, but the federal government headed by President Dwight Eisenhower (1890–1969) stuck to its conservative philosophy. It had made no preparations, preferring to allow **capitalism's** market supply and demand to control availability. Eventually, the President decided that wealth should not determine health. Manufacturers rushed to produce the vaccine, and in one case ignored industry standards: some children actually contracted polio from the vaccine made by Cutter Laboratories in California. Although properly manufactured vaccine was safe, the tragedy shook public confidence. Public reluctance to get vaccinated resulted in unnecessary outbreaks in 1955, but thereafter incidence dropped virtually to zero in the United States. By comparison, meticulous government planning, control, and vaccination in Canada resulted in elimination of the disease without a hitch. By 1961 Albert Sabin had completed his live oral virus vaccine. Eliminating the need for booster shots, which the Salk vaccine required, the Sabin version replaced Salk's, despite its very slight risk of inducing polio.

Buoyed by the progress of the global effort to eradicate smallpox (the last reported case was in 1979), in 1974 the World Health Assembly (WHA) decided to diversify the program and created the Expanded Program on Immunization (EPI). This sought to provide basic childhood disease immunizations worldwide. This was reinforced in 1985, when the **World Health Organization** and UNICEF established the Universal Childhood



A nurse is ready to offer assistance to a young boy struggling to walk with the aid of crutches and leg braces in Tokyo, Japan. Courtesy of the National Library of Medicine.

Immunization Initiative, and the Pan American Health Organization declared its initiative to eliminate polio from the Americas by 1990 (certified accomplished in 1994). Launching the Global Polio Eradication Initiative in 1988, the WHA announced its goal of worldwide polio eradication by 2000. National Immunization Days in countries such as India and China began in the mid-1990s, and in 1996 the Organization of African Unity initiated the campaign to “Kick Polio out of Africa.” In addition to providing four doses of the oral vaccine to infants with later supplementals, the global eradication campaign includes close surveillance for naturally occurring cases, and, when these are found, “mopping up” by targeted immunizations. By 2006 over \$5 billion, including \$247 million from Rotary International, had been spent worldwide immunizing over 2 billion children. In 1988 some 350,000 children in 125 countries suffered from endemic polio; less than two decades later, it was endemic in only Afghanistan, India, Nigeria, and Pakistan, with a worldwide count of fewer than 2,000 reported cases. In November 2007 the Bill and Melinda Gates Foundation joined Rotary International in committing an additional \$200 million to supplement dwindling funds. The target date for eradication has been extended to 2015. *See also* Measles, Efforts to Eradicate; Pharmaceutical Industry; Poliomyelitis and American Culture; Smallpox Eradication.

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FRED R. VAN HARTESVELDT

POPULAR MEDIA AND EPIDEMIC DISEASE: RECENT TRENDS. Plagues, viruses, and epidemic disease feature regularly in popular media and provide audiences with dramatic and gripping plots. Epidemic disease frequently functions as a catalyst to the overall narrative shedding light not only on motivations and struggles of the individual to survive but also on wider societal reactions to infection and containment. In popular media, the epidemiological specificities of the plague, epidemics, or diseases are often less important than the aftermath of epidemic disease and the social disruption that they cause.

Thus filmmakers are able to address wider questions about society, “normal” life, and powerful institutions. Fictional portrayals raise important questions including the search for appropriate solutions. In so doing, our “normal” codes of behavior can be interrogated: What is permissible or appropriate? What does it mean to be human? In addition, epidemic disease operates as a metaphorical device that allows critiques of contemporary society that reflect upon existing cultural, social, and political institutions in ways that would not otherwise be possible in factual media. The origins of disease and measures to contain such outbreaks frequently reveal a deeply pessimistic view of institutions (scientific, medical, political), social divisions, and the individual will for survival. By contrast, in popular fictional television, particularly soap operas, the focus concerns individual experience of disease. Thus, medical **diagnosis** can facilitate discussion of issues that would typically be taboo and transgressive in entertainment media.

Race for the Vaccine. Epidemic disease forms the basis of a number of popular **cinema** films. Frequently, the main protagonists are engaged in a desperate search for infected victims (often the first victim “patient zero”), and potentially lethal contact with the infected is required if a cure is to be developed. Narrative pace stems from the constraints of “time” where infection must be contained before it spreads to the wider population. Such themes can be identified in films as early as docudrama style thriller *Panic in the Streets* (1950), in which medical and police officers have just 48 hours to locate all those who came into contact with a man infected with **pneumonic plague** before an epidemic is unleashed. This theme of “race against time” is prevalent in cinematic representations of plague and disease, with many such films alluding to the **Ebola fever** and evoking global public fears and anxieties about the epidemic. Thus, in the film *Outbreak* (1995), a married couple who work for a federal disease laboratory must search for an infected monkey and a vaccine before the town is bombed by the military, which considers this to be the only solution.

Showing Not Telling: Destruction of the Body. Themes of epidemic disease can be identified across other cinematic genres, particularly within the contemporary horror film in which the theme of destruction of the body plays less on the broad fear of death than on the fear of one’s own body, of how one controls and relates to it. Showing rather than telling is directly related to the destruction of the body. The movies of the film trilogy by George Romero—*Night of the Living Dead* (1968), *Dawn of the Dead* (1978), and *Day of the Dead* (1985)—are cult horror classics dealing with an unknown infection that turns people into zombies. These films are highly regarded for their gory and explicit visual references to “body horror” mixed with dark humor and social satire. Others such as horror science-fiction film *28 Days Later . . .* (2002) and the sequel *28 Weeks Later* (2007) build on Romero’s mix of gore and social commentary offering a nightmare vision of a post-apocalyptic society caused by the release of diseased chimps infected with a “Rage” virus from a laboratory by environmental terrorists. As most of the population becomes infected, survivors must evade not only those infected but also the frequently draconian military efforts to contain the epidemic. The sequel *28 Weeks Later* deals with the repopulation of urban areas and depicts England under surveillance by American-led NATO forces. These films raise pessimistic questions of human nature, as social order breaks down bringing increased lawlessness, sexual violence, and looting, thus playing on our fears about human nature in crisis.

Lack of Trust in Military and Science. Plague and disease are commonly used as metaphors to address war and political issues, including political disappearances in Argentina, as in *The Plague* (1993). Sometimes the origins of plague are unknown, but a number of popular films involve human-engineered infections. In *The Crazies* (1973), a biological weapon is accidentally transferred to the drinking water of a small town. Dramatic tension stems from conflict between survivors and the military, and the subsequent breakdown in social order reveals scientists, military personnel, and survivors as unable to cooperate. Negative repercussions of biological warfare form the basis of *Omega Man* (1971), in which a military scientist survives and must evade flesh-eating zombies and find a cure. The use of viruses in **bioterrorism** features in *Twelve Monkeys* (1995) with a deliberately released lethal virus wiping out most of the population and forcing survivors to live underground. In *I am Legend* (2008) a human-made virus designed to cure cancer results in transmitting an infectious disease that turns recipients into mutants. The theme of fear of technological advances is similarly exploited in *The Andromeda Strain* (1971), in

which a team of scientists struggle to contain an extraterrestrial molecular virus. This film is based on medically trained Michael Crichton's novel and has been praised for its attention to scientific detail.

The AIDS Body and HIV Infection. During the early 1990s, a number of films emerged that focused on the HIV and AIDS epidemic. Some, such as *Longtime Companion* (1990) and *Philadelphia* (1993), deal with the discrimination, stigma, and prejudice experienced by those affected. Such portrayals of people living with AIDS aimed to highlight the human dimensions of the problem and sought to counteract the very negative media reporting which could be identified in the news media in which gay men (and injecting drug users) were positioned as "deserving victims." The representing of AIDS traverses difficult territory, in that it is sexually transmitted, and popular media struggled to depict gay relationships in any detail. More overtly political messages in *And the Band Played On* (1993) reflect on the first five years of AIDS in the United States. The conservative political climate is held responsible for the delayed reaction to the epidemic and the reluctance to direct resources to medical research.

Telling in Popular Television. Popular television miniseries have dealt with epidemic disease in terms of conspiracy and corruption; for example, in *Virus* (1995), a doctor tries to uncover why a strain of Ebola is spreading among the urban population of the United States and in so doing uncovers corruption and conspiracy within the medical profession and senior hospital administrators. Television drama provides important opportunities for long-term discussion of health issues through characters with whom audiences can identify. The medical drama *ER* (NBC) featured Dr. Jeanie Boulet, who contracts HIV from her sexually promiscuous husband. Heterosexual risk was similarly highlighted in soap operas *The Young and the Restless*, *All My Children*, and *Another World*, all of which featured women with HIV/AIDS. In the British soap opera *EastEnders* (BBC1) Mark Fowler was forced to challenge his own prejudices against gay people and intravenous drug users when he contracted HIV heterosexually. These socially realistic storylines represent an important commitment to social realism and were developed to counter public misconceptions of the disease as a "gay plague."

Accuracy, Sensationalism, and Impact on Audiences. The representation of infectious disease in popular film and television is frequently criticized by members of the medical and scientific profession for perpetuating scientific inaccuracies and for playing on public anxieties that may fuel panic in the event of an actual outbreak of epidemic disease. Yet popular representations of epidemics in popular media cannot be assessed on the grounds of accuracy and bias. Such representations are not perceived by audiences in the same way as factual reporting in news and documentary. As noted above, these fictional stories allow us to tackle other deep-rooted issues in society. This is not to argue that such portrayals have no impact on public understandings. Indeed, audience research studies have found that stories involving health and illness topics can have a positive and lasting impact, particularly in terms of understanding the psycho-social repercussions of infectious disease and in challenging sociocultural attitudes toward those affected. See also AIDS, Literature, and the Arts in the United States; Cinema and Epidemic Disease; Disease, Social Construction of; Literature, Disease in Modern; Poliomyelitis and American Popular Culture.

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LESLEY HENDERSON

POVERTY, WEALTH, AND EPIDEMIC DISEASE. Death comes to all, but the poor often die younger and from different illnesses than the non-poor. Since ancient Greece, **physicians** have noted that social conditions shape the **epidemiology** and outcome of disease. **Hippocrates**, writing in 400 BCE, noted that any proper medical investigation must "explore the mode in which the inhabitants live, and what are their pursuits." The yawning gap between health outcomes for the indigent and the wealthy has become more pronounced as public health and medical knowledge have advanced, enabling those with financial resources to protect themselves from acquiring disease and preventing themselves from succumbing to disease. Indeed, as Paul Farmer, a professor of social medicine at Harvard University, observes "the spectacular successes of biomedicine have in many instances further entrenched medical inequalities."

Poverty, Wealth, and Health. The positive correlation between health and wealth is shown in the accompanying box. This graph plots average life expectancy, a commonly used measure of a population's health, versus income per capita, a common indicator of national wealth. The figure demonstrates that residents of high-income countries enjoy better health, on average, than residents of lower-income countries.

According to the World Bank statistics for 2004, low-income countries (defined as countries with an average income per capita less than \$875 annually and encompassing more than 2 billion people) have an average life expectancy of 58.8 years, whereas high-income countries (defined as countries with an income per capita greater than \$10,726) have an average life expectancy of 78.7 years.

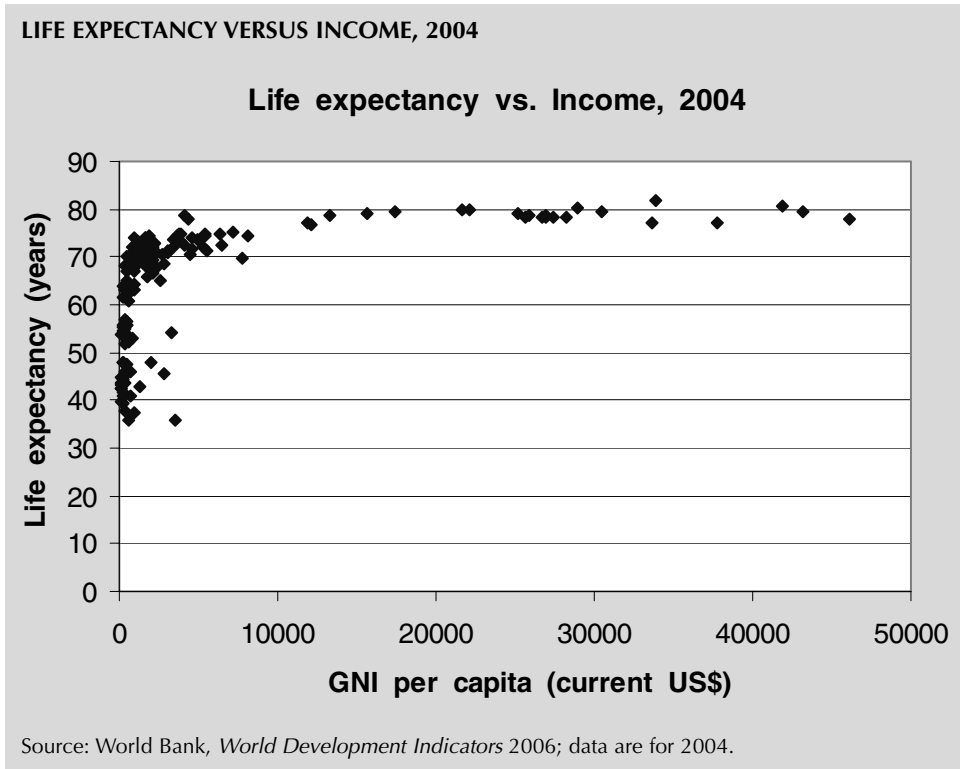
There are many possible factors driving the relationship shown in the graph. Perhaps it is mere coincidence. This seems unlikely given the robustness and reproducibility of the correlation over time. Traditionally, economists have interpreted the association as evidence that higher incomes lead to improved population health. The intuitiveness of this perspective is attractive. Wealth could reduce the risk of sickness, injury, and death through myriad pathways. Financial resources may be used to purchase clean water and sanitation, a comfortable home in a crime-free neighborhood, an adequate and nutritious **diet**, a health club membership, insurance, and high-quality medical care. Wealthier individuals often have more access to health information through media outlets or their social networks. The wealthy also tend to have more political clout—allowing them to advocate for better schools, a cleaner **environment**, and health benefits. A disproportionate share of medical research funds is allocated toward health concerns of the wealthy. In 1990 the Commission on Health Research for Development estimated that less than 10 percent of global health research resources were being applied to the health problems of developing countries, which accounted for over 90 percent of the world's health problems. This observation became known as the 10-90 gap. More current estimates suggest

that over U.S. \$105 billion is being spent on research and development for neglected diseases, yet the imbalance between disease burden and research funding persists.

However, the relationship between wealth and health may be more complex than originally thought. More recent economic and epidemiologic data support the view that the relationship between socioeconomic status and health is bidirectional. Health may induce wealth, but illness could also lead to indigence. A robust, fit individual is more capable of becoming an educated, productive, and higher-earning member of society than is one who is debilitated or diseased. Moreover, disease can impoverish households via medical and funeral expenses, lost wages, and the erosion of social networks. At the societal level, disease can interrupt supply networks, increase worker turnover, deter foreign investment, and hinder national savings. The shift in perspective, from viewing health as merely a byproduct of economic growth to an engine of development, was reflected in the 2001 **World Health Organization (WHO)** Report chaired by economist Jeffrey Sachs and entitled *Macroeconomics and Health: Investing in Health for Development*. Since 2000 a consensus has emerged that health and wealth, sickness and poverty, can lead to either a virtuous cycle of development and longevity or a vicious cycle of destitution and premature mortality. The eight Millennium Development Goals (MDGs), agreed to by all member states of the United Nations, as well as the leading international financial institutions form a blueprint for extending prosperity to the world's poor. Half of the MDGs are directly concerned with health issues—further evidence of the central role health has assumed in development circles.

However, it is not only absolute poverty that places individuals at greater risk for premature morbidity and mortality—relative position in society also appears to be important. Sir Michael Marmot (b. 1945) has been at the forefront of health inequalities research since the 1970s. Marmot was the principal investigator for a famous study involving thousands of British civil servants, known as the Whitehead study. The study demonstrated an inverse relationship between social class (proxied by employment grade) and the prevalence of multiple medical conditions. Marmot believes there is a connection between the adverse health outcomes for the disadvantaged in developing and developed worlds: “both low-grade civil servant and slum dweller lack control over their lives; they do not have the opportunity to lead lives they have reason to value.” Philosophically, Marmot's conception of poverty and development is aligned with that of Amartya Sen (b. 1933), the Nobel Prize-winning (1998) economist. Sen argues that the enduring deprivations caused by poverty, hunger, and the violation of basic liberties are common in rich and poor countries. It follows that freedom from such deprivations is necessary to achieve human development.

Poverty and Epidemics: AIDS and Obesity. Over 40 percent of the world's population, or 2.5 billion people, live on less than \$2 a day. The depredations of destitution lead to increased severity and vulnerability to epidemic disease. **Rudolf Virchow**, a renowned nineteenth-century German **physician**, is often cited as one of the first individuals to identify the social origins of epidemic disease. In today's world, the spread of the **human immunodeficiency virus (HIV)** is a conspicuous example of how socioeconomic status affects susceptibility to infectious disease. According to 2006 figures from the Joint United Nations Program on HIV/AIDS (UNAIDS), 39.5 million people were living with HIV. In 2006 over 4 million individuals were newly infected with the virus, and 3 million individuals died from AIDS and its related complications. Sub-Saharan Africa is the epicenter of the global AIDS **pandemic**. In 2006 two-thirds of all HIV-infected individuals



(about 25 million people) and the majority of HIV-related deaths occurred in Sub-Saharan Africa. Not surprisingly, Sub-Saharan Africa is also the poorest place in the world: over half of continent's 650 million people live on less than U.S. \$1 a day (the definition of extreme poverty). Of the 48 poorest countries in the world, 32 are located in this region. Poverty can increase vulnerability to HIV through many different mechanisms. Poverty prevents people from accessing regular medical and prenatal care. Without treatment for sexually transmitted infections (STIs), the indigent develop ulcerated and denuded genital mucosa, thus facilitating transmission of the AIDS virus. Expectant women may not be able to afford the medicines necessary to prevent viral transmission to their children during pregnancy or parturition. Preventing viral transmission through breast milk is only achievable if the mother has access to safe water for preparing infant formula, a luxury many cannot afford.

The global AIDS pandemic exemplifies the bidirectional relationship between disease and poverty. Winford Masanjala, an economist from Malawi, has summarized the effects of HIV at the household level: "AIDS undermines livelihoods by eroding affected households' resource base, thereby raising vulnerability to future collapse of livelihoods." Masanjala explains how AIDS erodes the four basic components of livelihood: human capital (via death of individuals), financial capital (via income depletion from death of breadwinners and diversion of resources toward health-care and funeral costs), agricultural resources (via the loss of livestock and labor), and social capital (via the loss of relatives and via disease-related stigma). At the macroeconomic level, AIDS strikes those in



Pigal, Edmé Jean, "I don't give to slackers." Caricature: An amputee beggar holds out his hat to a well-dressed man. Courtesy of the National Library of Medicine.

the prime of their productive life—killing farmers, teachers, political leaders, and doctors. A population of orphans and elderly is left behind. Such a radical demographic shift stymies income growth and could lead to economic collapse.

Yet it is not only infectious disease that stalks those living in poverty—obesity is becoming more prevalent among the relatively poor. According to Dr. Benjamin Caballero, director of the Center for Human Nutrition at Johns Hopkins Bloomberg School of Public Health, “The relationship between obesity and poverty is complex: being poor in one of the world’s poorest countries (i.e., in countries with a per capita gross national product [GNP] of less than \$800 per year) is associated with underweight and malnutrition, whereas being poor in a middle-income country (with a per capita GNP of about \$3,000 per year) is associated with an increased risk of obesity. Some developing countries face the paradox of families in which the children are underweight and the adults are overweight. This combination has been attributed by some people to intrauterine growth retardation and resulting low birth weight, which apparently confer a predisposition to obesity later in life through the acquisition of a “thrifty” phenotype that, when accompanied by rapid childhood weight gain, is conducive to the development of insulin resistance and the metabolic syndrome.” The Whitehead study showed that those on the lower rung of the socioeconomic ladder living in developed countries were more susceptible to chronic lung disease, cancer, and bronchitis and were more likely to engage in high-risk behaviors such as smoking, a high-fat diet, and a sedentary lifestyle.

Thus, the relationship between poverty and epidemic disease is bidirectional and observed across countries at every level of development. Using the expanded definition of poverty as lack of autonomy, empowerment, and freedom, we observe that premature morbidity and mortality plague the poor wherever they live. Recognizing that epidemic disease is shaped by socioeconomic realities allows effective interventions aimed at correcting both medical and social inequities to be envisioned. Acknowledging the role epidemic disease plays in economic development may provide the impetus for such interventions to be funded and enacted. *See also* AIDS in Africa; Capitalism and Epidemic Disease; Colonialism and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Human Papilloma Virus and Cervical Cancer; Industrialization and Epidemic Disease; International Health Agencies and Conventions; Irish Potato Famine and Epidemic Disease, 1845–1850; Medical Ethics and Epidemic Disease; Pest Houses and Lazarettos; Race, Ethnicity, and Epidemic Disease; Scapegoats and Epidemic Disease; Sexuality, Gender, and Epidemic Disease; Urbanization and Epidemic Disease; War, the Military, and Epidemic Disease; Water and Epidemic Diseases.

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MARCELLA ALSAN

PRESS. See News Media and Epidemic Disease.

PROTOZOON, –ZOA. Protozoa are unicellular organisms with a nucleus. There are over 200,000 species, of which about 10,000 are parasitic, and some infect all species of vertebrates and many invertebrates. However, the majority of significant human infections are caused by only a dozen or so species. There are three pathways into the human body: oral, sexual, or by a blood-sucking vector, usually an insect. Some of the intestinal protozoa can form cysts and live for years outside of their host.

There are four groups of protozoa, organized according to their means of motion. Sarcodina—amoeba or rhizopods—use pseudopods to move and are the most primitive protozoa. Mastigophora (flagellates) use whip-like flagella for motion, and Ciliophora (ciliates) use hair-like cilia. Sporozoa is the smallest of protozoa and is not motile in its adult stage.

The most widely dispersed severe disease from amoeba, amebiasis, is caused by *Entamoeba histolytica*. It affects about 10 percent of the world's population, causes a bloody diarrhea, and results in about 40,000 to 110,000 deaths per year. African Trypanosomiasis (**sleeping sickness**) is caused by two species of flagellates, *Trypanosoma brucei gambiense* and *T. brucei rhodesiense*, found in central Africa, transmitted by the tsetse fly, and causing 100,000 new cases per year. American Trypanosomiasis (Chagas' disease), found in Mexico and Central and South America, is caused by *Trypanosoma cruzi* and transmitted by the triatomid insect. About 24 million people are infected, and there are 60,000 new cases per year.

Leishmaniasis, also called Kala-azar (black fever) or Assam fever, is caused by *Leishmania donovani*, is transmitted by sand flies, and is located in Asia, Europe, Africa, and Latin America. About 12 million people are infected, and it causes a skin disease or a disseminated disease. *Toxoplasma gondii*, a sporozoa, can infect and reproduce in any mammalian cell. That makes it the most widely distributed parasite in the world. It infects about one-third of the world's human population and may cause death or congenital defects of fetuses or newborns. Most mammals and many birds can be infected, and a common reservoir is the intestinal tract of the domestic cat. Thus, cat feces play a large role in the transmission; however, some infections are transmitted by ingestion of undercooked meat.

Malaria is caused by four *Plasmodium* species (sporozoa) that are transmitted by the female *Anopheles* mosquito. About 500 million people are infected, and between 1 and 3 million people (mostly children) die each year from this protozoon. Malaria was described as far back as 2700 BCE and by **Hippocrates** in the fifth century BCE. It remains the leading parasitic cause of death in the world and is endemic in Africa, Asia, and Latin America.

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MARK A. BEST

PUBLIC HEALTH AGENCIES IN BRITAIN SINCE 1800. The history of public health agencies in Britain reflects wider shifts in attitudes toward state intervention in the lives of individuals and the centralization of political and economic power. The idea of public health as one of the responsibilities of a modern state emerged in France in the early nineteenth century, under the social reforms of Napoleon Bonaparte (1769–1821). European intellectuals and reformers were quick to adopt this idea: the German physiologist **Rudolf Virchow's** claim that “medicine is politics” reflected a growing sense that European citizens could expect their governments to get involved in maintaining and promoting the health of the nation.

But in Britain the notion of state intervention in the lives of individuals was widely seen as an infringement of **personal liberty**, running against the spirit of *laissez-faire* **capitalism**. Before the 1840s, British governments took little interest in centrally organized public health measures. Rapid **industrialization** and **urbanization** in the early nineteenth century, and terrible **poverty** in new industrial cities, generated some support for government action on this subject, as did a series of **cholera epidemics** in the 1830s and 1840s. The 1848 Public Health Act, passed against great opposition in Parliament, established a General Board of Health under the civil servant and sanitary reformer **Edwin Chadwick**, with the London **physician** John Simon (1816–1904) appointed Medical Officer for the City of London.

Simon's program of reforms became a model for subsequent British public health agencies. Though he was a physician, his work was based on public sanitation and statistical analyses of demographic data rather than on developments in medical theory and practice. Like Chadwick, Simon sought to improve the urban **environment** by removing sewage and providing clean water. The 1848 Act established the principle of central governmental intervention in public health. In 1872, following the success of this approach, a further Public Health Act required local councils throughout the country to appoint Medical Officers of Health (MOsH).

For the next 50 years, MOsH were the cornerstone of British public health. Their role was initially preventative—to identify, trace, and prevent local outbreaks of epidemic diseases such as cholera. Their work was supported by two central agencies. The General Register Office collected and published demographic data on health and disease, and the Local Government Board coordinated public health at a national level. The “bacteriological revolution” of the late nineteenth century, associated with the work of the French chemist **Louis Pasteur** and the German biologist **Robert Koch**, had little immediate impact on British public health. MOsH were, in general, more influenced by local social and economic factors than by developments in scientific theory. Despite the growing acceptance of state intervention in public health, it remained a controversial subject.

Fierce debates over the Contagious Diseases Acts in the 1860s and 1870s reflected continuing concern for individual freedom.

In the closing decades of the nineteenth century, Simon's "environmental" approach to public health was augmented by a new focus on poverty. Journalists, novelists, and social reformers drew attention to the health problems associated with poverty and to the plight of poor children in particular. Successive governments made many attempts to improve the health of children: compulsory primary education in the 1870s and 1880s, the central provision of milk for infants in the 1890s, free school meals in 1906, and the Schools Medical Service 1907. These measures culminated in the 1911 National Insurance Act, introduced by the first Liberal government in Britain, which provided old age pensions, medical care, and unemployment benefit for all—the Welfare State.

A new Ministry of Health, established at the end of the First World War (1914–1918), provided a fresh governmental focus for a multi-agency approach to public health in Britain. MOsH continued to support improvements in sanitation and housing and to monitor infectious diseases. The Schools Medical Service monitored the health, development, and nutrition of local children and coordinated health education. More widely, the apparatus of the Welfare State—pensions, unemployment benefits and health insurance—aimed to lift the working classes out of poverty by improving the environment in which they were born, grew up, and worked. But this apparent cooperation masked a growing tension between local and central agencies. The 1929 Local Government Act, an attempt to centralize power and financial authority, actually reduced the funds available to the poorest areas.

Despite these tensions, by the mid-twentieth century, the environmentalist approach to public health was widely seen as being successful. Epidemic diseases had largely been eradicated, and, despite the economic depression of the 1930s, the worst Victorian urban poverty had been eradicated. New ideas of citizenship emphasized the responsibility of individual citizens to look after their own health. Public health was increasingly redefined as "community medicine," with a new focus on the chronic disorders of old age and "diseases of affluence." This new approach was embodied in the National Health Service, established in 1948. Much authority and financial control over public health was transferred from local councils and MOsH to the Ministry of Health. The Ministry used general practitioners, now working under the National Health Service, and the increasingly influential mass media to encourage the public to take responsibility for their own health through healthy eating, exercise, and participation on state health programs such as **vaccination** and maternity care.

Since its foundation, the National Health Service has undergone an almost continuous process of reform. The balance has shifted back and forth between local and central control of public health, but the Service has remained under the supervision of the Ministry of Health and its satellite agencies. Current enthusiasm for local control of funds and medical policy means that public health is more than ever in the hands of individual British citizens. *See also* Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1862–1947; Demographic Data Collection and Analysis, History of; Germ Theory of Disease; Hospitals since 1900; Irish Potato Famine and Epidemic Disease, 1845–1850; Literature, Disease in Modern; Personal Hygiene and Epidemic Disease; Pharmaceutical Industry; Sanitation Movement of the Nineteenth Century.

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RICHARD BARNETT

PUBLIC HEALTH AGENCIES, U.S. FEDERAL. The origins of the United States Public Health Service may be traced back to the passage of an act “for the relief of sick and disabled seamen,” signed into law by President John Adams (1735–1826) on July 16, 1798. This original legislation was not actually concerned with public health, which was not a concern of the federal government at the end of the eighteenth century, but was motivated by a recognition on the part of the leaders of the young American nation that a healthy merchant marine was necessary to protect the economic prosperity and national defense of the country. There was no mechanism at the time for providing health care to sick American merchant seamen when their ships docked in American ports. The 1798 law, based on a British model, created a fund to be used by the federal government to provide medical services to merchant seamen in American ports. The Marine Hospital Fund was administered by the Treasury Department and originally financed through a monthly deduction from the wages of the seamen (although later the federal government provided the full funding for the program). Medical care was provided through contracts with existing hospitals and, increasingly as time went on, through the construction of new hospitals for this purpose.

The earliest marine hospitals were located along the East Coast, with Boston being the site of the first such facility. Hospitals were soon also established in a number of other cities on the eastern seaboard, such as Newport, Rhode Island, and Norfolk, Virginia. In time, hospitals were also established along inland waterways, on the Great Lakes, on the Gulf Coast, and finally on the Pacific Coast. The marine hospitals hardly constituted a system in the pre-Civil War period. Funds for the hospitals were inadequate, political rather than medical reasons often influenced the choice of sites for hospitals and the selection of **physicians**, and the Treasury Department had little supervisory authority over the hospitals. During the Civil War (1861–1865), the Union and Confederate forces occupied the hospitals for their own use, and in 1864 only 8 of the 27 hospitals listed before the war were operational. In 1869 the Secretary of the Treasury commissioned an extensive study of the marine hospitals, and the resulting critical report led to the passage of reform legislation in the following year.

The 1870 reorganization converted the loose network of locally controlled hospitals into a centrally controlled Marine Hospital Service, with its headquarters in Washington, D.C. The position of Supervising Surgeon (later Surgeon-General) was created to administer the Service. John Maynard Woodworth (1837–1879) was appointed as the first Supervising Surgeon in 1871, and he moved quickly to reform the system. He adopted a military model for his medical staff, instituting examinations for applicants and putting his physicians in uniforms. Woodworth created a cadre of mobile, career service physicians who could be assigned and moved as needed to the various marine hospitals. The uniformed services component of the Marine Hospital Service was formalized as the Commissioned Corps by legislation enacted in 1889.

The scope of activities of the Marine Hospital Service also began to expand well beyond the care of merchant seamen in the closing decades of the nineteenth century, beginning with the control of infectious disease. Responsibility for **quarantine** was originally a function of the states rather than the federal government, but an 1877 **yellow fever epidemic** that spread quickly from New Orleans up the Mississippi River served as a reminder that infectious diseases do not respect state borders. The epidemic resulted in the passage of the National Quarantine Act of 1878, which conferred quarantine authority on the Marine Hospital Service. Because the Service already had hospitals and physicians located in many port cities, it was a logical choice to administer quarantine at the federal level. Over the course of the next half a century, the Marine Hospital Service increasingly took over quarantine functions from state authorities.

As immigration increased dramatically in the late nineteenth century, the federal government also took over the processing of immigrants from the states, beginning in 1891. The Marine Hospital Service was assigned the responsibility for the medical inspection of arriving immigrants. Immigration legislation prohibited the admission of persons suffering from “loathsome” or dangerous contagious diseases, those who were insane or had serious mental deficiencies, and those who were likely to become public charges (e.g., because of a medical disability). Officers of the Marine Hospital Service were assigned to immigration depots to examine immigrants for medical fitness. The largest center of immigration was Ellis Island in New York, where Service physicians would examine 5,000 or more immigrants on a busy day. The Service also operated hospital facilities on Ellis Island to provide care for those arriving immigrants who needed to be hospitalized.

The newly emerging science of bacteriology was just beginning to make its impact felt on medicine in the late nineteenth century (e.g., by aiding in the **diagnosis** of infectious diseases). In 1887 the Service established a bacteriological laboratory at the marine hospital at Staten Island, New York. Originally concerned mainly with practical problems related to the diagnosis of disease, the Hygienic Laboratory, as it was called, was moved to Washington, D.C., in 1891 and became a center for biomedical research, eventually known as the National Institutes of Health.

Because of the broadening responsibilities of the Service, its name was changed in 1902 to the Public Health and Marine Hospital Service. The Service continued to expand its public health activities as the nation entered the twentieth century. For example, Service physicians cooperated with local health departments in campaigns against **bubonic plague** and yellow fever in cities such as San Francisco and New Orleans in the early part of the century. The increasing involvement of the Service in public health activities led to its name being changed again in 1912 to the Public Health Service (PHS). At the same time, the PHS was given clear legislative authority to “investigate the diseases of man and conditions influencing the propagation and spread thereof, including sanitation and sewage and the pollution either directly or indirectly of the navigable streams and lakes of the United States.” Thus, any kind of illness, whatever the cause (including environmental pollution), now came within the purview of the PHS.

During World War I (1914–1918), some PHS-commissioned officers were detailed to the Army and the Navy, but most PHS staff were involved in **war**-related efforts on the home front. The Service was given the responsibility of working with local health departments to keep the areas around military training camps free from disease. Venereal disease was a particular concern to the military, and a PHS Division of Venereal Disease was established in 1918 to control the spread of “social disease.” The wartime concern with

potential industrial hazards for workers served to stimulate PHS activities in the field of industrial hygiene. Following the war, the PHS was given the responsibility for the care of all returning veterans for a brief time, until the Veteran's Bureau was created in 1921.

In the two decades between the two world wars, the PHS expanded the population to which it provided health care beyond the traditional categories of merchant seamen and the Coast Guard. In 1921 the PHS assumed responsibility for individuals suffering from Hansen's disease when it converted the state **leprosy** facility in Carville, Louisiana, to a national leprosy hospital. Under the PHS, the hospital at Carville carried out pioneering research on the nature and treatment of leprosy. In 1928 the Service detailed a commissioned officer to serve as Director of Health of the Bureau of Indian Affairs of the Department of Interior, as well assigning a number of other officers to the Bureau to provide medical assistance in the field. The law creating the Federal Bureau of Prisons in 1930 included provisions for the assignment of PHS officers to supervise and provide medical and psychiatric services in Federal prisons, thus adding another category of beneficiaries to the roster of those served by the PHS.

The Public Health Service also increased its involvement in this period with issues of drug abuse and mental health. A Division of Narcotics was created in 1929, and the following year it was given the broader name of Division of Mental Hygiene (although drug abuse remained its major focus for some years). The 1929 law that established the Division also authorized the creation of two hospitals for the treatment of narcotics addicts, and these facilities were opened in Lexington, Kentucky, and Fort Worth, Texas, in the 1930s.

Under the New Deal, the PHS became more involved in the broader health concerns of the nation. The Social Security Act of 1935 provided the PHS with the funds and the authority to build a system of state and local health departments, an activity that it had already been doing to some extent on an informal basis. Under this legislation, the Service provided grants to states to stimulate the development of health services, train public health workers, and undertake research on health problems. These new authorities were embraced by Thomas Parran (1892–1968), who was appointed as PHS Surgeon-General in 1936. Venereal disease was an area of particular concern to Parran, who sought to focus the battle against **syphilis** and **gonorrhoea** on scientific and medical grounds. He played a major role in breaking down the taboo against the discussion of the subject in the **popular media**, and his efforts were instrumental in leading to the passage of the National Venereal Disease Control Act in 1938.

After being housed in the Treasury Department ever since its establishment, the PHS suddenly found itself in a new administrative home as the result of a government reorganization in 1939. President Franklin D. Roosevelt (1882–1945) aligned the PHS along with a number of social service agencies, such as the Social Security Board, in a newly created Federal Security Agency. The reorganization had little effect, however, on the functions and operation of the Service.

With the entry of the country into World War II (1939–1945), some PHS officers were detailed to the military services. The Coast Guard was militarized in November 1941, and 663 PHS officers served with the Guard during the war, four of them losing their lives. A concern about a wartime shortage of **nurses** led to the passage of the Nurse Training Act of 1943, creating a program known as the Cadet Nurse Corps, administered by the PHS. The program provided participants with a tuition scholarship and a small monthly stipend while attending a qualified nursing school. In return for this support, the Cadets agreed to

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work after graduation in essential nursing services for the duration of the war, whether in the military or in civilian life. By the time that the program was terminated in 1948, over 124,000 nurses (including some 3,000 African Americans) had graduated.

The war contributed to expansion in the Service's programs and personnel and also increased the involvement of the Service in international health activities. The 1944 Public Health Service Act codified on an integrated basis all of the authorities of the Service and strengthened the administrative authority of the Surgeon-General. This act also provided the authority under which the PHS developed a major postwar program of grants for medical research through the National Institutes of Health, building upon the earlier example of the extramural grants for cancer research given by the Service's National Cancer Institute since its creation in 1937.

Another legacy of World War II grew out of a wartime program of the PHS to control **malaria** in areas around military camps and in maneuver areas in the United States, most of which were established in the South. Over the course of the war, the Malaria Control in War Areas program, based in Atlanta, expanded its responsibilities to include the control of other communicable diseases such as yellow fever, **Dengue**, and **typhus**. The program was converted in 1946 to the Communicable Disease Center (CDC). The mission of the CDC continued to expand over the next half-century, going beyond the bounds of infectious disease to include areas such as nutrition, chronic disease, and occupational and environmental health. To reflect this broader scope of the institution, its name was changed to the Center for Disease Control in 1970. It received its current designation, Centers for Disease Control and Prevention (retaining the acronym CDC), in 1992.

In 1946 two major legislative acts had a significant impact on the PHS. The National Mental Health Act greatly increased PHS involvement in the area of mental health. The Act supported research on mental illness, provided fellowships and grants for the training of mental health personnel, and made available grants to states to assist in the establishment of clinics and treatment centers and to fund demonstration projects. It also called for the establishment within the PHS of a National Institute for Mental Health, which was created in 1949. The Hospital Survey and Construction Act, more commonly referred to as the Hill-Burton Act, authorized the PHS to make grants to the states for surveying their hospitals and public health centers, for planning construction of additional facilities, and to assist in this construction.

The Federal Security Agency was elevated to cabinet status as the Department of Health, Education, and Welfare (DHEW) in 1953, but this change in status of the Service's parent organization had little direct impact on the PHS at the time. The Service did assume several new tasks, however, in the 1950s and 1960s. For example, it became responsible for the health of American Indians in 1955, when all Indian health programs of the Bureau of Indian Affairs were transferred to the PHS. A new Division of Indian Health (now the Indian Health Service) was established to administer these programs. The Food and Drug Administration was made a part of the PHS in 1968, thus involving the PHS much more heavily and visibly in the area of regulation.

While expanding its responsibilities in a number of areas, the PHS also saw its activities circumscribed in one field in this period, namely environmental health. In the 1960s, water pollution control was moved from the PHS to the Department level, and eventually transferred to the Department of Interior. The creation of the Environmental Protection Agency (EPA) in 1970 led to the loss of PHS programs in areas such as air pollution and

solid waste to the new agency. Although some PHS-commissioned officers were detailed to the EPA to assist it in its work, the Service had lost its role as the leader of the federal environmental movement.

A major reorganization in 1968, prompted by the concerns of some that the PHS needed to be more responsive to the policies of elected public officials and more of a modern political bureaucracy, dramatically changed the leadership structure of the Service. From the reorganization of 1870 through the middle of the 1960s, the PHS had been led entirely by career commissioned officers (who represented less than 20 percent of PHS employees by the 1960s), with no member of the civil service having ever run a bureau. The Surgeon-General, although appointed by the president, had always been a career member of the Commissioned Corps. The 1968 reorganization transferred the responsibility for directing the PHS from the Surgeon-General to the Assistant Secretary for Health (a political appointee position). For the first time, a non-career official became the top official in the PHS. Although the Assistant Secretary for Health could come from the ranks of the PHS Commissioned Corps, this has not typically been the case. The Surgeon-General was no longer responsible for the management of the PHS but became largely an advisor and spokesperson on public health matters. Candidates for the position of Surgeon-General no longer necessarily came from the ranks of the Corps but were often appointed from outside the PHS and commissioned upon their appointment.

A series of further reorganizations over the next three decades continued to reshape the structure, but not the major functions, of the PHS. The PHS did assume responsibility for the first time for the health of certain members of the general public (as opposed to specific groups such as seamen or prisoners or Indians) with the creation of the National Health Services Corps (NHSC) in 1970. Under this program, the PHS sent physicians and other health professionals into clinical practice in areas where there were critical health manpower shortages. Beginning in 1972, the PHS could offer health professional students scholarships in exchange for a commitment to serve in the NHSC. A decade later, however, the PHS lost another group of patients when the health care entitlement for merchant seamen was terminated. By that time, the provision of health care to merchant seamen played only a small part in the work of the PHS, but nevertheless the closing of the remaining 8 marine hospitals and 27 clinics in 1981 represented the end of the activity for which the Service was originally created.

There has been no lack of challenges for the PHS since that time, with the **HIV/AIDS** epidemic being just one example of the health-care issues confronting the Service. The Service today, with some 50,000 employees, remains a component of the Department of Health and Human Services (DHHS), as the DHEW was renamed upon the creation of a separate Department of Education in 1980. A major reorganization in 1995 once again changed the leadership structure of the PHS. The PHS agencies, by this time numbering eight, no longer reported to the Assistant Secretary for Health, but directly to the Secretary of the DHHS. The eight agencies, or operating divisions, together with the Office of Public Health and Science (headed by the Assistant Secretary for Health and including the Surgeon General), compose today's Public Health Service. *See also* Hospitals in the West to 1900; Hospitals since 1900; Influenza Pandemic, 1889–1890; Influenza Pandemic, 1918–1919; Leprosy in the United States; Poliomyelitis, Campaign Against; Public Health Agencies in Britain since 1800; Public Health Boards in the West before 1900; Trade, Travel, and Epidemic Disease; Venereal Disease and Social Reform in Progressive-Era America; Yellow Fever in the American South, 1810–1905.

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JOHN PARASCANDOLA

PUBLIC HEALTH BOARDS IN THE WEST BEFORE 1900. The ancient Greeks and Romans rightly associated the preservation of health with clean living **environments**, healthy **diets**, and fresh **water**. Roman *aediles* were public officials charged with maintaining public sanitation, baths, drinking water supplies, and reasonably fresh food, and Rome's first emperor, Augustus Caesar (r. 31 BCE–14 CE) organized their efforts in the Eternal City and provincial capitals. Rome's Byzantine and Islamic successors retained some of this structure, adding hospices, **hospitals**, and **bimaristan** to care for the ill. In the Latin West the revival of Roman law and the development of cities needful of sanitary legislation and oversight were delayed until the twelfth and thirteenth centuries. Beginning in Italy, city councils and their officers oversaw rudimentary attempts to keep streets clean, drainage and sewage flowing, and food sold in markets healthy. Occupational guilds oversaw the practices of **physicians**, **surgeons**, and **apothecaries**, but there was little in the way of organized public health. Guilds and philanthropists supported poor relief, **leprosarria**, and hospitals, largely as means of maintaining social order.

The **Black Death** in the late 1340s ushered in a new age of concern and public health organization. Many Italian city-states appointed temporary, ad hoc committees of non-medical expert laymen to oversee intensified sanitation and charity efforts, and to protect the property of those who had fled or died. The Venetian Republic's temporary board closed its port, and, after a few bouts of plague, began **quarantine** practices. The Milanese dukes acted decisively in closing the city gates, isolating early plague cases in their houses, establishing a **pest house** outside the city and forcibly relocating the sick, and maintaining a **cordon sanitaire** at the edge of their duchy. Elsewhere in Continental Europe, city governments adopted the ad hoc committee approach, though very slowly, appointing the politically significant who relied on physicians for framing temporary policies and laws. Permanent health boards, still dominated by non-medical experts, began to appear in Italy from the later fifteenth century. Ducal Milan and newly ducal Florence (1527) led the way, with subject towns and cities following their leads. These early magistracies sent investigators around the territories and collected reports on sanitary and health conditions, and when plague or another **epidemic** hit, they appointed the necessary officials to affected locales and enacted appropriate legislation to prevent the spread of disease. By the seventeenth century, their authority trumped that of local church officials, who often wanted to hold religious gatherings the boards felt dangerous to public health. It was no coincidence that small monarchical states pioneered these coercive means and measures. In England the Tudor monarchs' Privy Councils handed down "orders"

during plague times. These applied foremost to London, but even there compliance was relegated to the parish level of municipal organization.

From the sixteenth through the eighteenth centuries, maintenance of public health and reaction to epidemic disease remained largely local concerns, despite the flourishing of new and reemerging infectious diseases (the **English sweat, typhus, syphilis, bubonic plague, smallpox**, scarlet fever). Though little changed administratively, a number of individuals made important contributions to public health thinking during the period, sometimes referred to as the **Scientific Revolution**. Many of these ideas resonated with the leaders of states that considered their populations to be economic and political resources to be protected and fostered. **Girolamo Fracastoro** developed an unprecedentedly coherent theory of **contagion**. Englishmen William Petty (1623–1687) and John Graunt (1620–1674) respectively constructed the bases for accurate population data collection and its analysis. In the wake of the **Great Plague of London** in 1665, Petty proposed the establishment of a permanent Health Council for the capital, as well as the construction of public plague isolation hospitals. Wealthy Quaker John Bellers (1654–1725) in his *Essay toward the Improvement of Physick* promoted a comprehensive national health service that would provide well-trained physicians, hospitals, and medical research into diseases. On the continent, the absolutist states took a paternalistic approach to the welfare of their people, but theory rarely translated into action. Germans Veit Ludwig von Seckendorff (1626–1692) and Gottfried von Leibniz (1646–1716) developed early statistical methods and advocated a state health council to oversee public health. Conrad Behrens of Hildesheim (1660–1726) wrote that a state had the obligation to provide for the good health of its people as a mater of natural law, and this meant preventing illness where possible, and treating the suffering to the extent possible.

Humanitarian and Lockean (classical liberal) strains of the eighteenth-century Enlightenment shifted the focus to the individual's right to protection by the state. Enlightened absolutists in Germany set up "medical police," and prison reformer John Howard (1726–1790) inspected prisons and pest houses from Ireland to the Black Sea and reported his findings on the human misery he witnessed. Public-spirited Quakers supported hospitals and trustworthy water supplies for the cities that were growing in number and size. In Germany, Johann Peter Frank (1748–1821) composed a meticulously detailed, nine-volume work outlining a system of state-controlled public welfare that relied on professionals and their emerging sciences. The French Revolution (1789–1796) established France's first national Health Committee, but it took Napoleon (1769–1821) to organize the ad hoc *bureaux de santé* (bureaus of health), commissioned in times of epidemics, under a central council—though only in Paris. A few other French cities followed suit in the 1820s and 1830s. Following the Revolution of 1848, the French government created a system of provincial health councils consisting of health professionals in each *département*. It also created a permanent advisory committee on public health that reported to the Minister of Agriculture and Commerce. The same revolution sparked a public health reform movement in Germany, one of whose leaders was Prussian **Rudolf Virchow**. Though crushed by the royal reaction, a quarter century later, Virchow in Berlin and **Max von Pettenkoffer** in Munich were cleaning up their respective capitals under the authority of new German Empire's Reich Health Office, a creation of the liberal Chancellor Otto von Bismarck (1815–1898).

Both the French and German advances were inspired by changes in England that began in the 1830s and constituted part of the so-called **Sanitation Movement**. **Edwin**

Chadwick shared the popular notion that physical and social environments determined good or bad health, and that poverty and filth contributed directly to disease. This included the dreaded **cholera** that struck London in 1831 and 1832. The capital had undergone intense **urbanization**, and the whole country **industrialization**, and these processes aggravated living conditions across the isle. Chadwick was key actor in drafting the reformative Poor Law Act of 1834, and he served on the Poor Law Commission that oversaw reform activity. A second commission, the Health of Towns Commission, followed in 1843, and, finally, a General Board of Health was established by the Public Health Act in 1848 (not coincidentally a year of epidemic cholera). Though it lasted only five years (at which point its initial mandate ran out), it established and directed local boards of health that were responsible for water, sewage, cemeteries, and other sanitary matters. Health matters reverted to the Privy Council until a royal commission report on sanitary administration led to the creation of the Local Government Board in 1871. Four years later, the Public Health Act created a full framework that directed all local boards of health, thus creating a meaningful national health oversight system.

Colonial America had relied on ad hoc committees to see the colonists through epidemic seasons, and by 1830 only five cities had boards of health. New York City began with a City Inspector of Health in 1804, but immigration, growth, industrialization, and the health and social problems and dangers that accompanied these outpaced a single official. By the 1840s the New York slums and recurring outbreaks of **yellow fever**, typhus, **typhoid**, smallpox, and cholera caused deep concern, as chronicled in physician and health inspector John Griscom's (1809–1874) *Sanitary Conditions of the Laboring Population of New York* (1848). As did other Sanitationists of the era, Griscom believed that most disease was preventable, and he outlined the steps to a cleaner and healthier city. Citizen committees picked up much of the slack until the New York Metropolitan Board of Health was established in 1866. It had a geographically wide mandate that was narrowed in 1870. The new New York City Health Department was presided over by a political appointee and consisted of four doctors who served as health commissioners, four police commissioners, and the health officer of the Port of New York. The post-Civil War years also saw the development of state health departments. Between 1869, when Massachusetts began the trend by following the recommendations of Boston's Lemuel Shattuck (1793–1859), and 1877, eight states and the District of Columbia established boards of health. This was followed in 1879 by the creation of the U.S. National Board of Health. *See also* Cholera: First through Third Pandemics, 1816–1861; Demographic Data Collection and Analysis, History of; Epidemiology, History of; Industrial Revolution; International Health Agencies and Conventions; Personal Liberties and Epidemic Disease; Plague and Developments in Public Health, 1348–1600; Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500; Public Health Agencies in Britain since 1800; Public Health Agencies, U.S. Federal; Public Health in the Islamic World, 1000–1600; Syphilis in Sixteenth-Century Europe; Yellow Fever in the American South, 1810–1905.

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JOSEPH P. BYRNE

PUBLIC HEALTH IN THE ISLAMIC WORLD, 1000–1600. Although structured and extensive **public health** organizations are products of modern states, there was a continuous concern for preserving the health of communities in the Islamic world, as there was in Europe, before the modern era. A variety of cultural and religious practices, such as circumcision or prohibition of eating pork, either attempted to or in effect served to preserve **personal hygiene** and communal health in medieval Islamic society.

Islamic disease theory and medicine, which was largely based on **Galenic** teachings of **humoral theory**, stressed the importance of preserving health and restoring the balances of the body's humors. Eating a well-balanced diet; bathing and purging regularly; and observing moderation in physical exercise, sexual intercourse, sleep, and emotions were recommended for maintaining good health.

The earliest Islamic hospitals—**bimaristan**—date to the tenth century. Early hospitals were founded in several major cities of the Islamic world including Baghdad, Damascus, and Cairo, and later in several Anatolian cities. Although these foundations grew in number and quality of organization, it is debatable to what extent medieval Islamic hospitals served as public health institutions.

As in neighboring Europe, epidemic disease appears to have been the most important factor that prompted the formation of public health measures in the Islamic world. The **Black Death (1347–1352)** and its recurrent waves affected the Islamic world immensely, as it did the rest of the Old World, and it pressed hard the various governing bodies to adopt measures to monitor, control, and fight the disease. As such, historical analyses of the chain of events in the medieval and early modern Islamic world allow one to document the extent to which the **plague and developments in public health** have been intertwined in the Old World. Practices such as **quarantine**, records of death tolls, control of burying of the dead, and maintenance of urban hygiene were some of the common measures adopted during epidemics.

Quarantine, which required that people and goods be detained and isolated for a number of days before they would be allowed to enter a town, was commonly practiced in the Mediterranean world. This ancient custom had been well known in the Islamic world since antiquity. Although there are occasional references to this custom in the sources, it is hard to determine to what extent regulations were being systematically enforced.

During outbreaks of plague, it was also a common practice for governments to monitor the death toll. Daily death tolls were meticulously kept in many cities of the Islamic world in an effort to observe the progress of the plague infestations. For instance, during the plague in Mamluk Cairo, the death toll was recorded for tax registers. Similarly, in six-

teenth-century Istanbul, the number of dead bodies that were taken outside of city walls was recorded on a daily basis.

Because of the supposed connection between **corpses and epidemic disease**, quick and effective burying of the dead was one of the primary concerns during outbreaks. At times, meeting the increased need for labor to carry out burying duties presented a serious challenge to governments. In early fifteenth-century Cairo, for example, the Mamluk Sultan hired the city's poor and beggars and paid them high wages to bury the dead and perform Muslim burial rituals. In another case, during a violent outbreak of plague in late fifteenth-century Istanbul, the city appears to have been nearly deserted as a result of communal **flight**, and chronicles describe the struggle of the government to find the necessary labor force to bury the dead.

As cities grew, maintaining urban hygiene became a major task for governments. For instance, the early modern Ottoman government began to give greater care to public sanitation: it sought to dry up marshy lands, keep water resources clean, and regulate garbage disposal practices in the Empire's cities. From the sixteenth century onward, local judges were made responsible for monitoring and controlling urban hygiene in Ottoman cities. They were also responsible for resolving legal disputes among individuals, which could also entail issues of health. For instance, local judges were consulted for obtaining a report confirming the health status of an individual or his/her illness.

Although the link between **personal hygiene and epidemic disease** was not accurately established in the early modern period, we do see an emphasis on domestic hygiene in most extant Islamic plague treatises. It was recommended, for example, to clean houses by sprinkling vinegar, sandalwood, and rosewater.

The rise of hospitals also helped the emergence and development of institutional **medical education** in the Islamic world. The first medical school opened in Damascus in the early thirteenth century, and new medical schools were established in various cities of the Islamic world. Islamic medical education reached its apogee in the sixteenth century with the establishment of Süleymaniye hospital and medical school in Ottoman Istanbul. Through establishing medical schools and patronizing medical works, the early modern Ottoman state was able to exert control over the production of medical knowledge. From the late fifteenth century onward, for instance, Ottoman plague treatises legally authorized the need to exit a plague-infested city, in contrast to the earlier treatises written in the Islamic world, which strictly forbade this practice.

From the last years of the fifteenth century, the early modern Ottoman state established the post of the Chief **Physician**, who was responsible for administering all health affairs of the empire. The Chief Physician was also responsible for appointing physicians to hospitals in the empire. These health measures paved the way for a gradual institutionalization of medicine and the public health in the Islamic world. *See also* Apothecary/Pharmacist; Black Death, Economic and Demographic Effects of; Hospitals in the West to 1900; Plague in the Islamic World, 1360–1500; Plague in the Islamic World, 1500–1850; Public Health Boards in the West before 1900.

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NÜKHET VARLIK

PUBLIC HEALTH POSTERS. Publicly displayed health warnings go back at least to Roman times. But public health posters as we know them today, especially following their extensive use in campaigns against **AIDS**, are scarcely a century old. A variant of posters in general (essentially large announcements, usually with a pictorial element, and usually mass-produced on paper for display on walls or billboards to a general audience), they made their debut in the first decade of the twentieth century when health campaigners began to adopt the techniques of mass commercial advertising. During the First World War (1914–1918), they came to be more widely relied upon, particularly in France where a tradition of poster art was exploited for an anti-**tuberculosis** campaign financed by the

Rockefeller foundation. They were also extensively deployed during the Russian Civil War (1918–1921) and in the new Soviet Union, above all in the battle against the rickettsial **typhus** louse. Unlike wartime propaganda posters, public health posters did not suffer the backlash of informational distrust, in part because in most liberal democracies during the interwar period they continued to be mainly produced and distributed by voluntary organizations such as the **Red Cross** and were perceived as educational tools in a humanitarian interest. By the Second World War (1939–1945) they were increasingly under the aegis of state health authorities, military and civilian, and were as frequently used in campaigns against rats and vermin, as in soliciting blood donation or informing on the dangers of sexually transmitted disease. Whereas in Africa and impoverished countries they continued to be important in campaigns against **smallpox**, **malaria**, and various other infectious diseases, in the West, where infectious diseases were thought to be all but conquered by the 1960s, they were often directed to the dangers of smoking. Ironically, with the advent of **AIDS**, in the context of the retreat of many Western nations from public health and welfare programs, state



Two Iranian children look at educational posters depicting healthy practices. Photo by Marc Riboud. Courtesy of the National Library of Medicine.

initiatives in health poster production were dramatically increased (albeit usually in multimedia campaigns franchised to major advertising companies who could utilize the latest production technologies and marketing strategies). Subsequently, their production in the West tended to revert to voluntary organizations whose audiences are no longer the homogeneous “public” of mid-century, but targeted groups perceived to be at risk. Thus, public health posters have been transformed into health posters for different “publics.”

Public health posters might be said to operate by evoking a controlled form of fear and anxiety for the purpose of the rational governance of personal and/or national life. It remains an open question, however, how far this or any other emotional response to them can be generalized, either in terms of the intent to instill it by the producers of posters, or in terms of viewers’ reactions. Quintessentially ephemeral objects—disposable, defaceable, and over-paste-able—intended to make an impression and then disappear (as, indeed, many of them have), it is almost impossible historically to measure their behavioral impact. Indeed, just how “public” their circulation was before the time of AIDS (and which posters, when and where) is not readily established. Historically, their greatest power may have been not with regard to public and preventive health, but rather, in destigmatising certain corporeal discussions and in consolidating discourses and authority structures around the body in health and illness. *See also* Disease, Social Construction of; Non-Governmental Organizations (NGOs) and Epidemic Disease; Personal Hygiene and Epidemic Disease; Poliomyelitis, Campaign Against.

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ROGER COOTER

PUBLIC HEALTH SERVICE, U.S. See Public Health Agencies, U.S. Federal.

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QUACKS, CHARLATANS, AND THEIR REMEDIES. Quackery or charlatanism can be defined in simple terms as a pretense to medical skill, usually by those lacking a formal or credible **medical education**. Although both are pejorative terms, charlatan is more often associated with itinerant healers who exhibited a flair for the theatrical. Historically, accusations of quackery or charlatanism often formed part of larger social and cultural interactions among medical professionals. Any number of practitioners accused their contemporaries of quackery and were themselves accused in turn by their rivals, as part of wider professional conflicts and turf wars or as retribution for perceived slights. In fact, though pretenders to medical skill and knowledge have existed throughout the history of medical practice, it is largely within the context of these professional interactions and rivalries that quackery has assumed particular importance. Accusations of charlatanism became a way for some medical practitioners to establish and defend their professional prerogatives by excluding other, rival, practitioners as “medical pretenders.”

The writings of ancient Greek **physicians** indicate that concerns about medical charlatanism date back to the very roots of Western medicine, but it is important to note that charlatanism was by no means unique to the West. For example, when Arabic physicians in the medieval Islamic world discussed quackery, they framed it in terms of fraud and ignorance—for them, the charlatan was someone who deliberately deceived his patients with a pretense to medical skill. It could also, however, be someone whose medical ideas were not based in what was understood to be the legitimate canon of medical literature, derived in large part from classical authors such as **Galen**. Those who were viewed by the predominantly male, Muslim professional class as “others” were also attacked as medical pretenders, particularly women, Christians, and Jews. Some Arabic authors viewed attempts by women to practice medicine as a dangerous form of deception and quackery; their gender was in itself sufficient to brand them as incompetent and illegitimate. By the same token, cultural attitudes toward Jews, in particular, and

toward Christians as well, colored the ways Muslim physicians discussed and portrayed Jewish and Christian practitioners.

That Arabic physicians discussed and debated the problem of medical charlatanism for centuries tells us that, in spite of their best efforts, they never entirely succeeded in eliminating rival practitioners. The same can be said for practitioners in Europe, who struggled with similar problems. In the European context, it became increasingly common from the Middle Ages for physicians to identify the self-taught and untraditional practitioners known as **empirics** as quacks and charlatans; the faults ascribed to empirics were almost universally applied to quacks, and vice versa. In seventeenth-century France, a small but powerful coterie of professional physicians railed against a long list of illegitimate practitioners, including foreigners, priests, and women, as well as empirics, alchemists, and **Paracelsians**. They published dozens of pamphlets attacking these practitioners and even appealed to the king in their efforts to eradicate them, but like their Arabic predecessors, they met with little success.

It could be argued that quacks were, in fact, the entrepreneurs of the medical marketplace, which explains why they were so numerous in both Western and non-Western contexts. Because their advertising was cheap and widely circulated, and their services and remedies were affordable, they were more widely consulted by the popular classes than were the more expensive physicians, and as a result, they were often an important part of the medical response to widespread medical crises such as plague and pestilence.

In fact, historians have noted that quacks and charlatans often abounded in times of plague, no doubt seeing a ready market for their cures in an increasingly panicked and fearful populace. During the great **London plague** of 1665–1666, for example, contemporaries recorded numerous instances of quacks and mountebanks advertising both prophylactic measures to ward off the plague and cures for those who had already contracted it. Some of these remedies included powdered unicorn horn and stones extracted from the intestines of camels, both of which would have carried an appealing veneer of exoticism for Londoners. Based on ancient notions of sympathy, the flesh of poisonous animals like vipers and toads was thought to attract the pestilential poison from the air and thereby protect those carrying or consuming it, which explains why quacks and mountebanks sold numerous amulets that contained traces of toad poison or arsenic. Significantly, many professional physicians and **apothecaries** advocated the same types of prophylaxis and treatment.

Undoubtedly, some charlatans preyed on popular fears of plague in order to turn a tidy profit. Accounts from the London plague of 1665–1666 report that some were selling an ounce of the miraculous (but useless) *aurum potable*, or potable gold, for 5 pounds—a huge sum of money in an age when most household servants earned no more than 10 pounds a year. These abuses led a number of prominent intellectuals to test claims of miracle cures, subjecting them to the new fashion for experimentation that was becoming popular in the latter half of the seventeenth century as part of the **Scientific Revolution**. Unsurprisingly, they discovered that unicorn horn, camel stones, and the rest had no discernible therapeutic properties, a conclusion that nonetheless did little to deter the throngs of paying customers.

As with empirics, however, quacks and charlatans could become useful in times of **epidemic** disease. Towns and cities sometimes turned to alternative practitioners for help when disease threatened to overwhelm the capabilities of legitimate physicians, and this



“Der Marktschrier” (“The Quack Doctor”). Market-day scene with a seventeenth-century quack doctor behind his stand. Engraving by W. French after a seventeenth-century painting by Gérard Dou. Courtesy of the National Library of Medicine.

in turn helped at least some of these alternative practitioners to secure footholds in the medical profession. In Italy, physicians attempted to regulate charlatans and quacks by actually issuing them with licenses to practice specific kinds of medicine, such as operations on the eye or the removal of diseased teeth. This seemed to reflect a widespread attitude among physicians that controlling and supervising alternative practitioners was a more practical measure than a futile effort to eradicate them altogether. This attitude, combined with the perceived utility of quacks during periods of epidemic disease, permitted an important degree of professional inclusion for alternative practitioners, which increased during the eighteenth and nineteenth centuries.

As the medical marketplace has become increasingly professionalized in the modern era, the policing of medical practice has assumed greater importance, a task taken up today by organizations such as the state licensing boards in the United States or the General Medical Council in Britain. In other countries, however, medical charlatanism remains a serious problem. For example, some of those with **HIV** or **AIDS** in parts of Africa have been encouraged by a wide range of charlatans to abandon Western medicines and to turn instead to a host of alternative remedies, often including homemade concoctions that patients are induced to buy but which have no demonstrated therapeutic benefit. Similarly, in parts of India and Southeast Asia where **dysentery** remains a serious health problem, charlatans masquerading as traditional healers have duped thousands of suffering patients into paying for ineffective remedies. Without a centralized and effective means of countering such practices, many physicians worry that this brand of modern-day quackery will only worsen the spread of epidemic disease. *See also* Folk Medicine; Magic and Healing; Medical Ethics and Epidemic Disease.

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MARK WADDELL

QUARANTINE. Quarantine is the enforced temporary isolation of humans (and animals) suspected of carrying a disease because of public health concerns. Quarantine is not the same as enforced isolation of those who are already sick in **leprosaria**, **pest houses**, **hospitals**, **sanatoria**, or their own homes. The practice of isolating and avoiding the ill, or those suspected of being ill, has a long history. The first recorded testimonies come from the Hebrew Bible (Old Testament) and there are examples of quarantining in the writings of **Hippocrates**, Thucydides (460–400 BCE), and **Galen**. In 549 the Byzantine Emperor Justinian (c. 482–565) produced the first effective quarantine laws. Such legislation established that travelers coming from territories struck by the plague should be isolated and avoided. As in Byzantium, China and other countries in Asia and Europe

practiced some form of quarantine during the **first plague pandemic**, seven centuries before the **Black Death** visited Europe.

Most scholars agree that source of the term was the city-state of Venice. In 1377 Venetian officials established a waiting period of 40 days for ships seeking entry to the port of Ragusa controlled by Venice. This prohibition included all goods, animals, crews, and passengers, and it was called *quarantine* or *quaranta giorni* (40 days). More controversial is the explanation behind the 40 day length that the isolation lasted. Some scholars maintain that the duration of the quarantine relates to the prevalent medical theory of the time, Hippocratic theory. Hippocrates set at 45 days the limit distinguishing between chronic and acute diseases, a distinction discussed in Europe from the later sixteenth century. Others relate it to the symbolic 40 days of Jewish ritual purification, of Jesus's time in the desert, and the 40 days of the Lenten season.

Of all the measures put in place to contain the spread of the plague that repeatedly struck Europe from 1347 on, quarantine appeared to be the most effective. As in the example of Venice, quarantine aimed to satisfy two main purposes. The first was to allow time for medical inspectors to examine the crew, passengers, and animal cargo of the vessel; the second (and most important) was to permit the development of any incubating disease the ship's passengers and crew might have brought with them.

A modified type of procedure was put in practice in the new world to protect the human cargo that European slave-traders forcefully transported from Africa to the Americas. After major **smallpox** and **typhus** epidemics in the seventeenth century hit the major slave trade ports of the new world, such as Havana, Cartagena, Rio de Janeiro, and Portobelo, all vessels, and more specifically all slave ships, were subjected to a quarantine period and to a careful inspection by physicians of the colonial medical corps. The main task for the medical inspectors was to ensure that the human cargo was free of any signs of epidemic disease. The slightest suspicion could result in the vessel's lying at anchor offshore for weeks. Naturally, quarantines, which by the mid-seventeenth century had become common all over the Caribbean, stimulated the smuggling of slaves and all sort of goods in the Americas, as well as the practice of bribery as a way of doing business in the region.

During European colonial rule, quarantine became standard in the cities and plantations of the Western Hemisphere, as a way of dealing with the threats of **yellow fever**, **cholera**, smallpox, and typhus. Quarantine was also widely used in France, Britain, Austria, Germany, Russia, and many other European and Asian nations from the fourteenth century on. Even though the microbiological revolution that linked germs with disease would not come until late in the nineteenth century, quarantine was enacted as an effective sanitary measure, and it became mandatory especially during epidemic times, such as during the cholera pandemics of the 1800s.

In the United States, quarantine facilities were first established in port cities from the early eighteenth century. They proved especially important as immigration increased and after the first cholera epidemics struck New York City in the mid-nineteenth century. Quarantining in the United States, even after Pasteur's bacteriological revolution, became a form of social stigmatization. "Undesirable immigrants," such as Russians, Italians, Austrians, Hungarians, and Irish, came to be regarded not only as symbols of disease, but as a menace to American social structure. They were picked out for quarantine in the ships coming from Europe, whereas passengers on the upper decks were allowed to disembark. Also, they were singled out in American cities and quarantined in secluded locations outside the city limits.

From the 1870s, quarantining of animals became a standard practice to prevent the spread of **animal diseases**, ranging from rabies to mad cow disease. It also has been consistently applied to astronauts after returning from space.

More recently, in an age when quarantine was thought to be a primitive tool for the control of disease, only necessary before the rise of modern medicine, humans were faced with the apparently unavoidable fate of quarantining. The late-twentieth-century epidemics of **AIDS**, **Ebola** virus, and especially **SARS**, prompted governments, of both developed and underdeveloped countries (though not the United States), to enact stringent quarantines. Quarantine, regardless of scientific and medical advances, will long remain the only effective defense against the spread of some diseases, particularly those associated with epidemic spread and high mortality. *See also* Cordon Sanitaire; Hospitals in the West to 1900; Leprosy, Societal Reactions to; Personal Liberties and Epidemic Disease; Plague and Developments in Public Health, 1348–1600; Plague: End of the Second Pandemic; Poverty, Wealth, and Epidemic Disease; Public Health Boards in the West before 1900; Slavery and Disease; Trade, Travel, and Epidemic Disease.

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PABLO F. GOMEZ

R

RACE, ETHNICITY, AND EPIDEMIC DISEASE. Race is among the most controversial factors used for understanding and tracking diseases in human populations. The classification of human groups under racial labels is largely a cultural creation and does not strictly correspond with biology. **Epidemic** disease factors previously thought to be related to race are now known to be caused by cultural behaviors, socioeconomic conditions, and environmental factors. Nonetheless, race has been, and continues to be, used for scientific, political, religious, social, and cultural classification of human populations.

Hippocrates used the Greek term for “race” in the first classical medical texts, and **Galen** perpetuated its use in the Western medical tradition from 170 CE on. The definition of “race” is, however, highly unstable and can change even within a single generation: for example, not long ago “Jewish” and “Irish” were considered racial categories. Also, because of such variability, race has worked as an effective tool in creating **scapegoats** for the appearance of epidemics. History is full of such examples and even today the subtle force of racial categorization assigns a racial determinant to diseases such as **HIV/AIDS**.

Differences in socioeconomic conditions and geographical patterns of longstanding human settlements—traditionally ascribed to race—have influenced patterns of epidemics’ distribution. The interaction between humans and the **environment**, which is studied through economic and sociocultural modeling, slowly shapes immune system characteristics, and these changes make certain human populations more susceptible to disease than others. Thus, diseases that are endemic in certain territories became epidemic when introduced to immunologically “naïve” populations. Most notable among these examples is the sixteenth-century collapse of Native American populations caused by epidemics of **smallpox, measles, tuberculosis**, and other “Old World diseases.”

By the time Europeans began their colonization of the Americas, they had lived in settled communities for centuries. This close-range association of humans and animals,

fostered by European economic and social models, permitted the biological interchange of **bacteria**, **viruses**, and parasites among multiple animal species and humans. Diseases such as tuberculosis, the common cold, and smallpox originated in animals and, over centuries of close contact, became endemic in European human communities, where children acquired them at an early age.

The behavior of most infectious illnesses, and the immune reaction to them, varies considerably depending on the age at which the person is first infected. Infections that are mild if first encountered in infancy can be deadly when humans encounter them in adulthood. This is particularly true for smallpox.

With the European colonization of the New World, Native American groups encountered for the first time diseases that had become endemic in the Old World after centuries of close cohabitation between animals and humans, and they suffered dearly from it. The 1507 smallpox epidemic on the island of Hispaniola—today's Haiti and Dominican Republic—marked the beginning of a demographic catastrophe in which almost 80 percent (in some cases, such as the Brazilian smallpox epidemic of 1660, as much as 90 percent) of the original inhabitants of the Americas perished. Thus, differences in immune characteristics, as defined by human groups' particular interaction with the environment, were behind the demise of Native Americans and the consequent rise of African **slavery** in the Americas.

It was precisely in the slave ships that **yellow fever** came to America. Until the sixteenth century, yellow fever affected mostly Europeans visiting the West coast of Africa, and the first recorded epidemic in the Americas struck the island of Barbados in 1647. Like smallpox, yellow fever is a milder disease when acquired during childhood, but it is vicious when acquired later in life. Most Africans, and later in the eighteenth-century European and Native Americans, living in the New World became immune to the disease by acquiring it during infancy and developing a lifelong immunity. Thus, "the disease of the strangers," as contemporary inhabitants of the West Indies called yellow fever, became a disease of new European colonists and invaders. This lesson was relearned the hard way by the British and French armies in their multiple, failed assaults on Caribbean cities and in later militarized colonization of western Africa, when they were defeated mainly by the endemic yellow fever virus.

In other historical cases, the assignment of particular diseases to particular human groups, as defined by their "race," does not correlate with any biological explanation. For instance, when the **Black Death** struck Europe in the fourteenth century, terrified Christians used ethnicity and religion to explain the origin of the disease. Though defended by royal and religious authorities, Jews in many parts of Europe were accused of "poisoning" "Christian" water supplies to initiate the waves of pestilence over European cities. Because of these claims, mobs murdered hundreds of Jews, while local magistrates imprisoned and exiled others during the plague epidemics of the fourteenth centuries. In Spain the concept of "purity of blood" (*limpieza de sangre*) reinforced the intolerance for Jews that led to their expulsion in the late fifteenth century.

European racial and ethnic prejudices accompanied the settlement of America. The inhabitants of nineteenth-century American cities affected by the **cholera** pandemics associated cholera with moral degeneracy, impiety, filth, and race and ethnicity. After striking New York in 1832, cholera became a symbol of the moral degeneracy of the city and its inhabitants. Throughout the nineteenth century, the Irish in particular were blamed as the spreaders of cholera's scourge. Stereotyped Irish characteristics, such as

alcoholism, moral degeneracy, and filthiness, were linked to the disease. Similarly, toward the end of the nineteenth century, immigrant Jews, Italians, and Asians came to be seen as carriers of disease, including typhus, cholera, and plague. Hundreds were quarantined, either after being evicted from their houses or upon their arrival at American ports.

As had cholera, AIDS has also been associated with race. AIDS had its origins in Africa, and because of specific sociocultural and economic circumstances, people of African descent have been disproportionately affected by the AIDS pandemic. But there is no definitive evidence linking African descent with increased propensity toward infection by the virus. The mechanisms behind this link are probably similar to the ones through which every major pestilence has been ascribed to particular ethnic groups, including particular socioeconomic conditions and cultural behaviors.

The association of race with epidemics has a long history. However, it was not until the nineteenth century, with the work of the German naturalist J. F. Blumenbach (1752–1840), that race achieved its current status in the categorization of human groups. Nonetheless, a nuanced analysis of the history of epidemic diseases shows that rather than being definitive, race is a temporal and fluid category, one that is not objective and does not relate to biological characteristics that determine susceptibility to disease. Although it is undeniable that differences in immune responses have been responsible for the behavior of epidemic diseases around the globe, such differences are the result of cultural patterns or geographical location and not racial characteristics. *See also* AIDS in America; Black Death, Flagellants, and Jews; Colonialism and Epidemic Disease; Disease, Social Construction of; Human Immunity and Resistance to Disease; Human Subjects Research; Irish Potato Famine and Epidemic Disease, 1845–1850; Latin America, Colonial: Demographic Effects of Imported Diseases; Mallon, Mary; Medical Ethics and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Yellow Fever in Colonial Latin America and the Caribbean.

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PABLO F. GOMEZ

RED CRESCENT. See Non-Governmental Organizations (NGOs) and Epidemic Disease.

RED CROSS. See Non-Governmental Organizations (NGOs) and Epidemic Disease.

REED COMMISSION. See Yellow Fever Commission.

REED, WALTER (1851–1902). After being imported into the Western Hemisphere from Africa via the slave trade, **yellow fever**, with a mortality rate of 20 percent, went unchecked for about 400 years. Recognition of the mosquito vector and its breeding ground, and the disproving of the fomite (infectious object or substance) or **contagion theory**, proved invaluable to eliminating this disease. Though others played key roles, the **physician** and medical researcher Walter Reed gets the most credit for this advance in public health, as well as for greater understanding of **typhoid fever**.

Walter Reed was born in Belroi, Virginia. He obtained a two-year medical degree in only one year at age 18, from the University of Virginia, and is the youngest person ever granted a M.D. from that university. Wanting more clinical experience, he obtained a second M.D. degree from Bellevue Medical College in 1870, because it had an associated hospital. He then went on to serve an internship at Kings County Hospital and Brooklyn City Hospital. He was noted for his conversational skills, optimism, and enthusiasm. After joining the Army, he practiced medicine at various frontier Army posts. His later years were spent conducting medical research activities in **epidemiology** and infectious disease. In 1890–1891, Reed studied pathology and bacteriology at the Johns Hopkins University Pathology Laboratory. In the last decade of his life, the targets of his investigations included **yellow fever**, typhoid, **cholera**, erysipelas, **malaria**, and **smallpox**.

Reed is most noted for his contributions to our understanding of the etiology (cause) and spread of typhoid and yellow fever (yellow jack) as a key member on both the Typhoid Board (1898) and the **Yellow Fever (Reed) Commission** (1900). Between 1596 and 1900, 90 waves of yellow fever hit what is now the United States, resulting in an estimated 100,000 deaths. During the American military preparation and campaigns in Cuba in 1898, diseases such as yellow fever and typhoid killed more America soldiers than did the enemy. The generally accepted theory at that time was that fomites (clothing or bedding) transmitted the disease from one person to another. From his research, however, Reed disproved the fomite theory and identified the causative agent as being in the blood, with the *Aedes aegypti* mosquito as the vector of yellow fever (a discovery pioneered in 1881 by Cuban physician Carlos Finlay [1833–1915]) and the housefly as one means of passing typhoid fever. Reed's research on yellow fever, based in Cuba, resulted in a

campaign to eliminate bodies of standing **water** that were **insect** breeding places, thus decreasing the disease incidence. Years later, this approach was introduced to Panama during the construction of the Panama Canal. A vaccine for yellow fever was first produced in 1937.

Reed died in 1902 from a ruptured appendix at age 51 and was buried in Arlington National Cemetery. The epitaph on his monument states: "He gave to man control over that dreadful scourge, yellow fever." The Walter Reed Army Medical Center is named in tribute to this remarkable man, soldier, physician, pathologist, and medical researcher. See also Colonialism and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Germ Theory of Disease; Sanitation Movement of the Nineteenth Century; War, the Military, and Epidemic Disease; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in the American South, 1810–1905.

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MARK A. BEST

RELAPSING FEVER. The most distinctive feature of relapsing fever can be discerned in its name. The disease, which is caused by the spirochete *Borrelia bacterium*, has a cycle of recurrent bouts of fever. Between each relapse is a period of a few days during which the victim appears to have returned to normal good health. The deceptive lull is then followed by another round of the fever's symptoms, with each recurrence becoming increasingly less virulent as the patient slowly becomes immune to the disease.

Relapsing fever takes on two forms based on the type of carrier that is present. One form is carried by ticks and the other by body lice. They both have the bacteria in their bodies and can infect humans by injecting the *Borrelia* into the bloodstream. The two types of relapsing fever can best be symbolized by the settings in which each thrives. The tick-borne variety is found in remote mountainous or desert regions, especially in North America. Victims are typically people who utilize isolated cabins or explore caves where rodent hosts have nested leaving behind the *Borrelia*-carrying ticks. This type tends to be endemic in nature. The **epidemic** form is the louse-borne relapsing fever, the outbreaks of which are far more deadly and fearsome. The louse-borne fever is a disease of poverty, overcrowding, poor **personal hygiene**, and poor health standards. It is often associated with **typhus**, another louse-borne disease that has some symptoms that are similar to relapsing fever. The two diseases sometimes travel together and can be clearly distinguished by the latter's recurrent cycles and by the presence of jaundice not found with typhus. Louse-borne relapsing fever is perhaps most prevalent during **wartime**, with refugees and returning soldiers helping to spread the fever. Arguably, the worst outbreaks have occurred in Africa following World War I (1914–1918) and, especially, World War II (1939–1945). In North America, where it is rare, it can be linked to the **Irish potato famine** immigration in the mid-nineteenth century.

The symptoms of relapsing fever begin with the sudden onset of a fever, one that can range as high as 102.5°F or more. This is followed by headaches, stiff neck, nausea, and

vomiting, as well as sore, aching muscles and joints. It can escalate to unsteadiness, seizures, facial droop, and even coma. The first bout of fever takes place about two weeks after infection, and it can last three to five days. In both types of relapsing fever, the initial febrile attack can end in a “crisis” phase that lasts approximately 30 minutes and can include severe shaking and chills followed by sweating accompanied by falling temperature and blood pressure. It is this stage that causes death in 10 percent of cases. This cycle of symptoms reoccurs within seven to ten days following the seeming disappearance of the disease. The number of such relapses can range from one, typical of the louse-borne type, to up to ten for the tick-borne variety. The entire series of relapses can continue for as long as 50 or more days, but the average is 18 to 20 days. This relapse cycle is caused by the ability of the *Borrelia* bacteria to create clones that evolve to ward off antibodies. Once the first round of bacteria has been dealt with by the body’s immune defense system, variations of the original are created. Thus, as one type is cleaned out, other, initially less prominent, clones take over and multiply, triggering another round of relapsing fever.

The long-term effects can include problems of the central nervous system that could result in seizures or stupor. *Borrelia* can also invade heart and liver tissue and produce inflammation. Relapsing fever is particularly dangerous for **children** and pregnant women. In the latter it can cause a spontaneous abortion or lead to stillbirth. The bacteria can also be passed on to the fetus, who would then have the disease at birth.

The average mortality rates for relapsing fever range around 5 percent and, with treatment, are as low as 1 percent. However, particularly with the louse-borne type, the death toll can be much higher especially among infants, the very old, and those who are malnourished and debilitated. It would not be unusual for such victims to die even before the first relapse, a fact that, on occasion, made it difficult to identify the disease. During the epidemic in Africa in the 1940s, the mortality rates went as high as 10 to 15 percent.

The **transmission** of the fever bacteria requires a reservoir host for the tick-borne type, usually some variety of rodent, including mice, squirrels, or chipmunks that carry the infected ticks. The louse-borne fever requires no such host animal because it feeds on the human body and is transported by it. This is what makes louse-borne relapsing fever so prone to erupt into an epidemic. The lice pick up the disease from humans who are already infected and feverish and then transport it to other humans, especially in areas that are unhygienic or severely overcrowded. The infection enters the human body when the lice are crushed into a bite-wound or into an area made raw from scratching. From there, it goes into the bloodstream eventually to start the relapsing cycle.

Whereas lice infestation of the body is very obvious, the bite of a tick carrying the fever often is not. The tick bites are painless and occur at night when the **insect** feeds. Thus, the victim may not even know that the infection has begun. The ticks acquire the disease from rodent hosts and pass it on to humans through saliva during feeding. The transmission can take place within minutes. When rodents leave a cabin or other vacant building, the humans who may move in become the ticks’ only available host.

A diagnosis of the disease involves a combination of a patient’s recent history and travel locations for the tick-borne fever and a visual discovery of body lice for the louse-borne fever. Clinically, relapsing fever can be confirmed through staining blood smears that will detect the spiral form of the *Borrelia* bacteria type. The blood work has to be performed during one of the victim’s febrile periods. Modern treatment includes the use of **antibiotics** such as doxycycline or tetracycline. Such treatment is generally very

successful, and there is rarely any antibiotic resistance. What has been learned, however, is that tetracycline can set off a Jarisch-Herxheimer Reaction, which triggers an increase in the symptoms of relapsing fever. This can occur within two hours of administering the antibiotic, and it can sometimes be fatal.

Prevention of relapsing fever differs depending on the type. With the tick-borne variety, it involves a common sense approach to utilizing wilderness areas, particularly if using remote cabins. Avoidance of rodents, the use of insect repellent such as DEET, and the wearing of proper clothes that cover the skin can help. This is particularly true while sleeping because of the nighttime feeding habits of ticks. Buildings or crawlspaces that may harbor rodents should be sprayed with a 0.5 percent solution of malathion insecticide. The louse-borne type thrives in more horrific environments where prevention demands a good deal of vigorous social and political activity. The disease must be combated by relieving overcrowded living conditions, by improving levels of personal hygiene in often-difficult conditions, and by the systematic disinfecting of camps and dwelling places. Once an epidemic starts, it also becomes necessary to use thorough de-lousing procedures of the clothes and bodies of the general population.

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ERIC JARVIS

RELIGION AND EPIDEMIC DISEASE. Religious beliefs have always been a primary lens through which people have viewed and understood the experience of epidemic disease. Religion entails the cultural practices and beliefs that have as their goal relationship and communication between human beings and those (usually) unseen spiritual entities or forces that are believed to affect their lives. As anthropologists have noted, the dominant motif of a religion—its fundamental characteristics—is often most clearly revealed in the ways in which it explains misfortune and sickness and by the steps recommended to avert them. Classifying such beliefs as “primitive” or “civilized” according to the degree to which they approach or diverge from some external, imposed ideal (whether monotheism or modern scientific medicine) is less useful than recognizing the extent to which all religions have offered a way of making sense of common human experiences of danger, suffering, and disease.

In the case of epidemics, religious beliefs are forged in the furnace of catastrophic mass disease and high mortality, affecting not just one or two unfortunates but large numbers of sufferers at the same time. For many societies, this represents a qualitatively different situation from individual experience of sickness and health, generating different explanations and responses. Because epidemics affect entire communities at a time, prescribed

actions are most often public and collective rather than private and individual, because the goal is to end the epidemic and restore health for the entire group.

Religion may offer more than one possible reading of events and could be integrated within or coexist alongside other, more empirically inflected, ideas of epidemic disease causation and cure. Ancient Assyria, for example, is known for its extensive medical corpus of naturalistic therapies, but Assyrian scholarly healers were also exorcists and priests who performed propitiatory rituals to soothe the angered gods and made no distinction between natural and supernatural causes of disease. Similarly, religious and naturalistic interpretations and practices have coexisted in Indian **Ayurvedic** medicine, Confucian China, medieval Islam and Christendom, early modern Europe, and in many societies today. Religion is thus not necessarily monolithic as an explanatory model, nor is it automatically exclusive of other models. Most often, people will find explanations that work for their particular set of imperatives. Being conscious of such diversity and pluralism of understandings allows us to recognize the robust creativity and resilience of human responses to epidemic disease across time and space.

Understanding Causes: A Twofold Model. The most important role that religion played in relation to epidemics was in explaining what was happening in terms that made sense to that particular culture. Usually, such explanations were two-pronged, looking upward to the supernatural realm and outward (or perhaps better, inward) to contemporary society. Epidemics were usually understood as having been let loose upon the world by supernatural forces: one or many gods, demons, or spirits of the dead. In most cases, these heavenly beings were not seen as acting randomly, but as responding to particular human actions that offended them. A society's identification of the behaviors that would prompt the infliction of mass suffering and death upon an entire people reveals a great deal about the values and worldview of that culture. These vary considerably among cultures, but usually revolve around definitions of the sacred—which could be polluted, profaned, or neglected by deliberate or inadvertent actions—and of acceptable standards of moral behavior within the community.

For all cultures, explaining epidemic disease is less focused on addressing the disease symptoms of individual sufferers, and much more about the cosmic disorder that such diseased bodies manifest. Epidemic disease represents the world out of joint, a disastrous upset of the expected cosmic harmony. Religion aims to identify the causes, redress the problem, and restore good relations between heaven and earth. To do this, adherents draw on specially designated human intermediaries. These men and women—priests, chanters, oracles, diviners, seers, prophets, soothsayers, exorcists, and other specialists—are attributed with special skills and status that enable them to clarify the wishes of the supernatural powers and identify the human failings responsible. From these individuals, too, would often come specific recommendations for remedial devotional and ritual action.

Divine Agency and Divine Cure. When epidemics are viewed as divine punishments for human error, the gods that send the disaster are also those who will lift it, if correctly approached. In both heavenly pantheons and monotheism, the gods are inherently dualistic, both benevolent and punitive, the source of the scourge and the means of deliverance. In ancient Mesopotamia (modern Iraq), the underworld god Nergal was a benefactor of humanity and protector of kings, as well as a “destroying flame” and “mighty storm,” a fearsome warrior god who looses war, pestilence, and devastation upon the land. His destructive powers are enthusiastically celebrated in a hymn in his honor from the second millennium BCE:

Lord of the underworld, who acts swiftly in everything, whose terrifying anger smites the wicked, Nergal, single-handed crusher, who tortures the disobedient, fearsome terror of the Land, respected lord and hero, Nergal, you pour their blood down the wadis [gullies] like rain. You afflict all the wicked peoples with woe, and deprive all of them of their lives.

Such hymns were part of placatory rituals designed to mollify the angry gods and restore their good humor by heaping up their praises.

This dualism is not unique to ancient Mesopotamia. Greco-Roman Apollo was god of learning and the arts, as well as the death-dealing archer raining plague arrows on those who offended him, as he did upon the Greeks at Troy. Yoruba divinities supervise all aspects of human existence, but punish with misfortune, disease, and epidemics. The most feared is Shopona, powerful as a whirlwind, who attacks by sending **smallpox**, insanity, and other crippling diseases. Judaism, Christianity, Islam, and monotheistic African religions like those of the Neer and the Masaai, have all recognized the supreme creator God as both author of their devastation and source of their liberation. In India, Sitala has been venerated since the sixteenth century as the goddess of smallpox. The heat of her anger causes the disease when she possesses the body, but if she is appeased and cooled by human propitiation, she will leave, and the sufferer will recover. Today, she is the major village deity in Bengal and elsewhere, annually celebrated as “the mother” of the village, who takes away the fear of smallpox.

Arguing One’s Case before an Angry God: The Plague Prayers of King Mursilis. Some of the earliest and most vivid examples of prayers composed to request divine aid against an epidemic come from ancient Anatolia (the Asian part of modern Turkey), from the reign of the Hittite king Mursilis II (r. c. 1321–1295 BCE) (see sidebar). Faced with a devastating 20-year pestilence, the king appeals to

THE PLAGUE PRAYERS OF HITTITE KING MURSILIS, FOURTEENTH CENTURY BCE

O, Stormgod of Hatti, my Lord, and gods of Hatti, my Lords, Mursilis your servant has sent me, (saying) go and speak to the Stormgod of Hatti and to the gods, my Lords, as follows: What is this that you have done? You have let loose the plague in the interior of the land of Hatti. And the land of Hatti has been sorely, greatly oppressed by the plague. Under my father (and) under my brother there was constant dying. And since I became priest of the gods, there is now constant dying under me. Behold, it is twenty years since people have been continually dying in the interior of Hatti. Will the plague never be eliminated from the land of Hatti? I cannot overcome the worry from my heart; I cannot overcome the anguish from my soul.

Translated at <http://www.utexas.edu/cola/centers/lrc/eieol/hitol-8-X.html>

. . . See! I lay the matter of the plague before the Stormgod of Hatti, my Lord. Harken to me, Stormgod of Hatti, and save my life! This is what I (have to remind) you: The bird takes refuge in (its) nest, and the nest saves its life. Again: if anything becomes too much for a servant, he appeals to his lord. His lord hears him and takes pity on him. Whatever had become too much for him, he sets right for him. Again: if the servant incurred a guilt, but confesses his guilt to his lord, his lord may do with him whatever he pleases. But, because (the servant) has confessed his guilt to his lord, his lord’s soul is pacified, and his lord will not punish that servant. I have now confessed my father’s sin. It is only too true. I have done it . . . Stormgod of Hatti, my Lord, save my life! Let this plague abate again in the land of Hatti.

Translated by Albrecht Goetze in *Ancient Near Eastern Texts Relating to the Old Testament*, 3rd revised edition, edited by James B. Pritchard (Princeton: Princeton University Press, 1969) pp. 395–96.

the gods through the intermediary of a priest reciting the prayer aloud. He begins with a dramatic evocation of unending death, reproaching the gods for their harshness—even, one might say, for their irresponsibility—in allowing the plague to last so long. He comes to the gods as an urgent petitioner, seeking answers to a terrible situation.

Like a defendant in a law case, Mursilis uses every means he can to present his case favorably to the gods ranged in judgment. He stresses his piety and devotion to the temples of all the gods, and his many attempts, so far unsuccessful, to convince them to lift the plague. He points out that the epidemic is against the gods' own self-interest, since so many have died that there is no one left alive to honor them. In the divine court, the accused must admit guilt. Consultation of oracles has revealed that Mursilis's father angered the storm god by breaking a treaty oath (sworn on the gods) and failing to maintain certain rites. Though himself blameless, Mursilis accepts that punishment of his father's sin has fallen on him. Moreover, because the king is the priestly representative of his people before the gods, royal offenses implicate the whole society in their punishment.

Confession disarms the angry judges, who are further appeased with the offering of gifts, in the form of sacrifices and libations. The identified offenses are rectified—the king repairs the broken oath and promises to restore the neglected rites. Finally, Mursilis reminds the gods to be merciful, like a good patron with an erring dependent. Gods and humans exist in a hierarchical but reciprocal relationship, which imposes responsibilities on each party: the king to admit faults and rectify offenses, the gods to be compassionate and receptive to pleas for help. The king has fulfilled his side of the bargain, and it is now time for the gods to do their part.

Heavenly Bookkeeping. Heavenly pantheons are envisaged in terms that make sense to a particular society. In China, from the twelfth century CE, the influence of Confucian ideals led to belief in a hierarchically organized celestial bureaucracy, with a Ministry of Epidemics presided over by five powerful deities, the Commissioners of Epidemics. These divine bureaucrats drew up heavenly balance sheets of good and evil deeds for every person on earth, rewarding meritorious acts with health and sending disease when the balance tipped too far toward the negative. Epidemics occurred when the score sheets of an entire community were so unfavorable as to be judged beyond saving. Like bureaucrats everywhere, the Commissioners themselves stayed in their offices and sent their assistants to earth to carry out their commands. A host of plague gods (*wenshen*) acted as their emissaries, carrying out annual inspections of morals and inflicting epidemics on those deserving of punishment.

As the active causative agents, it is the *wenshen* who receive cultic veneration. Images of the plague gods were set up to receive homage and worship, and festivals in their honor were held around the time when they were believed to be making their annual tours of inspection, to persuade them to return to heaven without marking the community down in their black books. Similar festivals were also held when an epidemic broke out. Prayers and ceremonies of cleansing and purification culminated in a procession to drive out demons (who could be enlisted by the plague gods) and see the gods on their way. The gods' departure was visibly enacted by placing images of the *wenshen* on boats made of paper or grass that were then floated away or burnt.

What Makes the Gods Angry? Crimes that stir up the gods vary according to cultural priorities. In the plays of the Greek poet Sophocles (496–406 BCE), Oedipus's murder of his father, the king, and his marriage with his mother, though unwitting, polluted the land in the sight of the gods and cried out for vengeance. Only the suicide of the queen and

Oedipus's own blood offering (he blinds himself) and banishment could begin to wipe the stain clean. Disrespect or profanation of a divinity's cult was equally fatal. In the *Iliad*, Apollo inflicts an epidemic on the Greek army at Troy after their king, Agamemnon, captures the daughter of the priest of Apollo and refuses to ransom her back to her father. Yoruba deities were angered not by moral shortcomings but by failure to maintain their cult properly, including neglect, disrespect, and breaking taboos. Hindu and Buddhist ideas of reincarnation and inherited karma raised the possibility that epidemics could be heaven-sent punishments for unrighteousness or misdeeds in a previous life.

Judaic understanding of the causes of epidemics was determined by Israel's sense of mission as God's chosen people. Directed against Israel's enemies, pestilence was an aspect of God's unique sovereignty, his unlimited power over all creation, and his ability to trump the gods of any other peoples. Yet Yahweh could also turn this fearful weapon upon his own people. This was the burden as well as the promise of the covenant between nation and God, a mutual agreement that promised divine favor and protection on condition that Israel faithfully obeyed the divine commandments. The polarities of judgment and deliverance, destruction and sustenance, are thus central to the relationship between God and his people: "I will kill and I will make to live, I will strike, and I will heal, and there is none that can deliver out of my hand" (Deuteronomy 32:39–41). The only hope is repentance of sin and cleaving once more to God, for he has promised compassion after judgment, rewards after suffering, the renewal of divine favor, and blessing upon a chastised and penitent nation.

This concept of a God at once merciful and severe, who punishes his people for their own good, is also a central feature of Christian and Islamic understandings of epidemic disease. When plague broke out in the mid-third century CE, Christianity was a minority religion in a hostile Roman world. According to bishops Cyprian of Carthage (d. 258) and Eusebius of Caesarea (c. 260–340), although the epidemic appeared to strike down pagan and Christian indiscriminately, the purposes and end results for each were very different. For the enemies of Christ, the plague was a justly deserved punishment that led straight to eternal torment. But for Christians, the plague was to be welcomed as a way of testing one's faith and making sure the believer followed Christ's injunctions to care for the poor and the sick. Christians who died were called to paradise and eternal rest, and those who died caring for others were equal to the martyrs in the way they testified to the faith at the cost of their own lives. Thus, a paradoxical interpretation of hope and mercy was wrested from a seemingly calamitous situation. Early Islamic teachers similarly viewed epidemic disease as differentially freighted according to belief: for infidels, plague was a punishment and a disaster, but for faithful Muslims, it was a mercy and a reward, a martyrdom sent by God that led directly to paradise.

When Christianity became the state religion of the Roman Empire, this kind of dialectic explanatory model was less appropriate. Instead, like the Israelites, Christians recognized God was punishing them for their sins, chastising them into better behavior. Thus, Pope St. Gregory the Great (c. 540–604), in a sermon preached in Rome during an episode of the **Plague of Justinian** in 590, stated, "May our sorrows open to us the way of conversion: may this punishment which we endure soften the hardness of our hearts." Interior repentance and conversion of morals had to be proven by collective rituals performed under the divine gaze by a united and reformed community, "so that when he seeth how we chastise ourselves for our sins, the stern Judge may himself acquit us from the sentence of damnation prepared for us." Some later Islamic authorities also

interpreted plague as divine castigation of sins, such as adultery, prostitution, usury, or drinking alcohol, with a consequently greater emphasis on reformation of morals, as well as individual prayer and collective processions.

Spirits of the Dead: Community beyond the Grave. As agents of epidemic disease, the ancestor spirits of certain African religions share many characteristics with the gods: they watch over the living and expect to be honored with correct cultic veneration. Like the gods, they are both agents of affliction and sources of healing. They are angered by neglect of their rites, breaches of taboo, and flouting of acceptable behavior. Like the relatives they once were, they can be difficult, exacting, and demanding, holding grudges until they are properly propitiated. Kongo *nikisi* spirits, the oldest and most powerful of a hierarchically ranked series of ancestor spirits, are each associated with a particular disease. Epidemics are caused by Mayimbi spirits, particularly potent *nikisi* who belong to a family of “smashers.” Severe epidemics are the work of male Mayimbi, whereas less serious outbreaks are attributed to female Mayimbi spirits. To appease their anger and give them the honor and respect they require, these spirits must be invoked and propitiated by sacrifices.

Ancestor spirits may also be more constrained than gods by close-knit ties of kinship joining the living and the dead in community, with their sphere of abilities limited to their own living relatives. In societies with strong traditions of sacred kingship, even if disrupted or abolished by colonial rule, such as the Sukuma and the Kongo, only the spirits of deceased chiefs can cause an epidemic afflicting many families at once. During their lifetimes, chiefs were religious representatives of the entire territory, responsible for the correct performance of rituals maintaining the health of the community, and this power continues after death.

Elsewhere, relations between the living and the dead could be more fraught, as in the Chinese belief in hostile or hungry ghosts, vengeful spirits of the unquiet dead, who had suffered premature or violent deaths. Their bodies unclaimed, their rites neglected, they cannot return home, but instead roam the countryside, searching for victims. Alone, they inflict disease on individuals, but joined together in packs, they are even more dangerous, capable of causing epidemics. These spirits are the polar opposites of African ancestor spirits, unconstrained by family ties, representing an uncontrollable, potentially lethal supernatural force, defining these particular dead as more demonic than human.

Hostile Demons and How to Get Rid of Them. As supernatural agents of epidemic disease, gods and ancestors share the essential quality of moral duality: they might punish, but they will also heal. Humans enter into cultic relations with them as a way of keeping the lines of communication open, so that disagreements can be resolved and harmony restored. But demons are another matter, fundamentally malevolent and chaotic. Different strategies are therefore required. Where gods and ancestors are praised and petitioned, demons are exorcised, battled, and even tricked. In Vedic India (c. 1700–800 BCE) and in China from at least the sixteenth century BCE, all diseases, including epidemics, were thought to be caused by demons, who attacked the body from outside and possessed it. A Chinese dictionary from the second century CE defined epidemics as *corvée*, or harsh servitude from which there is no escape, clarifying that “it refers to the *corvée* exacted by demons.” With incantations and prayers, Vedic and Chinese healers engaged in a ritual battle to expel demons from the body. Subsequently, in China, belief in demonic origins of epidemics existed alongside or was combined with the heavenly bureaucracy discussed above. Demons might act on their own, but more often they were thought to be under the control of the *wenshen*, or plague gods.

Demons sometimes appear in Christian art as secondary supernatural agents of the plague. However, if demons are allowed to harry humanity with epidemic disease, it is only because God has given permission for them to do. The demons act not in their own right but as part of the divine plan. Sometimes they cooperate with angels in imposing punishment on sinful humanity. Nevertheless, such a withdrawal of active divine agency from the task of chastising sinners does leave open the possibility for others, such as saints and holy people, to wrest control from the demons and provide protection from the plague.

Heavenly Helpers. In addition to the supernatural beings who cause the plague, many religions provide for lower-level heavenly helpers. Bhaiaiyaguru, the medicine Buddha, dispenses a range of healing benefits, including protection against epidemics. Until the decline of smallpox as a serious threat in the modern era, several Shinto deities in Japan were petitioned for protection against smallpox and other epidemics. Both the Christian belief in a triune godhead and the cult of the saints offered many possibilities for playing one heavenly power against another. Before an angry God the Father, Christians could appeal for relief to Christ the merciful son. If Christ is enraged, then one might invoke his mother, the Virgin Mary, known to be especially forgiving of sinners and enjoying a mother's privilege in overriding or deflecting her son's destructive impulses. As the special friends of God, the saints were also well placed to intercede with the deity, acting as impassioned advocates before the throne of the divine judge. Whether name saints, local patrons, or specialist healing and plague saints, they could be relied upon to respond to their worshippers' appeals.

Religion as Help and Hindrance. By providing an explanation of events that was judged meaningful and satisfactory by a particular society, and by offering concrete solutions that were believed to avert or change events, religion has offered believers a way of making sense of the world and thereby, perhaps, gaining some measure of control over it. In times of epidemics, religion often functions as a significant coping strategy. Such positive psychological effects have sometimes been paid insufficient attention when historians have considered the psychological effects of epidemics upon any given society.

Many religions emphasize care of the sick as part of their work in the world and have contributed significantly to the creation of institutions and personnel providing much-needed nursing and medical care of victims of epidemic disease. In some instances, such as the practice of variolation as a part of the worship of the smallpox goddess Sitala in India, or the emphasis of cleansing and ritual purity, religious beliefs can have demonstrable positive therapeutic effects.

Conversely, religious rituals involving the coming together of many worshippers at a time, such as processions and pilgrimages, often facilitate the spread of epidemic disease. Along with conquering armies, missionaries can be the cause of spreading epidemic diseases to previously unexposed populations they are attempting to convert (though modern Christian missionaries usually shared the miracles of modern medicine along with those of the Gospel). All too often, conquering Europeans interpreted the resulting catastrophic mortality of indigenous peoples in waves of epidemic diseases as divine judgment on the savage heathens. This use of religious beliefs to justify stigmatization and persecution of minorities and outsiders—Jews, women, the poor, the lower classes, foreigners, racial minorities, homosexuals, practitioners of other religions—of whom the dominant group does not approve is the most troubling element of the encounter of religion and epidemics, and as the recent history of the AIDS epidemic has demonstrated, it remains

very much with us today. In sum, religion cannot be ignored in any attempt to understand past, present, and future encounters with epidemic disease. *See also* AIDS in America; Astrology and Medicine; Biblical Plagues; Black Death (1347–1352); Black Death and Late Medieval Christianity; Black Death, Flagellants, and Jews; Black Death: Literature and Art; Chinese Disease Theory and Medicine; Colonialism and Epidemic Disease; Contagion Theory of Disease, Premodern; Disease, Social Construction of; Hospitals in the West to 1900; Islamic Disease Theory and Medicine; Leprosarium; Leprosy, Societal Reactions to; London, Great Plague of (1665–1666); Non-Governmental Organizations (NGOs) and Epidemic Disease; Plague Literature and Art, Early Modern European; Plague Memorials; Public Health in the Islamic World, 1000–1600; Race, Ethnicity, and Epidemic Disease; Scapegoats and Epidemic Disease; Syphilis in Sixteenth-Century Europe.

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LOUISE MARSHALL

RHAZES (ABU BAKR MUHAMMAD IBN AKRIYYA AL-RAZI; 865–925). The Persian Al-Razi, known in the West as Rhazes, studied medicine in Baghdad and became one of the greatest **physicians** of the medieval period, writing over 200 works. Half of them were on medicine, but others covered topics including philosophy, mathematics, and astronomy. He was named after the place where he was born and died, Rayy, near Tehran in modern Iran.

The largest and most important of his medical works, *Kitab al-Hawi fi al-tibb* (The Comprehensive Book of Medicine), is a collection of notes he made from everything he



“Rhazes of Baghdad Used Harp Strings for Sutures.” Courtesy of the National Library of Medicine.

had read, as well as observations from his own medical experience. Alone among his contemporaries, Rhazes names every author he quotes, and when the statement is his own, he prefixes it with the word “mine”. Translated into Latin in the thirteenth century, *Kitab al-Hawi* was repeatedly copied and had a major influence on medical practice in Europe. In the famous first chapter of Volume XVII of this work, “On **Smallpox, Measles and Plagues**,” which circulated separately, Rhazes described the symptoms of smallpox and measles as constant fever, inflammation, itchy nose, severe backache, and disturbed sleep. He added that a sure sign of an impending smallpox **epidemic** is an exceptionally hot autumn followed by a dry winter. When a rash erupted, he advised patients to keep warm and not to breathe cold air; for scars, he recommended peanut-oil paste. To prevent spreading of the rash into sensitive parts of the face, he recommended a special kohl for the eyes, sucking pomegranates for the mouth and throat, and an ointment containing horned poppy for the nostrils. Rhazes adopted the theory that pestilence is caused by corrupt **air** (miasma) and, contrary to Muslim opinion at the time, he strongly advocated **flight** to avoid epidemic disease.

Rhazes states that pestilence occurs at the end of summer and autumn when the wind is southerly and the air heavy. To avoid hot, contaminated air, he wrote, houses should be built on high ground, facing north; infection with **leprosy**, scabies, **tuberculosis**, and plague occurs in confined places. To lessen the effect of putrid air, he recommended fumigation with sandalwood and camphor, and sprinkling the place with rosewater. The patient should drink chilled water and take a mixture of aloes, saffron, and myrrh daily; from **Galen**, Rhazes also recommended a potion of Armenian clay with vinegar, or snake theriac.

Toward the end of his life, Rhazes went blind from cataracts; he must have died frustrated and unhappy, for he refused treatment, saying he had seen enough of the world. See also Diet, Nutrition, and Epidemic Disease; Humoral Theory; Islamic Disease Theory and Medicine.

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SELMA TIBI-HARB

ROCKEFELLER FOUNDATION. See Non-Governmental Organizations (NGOs) and Epidemic Disease.

ROMANTICISM. See Tuberculosis and Romanticism.

ROSS, RONALD (1857–1932). A **Physician** and malariologist of Scottish origin, Ross was the son of General Sir Campbell Claye Grant Ross (b. 1824), an officer of the British Army stationed in India. Encouraged to study medicine, Ross duly entered London’s

St. Bartholomew's Hospital medical school in 1874. He began his career in the Indian Medical Service in 1881. After four months at the Army Medical College at Netley, he was commissioned to Madras. Over the next seven years, he served in Vizianagram, Moulmein, Burma, and Port Blair. On a leave of absence in 1888, Ross studied bacteriology at his former medical school. Upon returning to India, he was appointed Acting Garrison Surgeon in Bangalore, which he considered "the best station" in southern India, and where he developed an interest in the breeding habits of mosquitoes.

Ross published his first medical paper in 1893 on the subject of **malaria**. This led him to correspond with **Patrick Manson**, a London-based authority on tropical medicine. During a visit to London in 1894, Ross met Manson, who disclosed his view that malaria was transmitted by mosquitoes. In 1895 Ross returned to India where he continued his malaria research under Manson's guidance; their correspondence generated 173 letters over the next four years. Initially using *Culex* mosquitoes, the carriers of **bird malaria**, Ross's research became productive in 1897 when he was posted to Ootacamund, a malarial region. In Secunderabad, Ross first began to experiment with the "dapple-winged," or *Anopheles*, mosquito. Dissections of the **insect's** gastrointestinal tract eventually

revealed the malaria parasite. Ross continued his work throughout 1898 in Calcutta, where he used birds to research the parasite's life cycle. Working in a disused laboratory, he traced the parasite to the *Anopheles'* salivary glands. By July 1898, he could prove that avian malaria was transmitted from infected birds to healthy ones through the vector's bite. Ross communicated a full account of his work to Manson, who presented his findings before the new tropical diseases section at the British Medical Association's annual meeting. The research was subsequently published in leading British medical periodicals.

In February 1899, Ross retired from the Indian Medical Service and was appointed to a lectureship at the newly founded Liverpool School of Tropical Medicine. Subsequent publications, including *The Prevention of Malaria* (1910), laid the foundations for combating malaria. In 1901 Ross was elected a Fellow of both the Royal College of Surgeons and the Royal Society; he was Vice-President of the latter between 1911 and 1913. In 1902 Ross became the first Briton to be awarded the Nobel Prize in Physiology and



Dr. Ronald Ross. Courtesy of the National Library of Medicine.

Medicine. The same year, he was appointed to the Order of Bath and was knighted in 1911. In 1912 he was made an honorary chair at the University of Liverpool, where he taught until 1916. Four years earlier, he had relocated to London, when he was appointed as a consultant physician to King's College Hospital. During World War I (1914–1918) he was appointed as a malaria consultant to Indian troops. A final memorial to his achievements came in 1926 when the Ross Institute opened in Putney; it moved to Bloomsbury in 1934. Soon after the institute's inauguration, Ross suffered a stroke and was confined to a wheelchair. Eager to secure his role in the discovery of malaria's transmission, Ross published his memoirs in 1930, minimizing both Manson's and Italian entomologist Giovanni Batista Grassi's (1854–1925) contributions to tropical medicine. He died two years later on September 16 at the Ross Institute. *See also* Colonialism and Epidemic Disease; Malaria and Modern Military History.

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JONATHAN REINARZ

RUSH, BENJAMIN (1746–1813). Both a political leader and **physician**, the Philadelphian Benjamin Rush promoted clinical research despite the fact that his advocacy of **humoral theory**–based “depletion” therapies (such as bloodletting) were ultimately harmful. Educated at the College of New Jersey (Princeton) and taking a medical degree at the University of Edinburgh, Scotland, Rush returned to practice medicine in Philadelphia while teaching chemistry and writing extensively on medical topics. His fame spread as a result of his scores of publications, and he eventually taught several thousand students over the course of his career. Both civic-minded and a champion of **inoculation**, in 1774 he was one of the founding physicians of Philadelphia's Society for Inoculating the Poor.

Rush was also a member of the Continental Congress and a signer of the Declaration of Independence. In the first years of the Revolutionary War, he served as surgeon general and physician general for the army, but resigned in 1778 in protest over what he saw as the mismanagement of army hospitals then under the supervision of an officer appointed by George Washington (1732–1799). Nonetheless, he remained a consultant to the Congress on military medicine, and his important *Result of Observations* outlines the means by which American troops could best be protected from the ravages of disease.

The careful observations Rush made during the Philadelphia **measles** epidemic of 1789 reflect the high medical standards developed during the Scottish Enlightenment. These were included in his *Medical Observations and Inquiries*, which he later expanded and republished. During the great Philadelphia **yellow fever epidemic** in 1793, Rush proposed that treatment had to be calibrated to the severity of fever: the higher the fever, the stronger the therapy, which in Rush's view, meant purgatives and bloodletting (which he

even applied to himself). However benighted these treatments seem to modern readers, Rush was nonetheless tireless in his care for victims of the epidemic and recorded meticulous notes on its progress. His publication of the account written for a general lay audience, *An Account of the Bilious Remitting Yellow Fever, as It Appeared in the City of Philadelphia, in the Year 1793* (1794), made him famous internationally. The book provides a narrative of the epidemic's appearance and progress, attributes its cause to "exhalations" from rotting produce and swamps (akin to the "bad air" or *malaria* that provided the name of that other tropical disease in which mosquitoes are the vector of transmission), observes quite accurately the two stages of the disease in patients, and carefully charts the daily death rates of the epidemic. Although the book reflects the Enlightenment's penchant for meticulous (and sometimes irrelevant) recording of data, it is also a defense of Rush's views on the origins and effective treatment of the epidemic.

At the time of the epidemic, Philadelphia was the capital of the new republic, its largest city, and its busiest **trade** port, intensifying the notoriety of and anxiety about the mosquito-borne tropical disease, probably carried there by refugees from political turmoil in Haiti. Eventually many citizens, including members of Congress and President Washington, fled the city. To his credit, Rush remained treating the sick, putting himself at risk since nearly a tenth of the population died.

Later in his life, Rush became an ardent abolitionist and enlisted the help of African Americans during the yellow fever epidemic. See also Demographic Data Collection and Analysis, History of; Measles in the Colonial Americas; Medical Education in the West, 1500–1900; Scientific Revolution and Epidemic Disease; Yellow Fever in North America to 1810.

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THOMAS LAWRENCE LONG

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SABIN, ALBERT (1906–1993). Albert Sabin is best known for the development of an oral, attenuated-live-virus vaccine against **poliomyelitis**. An outstanding contributor to virology and **epidemiology**, he championed the vaccine for mass **vaccination** programs to achieve eradication of the disease in the United States and around the world. He vehemently opposed the use of the killed-virus vaccine developed by **Jonas Salk** and never acknowledged that his own vaccine can mutate back to virulence and cause paralysis. Nevertheless, the Sabin vaccine remains the preferred vaccine worldwide.

Sabin was born in Bialystok, Poland, where his parents were silk weavers. After immigrating to the United States in 1921, he earned his medical degree from New York University in 1931. Fresh out of medical school, in a decision that changed the course of his life, he postponed his residency and began working with polio during a major **epidemic** in New York City. He continued his research starting in 1935 at the Rockefeller Institute for Medical Research in New York. Four years later, eager to combine laboratory research with patient care, he moved to the University of Cincinnati College of Medicine and the associated Children's Hospital. During World War II (1939–1945) Sabin spent time in North Africa with the U.S. military studying polio and documenting his confirmation of **Wade Frost's** model of the virus as an intestinal pathogen spread through tainted water supplies. His research continued in Cincinnati, where he developed the polio vaccine. This he accomplished in 1956, just as the world hailed the first successful vaccine by Salk.

After field testing his oral vaccine in the Soviet Union, Sabin oversaw successful mass immunization campaigns in Europe, South and Central America, Asia, and the Soviet Union. In 1960 the U.S. Public Health Service approved the use of the vaccine in the United States. It became the essential tool for the defeat of polio in the Western Hemisphere and in Europe. Sabin urged vehemently that his vaccine was more effective, cheaper, and easier to administer than the Salk vaccine. But the overriding advantage was the vaccine's ability to induce immunity in the gut, which is where poliovirus multiplies.

As it disseminates in the feces, it might, he believed, naturally immunize nonvaccinated persons. This, he concluded, was essential to preventing the spread of wild poliovirus in communities. To facilitate its universal use, in 1972 he donated the rights to the vaccine to the **World Health Organization** (WHO). In 1988 the WHO—following the model of the eradication of smallpox—set the goal for polio's worldwide eradication for the year 2000. The goal was not realized, and its feasibility remains in question.

Although Sabin understood the potential for large-scale vaccination programs, he remained narrow-minded when it came to the merits of his own vaccine. Though it is cheap and easy to administer, in very rare cases it can revert to virulence—an outcome that is prompting research into new vaccines. Sabin disputed the evidence for reversion and continued to research this problem until his death. Though he had a difficult personality, his exceptional contribution to the epidemiology and eradication of poliomyelitis is undisputed. *See also* Children and Childhood Epidemic Diseases; Human Immunity and Resistance to Disease; Immunology; Personal Hygiene and Epidemic Disease; Poliomyelitis and American Popular Culture; Poliomyelitis, Campaign Against; Salk, Jonas E.; Smallpox Eradication.

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ANGELA MATYSIAK

ST. VITUS' DANCE. St. Vitus' Dance refers to an historical condition that included the uncontrollable compulsion to dance, hop, and leap, which could last for days and sometimes caused the sufferer's death from exhaustion. The term is today synonymous with "**Sydenham's chorea**," but it derived from a series of dancing **epidemics** that struck Europe during the medieval and early modern periods. In 1021, chroniclers tell us, several people began dancing outside a church in the town of Kölbzig in Saxony. An angry priest cursed them to dance for a year, which they did. Some argue that this is the first case, albeit distorted into allegory, of a dancing epidemic. In Maastricht, Netherlands, in 1278, 200 are said to have drowned after the collapse of a bridge on which they had been dancing emphatically and perhaps uncontrollably. The largest epidemic began in 1374 and ended in 1378, extending from Aachen in the north of Germany to Strassburg (Strasbourg) in the southwest. Chroniclers talk of thousands of dancers, screeching with pain, begging bystanders to tie sheets tightly around their waists while they called on the mercy of saints. Most assumed that they were possessed by demons, and the chronicles speak of many deaths. A small outbreak occurred around 1463 when several people danced compulsively near Trier, Germany. Better documented is a Strasbourg epidemic that began in mid-July 1518. As many as 400 people danced uncontrollably for days or even weeks. Isolated cases, affecting one or a few people, have also been recorded in fifteenth-century Switzerland and twentieth-century Turkey. No more epidemics of dancing occurred in Europe after 1518, but reports of "Tigretier" in Abyssinia, Africa, in the nineteenth century sound very much like St. Vitus' Dance, as does a major outbreak of dancing in

Madagascar in 1863. Chronicles and medical reports are unequivocal in stating that the victims of these outbreaks danced. They may have twitched and convulsed as well, but their movements were quite recognizable as dancing. Indeed, the Dutch artist Pieter Brueghel drew victims of what he called victims “St. John’s Dance” during the 1540s. He shows them performing the semblance of a dance, although they are clearly distracted and in pain.

There is little consensus as to the cause of these outbreaks. It has been claimed that the dancers suffered from ergot poisoning. Yet **ergotism** is not compatible with sustained dancing. Equally unsatisfactory is the claim that the dancers were members of a religious cult. The dancers did not dance voluntarily, and the church did not consider them heretical or blessed. Many have opted for the category of hysteria or conversion disorder, seeing the dance as a response to intolerable stress, a physical manifestation of despair. This is plausible: it seems that during the 1500s some expected to develop St. Vitus’ Dance every year after feeling mounting anxiety lasting weeks. This is strongly reminiscent of the Italian tradition of the tarantella dance, for which preexisting psychological stress was an important element. Indeed, like those who performed the traditional tarantella, the St. Vitus dancers may have been in a state of trance, a conclusion also supported by chroniclers’ reports and the otherwise astonishing endurance of the dancers. Those in a state of trance usually behave in ways consistent with their own and their culture’s expectations. It may therefore be significant that there was a well-established belief, especially in the Rhine region, in the danger of a compulsive dance being inflicted by St. Vitus, St. John, or the Devil. Those whose resistance to such beliefs had been lessened by hunger, poverty, and religious crisis, may have succumbed to a trance state in which they behaved according to such deeply laid fears. This would also explain why exorcism rituals and visits to St. Vitus shrines so often cured the afflicted. Importantly, similar beliefs in the possibility of unwanted possession leading to dance seem to have existed in the popular cultures of Abyssinia and Madagascar. If this interpretation is correct, St. Vitus’ Dance is an example of a reprobate trance, and its disappearance is explained by the fading away of the mystical or demonological beliefs that made it possible. *See also* Social Psychological Epidemics.

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JOHN WALLER

SALK, JONAS E. (1914–1995). Dr. Jonas Salk developed the first safe and effective vaccine against **poliomyelitis**. The introduction of the inactivated polio vaccine in 1955 was one of the most important medical advances of the twentieth century.

Jonas Salk was born in 1914 in New York City to Russian immigrant parents. He was a young child during the beginnings of **epidemic** polio, which mostly affected the children of the United States. Jonas Salk attended New York University School of Medicine and became a **physician**, but he was drawn to research rather than to direct patient care. Salk’s interest in virology (the study of viruses) was piqued by a lecture in medical school. The



Cheryl Halpin (foreground) watches Dr. Jonas Salk on television in 1955, inoculating a child with polio vaccine, as part of a closed-circuit television show from the University of Michigan. Courtesy of the National Library of Medicine.

lecturer stated that the only way for a person to become immune to a viral disease was to suffer the disease, because a killed vaccine would not work on **viruses**. In addition, he said that it was possible to make a person immune to the bacterial disease **diphtheria** by **inoculation** with a vaccine made from killed **bacteria**. Salk felt that both statements could not be true. After completing his medical training, he entered the University of Michigan and assisted in research to develop a successful killed influenza virus.

Salk was then recruited to the University of Pittsburgh in 1947. He received a research grant to participate in a poliovirus-typing project commissioned by the National Foundation for Infantile Paralysis (NFIP). A new technique was adopted in Salk's lab that allowed the growth of the virus on monkey kidney tissue. Polio virus could suddenly be grown in large amounts, reducing time and costing less money, and reducing the sacrifice of monkeys. After the development of this technique, he killed the virus with formalin and ensured that no live virus remained in the vaccine preparation. After testing successfully in rhesus monkeys, a small trial was conducted using previously infected children. Salk vaccinated the children with the same type of polio that they had previously been exposed to and measured the increase in immunity. This ingenious approach ensured that the children were exposed to no risk. The pivotal placebo-controlled trial of the vaccine involved 1.8 million American children in 1954. **Vaccination** provided a

greater than 80 percent protection rate against infection from epidemic polio. In 1956 **Albert Sabin** completed a live-virus oral vaccine in an effort to create mass immunizations. Controversy thus ensued over which kind of vaccine was better, and today Salk's original vaccine is still used, though Sabin's is preferred. Five years after introduction of the Salk vaccine, the incidence of poliomyelitis cases dropped 90 percent, and the vaccine proved to be safe, potent, and effective.

In 1960 Jonas Salk established the Salk Institute in California, a nonprofit research institution devoted to biological research related to health. After his work on the polio virus, Salk began research on the AIDS virus and contributed his remaining career in search of a cure. *See also* Animal Research; Children and Childhood Epidemic Diseases; Human Immunity and Resistance to Disease; Human Subjects Research; Poliomyelitis and American Popular Culture; Poliomyelitis, Campaign Against; Sabin, Albert.

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LARA J. KUNSCHNER

SANATORIUM. A sanatorium (pl. -toria) is a place to which sick people go to recuperate or recover from disease. Nineteenth-century Germans who pioneered the use of the term, derived from the Latin *sanare* (to heal), distinguished sanatorium from sanitarium—derived from *sanitas* (health)—though Americans have often blurred the distinction. A sanatorium utilizes a regimen of rest, diet, exercise, and other forms of therapy in aiding recovery. These facilities may be dedicated to any physical problem, from venereal disease to broken limbs, but sanatoria were most often built to aid early-stage pulmonary **tuberculosis** (TB) patients.

Before the discovery of the tubercle bacillus by **Robert Koch** in 1882, Western medicine understood the disease in traditional, Galenic terms and emphasized rest, clean **air**, and special **diets** as treatment. Seventeenth-century English **physician Thomas Sydenham** and his friend, physician and philosopher John Locke (1632–1704), recommended horseback riding as a suitable passive exercise. In 1791 Quaker physician and founder of the Medical Society of London John Coakley Lettson (1744–1815) opened the Royal Sea Bathing Infirmary at Margate in Kent, England, for patients with scrofula, a form of TB. Sea air had long been recommended to wealthy English patients, but Lettson designed Margate for London's poorer denizens. Residents bathed in the sea and slept in the open on covered verandas, and by 1800 the number of beds had risen from 36 to 86. Sir James Clark's (1788–1870) *Sanative Influence of Climate* (1841) opened a new chapter in residential treatment of TB. The same year saw the opening of the Brompton Hospital for Consumption near London, and of the first Swiss sanatorium in Davos, later made famous by German novelist Thomas Mann (1875–1955) in *Magic Mountain* (1924). German physician Hermann Brehmer (1826–1889) devoted his 1853 dissertation to the advantages of high altitude treatment for pulmonary TB. He noted that autopsied TB

victims had small hearts and concluded that the thinner air would reduce pressure on the organ and help cure patients. Brehmer opened the first sanatorium for pulmonary TB at Görbersdorf in the mountains of Bavaria in 1854. Linking atmosphere with diet and advocating walking for exercise, he invented for the weary the park bench placed alongside the path.

Tuberculosis grew increasingly common in later nineteenth-century Europe and America, becoming the leading cause of death among adults. The Romantic Movement in the arts clasped the wan consumptive to its breast and provided a model of the “recuperative power of nature” for treatment. *Abandon the filth and stress of the urban cesspool and embrace the clean, health-restoring nature of flashing sea or majestic mountaintop; and do so under the strict regimen of a sanatorium*, it seemed to advise. Of course, who but the well-off could afford to travel, let alone pay for such treatment? The tubercular poor remained all but invisible.

In the United States, tuberculosis patients, such as the gambler, gunslinger, and dentist “Doc” Holliday (1851–1887), sought the dry desert air of the frontier Southwest or Colorado. New Yorker Edward Livingston Trudeau (1848–1915) contracted TB while tending his consumptive brother in the 1860s. Gaining nothing by a stay in the South, he decided to live out his days in the Adirondack Mountains, where he had vacationed as a child. He was soon showing signs of improvement, regaining weight and strength. In 1882 he read about both Brehmer’s theories and his sanatorium, as well as about Koch’s discovery of the **bacterium** causing tuberculosis. Collecting funds from friends, Trudeau purchased property on Saranac Lake and in 1884 opened the Adirondack Cottage Sanatorium. Fascinated by Koch’s findings, he furnished his establishment with a research laboratory, putting his medical experience—and **microscope**—to good use. By 1900 Saranac had 12 buildings and served as a model for other nearby sanatoria as well as for facilities in Pennsylvania and other neighboring states. Across the United States in 1900 there were 34 sanatoria with 4,485 beds, most in the Northeast with a few in arid western states. In 1904 there were about a hundred American sanatoria, and by 1910 another 300. America was participating in the so-called Sanatorium Movement that followed Koch’s discovery. Sanatoria now not only served the patient with a restful, healthful environment, but it also isolated him or her from wider society, a growing concern as microbiologists uncovered the mysteries of the disease and its transmission.

The 1890s witnessed a worldwide concern for both consumptives and lepers, and the decade saw a parallel flourishing of **leprosarria** and sanatoria. In 1901 the editor of *The Sanitarian* magazine reported on European and American progress in establishing sanatoria. England had about 2,000 beds (this number would double over the next decade), whereas France had well over 3,000 and was building or had finished 10 new facilities. Czarist Russia had five facilities, with more “under way,” and Italy had eight new sanatoria under construction. The Netherlands, Norway, Denmark, Sweden, Spain, Portugal, and the Habsburg Empire each had one or more sanatoria for consumptives being built, most with royal funding. The French tended toward smaller facilities, with contemporary medical opinion favoring 12 to 20 patients, whereas the German Heidehaus near Hanover, founded in 1907, had four physicians and ten nurses tending 200 patients in 1914. Canada’s first anti-tuberculosis society appeared in 1895 and created the Cottage Sanitarium on Muskoka Lake, Ontario, two years later. By 1901 Canada had two facilities with a total of 75 beds, whereas New York State alone had ten private sanatoria with 600 beds and a new state institution “projected.” The first state facility in the United States was the Sharon Sanatorium,

founded in 1898 some 18 miles from Boston.

By the early twentieth century, Romanticism had run its course, **germ theory** had established itself, and the **Sanitation Movement** had established links among disease, **poverty**, and filth. Tuberculosis slowly morphed from a fashionable disease of aesthetes to a pestilence of the urban poor. The Sanatorium Movement became linked to social philanthropy and public health, and newer sanatoria were increasingly urban and institutional rather than rural and idyllic. By 1910, 61 of Britain's 90 TB sanatoria were public. When physician Hermann M. Biggs (1859–1923), Public Health Officer for New York City, established a rural sanatorium at Otisville, he instituted a “work cure” instead of the typical “rest cure” for the city's lower class consumptives. Shortly after, he had Riverside set up as a virtual prison for nonvoluntary committals who presented a public health risk to New York. Although charitable, religious, and for-profit sanatoria continued to thrive, the percentage of beds in public facilities continued to climb even faster. Between 1907 and 1916, Pennsylvania had the largest state system of sanatoria; between 1904 and 1919, its number of beds increased from 660 to 3,972. Pennsylvania's public sector controlled 32 percent of beds in 1904, 50 percent in 1908, and 73 percent in 1919. Camp Mont Alto grew from 28 to 730 patients between 1907 and 1910, and housed 1,150 in 1916, making it the largest sanatorium in the country. Still, in 1916 there was but one bed for every three Pennsylvanians who died of TB that year. Those sanatoria that admitted African Americans generally segregated blacks and whites, and the first public sanatorium specifically for black Americans was established near Burkeville, Virginia, in 1917. By 1925 there were 536 sanatoria in the United States with a total of 73,338 beds, or an average of 137 per institution.

The 1920s saw a slowdown in the creation of new sanatoria in Europe as the incidence of the disease fell. The movement had its impact on architectural style, however, as

HOW TO REST IN AN AMERICAN SANATORIUM (1909)

Rest out of doors is the medicine that cures consumption. Absolute rest for mind and body brings speedy improvement. It stops the cough and promotes the appetite. The lungs heal more quickly when the body is at rest. Lie with the chest low, so the blood flow in the lungs will aid to the uttermost the work of healing. The rest habit is soon acquired. Each day of rest makes the next day of rest easier, and shortens the time necessary to regain health. The more time spent in bed out of doors the better. Do not dress if the temperature is above 99 degrees, or if there is blood in the sputum. It is life in the open air, not exercise, that brings health and strength. Just a few minutes daily exercise during the active stage of the disease may delay recovery weeks or months. Rest favors digestion, exercise frequently disturbs digestion. When possible have meals served in bed. Never think the rest treatment can be taken in a rocking-chair. If tired of the cot, shift to the reclining chair, but sit with head low and feet elevated. Do not write letters. Dictate to a friend. Do not read much and do not hold heavy books. While reading, remain in the recumbent posture.

Once having learned the simple facts that must be noted and the simple laws that must be followed, once having placed oneself in a position to secure the rest, the fresh air, and the health diet, no better next steps can be taken than to observe the closing injunction in the rules for rest:

There are few medicines better than clouds, and you have not to swallow them or wear them as plasters,—only to watch them. Keeping your eyes aloft, your thoughts will shortly clamber after them, or, if they don't do that, the sun gets into them, and the bad ones go a-dozing like bats and owls.

From William H. Allen, *Civics and Health* (Boston: Ginn and Co., 1909) online at <http://chestofbooks.com/health/>



Sanatorium, Albuquerque, New Mexico, built in 1934. Courtesy of the National Library of Medicine.

architects adopted the clean, smooth, include-nothing-on-which-dust-might-accumulate imperative in Bauhaus and other modernist styles. For example, pioneer Finnish architect Alvar Aalto (1898–1976) designed Paimio Sanatorium (1929–1932) 20 miles from Helsinki.

The introduction of streptomycin as a relatively effective treatment against TB in 1943, and its even more effective combination with para-aminosalicytic acid (PAS) in 1948, brought the age of the sanatorium to a close. An experiment in Madras, India, in 1959 showed that outpatient treatment with the new medications could be as effective as hospitalization. Mountain health resorts were transformed into playgrounds for winter sports—a role Davos plays just as well as it ever served as a health resort. Although sanatoria disappeared from or changed functions in most national landscapes, only the Soviet Union and post-Soviet states retained the facilities and regimens for TB into the twenty-first century. *See also* Disease, Social Construction of; Environment, Ecology, and Epidemic Disease; Industrialization and Epidemic Disease; Industrial Revolution; Leprosy in the United States; Leprosy, Societal Reaction to; Tuberculosis and Romanticism; Tuberculosis in England since 1500; Tuberculosis in North America since 1800; Urbanization and Epidemic Disease.

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JOSEPH P. BYRNE

SANITATION MOVEMENT OF THE NINETEENTH CENTURY. The sanitation movement of the mid-nineteenth century in Europe and the United States had at its heart a profound tension between the classic nineteenth-century principle of **personal liberty** and the growing importance of collective health and citizenship. The sociopolitical ramifications of this tension played a major part in determining the course of the movement. From it emerged a highly influential view of the proper relationship between medicine and the state, one mediated in Europe and the United States by the creation and expansion of new **public health agencies**.

But this movement did not exist in isolation. It was part of a broader aspiration among the newly affluent middle classes—initially in Britain, the first Western country to industrialize, and later in Europe and the United States—to place their own standards of morality, civility, and hygiene at the heart of life in industrial societies. Sanitation reform became, in the words of the contemporary historian Anthony Wohl, “a kind of *fundamental* reform,” one necessary to improve not only health but also wealth, welfare, and morality.

Industrialization and Urban Poverty. In 1800 80 percent of the British population lived in rural villages. By 1900, 80 percent lived in towns and cities. This startling statistic reflects the dizzying social and economic transformations of the Industrial Revolution in the nineteenth century. **Industrialization** and continued **urbanization** brought great wealth for the middle and upper classes, but also levels of urban **poverty**, squalor, and disease never before experienced in Europe. **Epidemic** diseases such as **cholera**, first seen in Britain in 1831, swept through overcrowded slums. Industrialization made the country as a whole rich, but its poor—the workforce on which industry depended—were sick and getting poorer.

A key question for nineteenth-century intellectuals was how to respond to this new industrial poverty. In the early decades of the century, *laissez-faire* **capitalism**—the principle that trade and industry should be subject to as few regulations as possible—dominated British public life. This idea was embodied in the work of the British economists Adam Smith (1723–1790) and Thomas Malthus (1766–1834), who argued that free trade was the basis of Britain’s industrial success. According to **Malthusianism**, poverty indicated a moral failure on the part of the poor to learn the lessons of the free market.

One expression of *laissez-faire* capitalism was in the provision of fresh **water** and the disposal of sewage in the new industrial cities. Water was provided by private companies or from communal street pumps, and sewage was collected in cesspools or emptied into rivers—often the only source of drinking water. Through the lens of modern bacteriology, it seems obvious that this cycle of contamination was implicated in the transmission of epidemic diseases. But to the inhabitants of these cities, sewage disposal was only one aspect of urban life, all of which seemed dirty and diseased. Overcrowded slum housing, slaughterhouses, and heavy industries, the pigs and chickens kept by the poor, the three million tons of dung deposited by horses on British streets every year—early sanitation reformers saw all aspects of the urban **environment** as causes of disease.

Sanitation Reform and Social Reform. Many social reform movements in this period were based on the new Christian evangelical movements of the 1830s and 1840s. The sanitation movement possessed this element of **morality**: epidemics were seen not as God’s punishment of sin, but rather as the failure of humans to look after His creation and His poor. This reflects a gradual movement away from *laissez-faire* ideology, as the middle classes began to take a paternalistic—some said patronizing—interest in the health and welfare of the industrial poor.

Two strands, one public, one private, characterized the sanitation movement. The public strand, led by members of the urban middle classes such as physicians, politicians, and journalists, emphasized the material, collective aspects of sanitation—sewers, clean water, and so on. The private strand, associated with groups of middle-class women such as the Ladies Sanitary Association, took an interest in individual behavior and circumstances. These groups entered and inspected the homes of the poor and offered education in cleaning and cooking. These strands were not separate but rather complementary, and their interests coalesced on many subjects. In the 1830s, for example, both were involved in a campaign to provide public washhouses in which the poor could wash themselves and their clothes.

A leading figure in the public strand of the British sanitation movement was the lawyer and civil servant **Edwin Chadwick**. Chadwick had been a student of the English Utilitarian philosopher Jeremy Bentham (1748–1832), and he adopted the Utilitarian principle of using government to produce “the greatest happiness of the greatest number.” From 1834 Chadwick worked for the Poor Law Commission, a government organization investigating poverty in Britain. From 1837 the British government introduced official registration of births and deaths. Early returns from this scheme revealed a very high infant death rate in poor urban areas—153 infant deaths per 1,000 live births, compared with fewer than 16 per 1,000 in the West today. This, and Chadwick’s work for the Commission, convinced him that disease was associated with poverty.

Chadwick’s Report. In 1839 Chadwick was asked to investigate the health of the British working class, and in 1842 he published a *Report on the Sanitary Condition of the Labouring Population of Great Britain*. His main conclusion was that rotting organic matter such as sewage and food waste released a smelly and poisonous “**miasma**,” and that this form of air pollution was responsible for transmitting infectious epidemic diseases such as cholera. In his view, slums were not only a danger to those who inhabited them: the miasma they generated could spread disease to a whole town. This “miasmatic” model of disease provided a rationale for Chadwick’s proposed program of “environmental” sanitation reform—improving water supplies, building sewers and drains, regulating refuse disposal, and controlling industrial pollution.

Though widely seen as a challenge to personal liberty, Chadwick's program of reform received governmental approval with the 1848 Public Health Act. The Act established a General Board of Health to oversee public health and sanitation reform, with Chadwick as chairman and the London physician John Simon (1816–1904) as medical officer. But many local authorities resented Chadwick's autocratic chairmanship, and in 1855 he was forced to resign. Despite his pioneering work in this field, the most radical sanitation reforms took place under Simon's supervision after Chadwick had left the Board. Simon favored a neo-**contagionist** model of epidemic disease, in which disease was spread from case to case by waterborne particles, and this model provided an equally strong rationale for sanitation reform.

In 1858 the engineer Joseph Bazalgette (1819–1891) was commissioned to build a massive integrated sewer system for London. In the hot summer of that year, the level of the River Thames fell, and the smell of rotting sewage on its banks caused Parliament to be suspended for several weeks. Several years of these “great stinks” and a major cholera epidemic in 1866, brought home the need for further sanitation reform and the urgent completion of Bazalgette's scheme. The swift change in public attitudes toward sanitation reform in this period is illustrated by the fact that the 1866 Sanitary Act, though far more interventionist than Chadwick's 1848 Public Health Act, faced little opposition in parliament and the press.

The Sanitation Movement in Europe and the United States. Both Europe and the United States experienced cholera epidemics in the first half of the nineteenth century, but it was not until the 1870s that the condition of their industrial cities began to reach crisis point. And political instability—particularly the European revolutions of 1848 and the American Civil War—complicated sanitation reform. The emergence of bacteriology and new theories of disease transmission in France and Germany in the late nineteenth century added a scientific dimension to the activities of the sanitation movement in these countries. In Germany sanitation reform became part of Otto von Bismarck's (1815–1898) program of political unification, industrial modernization, and social welfare. In France, meanwhile, two “great stinks” in Paris in the 1880s triggered a nationwide program of sewer construction and slum clearance. But this aggravated underlying class tensions in French society. Could working-class neighborhoods—seen by many as the principal source of smell and disease—be cleaned up without alienating and radicalizing their inhabitants?

Though Chadwick's work had inspired some sanitation reformers in the United States in the 1840s and 1850s, the social and political turmoil of the Civil War hampered their efforts to establish a federal agency for sanitation reform. In the aftermath of the war, many cities and states established health boards, which oversaw food quality, water supplies, and the containment of epidemic disease. The National Board of Health, established in 1879, took responsibility for coordinating scientific research into contagious diseases and sanitation engineering at a national level. As the influence of the sanitation movement spread across Europe and the United States, the incidence of epidemic diseases declined sharply. Public health reformers began to shift their emphasis away from sanitation reform, embracing a wider concern for the social and medical problems associated with urban poverty.

Interpreting the Sanitation Movement. Historians have traditionally seen the sanitation movement as a straightforward battle between “miasmatists” and “contagionists.” But its impact remains controversial. Recent research suggests that the story is more complex, reflecting the success of social, economic, and administrative reform rather than the

triumph of science and medicine over disease. The sanitation movement reflected the cultural, social, religious, and political concerns of those involved. Its success owed as much to new techniques of data analysis and the skill of sanitation engineers as to any developments in medical practice or scientific theory. *See also* Capitalism and Epidemic Disease; Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1863–1947; Demographic Data Collection and Analysis, History of; Disinfection and Fumigation; Environment, Ecology, and Epidemic Disease; Industrial Revolution; Personal Hygiene and Epidemic Disease; Public Health Agencies in Britain since 1800; Public Health Boards in the West before 1900; Religion and Epidemic Disease.

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RICHARD BARNETT

SARS. *See* Severe Acute Respiratory Syndrome.

SCAPEGOATS AND EPIDEMIC DISEASE. Epidemics generate profound social disorder. In response, the individuals who risk infection during **epidemic** episodes seek explanations for the fundamental causes of disease outbreaks. Throughout history, societies have created scapegoats by blaming otherwise innocent people in order to rationalize and explain the origins and course of disease outbreaks. These patterns of scapegoating often mirror existing social prejudices, as the socially disempowered become objects of blame. The designation of certain groups or individuals as scapegoats may be based partially in fact. Poor living conditions, for example, put some at greater risk for infection and mortality; these demographic realities thus made it appear logical that such individuals were particularly dangerous. In other cases, persecution stems from existing cultural biases with perceptions of danger bearing little relation to actual disease risk. Religious, ethnic, political, economic, and sexual prejudices all factor into the process of scapegoating, and these affiliations are not mutually exclusive. Though not intended to be exhaustive, the following representative cases of epidemic scapegoating demonstrate its long history across time and place.

People often turn to religion to explain disease outbreaks. By extension, religious persecution has been a frequent response to epidemics. During the **Black Death**, Christian

majorities accused Jews of poisoning wells and spreading plague in Strasbourg, Basle, Mainz, and other sites. Likewise, when **cholera** struck the United States in the 1830s, many Americans believed the epidemic was a divine punishment for immorality. Protestants blamed cholera on individuals who disobeyed God's law, including the population of Irish Catholics in the nation. In the 1980s and 1990s, fundamentalists such as Pat Robertson and Jerry Falwell defined **AIDS** as divine retribution against homosexuals.

As the above examples illustrate, religious scapegoating overlaps with other discrimination. Ethnic scapegoating targeted Jewish and Irish Catholic immigrants to the United States as inherently diseased. The perceived links between disease and ethnicity have changed over time, as cultural and biological understandings of difference give new meanings to prejudices. In sixteenth- and seventeenth-century Geneva and Milan, Spaniards and other foreigners found themselves accused of conspiracy to spread plague among locals. By the nineteenth century, new biological understandings of **race** and **heredity** linked certain ethnic groups to specific diseases. Eastern European Jews were blamed for spreading **typhus** and cholera in 1890s New York, whereas whites targeted residents of San Francisco's Chinatown for spreading and concealing plague in the early 1900s. In the 1980s, attempts in the United States to explain the source of **HIV** focused on Haitians, although it would later be clear that the disease probably spread *from* the United States to the Caribbean instead. The perceived connection between disease and foreigners persists.

Epidemic scapegoating also stems from political and socioeconomic conflicts. Many infectious diseases disproportionately affect people who lack decent housing, nutrition, or sanitation. Furthermore, many people blame **poverty** on individual moral failings, and thus hold poor people responsible for their disease-ridden living conditions. As diseases spread to other parts of the community, the more affluent classes are prompted to see the poor as harboring disease. **Mary Mallon**, or "**Typhoid Mary**," has come to typify the links between working classes and infectious disease. Mallon, a typhoid carrier, worked as a cook for wealthy New Yorkers and unknowingly contaminated dozens. Public health authorities blamed her refusal to stop cooking on ignorance and disregard for others' lives, while ignoring the economic constraints that obliged Mallon to make a living through cooking. Likewise, disease outbreaks such as **cholera**, **tuberculosis**, and hookworm, transmitted more easily in overcrowded living conditions, are often blamed on lower economic classes.

Socioeconomic and political scapegoating does not always target lower classes. Disempowered people have also blamed dominant groups for introducing disease. Disease here is understood as a conspiracy to exterminate certain peoples. Citizens of many Allied nations accused Germany of creating **influenza** as a biological weapon during World War I, and the British were blamed for importing cholera and **malaria** to Egypt after World War II (1939–1945). Leonard Horowitz and others have argued that the U.S. Government created HIV as a tool to commit genocide against African Americans and Hispanics. In many cases, distrust stems from historically hostile relations between groups; indeed, some conspiracy theories have a basis in past or present intimidation and threats. Whatever the reality, political and class distrust creates miscommunications that hamper effective public health initiatives.

Like politics and economics, gender profoundly affects assumptions about contamination. During the second plague pandemic, women blamed for spreading plague were accused of witchcraft and executed. In the late fifteenth century, **syphilis** became a major

problem in Europe, and many female prostitutes were condemned as sources of venereal infection. Likewise, in the 1860s, the British Parliament passed a series of Contagious Disease Acts for both Britain and its colonies. This legislation held female prostitutes (rather than their male patrons) responsible for infecting soldiers and civilians. Women have not been the only sexual scapegoats. In the early 1980s, scientists and civilians considered homosexual men as the prime casualties of HIV (initially termed Gay-Related Immunodeficiency). When heterosexual individuals began to acquire the disease, members of the gay community became scapegoats. Gender and sexuality continue to create the basis for scapegoating in epidemic diseases.

As the above examples illustrate, many different factors combine to construct the epidemic scapegoat. Mary Mallon, for example, was a poor, Irish Catholic immigrant woman and a threat to middle class, Anglo-Saxon Protestant norms on many levels. Similarly with HIV, religious, political, and gendered beliefs weave together to shape perceptions of risk.

In epidemic scapegoating, individuals attempt to impose order during a period that is fundamentally disordered and to assign blame for a seemingly random disease to a definable target group of individuals. Yet infectious diseases are always more complex sociological phenomena, the causes of which are never so simply defined. *See also* AIDS in Africa; AIDS in America; Biblical Plagues; Black Death, Flagellants, and Jews; Leprosy, Social Reactions to; Mallon, Mary; Personal Liberties and Epidemic Disease; Poison Libels and Epidemic Disease; Religion and Epidemic Disease; Sanitation Movement of the Nineteenth Century; Sexual Revolution.

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JULIA F. IRWIN

SCHAUDINN, FRITZ RICHARD (1871–1906). Fritz Richard Schaudinn's brief career focused on protozoology (the study of **protozoa**) and parasitology. His research culminated with the identification of the bacterial cause of venereal **syphilis**. Schaudinn was born in the village of Roesiningken in East Prussia. In 1890 he matriculated into Berlin University with the intention of studying philology, but he was soon drawn to zoology and studied protozoa with his mentor, Franz Eilhard Schulze (1840–1921). He received his doctorate in 1894 and in 1901 he was appointed director of the German-Austrian zoological station in the town of Rovigno near Venice, Italy. Here he conducted research on the etiology of **malaria** and proved that an amoeba is the cause of tropical **dysentery**. Schaudinn was recalled to Berlin in 1904 to head the newly created parasitology laboratory at the Imperial Health Office, and it was here that he started his investigations into the cause of syphilis. In the following year, he was appointed director of the Research Institute for Naval and Tropical Diseases in Hamburg, but he died from sepsis following a pararectal abscess before he could assume this post.

In early 1905, John Siegel (1861–1941), a parasitologist under the direction of Franz Schulze at Berlin, published a series of papers in which he pointed to *Cytorrhynchus luis* as

the cause of syphilis. As part of his duties with the Imperial Health Office, Schaudinn was called upon to confirm Siegel's findings. He started by investigating biopsy materials from syphilitic patients, provided by Erich Hoffmann (1868–1959), a clinical dermatologist and syphilologist. Rather than confirming Siegel's claims, however, he discovered a different microorganism in his syphilitic samples, which he initially named *Spirochaeta pallida*. In March 1905 Schaudinn and Hoffmann presented their results and noted that they had repeatedly found *Spirochaeta pallida* in their syphilitic materials, but they cautiously chose not to declare it the cause of the disease. Over the next few months, Schaudinn continued to study this microorganism and determined that based on its structure it was actually a new genus of protozoa, so he renamed it *Treponema pallidum*. Then, on May 17, 1905, Schaudinn publicly presented his discovery to the Berlin Medical Society and revealed research that more clearly identified *Treponema pallidum* as the causative agent of syphilis. Despite his initial caution, Schaudinn met with sharp criticism from Siegel and his supporters, including their shared mentor, Franz Schulze, who continued to advocate for the causal role of *Cytorrhcytes luis* in syphilis. Over the next few months, however, researchers from around the world confirmed Schaudinn's observations. Tragically, because of his untimely death, Schaudinn did not witness **Paul Ehrlich's** development of a cure for syphilis that depended on his identification of the microorganism that caused the disease.

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WILLIAM H. YORK

SCHISTOSOMIASIS. Schistosomiasis is a parasitic disease afflicting over 200 million people throughout the world, principally in areas of **poverty** and inadequate public health facilities. The causative agents are species of trematodes, or flukes, in the genus *Schistosoma*. *Schistosoma mansoni*, *S. hematobium*, and *S. japonicum* cause the vast majority of infections, with *S. mekongi* and *S. intercalatum* accounting for the rest. *S. japonicum* also infects a variety of domestic animals and therefore has epidemiologic significance. *S. mansoni* is the only species found in the western hemisphere and is seen in Brazil, Venezuela, Surinam, and parts of the Caribbean. *S. mansoni* and *S. hematobium* are both encountered in most African countries and on the Arabian peninsula, with *S. hematobium* found alone in parts of the Middle East. *S. japonicum* is found in China, the Philippines, and parts of Indonesia. *S. mekongi* is found in Laos and Cambodia, and *S. intercalatum* in Sub-Saharan Africa. Many other species infect birds, sheep, cattle, dogs, cats, and other mammals, but not humans. Most trematodes are bisexual, but *Schistosoma* are unisexual and reproduce by mating.

History. Schistosomiasis is an ancient disease. Eggs have been found in Egyptian mummies of the twelfth century BCE, and ancient Egyptian papyri describe hematuria. The first description of the adult worm (*S. hematobium*) was made in 1851 by Theodor

Bilharz (1825–1862), a German physician working in Cairo, who also described its terminal (end)–spined eggs. Other than the additional finding of lateral (side)–spined eggs (perhaps another species) no further progress was made until the turn of the century. In 1904 *S. japonicum* was described by John Catto; the circle was closed in 1913 when Japanese biologist Keinosuka Miyairi (d. 1946) found the intermediate host of *S. japonicum* to be a freshwater snail. This work was confirmed by British biologist Robert Leiper (1881–1969), and differentiation of *S. mansoni* and *S. hematobium* into two distinct species was confirmed by noting specific intermediate host snails for each. By the close of World War I (1914–1918), the three major species and their life cycles were known, and efforts could be directed at prevention and treatment.

However, progress was slow because of lack of effective therapeutic drugs and difficulties with snail control. Not until the 1970s, when drugs such as niridazole, metrifonate, and oxamniquine appeared, were greater strides made. These were effective, were less toxic than previous pharmaceuticals, and could be orally administered. Praziquantel, developed in the 1970s and in use by the 1980s, proved to be superior because it covered all three species and was low in cost and toxicity. It is the mainstay of most control programs today.

Life Cycle. Like other trematodes, *Schistosoma* have a life cycle involving two separate hosts. On exposure to freshwater, free-swimming larvae, called cerceriae, penetrate the skin within three to five minutes of contact. The larvae, now called schistosomulae, make their way into the circulation system through the heart and lungs and terminate in the portal circulation in about five to ten days. Here the larvae grow to adults and mate. The females migrate upstream to venules (small veins) around the intestinal or bladder walls. There, about four to six weeks after initial skin penetration, eggs are laid, about half of which pass upstream to lodge in the portal venules of the liver (in *S. mansoni* and *japonicum*). The other half penetrates the venules and the bladder or intestinal wall to be passed to the outside world. *S. haematobium* are passed in urine, whereas the other species are passed in the stool. Adult worms live an average of 3 to 7 years, though exceptional life spans of up to 30 years have been reported.

If the eggs reach freshwater, they hatch, releasing another larva, the miracidium. The miracidia penetrate the soft parts of certain species of snails and develop into sporocysts. These give rise to numerous daughter sporocysts, which grow and migrate out of the snail to become the cerceriae that reinitiate the cycle. In the case of *S. japonicum*, a similar life cycle exists in domestic animals, including cattle, water buffalo, pigs, dogs, and cats, whose eggs contribute to the disease burden.

Human Pathology and Disease. The life cycle of the *Schistosoma* parasite determines the clinical and pathologic findings. Penetration of the cerceriae for the first time often elicits little reaction. Repeated exposure results in an allergic reaction, cercarial dermatitis, an inflammatory papular rash limited to the exposed area of skin. It may also result from repeated exposure to nonhuman cerceriae, most commonly from birds, and it is often referred to as “swimmer’s itch.”

Passage of the larvae through the lungs is usually silent, but heavy infections cause symptoms and signs of inflammation (pneumonitis). Cough, wheeze, and scattered X-ray changes may be noted.

The onset of egg laying, in a heavy infection, is associated with an allergic reaction known as acute schistosomiasis or the “Katayama syndrome.” It is most commonly seen with *S. japonicum* but occurs with the other varieties as well. Symptoms and signs are

fever, pneumonitis with cough and X-ray changes, abdominal pain, diarrhea, and enlargement of the liver, spleen, and lymph nodes. In light infections this stage may pass unnoticed, and it is less often seen in endemic areas.

Subsequent stages, referred to as chronic schistosomiasis, take months to years to manifest. The pathology is almost entirely the result of inflammatory changes from the eggs, which secrete enzymes and other antigens that provoke a granuloma-forming inflammatory reaction. The most common early symptom of urinary tract involvement is hematuria, whereas prolonged infections may result in bladder cancer and urinary tract obstruction at various points along the tract. The intestinal forms are characterized by intermittent diarrhea, abdominal discomfort, and intermittent blood loss. In these, about 50 percent of eggs laid pass upstream to the liver where they elicit a similar inflammatory reaction around the portal venules. Less commonly, eggs may be found in "ectopic" foci, such as the spinal cord, brain, lungs, and genitalia, with symptoms dependent on the location.

In general, the symptoms of schistosomiasis are mild and chronic, and the economic impact of the disease is hard to estimate. Studies have shown evidence of growth retardation and decline in cognitive function in heavily infected children. There is some dispute about how much disability on a global scale is attributable to schistosomiasis, partly because of the nonspecific nature of the symptoms and the frequent coexistence of other diseases.

There is an immune response to this infection, but it is incomplete and complex. Research in this area is ongoing in hopes of developing a vaccine. Initial infections in childhood trigger an antibody response that facilitates removal of new invading schistosomes, but this seems to have little effect on adult worms, which are thought to be resistant to immune mechanisms. A portion of acquired immunity may be related to age alone.

Diagnosis and Treatment. The diagnosis of schistosomiasis is best made by finding the eggs in stool or urine samples. Light infections may require more sensitive procedures such as rectal (or colon) biopsy. Blood serum tests are helpful, especially as screening tests or for epidemiological studies. Antibody tests generally take two to three months to become positive (thus, they are of limited help in acute cases), and they are subject to some error. Antibodies remain measurable for up to two years after successful treatment. Measurement of the antigen in the bloodstream is possible and quite specific, but it may miss light infections. Ultrasound studies of the liver are helpful as screening tests, but they are not precise in finding the parasite.

Great progress has been made in recent decades in the treatment of schistosomiasis. The drug of choice today is praziquantel, which is administered orally in one or two daily doses and is effective against all three major species. Side effects are mild enough for the drug to be used in mass treatment campaigns, and it is considered safe in pregnancy. Praziquantel is not effective, however, against the schistosome stage.

Assessing cure requires follow-up stool or urine samples at three or more months after treatment and an assessment of the viability of any eggs found. There is generally good reversal of bowel and urinary tract pathology after treatment, and improvement is seen in liver inflammation, if it is not too far advanced.

Epidemiology and Control. The geographic distribution of schistosomiasis is dependent on the distribution of the intermediate host snails. Human contact with water that is contaminated with human, and in some cases (particularly in the Orient) animal excreta,



Two young children suffering from schistosomiasis, a debilitating water-borne disease. WHO photo. Courtesy of the National Library of Medicine.

perpetuates the infection. This combination occurs commonly in poor environments, where sewage disposal is primitive, and farming practices, swimming, and bathing enhance water contact. It is generally an endemic disease, though outbreaks have occurred, such as the outbreak in troops in the Philippine Islands during World War II and an occurrence that spread upstream in the 1990s after the damming of the Senegal River. The highest prevalence and intensity of infection is generally in 8- to 12-year-olds. The prevalence and intensity tend to decline later in life, perhaps as a result of reduced exposure to freshwater (because of new occupations, etc.) and of a partial immunity that develops over time. Endemic populations often have prevalence rates (of egg excretion) in the range of 30 percent to 50 percent, but lifetime infection rates of over 90 percent.

Strategies to control this disease require interruption of the life cycle at one or more points. Such strategies generally include the following approaches: sewage management to avoid contaminating water, provision of clean water for washing and bathing, drug therapy, and education programs. Work with mollusk poisons to control the snails is in less favor today because of cost and environmental concerns. The efficacy, relative cheapness,

and safety of praziquantel have made drug therapy with this agent, combined with education measures and provision of clean water, the most cost-effective approach today. A serious concern in all programs employing praziquantel is the emergence of **drug-resistant** parasites. These have been reported, and failures of treatment are seen, but thus far, resistance does not seem to be increasing. Caution and surveillance are, however, in order.

Great progress has been made in recent years in controlling schistosomiasis in the Orient, South America, Caribbean, and North Africa, utilizing the aforementioned control measures. Less successful has been control in Sub-Saharan Africa, where little progress has been made. The **World Health Organization** estimates that of the 200 million cases in the world, 150 million occur in Sub-Saharan Africa; there, 70 million have had hematuria, 10 million have had hydronephrosis, and 130,000 have hematemesis yearly. In response, the recently constituted Schistosomiasis Control Initiative, a mix of public and private consortiums funded primarily by the Melinda and Bill Gates Foundation, is addressing this deficiency. The goal is to select high-risk groups as pri-

mary targets for control programs and help local governments to implement these programs. The initiative includes research, surveillance, chemotherapy, education, and other measures.

Research on a vaccine against schistosomiasis is being actively pursued, but thus far there is nothing available. Some candidate vaccines are in early stages of trial. *See also* Children and Childhood Epidemic Diseases; Diagnosis and Diagnostic Tools; Ectoparasites; Environment, Ecology, and Epidemic Disease; Human Body; Human Immunity and Resistance to Disease; Personal Hygiene and Epidemic Disease; Pilgrimage and Epidemic Disease; Vaccination and Inoculation; Water and Epidemic Diseases.

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J. GORDON FRIERSON

SCIENTIFIC REVOLUTION AND EPIDEMIC DISEASE. Historians use the term Scientific Revolution to describe a radical shift in human understanding of nature and natural processes during the later European Renaissance and Early Modern periods. Lasting from the mid-sixteenth through the seventeenth centuries, this revolution was the work of scientists, physicians, and other researchers who moved away from the medieval and Renaissance natural philosophy, based on classical knowledge, religion, and folklore, toward a discipline of science based on principles of empiricism, experimentalism, and the communication of one's findings, often summarized by the term scientific method. This overthrow of tradition resulted in the emergence of new systems of knowledge. These were proposed by a range of innovative thinkers who challenged both the utility of ancient philosophy and the accumulated authority on which that philosophy rested. Some of the foremost exponents of these "new philosophies" included the French mechanical philosophers Pierre Gassendi (1592–1655) and René Descartes (1596–1650), the astronomers Nicolaus Copernicus (1473–1543) and Johannes Kepler (1571–1630), the Italian mathematician and astronomer Galileo Galilei (1564–1642), and the English virtuosi Robert Boyle (1627–1691) and Isaac Newton (1642–1727).

In the field of medicine, prominent reformers included the Flemish anatomist Andreas Vesalius (1514–1564), whose *Workings of the Human Body* (1543) revolutionized the study of anatomy, and the English physician William Harvey (1578–1657), who first described the circulation of the blood. Other prominent medical reforms were linked to the rise of **Paracelsianism** and its novel theory of disease. Originally proposed by German **empiric Paracelsus** and taken up by followers such as Jan Baptista van Helmont (1577–1644), this new theory rejected the dominant **humoral theory** of Galen and sought to explain illness as the disruption of an internal vital principle called the *archaeus*, which could be negatively affected by "seeds" of disease entering the body from the external environment. Paracelsians rejected traditional organic remedies for inorganic metals and salts in tiny doses.

Atomism, Mechanism, and Fermentation. Paracelsus and his followers were not the only thinkers to propose the idea of disease “seeds.” In the early sixteenth century, for example, the Veronese physician **Girolamo Fracastoro** applied the ancient philosophy of atomism to the problem of disease and proposed that **syphilis** and other **epidemic** diseases could be explained by the presence of *seminaria*, or “tiny seeds,” which were responsible for sickening otherwise healthy individuals. As part of the **miasma theory** of disease, he suggested that these seeds or particles were part of the “bad air” generated by certain **environments** and pollutants, but Fracastoro combined this idea with **contagion theory** by observing that these *seminaria* could be passed from one individual to another, particularly with diseases like syphilis. Fracastoro’s notion of a material cause for disease transmission is viewed by some as a direct ancestor of modern **germ theory**.

More than a century after Fracastoro, atomism came more prominently into vogue. Arguably the most significant of the “new sciences” that emerged during the Scientific Revolution was the materialistic mechanical philosophy, which sought to explain all natural phenomena in terms of matter and motion. Pierre Gassendi, a French Catholic priest, revived the atomism of the ancient Greek philosopher Epicurus (341–270 BCE), in which phenomena were explained by the movement of atoms through a void; differing in their size, shape, and weight, these atoms could combine and disperse to an almost infinite degree. At the same time, the French philosopher René Descartes proposed a system in which phenomena as disparate as light, magnetism, and sound were explained by the movement and contact of corpuscles, or tiny pieces of matter.

These ideas had a profound effect on thinkers in the seventeenth century, and so it is unsurprising that, like Fracastoro, some philosophers would seek to apply atomistic or mechanical explanations to the problem of epidemic diseases. For example, Robert Boyle, often considered the father of modern chemistry, considered that **bubonic plague** might be transmitted by discrete corpuscles. To Boyle, these “plague corpuscles” seemed the most likely explanation for the manner in which the plague appeared to move between individuals and places. Atomism in particular became strongly linked with miasmatic theories of transmission, in which it was generally assumed that tiny particles of disease could attach themselves to persons exposed to miasmas, or pockets of “bad air.” These particles could remain attached to a person’s clothing or hair for some time, affecting them and others around them even once clear of the miasma, making travel through congested urban areas such as London a potentially hazardous exercise.

Not all notions of epidemic disease were linked with corpuscularian or atomistic theories, however. The English physiologist Thomas Willis (1621–1675) was, like Boyle, a member of the Royal Society of London (founded in 1660) and an avid experimentalist, placing him squarely at the epicenter of the Scientific Revolution. He was also a vocal disciple of Paracelsus and sought to explain vital processes such as respiration and digestion by means of a chemistry of fermentation. Observing that fevers often accompanied diseases like plague, Willis suggested that the active fermentation of the blood, producing a high fever, was the body’s attempt to expel the “pestilential poison” of the disease. The innovative theories advanced by Boyle, Willis, and their contemporaries would reshape general understanding of physiology and of the body’s response to disease.

New Technologies. The Scientific Revolution spawned not only radical changes in ideas about the world, but the advent of new technologies as well. Prominent among these

was the telescope, used by Galileo around 1609 to discover the four largest moons of Jupiter, and the **microscope**, which was to play an important role in the study of living things and, importantly, diseases such as plague.

The advent of the microscope in particular was closely linked to prevailing ideas concerning the particulate or corpuscular nature of disease in the seventeenth century. The English journalist Marchamont Nedham (1620–1678) took his cue from Girolamo Fracastoro's notion of *seminaria* and looked for visual evidence of what he described as “certain Atoms, Corpuscles, or Particles, sometimes animated into little invisible worms as in the case of Pestilential infection.” In his *Medela Medicinae: A Plea for the free Profession, and a Renovation of the Art of Physic Tending to the Rescue of Mankind from the Tyranny of Diseases* (1665), Nedham noted that these “little worms” had also been observed by the eminent German Jesuit philosopher and polymath Athanasius Kircher (1602–1680), who had examined human blood under the microscope and reported, according to Nedham, that “upon the opening of buboes and tumors, they have been found full of innumerable vermicules [little worms] indiscernible by the eye.” Dutch scientist **Antony van Leeuwenhoek**, famed today for his close observation of spermatozoa under the microscope, also reportedly observed what he described as “animacules”—tiny animals—when examining the blood of an infected individual. The increasing use and sophistication of these technologies would eventually have a profound effect on **epidemiology** and the subsequent treatment of epidemic disease.

Organization, Communication, and the State. Because most scientists were not connected with the academic life of universities, they needed to create new methods of communicating their findings and discoveries. Scientific societies like the privately organized Royal Society in London, the state-directed French Academy of Science (1666), and several independent Italian academies were organized to facilitate discussion and the sharing of information and to promote scientific endeavors. Beginning in 1453, books by researchers and practitioners began to be printed in large numbers, and they increasingly appeared in vernacular languages for wide national audiences. Within these audiences were leaders and bureaucrats in the rapidly evolving European states. Information was power, and states began collecting data on, for example, epidemic death tolls, in attempts to rationalize and centralize state responses to disease. In the seventeenth century, mathematics—from Descartes's coordinate geometry to Newton's calculus—became a tool for scientists and a language for communicating information. Both probability theory and statistical method emerged around mid-century and helped lay the groundwork for epidemiology. One of the earliest examples of statistical analysis was English haberdasher *cum* demographer John Graunt's 1662 study of the London Bills of Mortality, which had been started under King Henry VIII (1491–1547) and listed the weekly numbers of dead by cause of death. Governments also gave greater weight to medical expertise, and in the sixteenth century, physicians began appearing on health boards and health magistracies, and their developing theories on contagion helped spur the widespread use of such measures as **quarantines** and isolation, and the institution of **pest houses** and **cordons sanitaires**. See also Colonialism and Epidemic Disease; Demographic Data Collection and Analysis, History of; Greco-Roman Medical Theory and Practice; Medical Education in the West, 1500–1900; Plague in Europe, 1500–1770s; Public Health Boards in the West before 1900.

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MARK A. WADDELL

SCROFULA. See Tuberculosis.

SECOND PLAGUE PANDEMIC. See Black Death (and related articles); Plague: End of the Second Pandemic; Plague in Britain, 1500–1666; Plague in China; Plague in Europe, 1500–1770s; Plague in Medieval Europe, 1360–1500; Plague in the Islamic World, 1360–1500; Plague in the Islamic World, 1500–1850.

SEMMELEIS, IGNAZ (1818–1865). Ignaz Semmelweis is most famous for advocating sanitary techniques, but his true innovation was redefining a disease in terms of a single cause, which, by definition, made the cause universal and necessary. This opened the way to systematic prophylaxis (prevention) and treatment and to coherent explanations of disease phenomena.

Semmelweis was born in Budapest, Hungary. After completing an M.D. degree at the University of Vienna, he was appointed an assistant in the Viennese maternity hospital. There he confronted the horrible reality of childbed fever. Childbed fever, now called puerperal sepsis, ravaged European maternity clinics. In some years, some facilities had mortality rates above 70 percent, but the Viennese clinic maintained a relatively favorable rate of about 8 percent. The situation in Vienna, however, was unusual: its maternity facility had two divisions. In the first, staffed by obstetricians, mortality averaged about 10 percent, whereas in the second division, which utilized midwives, mortality averaged about 2 percent. Semmelweis tried desperately to understand the higher mortality rate in his division. He required that all procedures be the same in both divisions—even to the extent that all patients received the same food and were delivered from the same position. Nothing helped.

When Semmelweis's colleague Jakob Kolletschka (1803–1847) died after being accidentally cut while performing an autopsy, his corpse revealed morbid remains similar to those found in deceased maternity patients. Semmelweis speculated that, if the remains were similar, perhaps the cause was the same. In Kolletschka's case, the cause was contamination by decaying matter from a cadaver. Semmelweis realized that his first division maternity patients were also exposed to decaying organic matter conveyed on the hands of medical personnel. This did not happen in the second division because the midwives did not conduct autopsies. In May 1847, Semmelweis began requiring everyone to wash regularly in a chlorine solution. Within days, the mortality rate dropped to the same level as in the midwives' division.

The chlorine washings, which Semmelweis probably adopted from the British, were tried here and there throughout Europe. However, in presenting his results, Semmelweis insisted that every case of childbed fever had the same one cause—decaying organic matter. This claim was inconsistent with the traditional view that every disease could have various causes, and initially both those who accepted chlorine washings and those who did not rejected it. Beginning in the mid-1860s and continuing through the century, however, Semmelweis's views were repeatedly discussed in German and French medical literature. Gradually, his way of thinking prevailed.

Frustrated at what he saw as reluctance to accept new ideas, Semmelweis's writings became strident. By 1865 he may have become deranged (although the evidence is inconclusive). In August he was committed to an asylum in Vienna where he was forcibly restrained. Two weeks later he died, probably from wounds inflicted in the asylum. *See also* Children and Childhood Epidemic Diseases; Contagion and Transmission; Disinfection and Fumigation; Germ Theory of Disease; Hospitals in the West to 1900.

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K. CODELL CARTER

SEPTICEMIC PLAGUE. *See* Pneumonic and Septicemic Plague.

SEVERE ACUTE RESPIRATORY SYNDROME (SARS). Severe Acute Respiratory Syndrome (SARS) originated in southern China in November 2002 and rapidly swept the globe to appear on five continents. From February to July 2003, it affected over 8,000 people worldwide, leaving at least 774 dead (including 349 in China, 299 in Hong Kong, 44 in Canada, 39 in Vietnam, 37 in Taiwan, and 33 in Singapore). A few sporadic cases continued to appear in China and Taiwan until April 2004.

A highly contagious lung infection, the illness was characterized by fever, cough, and difficulty breathing. It could result in hindrance to breathing such that death resulted in 10 percent or more of cases, even when good medical care was available. With a predilection for infants and the elderly, SARS also affected many health-care workers including **physicians, nurses**, and their family members.

After a few false leads, laboratories working independently on three continents identified the causative agent in late March 2003. It was new a strain of coronavirus, called SARS CoV. Such RNA **viruses** are named for their “crown-like” (corona) appearance on electron microscopy.

However, a pathogen is only one cause of any infectious disease; it is necessary for infection and spread, but it is not always sufficient to trigger an outbreak. **Environmental** and social factors also contribute to the appearance and spread of disease. In the wake of the September 11, 2001, attacks on the United States, some people wondered if this new disease was a deliberate act of **bioterrorism**. Their suspicions were soon dispelled.

Global air **travel** was another important factor in the spread of SARS. Initially unrecognized as a distinct new disease, SARS began in the southern Chinese province of Guangdong. An ailing doctor from Guangdong went to Hong Kong where he stayed on the ninth floor of the Metropole hotel. Sixteen hotel guests and visitors to that floor acquired the infection, probably while waiting for the elevator. Some carried the disease home to Vietnam, Singapore, or Canada. Many other cases arising in those countries would eventually be traced back to links with the Metropole hotel.

Disease can also be spread by technology and health workers. It was possible to transmit infection by care-giving and through special instruments for investigating and treating breathing disorders. Furthermore, health successes may backfire. The concept of pathocenosis, elaborated by medical historian Mirko Grmek (1924–2000), suggests that in any given time and place, prevailing diseases exist in a kind of harmony. When one condition disappears, another can come along to take its place. As a result, we can ask if SARS exploited a window of opportunity in the developed world created by the systematic use of **vaccinations** against **influenza** and childhood illnesses.

There is no specific treatment for SARS. In every center, the outbreak was contained by traditional methods: isolation of sufferers, **quarantine** of contacts, and use of protective clothing and sterile techniques by caregivers. Sick people were supported by oxygen and artificial respiration. Hospital security was increased; visiting was prohibited. Upon arrival each day, workers were required to have their temperatures taken and to **disinfect** their hands. All schools were closed in Singapore, Beijing, and Hong Kong, whereas isolated school closures were implemented in other centers. Consideration was given to closing airports, but health screening was preferred. Air passengers were monitored for fever and questioned about symptoms. Research on a vaccine continues.

SARS taxed the chronically underfunded public health services of several countries, and in its wake it left many other sequelae: medical, social, economic, political, and legislative. Medically, the outbreak made heavy demands of public health workers and infectious disease specialists. In Canada, cases appeared in Vancouver and Toronto, but the impact was much wider. For example, hospitals across the entire province of Ontario were quarantined for many weeks resulting in emotional turmoil. New rituals of hand-washing and temperature control were implemented. Some patients with SARS had access to specialized technologies for respiratory support, but it became clear that a larger outbreak would soon exhaust existing resources. Too often neglected, disease prevention grew in importance.

Socially and culturally, SARS unleashed personal fears and irrational xenophobia. Travelers from Asia and people of Asian origin experienced outright discrimination, as they were wrongly thought to be carriers of the pathogen. Questions were raised about normally harmless customs. Who should attend funerals for those dead of SARS? Should common communion cups be dispensed with in Christian services? Should collective prayer be banned?

Economically, SARS resulted in massive disruption, directly because its costs and indirectly through its effects. Concerts, plays, and conferences were cancelled, and normally busy hotels, theatres, and restaurants stood empty. This situation was thought to have been aggravated by **World Health Organization** travel advisories against Hong Kong, Beijing, and Toronto. Some of the direct expenditures were later found to have been unnecessary. For example, sales of costly N95 face masks escalated, and supplies were depleted, although those masks were later shown to offer no advantage over

others. The perceived need to stimulate travel to Toronto prompted a mega-concert by the Rolling Stones on July 20, 2003. Nevertheless, some evidence suggests that the financial hardship resulting from SARS was shorter lived and less severe than had been predicted.

Politically and legislatively, SARS revealed flaws in the existing safety nets for infection control. The disease occurred only in a few cities, but its legislative and policy impact was felt on a global scale. In its wake, more funding was directed to public health agencies, “**pandemic** planning” became standard practice, and restructuring of government ministries occurred.

Finally, SARS highlighted the continued vulnerability of the human organism to natural pathogens. When in the following year avian flu emerged as a health concern, the serious attention it received from media and governments, despite a paucity of human cases, was prompted by the recent passage of SARS. Looking back, many experts believe that a devastating pandemic was avoided more by good luck than by good management. Even as they deal with the nature and control of the disease, publications about SARS also emphasize the “lessons learned” from its brief but sharp debut in 2003.

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JACALYN DUFFIN

SEXUALITY, GENDER, AND EPIDEMIC DISEASE. The association of sexuality or gender with epidemic disease has an ancient pedigree in the Western world. Two themes seem to dominate: transgressions of sexual taboos or moral prohibitions are seen as causing disease, and stigmatized categories of people are viewed as particularly dangerous vectors of **transmission** or reservoirs of disease. Of course, issues of taboo and stigma aside, a large number of potentially fatal diseases are simply transmitted through the sex act, ironically making the act of procreation a potentially deadly one.

The Linguistic Production of “Plague” and “Pestilence”. The neutral medical term “**epidemic**” (*epi* + *dēmos* meaning “around or close to the people”) appears in English in the early seventeenth century. Its coinage at the dawn of modern science suggests

a turn away from the prevailing notion of widespread disease as a divine punishment that is contained in the far older medieval term “plague,” which appears in French and English in the fourteenth century. The term “pestilence” (the condition of plague, particularly **bubonic plague**) has a similar linguistic history to that of “plague,” appearing in English in the early fourteenth century, at which point it already appears to have had a figurative sense of “that which is morally pestilent or pernicious; moral plague or mischief, evil conduct, wickedness; that which is fatal to the public peace or well-being” (Oxford English Dictionary). By the use of such terms for phenomena that were mysterious, unpredictable, and uncontrollable, premodern societies were able to attribute meanings to widespread diseases, often at the expense of socially marginalized people (such as women) or socially stigmatized behaviors (such as sexual relations).

The Ancient World. The Hebrew Scriptures provide numerous instances of plague as the visitation of divine punishment, often associated with gender and sex. Genesis 12, for example, narrates Abraham’s removing to Egypt during a famine, where his wife Sarah poses as his sister only to be brought into the pharaoh’s house, ostensibly to become a concubine, for which God sends a plague upon Pharaoh. In Numbers 25:1–2 the association of plague with sexual transgressions and gender is explicit: “And Israel abode in Shittim, and the people began to commit whoredom with the daughters of Moab. And they called the people unto the sacrifices of their gods: and the people did eat, and bowed down to their gods” (King James Version). In this instance and in the vast Hebrew prophetic literature, intermarriage with non-Hebrew tribes is metaphorically configured as religious apostasy, and religious apostasy is metaphorically configured as consorting with prostitutes.

If Classical Greco-Roman cultures failed to associate epidemic disease with moral error or sin, they nonetheless understood plagues as divine punishments for displeasing the impetuous gods by acts often involving sexual elements. In Homer’s (c. 8th century BCE) *Iliad*, for example, the god Apollo hurls a plague upon the Greeks camped outside of Troy because of the trophy abduction of a virgin daughter of a priest of Apollo. Similarly, the incestuous patricide Oedipus at the beginning of Sophocles’ (c. 495–406 BCE) *Oedipus Rex* confronts a plague sent to punish his kingdom for its having harbored the murderer of his predecessor on the throne.

Although the Christian scriptures seem to make little of disease as a divine punishment, the last book of the Christian scriptures, the apocalyptic Book of Revelation, includes nearly a dozen verses describing end-times plagues. Not surprisingly, these are associated with the allegorical figure of the Whore of Babylon, who rides upon a symbolic Beast and who carries a defiling cup of iniquity. Thus, the most mythological of Christian scriptures associates plague with both divine judgment for sin and perverse female sexuality.

The Medieval and Early-Modern Worlds. In medieval Western Europe, which was dominated by Roman Catholic Christianity, epidemic disease was often understood as the product of immorality as well as an occasion for repentance. The association of sin and sickness provided more than an **epidemiology** in the medieval mind. Sin itself was viewed as a soul sickness, and in medieval Christian theology the most pervasive epidemic disease was Original Sin, the result of Adam and Eve’s fall, infecting all humans. Both the seven deadly sins and a multitude of physical illnesses were understood as symptomatic of the epidemic Original Sin, which is transmitted to the next generation of humans through the sexual intercourse of their parents. God’s displeasure with moral transgressions including prostitution and adultery led to plague, and plague led in many late medieval and early modern cities to the closing of brothels and to intense sermons against sexual sin.

At the end of the fifteenth century, the emergence of a new venereal pox epidemic, **syphilis**, coincided with new historical and social forces, including the rise of imperial ventures (expanding international travel) and the birth of Protestantism. **Syphilis in sixteenth-century Europe** was frequently attributed to infection by foreigners. Moreover, women were viewed as dangerous reservoirs of the disease. Protestant moralism, which particularly took aim at what it considered the sexual license and corruption of Roman Catholicism, militated against prostitutes and brothels. Medical authorities even argued whether or not remedies should be attempted, not because of questions about medical efficacy but because they viewed the disease as a divine judgment for lust in which the physician should not intervene.

Modern Medicine, Primitive Metaphors. Moralizing epidemiology did not end with the eighteenth-century Enlightenment and the development of modern medical science, including **germ theory**, which attributes a microbial cause to epidemic disease. Perhaps the most iconic epidemic disease of the nineteenth century, **tuberculosis** (known more commonly at the time as “consumption”), was associated with women (particularly high-strung or high-living women) and with effeminate men (who lacked the manly virtues of self-control and restraint and who were prone to hysteria). A product of a bacterial infection that was assisted by the explosive growth of urban dwellers during the **Industrial Revolution**, tuberculosis figured prominently in the era’s Romantic novels, melodramas, and operas as the affliction of ruined women and weak men.

Across the twentieth-century Western world, sexual taboos tended to dissolve, especially during the 1920s and from the early 1960s on (the Sexual Revolution). In both cases, increased social options for women (and in the latter the birth control pill) led to freer and often riskier sexual activity. Though increasingly controllable, **sexually transmitted disease** case rates grew, often dramatically, and new forms of venereal disease emerged.

AIDS: Postmodern Plague. Since its emergence in the early 1980s, **acquired immune deficiency syndrome** (AIDS) has also absorbed numerous metaphorical meanings because of its association with stigmatized behavior (for example, intravenous drug use, anal sex, or sex with multiple partners) and stigmatized or marginalized social groups or populations (gay men, urban African Americans, Caribbean immigrants, and Africans). Few epidemics have become as deeply entangled in attitudes toward sexuality and gender roles as has AIDS, in discussions of both its epidemiology and its prevention. The fact that some body fluids (like semen, vaginal secretions, and blood) are vectors of transmission for the human immunosuppressive virus (HIV) has meant that public health education required a frank discussion of the containment of these fluids to prevent HIV infection. See also *Biblical Plagues; Disease, Social Construction of; Gonorrhea and Chlamydia; Religion and Epidemic Disease; Scapegoats and Epidemic Disease; Sexual Revolution; Venereal Disease and Social Reform in Progressive-Era America; Tuberculosis.*

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THOMAS LAWRENCE LONG

SEXUAL REVOLUTION. The sexual revolution is the global shift in attitudes, behaviors, and legal regulations that occurred with respect to sexuality in the 1960s and 1970s. Born out of the broader “rights” movements of the era (i.e., the civil rights, feminist, gay rights, peace, and counterculture movements), the sexual revolution has had a major impact on **epidemiology**, as well as on the **diagnosis** and treatment of venereal and nonvenereal diseases and **epidemics**.

A Brief History of the Sexual Revolution. Most historians define 1960 as the start of the sexual revolution because it marks the year in which the **pharmaceutical** company Searle released the birth control pill. The pill had an immediate social impact: it was the most effective form of contraception (up to 99 percent when used properly) in history, and gave women extraordinary control over their bodies. For the first time, women could engage in sex without the fear of becoming pregnant, while the development of **antibiotics** in the 1940s made the most dreaded venereal diseases, such as syphilis curable. The fear of **AIDS** would not become a major concern for another two decades. This led to an explosion in sexual experimentation and the number of professional women who could now enter the workforce without worrying about motherhood.

Through his magazine *Playboy*, Hugh Hefner (1926–) promoted the findings of Alfred Kinsey (1894–1956; *Sexual Behavior in the Human Male*, 1948; *Sexual Behavior in the Human Female*, 1953) and Masters and Johnson (*Human Sexual Response*, 1966) as evidence that a sexual revolution was well under way. *Sex and the Single Girl* (1962), written by Helen Gurley Brown (1922–), the editor of *Cosmopolitan* magazine, echoed the message that was being conveyed by her male counterpart Hefner. Seen by conservative segments of society as promoting promiscuity and adultery, most young, single, sexually liberated urban women used the book as a “how to” manual to guide them through professional and romantic relationships.

With the threats of pregnancy, disease, and social stigmatization gone, many of the traditional restrictions on sexuality seemed no longer justifiable. With the birth control pill came the legitimization of feminism and reproductive rights (especially abortion). As women became more concerned with reclaiming power over their lives and bodies, they began questioning sexual expression and the social construction of medicalized sexuality. They began seeking advice about sexual health from laywomen and exploring alternative treatments to gynecological diseases; the Boston Women’s Health Book Collective’s *Our Bodies Ourselves*, first published in 1970, addressed both of these concerns. Feminists also began promoting the exploration of sexuality—especially through mainstream texts such as *The Female Eunuch* (1970) by Australian scholar Germaine Greer (1939–) and Alex Comfort’s (1920–2000) *The Joy of Sex* (1972).

More radical men and women explored their sexuality through the “free love” movement. Free love and other sexual movements, such as “swinging” in Britain, became prominent strains of the counterculture movement especially after the “Summer of Love” (1967), when peace activists and hippies merged to chant the famous 1960s slogan “make love not war.” In between anti-Vietnam protests (in the United States) and anti-nuclear demonstrations (in the United Kingdom), the men and women of this branch of the counterculture movement began exploring their sexuality without the constraints of marriage and monogamy. Popular modes of sexual expression included interracial, homosexual, and bisexual relationships; open cohabitation of unmarried couples; communal living; casual sexual encounters; and political “love-ins.” These were popularized by celebrities such as John Lennon (1940–1980) and Yoko Ono (1933–), who held a “Bed-in for Peace” in their honeymoon suite at the Amsterdam Hilton Hotel in March 1969. Another component of the hippie/free love lifestyle was illegal drug use. Drugs of choice included marijuana and harder psychedelics such as LSD and mescaline; in the 1980s, cocaine, crack, and heroine became the drugs of choice for individuals still practicing this lifestyle. The sexual revolution thus contributed to the transformation of illicit drug use into a national, and global, **epidemic**, especially as the hippie movement spread to Canada, Denmark, the Netherlands, Australia, New Zealand, Brazil, Mexico, and Japan.

The sexual revolution also had a profound impact on same-sex relationships. Sensing a window of opportunity, gays, lesbians, bisexual, and transgendered individuals began to seek equal civil and political rights. After the New York City Stonewall Riots of 1969, activists formed the Gay Liberation Front (GLF), which spearheaded the burgeoning gay rights movement. The GLF’s activism was quickly inherited by a number of other consciousness-raising groups, a technique that gay activists borrowed from feminists. Both feminists and gay activists used the sexual revolution to bring down social and legal barriers that had been restricting their activities for centuries: homosexuality was finally demedicalized in the 1970s (up until late 1974, the American Psychiatric Association considered it a psychiatric disorder), and American women were given the unfettered right to have an abortion through the 1973 U.S. Supreme Court decision in *Roe v. Wade*.

The open discussion of pornography and the legitimization of some aspects of the sex trade were also outcomes of the sexual revolution. Magazines such as *Playboy* had succeeded in making sexual expression and the display of nude bodies commonplace. No longer a taboo subject, pornography went from being a sin to being a “tasteful” form of adult entertainment. Even though their freedom of speech was protected by the First Amendment of the U.S. Constitution, Hefner, and his more controversial competitor Larry Flynt (1942–), publisher of *Hustler* magazine, faced scrutiny from feminists, such as Gloria Steinem (1934–), who described pornography—even soft-core pornography—as a form of violence against women.

As sex on the silver screen became a prerequisite for a box-office hit, Westerners became more and more comfortable with the commercial sex trade. Prostitution was decriminalized in a number of countries, including regions of Australia, as well as Germany, Switzerland, and the Netherlands. In the last nation, prostitutes even became unionized, tax-paying workers. The sex trade, like pornography, also attracted the attention of activists, such as Andrea Dworkin (1946–2005), who maintained that the selling of female bodies only increased the exploitation and violence that women were already facing in society.

The Impact of the Sexual Revolution on Epidemic Disease. Although some scholars continue to debate whether or not there actually *was* a sexual revolution, one fact is undeniable: the changes in sexual attitudes and activities revolutionized the way societies think about epidemics, plagues, and diseases. The sexual revolution profoundly impacted the way in which men, and especially women, perceive their bodies. Before the 1960s, modern society permitted only physicians to examine, diagnose, and treat ailments of the female body. The women's health movement, which was an offshoot of the second wave feminist movement of the 1960s and 1970s, gave women the power, and the permission, to bypass doctors and heal themselves.

One radical branch of the women's health movement, self-help gynecology, which was promoted by Carol Downer (1933–) and Lorraine Rothman (1932–), even taught women how to perform self-breast and cervical examinations. Although the former has now become part of standard medical practice, at the time, touching one's breast, or looking at one's cervix in order to detect possible abnormalities (such as cysts and tumors) was unheard of. These self-help groups made women more aware of their health and more knowledgeable about epidemic diseases, such as breast and cervical cancer, and their causes (i.e., **HPV**, **heredity**, the **environment**). Women are now active participants in their own health care and routinely seek medical attention for these epidemics by requesting testing such as pap smears and mammograms.

The consciousness-raising that was promoted by feminist groups eventually served as the foundation of the men's health movement, which rose to prominence in the early 1980s. During the 1960s and 1970s, very few individuals thought about sexually transmitted diseases while experimenting with their sexuality. Antibiotics had, after all, eliminated the consequences of venereal diseases such as **syphilis**, **gonorrhea**, and chlamydia; antiviral medicines would tame herpes and **hepatitis B**. Even so, the increase in sexual activity meant significant increases in cases of sexually transmitted diseases. Everything changed when AIDS entered the scene in the early 1980s. Initially branded a homosexual disease because of its incidence in the promiscuous gay population, AIDS actually helped create an organized men's health movement. Although its main focus was originally the AIDS **pandemic**, the men's health movement has, over the past decade, begun to branch out into other areas such as prostate cancer and heart disease prevention. Leading the way are groups such as the Gay Men's Health Crisis (established in New York in 1982), the Men's Health Forum (established in the United Kingdom in 1994), and the Men's Health Network (established in Toronto in 2000).

Free love and the liberalization of sexual relations also transformed the ways in which epidemic diseases are diagnosed and treated. Because individuals are, in the post-sexual revolution era, far more likely to have multiple sex partners, epidemiologists usually treat the identification of sexually transmitted diseases as they would any other outbreak. In other words, they routinely identify the common (or point) source (i.e., the diagnosed patient), and then try to determine how the disease might have propagated (i.e., they determine with whom the diagnosed individual had sexual relations). This approach, especially if it concerns a patient diagnosed with HIV/AIDS, usually involves contacting and testing other potentially infected individuals, as well educating the local community. It is here, more than with any other disease, that personal privacy rights conflict with public safety mandates.

Liberalized prostitution, one of the outcomes of the sexual revolution, has long been demonized as a major contributor to the spread of epidemic diseases. However, it is

unclear whether or not this is true because it is difficult to study prostitutes and disease transmission. Nevertheless, in an effort to reduce the spread of epidemic disease through prostitution, nations have taken one of three approaches to the sex trade: outlawing it completely; instituting regulations to monitor the health of sex workers; and/or educating sex workers about treatment and prevention. Prohibiting prostitution is probably the least effective approach because it only drives the practice underground, where epidemic diseases, such as HIV and hepatitis, can spread even more rapidly. This is especially true when unprotected sex is combined with intravenous drug use. The rationale behind regulation is that because the sex trade is impossible to eliminate, the best way to deal with it is to reduce its negative ramifications. The Netherlands, for example, requires routine health check-ups from prostitutes. If they fail an examination, or do not submit to state requirements, they could lose their licenses. The U.S. state of Nevada and the nation of Australia, where prostitution is legal, have been particularly successful in educating prostitutes about safe sex. *See also* AIDS, Literature, and the Arts in the United States; Cinema and Epidemic Disease; Human Papilloma Virus and Cervical Cancer; Medical Ethics and Epidemic Disease; Pharmaceutical Industry; Personal Liberties and Epidemic Disease; Public Health Agencies, U.S. Federal; Sexuality, Gender, and Epidemic Disease.

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TANFER EMIN TUNC

SIMOND, PAUL-LOUIS (1858–1947). Paul-Louis Simond was a French **physician** who discovered that the rodent flea transmitted the plague **bacterium** and was thus responsible for human cases of **bubonic plague**. Born to a French Protestant clergyman in Beaufort-sur-Gervanne, Simond graduated as a **physician** from the French Naval Medical School at Bordeaux in 1887. His medical thesis on **leprosy** in French Guyana won a prize, and he was posted to Indochina and the South China coast. His career changed dramatically after he took the course in bacteriology in 1895–1896 at the Pasteur Institute of Paris, where he was assigned to the laboratory of Elie Metchnikoff

(1845–1916). In 1897 the Pasteur Institute sent him to India to relieve **Alexandre Yersin** and to continue the latter's program of administering the Pasteur antiplague serum to Indian patients. In 1898 Simond developed his flea transmission theory after he noticed that a small blister-like lesion was usually found on the foot or leg of Indian plague patients. In his makeshift laboratory, he discovered organisms resembling the plague bacillus in the stomach of fleas that had fed on infected rats. The *Annales de l'Institut Pasteur* published his article in 1898. It stated boldly, on the basis of a limited number of experiments, that the bite of rat fleas constituted the mode of infection for both rats and humans. Elated at his discovery, Simond could not resist remarking that he "had uncovered a secret that had tortured man since the appearance of plague in the world."

Such luminaries as **Robert Koch** and **Patrick Manson** were partial to Simond's theory but wanted more evidence. They formed a small minority. Experts on the German and Indian Plague Commissions disregarded the flea and held that although rats were important during initial outbreaks, thereafter human agency played the greater role in spreading bubonic plague. It was not until the second Indian Plague Commission of 1905 conducted its own field and laboratory experiments that Simond began to receive scientific credit. It took a further three years before the conservative Indian Medical Service finally accepted the flea's role in plague transmission.

From India, Simond went to Indochina (Vietnam) where he was named Director of the Pasteur Institute's branch in Saigon (1898–1900). His next Pasteurian assignment took him to Brazil from 1901 to 1905 where, together with Emile Marchoux (1862–1943) and Alexandre Salimbeni (1867–1942), he formed a three-man team assigned to study the **yellow fever** control methods of Oswaldo Cruz (1872–1917) in Rio de Janeiro. Simond was able to apply these methods in the French colony of Martinique in the Caribbean in 1908–1909.

His final posting was as Director of Health Services for the French Colonial Army in Indochina during the First World War. In 1917, a falling-out with military authorities led him to resign his military commission. Too often neglected in general medical histories, Simond deserves a place beside his fellow Pastorian Alexandre Yersin in the history of bubonic plague.

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MYRON ECHENBERG

SIMPSON, WILLIAM JOHN RITCHIE (1855–1931). An expert on hygiene and control of **epidemic** diseases (in particular **bubonic plague**) in the tropics, William Simpson was a professor of public health and an advisor to British colonial governments. Born in Scotland, he graduated from the University of Aberdeen and in 1880 was awarded his M.D. degree along with a diploma in public health from Cambridge University. He served as a Medical Officer of Health, first in Aberdeen from 1881 to 1886 and then in Calcutta in 1886–1897. He moved to London in 1897 and joined **Patrick Manson** to establish the

London School of Tropical Medicine in 1899. Simpson also held the Chair in Hygiene at King's College, London. From 1900 to 1929 he took brief trips to advise colonial governments on the control of plague or sanitation more generally, including to Cape Town (1901), Hong Kong (1902), Singapore (1906), the Gold Coast, Sierra Leone, and Southern Nigeria (1908), Uganda and Zanzibar (1913), the Gold Coast (1924), and Northern Rhodesia (1929).

As Medical Officer of Health in Aberdeen, Simpson developed an interest in epidemics through his study of outbreaks of diseases characterized as zymotic (including **smallpox, measles, scarlet fever, diphtheria, typhoid fever, typhus, and whooping cough**). These were believed to result from chemical reactions acting as catalysts for a chain of disease processes. He also began to study **germ theories** of disease that developed from laboratory research, although he was at first skeptical about the value of such research for public health practice. By the time he helped found the London School, he had become a lifelong advocate of laboratory research. He related many of his findings in *A Treatise on Plague Dealing with the Historical, Epidemiological, Clinical, Therapeutic and Preventive Aspects of the Disease* and in *The Maintenance of Health in the Tropics*, both published in 1905.

On his trips abroad, Simpson put into practice ideas about plague control from research at the London School. For example, in Cape Town he drew on the newest laboratory research to institute a plague **vaccine** campaign. His medical colleagues and other citizens, however, found the campaign suspect, and it died away. In contrast, his colleagues and colonial authorities wanted to rely on a much older method of plague control: the separation of those they deemed dangerous, in this case all black Africans, whether they were healthy or not. Although he considered it inadequate, Simpson sanctioned the segregation. At issue was the local belief that black Africans were to blame for the epidemic's severity and Simpson's belief that segregation or isolation was only one of several means to control plague.

As do contemporary international health experts who travel from one epidemic to another, Simpson tried to reconcile practices to control plague that were new—such as plague vaccines—with older, established practices, such as segregation and isolation. See also Colonialism and Epidemic Disease; Disease, Social Construction of; Pest Houses and Lazarettos; Plague in Africa: Third Pandemic; Race, Ethnicity, and Epidemic Disease; Scapegoats and Epidemic Disease.

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MARY SUTPHEN

SLAVERY AND EPIDEMIC DISEASE. Slavery is an ancient practice. Even two centuries after the abolition of slavery in Europe and the Western hemisphere, numerous societies still have state-sponsored slavery or sustain slave-like working conditions. Though defined by the slave's status as chattel property, the physical circumstances of slavery have often included overcrowding, forced labor, poor nutrition and sanitary conditions, and forced travel through or to vastly different ecological **environments**. These provide the perfect environment for the emergence and proliferation of **epidemic** diseases.

Slavery was common in antiquity and the Middle Ages, and Arab slavers notoriously removed millions of Central and East Africans to North Africa, Arabia, and the Indian Ocean. In Western Europe the practice of slavery waned with the practice of serf labor but was revived to address the huge labor shortages caused by the **Black Death** and the late medieval colonial developments in the eastern Mediterranean and Atlantic isles. It was not until the mid-sixteenth century, however, that massive epidemics occurred in association with the slave trade. The surge is related to Europeans' transformation of slavery into a transatlantic enterprise. This followed their discovery that the natives of the Western Hemisphere made very poor slaves; in no small part this was because of the natives' susceptibility to European diseases. And so the Europeans turned to Africa for labor. The process of capture, enslavement, and forced **migration** of approximately 12 million West Africans to the Americas over three centuries defined the "New World" culturally and socially and was responsible for an unprecedented intercontinental biological interchange.

Bacteria, viruses, and parasites were transported in the ships linking Africa, the Americas, and Europe. These biological entities, regardless of their alleged origin, had been confined to geographic and human reservoirs for millennia, and human populations living with these microorganisms evolved to develop specific immune characteristics that kept germs at bay. Like the common cold today, their presence was endemic, and the usual presentation of the diseases they caused mild, when compared to the crippling symptoms of an epidemic. The transatlantic biological interchange set in motion by the colonization of the Western Hemisphere and by the slave trade put human populations and the germs associated with them into contact—populations that had been separately evolving, culturally, socially and biologically, for millennia. This set the perfect stage for an explosion of epidemics for which the only precedent in mortality and in geopolitical and social impact was the Black Death.

The introduction of African slavery to the New World was intimately related to the interchange of pathogens that caused native Central and South Americans' demographic collapse. Disease did not spare any group. Africans died by the thousands of **smallpox**, the same Old World disease that obliterated Incan, Mayan, and Aztec civilizations. However, Africans brought with them their own share of pestilences such as **malaria, yellow fever,** and filariasis, among others. But if there were one pestilence that was central in the shaping of the South American continent, it was yellow fever.

Yellow Fever is a mild affliction in its endemic state, but it became vicious when it traveled. It first emerged as a source of epidemics in the port cities of West Africa where enslaved Africans were appraised, sold to merchants, and shipped to the New World. Thousands of sailors died during the middle passage (the journey from Africa to the slave trade ports in the Caribbean and in South and North America), and many others once ashore. Slave ships, with their crew of susceptible European hosts and half-empty **water** casks, provided with the perfect transcontinental transport system for the yellow fever virus and its fastidious vector, the mosquito *Aedes*. The disease needed to survive in the body of susceptible hosts, jumping from one European to another after either killing them or immunizing them, for the 12 weeks that the middle passage usually lasted.

In 1647 yellow fever arrived at Barbados. Its pronounced symptoms and high mortality (approximately 10 percent) terrorized Native Americans, Europeans, and Creoles all the same, whereas immune Africans could ignore it. Yellow fever spread throughout the ports of the Americas as far north as Boston and New York in the English Colonies. It even reached Europe and struck Lisbon, Barcelona, St. Nazaire in France, and Swansea in

Wales. Although this very African epidemic did not seem to affect Africans, the story of malaria was different.

Even though Africans had been living with malaria for millennia, the parasitic characteristics of the *plasmodium* (the parasite causing malaria) did not allow African bodies to acquire immunity. Thus, malaria's scourge came within slaves' bodies and became endemic on the American continents. Though not immune, Africans had undergone a process of natural selection that made them able to survive the quartan fevers of the *falciparum* variant of the disease, but with one drawback. The special malaria-resistant red blood cells Africans developed were less effective at withstanding low blood oxygen concentration, hypoxemia, or body stress's hormone's surge and acidic conditions. These sickle-shaped cells are responsible for the condition known as sickle cell anemia, a disease specific to those of African descent.

In the New World, slavery also provided the perfect infrastructure for disease dissemination. Most African slaves were brought to the Americas to labor in two particular working spaces, the plantation and the mine. European colonists created or controlled both of these ecologically disruptive spaces, which proved to be perfect breeding grounds for the native *Anopheles* mosquito. These mosquitoes proliferated in close proximity to humans in the warm residual waters re-collected in the ubiquitous white clay receptacles used on the sugar plantations and in the rainwater-filled ponds left by silver and gold mining. From here, scores of *Anopheles* emerged and feasted on humans, while transmitting the deadly *falciparum*.

Four out of ten Africans died between the time they embarked from African shores and the end of their first year in the New World. Although there are no reliable statistics, it is not a stretch to say that most of these men, women, and children—predominantly men because of the nature of the demand for field hands—died of disease. Two epidemic diseases share responsibility for this humanitarian catastrophe: smallpox and **typhus**.

Sailors and captains; British, Portuguese, French, and Spanish governmental officers; **physicians** of European royal medical corps such as the Spanish *protomedicato*; and clergymen such as the Jesuit priests Alonso Sandoval (1577–1652) and Pedro Claver (1581–1654), all testify to the common occurrence of smallpox among African American slave populations. The conditions in which Africans were shipped from Africa made of the middle passage a truly Darwinian selective rite of passage in which only the strongest survived. African slaves were confined in overcrowded quarters for three or more months. In the poorly ventilated stowage decks of the slave ships, they shared everything from blankets to eating utensils. These are, of course, the perfect conditions for the dissemination of smallpox and epidemic typhus, among other diseases.

Sailors and captains of vessels under all flags left testimony about the terrifying experience of smallpox epidemics on board the slave ships and the economic catastrophe that it represented, in their desperate diary entries. After major smallpox epidemics struck cities such as Havana, Portobello, Rio de Janeiro, and Cartagena, authorities prohibited infected slave ships from unloading their cargoes in any American ports until after a strict **quarantine** period and careful inspections by medical officers. Unwilling to undergo this hardship, captains took no risks, and thousands of slaves were thrown overboard in the middle of the Atlantic at the slightest symptom of disease.

The arrival of new African slaves brought virgin material for the smallpox virus. Epidemics shook all the major cities of the New World until late in the nineteenth century, after decades of vaccination and, most importantly, the abolition of slavery. Slave

owners considered epidemics in slaves' quarters catastrophic, more often because of their economic impact than because of humanitarian concerns. Compulsory inoculation of the susceptible population became standard in North America after 1816 and in the rest of the Americas somewhat later. But there was no procedure that could protect slaves from the "ship's disease," a pestilence that roamed between the decks where they were confined in their passage from Africa to the Americas.

Epidemic typhus, the violent version of the milder endemic typhus is caused by *Rickettsia prowazekii*. The conditions predominating in the slave ships were perfect for the transmission of this affliction, one that prefers filthy environments and bodies. The unhygienic conditions in the lower decks of the *negros* (Black slave) ships were perfect for the blistering spread of the *Rickettsia* through its vector, the human louse *Pediculus humanus corporis*. Scores of slaves perished because of the ship's disease, many of them even before reaching the shores of the New World. The terrifying symptoms brought on by the louse-borne typhus, the high fevers and unmistakable rash, signaled the fate of scores of slaves who were thrown overboard in a desperate measure to save the cargo.

Cholera also deeply concerned slave traders and owners in the Americas. The unsanitary conditions in both rural and urban slave quarters in North and South America facilitated the spread of cholera's *Vibrio* bacteria. As in the rest of the world, the **pandemics** that raged in the New World during the nineteenth century were not ameliorated until 1853, when **John Snow** associated cholera dissemination with contaminated water sources. The bacterium would remain undiscovered until late in the century. Thus, during the first half of the century, measures that had proven to be at least partially effective against diseases such as smallpox or yellow fever were fruitlessly implemented when cholera struck. Contemporary conceptions of the disease's etiology and racial associations tinged the reports of the cholera epidemics in the Americas. As cholera was thought to be associated with filth, moral degeneracy, and degraded conditions, Euro-Americans and Europeans categorized it as a "black" disease. Though African slaves and even freed slaves, because of their diminished living conditions, were more prone to come in contact with *Vibrio cholerae*, the disease was very democratic, sparing no segment of society. Nineteenth-century reports attributed higher cholera rates among African Americans to slaves' dietary preferences and to inferior moral conditions. However, it was slaves' living conditions that really put them in harm's way. On the plantations of the Americas, most slaves lived in crowded quarters with minimal sanitary facilities, and when living in urban settlements, slaves and freed blacks were confined to the most impoverished neighborhoods. This, added to slaves' chronic malnourishment and strenuous working conditions, made them an easy prey for the cholera germs.

The "pest houses" that had been created for pox quarantine were now used to isolate slaves who were stricken by the disease. Cholera prompted town councils to establish public health boards and appropriate money for the treatment of the destitute, including slaves. Owners of slaves closed factories and plantations and urged "their" blacks to stay in quarters while paying especially good attention to cleanliness and Christian moral standards of living. In the end, society's preoccupation with the unfathomable characteristics of cholera's contagion, the puzzlement it caused by affecting black and white, moral and immoral, all the same, helped to elevate the standards of living of slaves in British and Spanish colonies. *See also* Cholera: First through Third Pandemics, 1816–1861; Colonialism and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria in the Americas; Poverty, Wealth, and Epidemic

Disease; Race, Ethnicity, and Epidemic Disease; Smallpox in Canada and the United States since 1783; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Yellow Fever in Colonial Latin America and Caribbean; Yellow Fever in North America to 1810; Yellow Fever in the American South, 1810–1905.

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PABLO F. GOMEZ

SLAVES. See Slavery and Epidemic Disease.

SLEEPING SICKNESS. The term African sleeping sickness comprises two fairly distinct clinical and epidemiologic disorders caused by **protozoa** of the genus *Trypanosoma* and spread by the tsetse fly. The two causative organisms, *T. brucei gambiense* and *T. brucei rhodesiense*, are considered subspecies of the *T. brucei* complex. A third member of the complex, *T. brucei brucei*, only infects **animals**. *Gambiense* disease occurs in central and West Africa, whereas *rhodesiense* disease is found in eastern and southern Africa, all within about 15 degrees north and south of the Equator.

History. African sleeping sickness is an old disease. The first written notation is by the fourteenth-century Arab writer Al-Qualquashaudi, who commented on “a sleeping sickness” common around the kingdom of Mali, but it was not until the eighteenth century that Europeans took notice. In 1742 John Atkins, a British naval **surgeon**, first described its presence on the coast of Guinea. In 1803 Thomas Winterbottom (1765–1854), working in the newly organized colony for freed slaves in Sierra Leone, described the same disorder and noted the presence of enlarged cervical (neck) lymph nodes, later called “Winterbottom’s sign.” In the last quarter of the nineteenth century, when the European rush to colonize vast areas of Africa prompted large population shifts and severe economic disruption, infected Africans and colonists introduced many new cases of sleeping sickness into virgin tsetse fly areas, creating epidemic conditions. Mortality estimates in central Africa in the years 1895–1905 run as high as 500,000. In 1901 a huge epidemic of sleeping sickness, possibly of the *rhodesiense* type, broke out on

the north shore of Lake Victoria and eventually took about 200,000 lives. During this outbreak, Aldo Castellani (1874–1971), a bacteriologist and member of a team sent by the London School of Tropical Medicine to investigate, first found trypanosomes in the spinal fluid of victims. Further work, encouraged by the arrival in Uganda of David Bruce (1855–1931), a British doctor who had discovered trypanosomes as the cause of an African cattle disease called “nagana,” clarified their importance. Trypanosomes were also found in cases in West and Central Africa.

By 1909 the full cycle of the parasite in *Glossina* flies was elucidated. In subsequent decades the disease distribution was more clearly mapped, and its two forms established. Control measures were instituted, and the epidemics subsided, though later relaxation of surveillance resulted in subsequent outbreaks. Early treatment with atoxyl, an arsenic derivative important also in the history of syphilis treatment, was moderately effective but could cause blindness. Bayer 205 (Germanin) and tryparsamide followed, and Melarsoprol, currently in use today, was developed in the 1940s. Eflornithine, originally developed as a possible anti-cancer drug, became available in the 1980s for late stage *gambiense* disease.

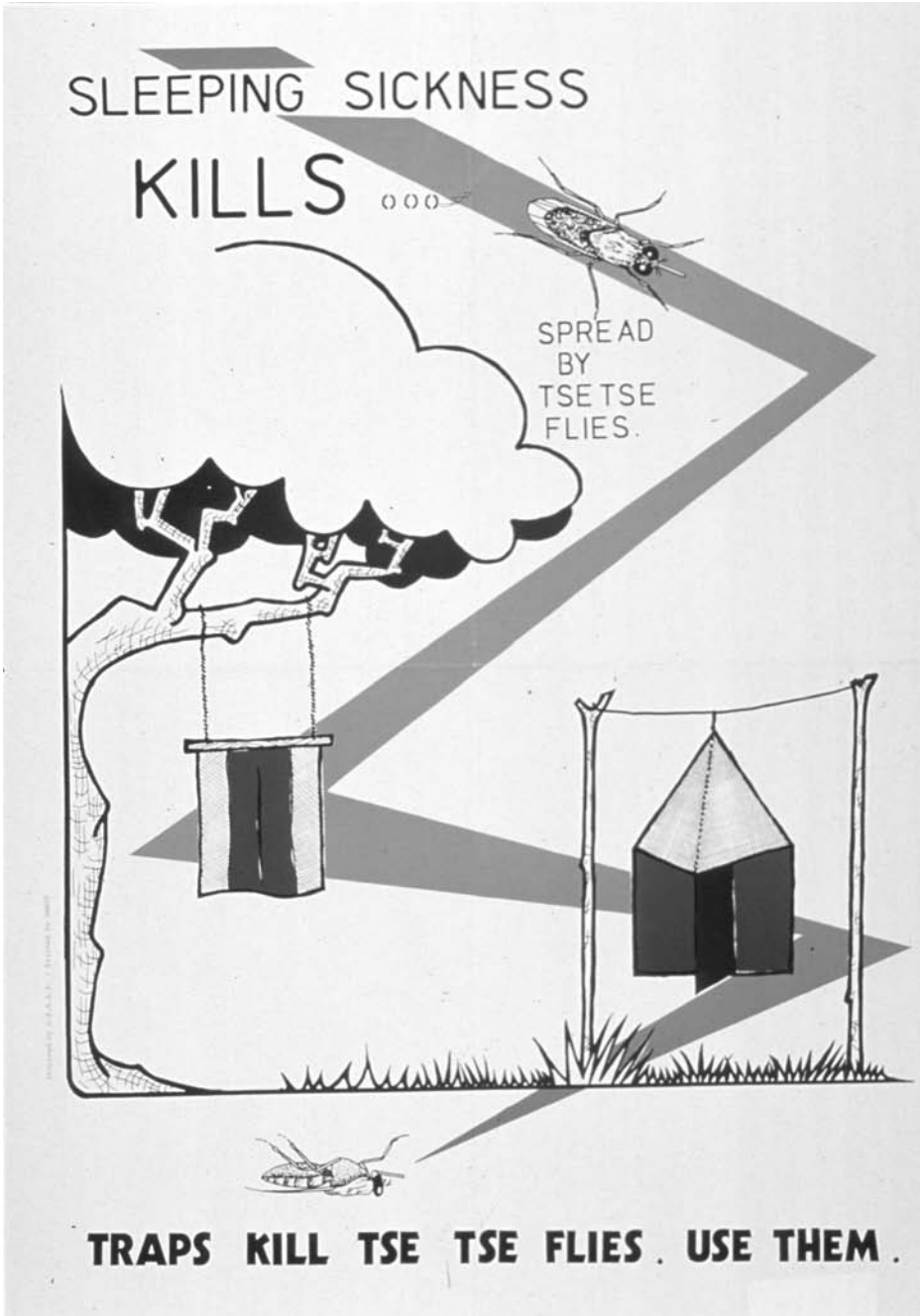
Organism and Vector. *Glossina* (tsetse) flies live in vegetation around rivers and lakes and do not venture far away, which accounts for the localized nature of disease distribution. The protozoa enter the digestive tract of the fly when the fly bites and sucks the blood of an infected victim. The protozoa multiply in the fly’s midgut and migrate to the salivary glands where they develop to an infective stage 18 to 35 days after initial feeding. New bites introduce the organisms into new hosts, where they circulate as motile forms characterized by a flagellum and undulating membrane, which propel them. They also migrate to lymph nodes and eventually to the central nervous system (CNS).

Parasites often cause harm over a period of time because they have mechanisms to survive for a long time in their “host.” For survival in the host’s body, the trypanosome’s outer membrane is coated with a layer of “variant surface protein” (VSP) that protects it from the host’s immune system. The human host manufactures antibodies to attack the protein, only to find that the parasite can produce new variants of this protein.

Pathology and Clinical Disease. Two different human organ systems are particularly affected by sleeping sickness. Early in the disease, the victim’s lymph nodes and spleen enlarge as a result of inflammation induced by the parasite. All three layers of the heart suffer an inflammatory reaction, including the conduction system that governs the heart’s contractions. Inflammatory changes in the central nervous system involve the covering layers of the brain and around blood vessels, leading to clots, small hemorrhages, and localized areas of inflammation.

Different strains of the organism lead to different disease patterns. *T. b. gambiense* infection follows a chronic course. For months to years victims have no symptoms, even though trypanosomes may be found in blood or lymph nodes. At some point nonspecific symptoms appear, consisting of mild fever, headaches, and fatigue, which come and go. During this phase the lymph nodes begin to enlarge, especially in the neck (referred to as Winterbottom’s sign). Only years after onset, the symptoms of **encephalitis**—decreased thinking ability, sleepiness, tremor, and sometimes psychosis—gradually appear. Eventually severe somnolence prevails, the victim becomes wasted from poor nutrition, and he or she often succumbs to pneumonia.

T. b. rhodesiense infection, however, is a more acute disease, lasting weeks to months. Initially a dark red, painful swelling (chancre) around the tsetse fly bite can appear and



Poster distributed by the African Medical and Research Foundation in Nairobi, Kenya displaying that the use of traps kills tsetse flies that spread sleeping sickness. Courtesy of the National Library of Medicine.

last two to three weeks. With or without a chancre, fever begins within one to three weeks of the bite. Lymph nodes may enlarge. Invasion of the CNS follows fairly shortly, characterized by headache, then signs of encephalitis (as noted above) which progress more rapidly to death. An irregular, faintly pink rash may be seen in lighter skinned persons.

Diagnosis and Treatment. Today the diagnosis of sleeping sickness is made with a combination of clinical and laboratory findings. Some factors—geographic location, the chancre and rash (if visible), and enlarged lymph nodes—remain important features in suspecting sleeping sickness, but specific diagnosis rests on demonstrating the presence of the parasite. Treatment of trypanosomiasis is still difficult because we do not have simple, nontoxic medicines that kill the parasites.

Epidemiology and Control. Sleeping sickness is acquired only where tsetse flies live and is therefore what epidemiologists term a “focal disease.” Larger outbreaks occur when parasite-infested individuals move into uninfected tsetse fly areas and/or when control efforts are neglected. The two types of sleeping sickness do not overlap, and Uganda is the only country where both are found (in different foci). Animals constitute the major reservoir of *rhodesiense*, whereas humans (and to some extent pigs) are reservoirs of *gambiense*. Control efforts have utilized a combination of finding and treating cases, fly trapping, clearing of fly breeding areas, and animal destruction. Today most programs emphasize case finding and treatment, coupled with varying degrees of fly control. Because this disease is linked to specific vectors, controlling the flies during outbreaks helped to eliminate the disease from the Gambia, Senegal, Ghana, Sierra Leone, and Guinea-Bissau. Because of political unrest and lapse of control programs there was resurgence in central African states in the 1990s, peaking at over 37,000 reported cases in 1998 (estimated to be a fraction of the total). More recently, as a result of better control measures, the outbreaks have been subsiding rapidly. Vaccine development is unlikely because of the parasite’s ability to alter its VSP. Development of cheaper, safer drugs should put even more emphasis on case finding and treatment. *See also* Colonialism and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Pesticides; Urbanization and Epidemic Disease.

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J. GORDON FRIERSON

SMALLPOX. Smallpox is the only infectious disease that has been eradicated as a human infection by medical intervention. Smallpox was a disease characterized by fever and eruptive rash caused by infection with the *variola virus*, principally by *Variola major*, its most virulent form. *Variola* is a member of the poxvirus family and is a relatively large, brick-shaped, envelope-coated DNA virus. *Variola* has no other host than human beings, the characteristic that made smallpox a candidate disease to be eliminated from the human population. It was primarily transmitted to a new host via inhalation of droplets from an infected person at close range, although it was also possible to transmit the disease through contact with infected clothing or bedding.

After an incubation period of about 12 days, the onset of smallpox was abrupt and debilitating, marked by a high fever, headache, muscle and back pains, and occasionally vomiting and convulsions. Two to five days after onset, the characteristic rash erupted, and in a few more days, pustules formed. In uncomplicated cases, just over a week after the first eruptions, the pustules began drying and forming scabs. By the third or fourth week after onset of the disease, the scabs fell off, and the victim was well again with lifetime **immunity** to the virus.

Smallpox caused by *Variola major* had a mortality rate of 25 to 30 percent. Fatal cases progressed more rapidly and dramatically. Blood poisoning could lead to massive hemorrhaging into the skin and internal organs followed by rapid death. In other cases, the pustules, which appeared more densely on the face, the palms of the hands, and the soles of the feet than on the trunk, became confluent and signaled a lethal infection. The pustules often left a scarred or "pocked" face that marked the victim for the rest of his or her life. Smallpox could also cause blindness and male infertility.

In the late nineteenth century, a milder form of smallpox first appeared in southern Africa, later spreading to Brazil, North America, and parts of Europe. Caused by a less virulent strain of *Variola* known as *Variola minor*, its mortality rate was 1 percent or lower.

History. There are accounts of many ancient **epidemics** that might have been caused by smallpox, but none described the symptoms sufficiently to permit accurate diagnosis in hindsight. The first medical account comes from **Rhazes**, a ninth-century physician in Baghdad, who differentiated between smallpox and **measles** and described smallpox as a common, nonlethal disease of **children** in southwest Asia. Not until the sixteenth and seventeenth centuries in Europe did it emerge as a feared epidemic disease. There is debate among scholars as to whether *Variola major* mutated into a more virulent form at that time or whether previous diagnoses of smallpox were wrong.

Beginning in the sixteenth century, however, smallpox played a deadly role in the efforts of European nations to colonize other areas of the world. Native American tribes with no immunity were decimated as Spanish, Portuguese, French, and English explorers marched across North, Central, and South America. In 1630 native Siberians were decimated when Russian colonists triggered the first smallpox epidemic in that region. In 1713 the Dutch brought the disease to South Africa and decimated the native Khoikhoi, and in 1789 Australian aborigines were felled by smallpox after English settlers landed at Sydney.

Smallpox was also known in Asian cultures. By the thirteenth century, the Chinese practiced *variolation*—the **inoculation** of a healthy person with smallpox from a diseased person with the desire to cause a mild form of the disease, induce immunity, and prevent a possibly lethal case. Smallpox remained endemic in the cities of China and, like the Great Wall itself, served as a barrier against Mongols and others who might try to invade. Indeed, after conquering the western Mongols, the Chinese excused them from making obeisance to the Emperor in Beijing, accepting their tributes at sites north of the Great Wall in order to protect them from the disease.

It is not known exactly when or where variolation was developed, but by the early eighteenth century, it was being practiced by wealthy Europeans such as Lady Mary Wortley Montagu (1689–1762) and in colonial North America by the Massachusetts minister **Cotton Mather**. The practice was not embraced widely because there always remained the danger that an inoculated person could infect others and set off an epidemic.

Near the end of the eighteenth century, physician **Edward Jenner** noticed that variolation failed to produce symptoms in people who had previously contracted cowpox, and that milkmaids and others who contracted cowpox did not contract smallpox during epidemic outbreaks. Jenner conducted a trial of a procedure he termed “**vaccination**,” from the Latin word *vacca*, “cow.” He inoculated individuals with cowpox matter and later conducted traditional variolation. The variolation failed to produce any signs of illness in those vaccinated.

In 1798 Jenner published his results, and by 1801 more than 100,000 people in England had been vaccinated. Millions across Europe were vaccinated by 1815. In 1840 an act of Parliament made variolation illegal in England and empowered local officials to vaccinate the poor from public funds. Between 1853 and 1873, vaccination in England became compulsory, with civil fines levied for failure to comply. Prussia likewise pursued compulsory vaccination, and the result for both England and Prussia was the near **eradication** of the disease by 1900.

Resistance to compulsory vaccination grew in the last quarter of the nineteenth century. Anti-vaccinationists argued that healthy children should not be forcibly injected with an agent that caused cowpox. The smallpox vaccine, known officially as “calf lymph” and produced commercially by scraping infected matter from cowpox pustules from infected calves, was subject to contamination at many points in production. By 1895, the governments of France, Germany, Italy, and Russia had enacted laws requiring vaccines and antitoxins, known collectively as *biologics* or *biologic products* because they were injected into the human body, to be licensed by government laboratories. In the United States, however, no oversight was enforced until 1902, following the deaths of 13 children in one city who received **diphtheria** antitoxin contaminated with tetanus spores. Initially, the law required proof that the vaccine was not contaminated during production. In 1934 a further regulation was issued in the United States requiring proof that commercially produced vaccines were effective.

Edward Jenner realized that his cowpox vaccine had the potential to annihilate smallpox, even if it did not happen quickly. Smallpox vaccination eliminated the disease from Britain by 1940, from the United States by 1950, and from China by 1965. In 1972 the United States ended the routine use of smallpox vaccine. Ten years later, the vaccine was no longer even available to civilians in the United States, and in 1990 the U.S. Department of Defense discontinued vaccinating military recruits.

Since 1979 samples of *Variola major* have been maintained in freezers at the U.S. Centers for Disease Control in Atlanta, Georgia, and in the Moscow Research Institute for



The heavily pockmarked hands, legs, and feet of a smallpox victim on the Ivory Coast. WHO photo. Courtesy of the National Library of Medicine.

Viral Preparation's High Containment Laboratories. The genome of the virus has been sequenced, and numerous discussions have occurred about whether the frozen samples should be destroyed, lest they accidentally be released into a nonimmune population. After the terrorist attacks in the United States of September 11, 2001, and the anthrax attacks shortly thereafter, there was considerable fear that smallpox virus had been obtained and stored illegally and thus might be used as a **bioterror** agent. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 included provisions for supporting smallpox vaccine development. Vaccinations for first responders began in January 2003, but within months, concerns arose about vaccine safety after reports that some recipients had suffered fatal heart attacks. Congress enacted a vaccine compensation plan for those injured, but by June 2003, a Federal Advisory Committee on Immunization Practices recommended that the program be ended. Since that time, the United States and the **World Health Organization** have moved to establish stockpiles of smallpox vaccine in the event that *Variola major* is released as a bioterror agent. See also Animal Diseases (Zoonoses) and Epidemic Disease; Biological Warfare; Colonialism and Epidemic Disease; Diagnosis of Historical Diseases; Public Health Agencies, U.S. Federal; Smallpox Eradication; Smallpox in Canada and the United States since 1783; Smallpox in Colonial Latin America; Smallpox in Colonial North America; Smallpox in European Non-American Colonies; Smallpox in Premodern Europe; Smallpox in the Ancient World.

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VICTORIA A. HARDEN

SMALLPOX AND THE AMERICAN REVOLUTION. By 1775 **smallpox** had long been endemic in England, but colonials were rarely immunized against it by natural exposure as children. Adults could be inoculated and suffer a weak but **immunity**-conferring case, but this required a four-week **quarantine** while the patient was contagious. Many of Continental Army General George Washington's (1732–1799) rural recruits had been isolated from the colonial urban outbreaks, and natural infection by the **virus** would send these men reeling, exacting a mortality rate of around 14 percent.

In the summer of 1775, at the outset of the **war**, Washington acted very cautiously as smallpox ravaged Boston, the British-held city around which his army was posi-

tioned. Knowing firsthand what damage smallpox could inflict, Washington did all he could to isolate his army from the disease that wracked the civilian population. “Camp followers” who cooked and did laundry underwent close medical scrutiny and surveillance. Access to American camps was restricted, and refugees from Boston were checked closely for signs of disease: he knew that the British might use infected citizens as a type of biological weapon. Above all, he refused to assault the city, a decision that prolonged the siege to nine months and allowed the redeployment of the British Army rather than its defeat or surrender. British troops had often been exposed to smallpox as children, and the besieged commanders had no issue with inoculating those who had not.

When British Commander General William Howe (1729–1814) finally evacuated Boston on March 17, 1776, Washington remained convinced that he had left the city poisoned with smallpox. Only troops who had been immunized were allowed to take the heights directly overlooking the city, and as late as July, only immunized or immune troops could enter liberated Boston. At first reticent to hobble his army with recuperating inoculation patients, Washington rapidly embraced the practice, and only 1 in 500 American troops died of the virus.

While Washington was settled in around Boston, the American Northern Army led by General Richard Montgomery (1736–1775) headed north to seize Montreal and Quebec and bring Canada into the war on America’s side. Had this ploy succeeded, Canadian provinces might have emerged as U.S. states. As with Boston, Quebec was suffering an outbreak of smallpox, and American leaders suspected spies of spreading the disease to the vulnerable American siege lines around the city. When the American assault took place on the night of December 30–31, 1775, 300 of the 1,100 colonials were laid up sick. The attack failed, and Montgomery was killed. American General Benedict Arnold (1741–1801) continued the siege, but smallpox and other diseases ravaged his shrinking army. Men succeeded in

GEORGE WASHINGTON’S ORDER TO INOCULATE RECRUITS FOR SMALLPOX (1777)

To Doctor William Shippen, Junior.

Head Quarters, Morristown, January 6, 1777.

Dear Sir: Finding the small pox to be spreading much and fearing that no precaution can prevent it from running thro’ the whole of our Army, I have determined that the Troops shall be inoculated. This Expedient may be attended with some inconveniences and some disadvantages, but yet I trust, in its consequences will have the most happy effects.

Necessity not only authorizes but seems to require the measure, for should the disorder infect the Army, in the natural way, and rage with its usual Virulence, we should have more to dread from it, than the Sword of the Enemy. Under these Circumstances, I have directed Doctr. Bond [Dr. Nathaniel Bond], to prepare immediately for inoculating this Quarter, keeping the matter as secret as possible, and request, that you will without delay inoculate all the Continental Troops that are in Philadelphia and those that shall come in, as fast as they arrive. You will spare no pains to carry them thro’ the disorder with the utmost expedition, and to have them cleansed from the infection when recovered, that they may proceed to Camp, with as little injury as possible, to the Country thro’ which they pass. If the business is immediately begun and favored with common success, I would fain hope they will soon be fit for duty, and that in a short space of time we shall have an Army not subject to this, the greatest of all calamities that can befall it, when taken in the natural way.

[Signed by Washington.]

From *The Writings of George Washington*, edited by John C. Fitzpatrick (Washington: U.S. Government Printing Office, 1931–1944) 6: 473–74.

inoculating themselves but failed to isolate themselves while infectious, spreading the disease to their comrades. Bostonian rebel John Adams (1735–1826) was prompted to write, “This pestilence completed our destruction.” American General John Thomas (1724–1776) took command in early May with some 1,900 men, about half of whom were sick at any given time; he, too, took ill and died after a month. Fully 30 percent of the American Northern Army died of disease, and the Americans were in full retreat from Canada by late June 1776.

In July 1781, British General Alexander Leslie in Portsmouth, Virginia, wrote to his colleague General Charles Cornwallis (1738–1805) in Yorktown: “Above 700 Negroes are come down the River in the Small Pox—it will ruin our market, which was bad enough before. I shall distribute them about the Rebell Plantations.” From the time of Benjamin Franklin (1706–1790) to the present colonial historians have believed this to mean that Leslie was going to use infected slaves to spread the pox. Recently, however, historian Philip Ranlet viewed this in a different light, interpreting Leslie to mean that escaped slaves who had caught the pox in Portsmouth would be returned to their owners, who presumably would have them isolated for recuperation. The harried British had no interest in weakened laborers and few supplies to spare for their care. When Leslie’s troops relocated to Yorktown, they left the ailing African Americans behind. Even so, some who accompanied Leslie were carriers and spread the disease further. Cornwallis expelled hundreds of sickened blacks as his own troops suffered from diseases other than smallpox, for which they had been inoculated. *See also* Colonialism and Epidemic Disease; Slavery and Epidemic Disease; Smallpox in Colonial North America; War, the Military, and Epidemic Disease.

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JOSEPH P. BYRNE

SMALLPOX ERADICATION. Smallpox is thus far the only infectious disease to have been eliminated by human activity from nature. Following an exhaustive study of documentation gathered from several countries where smallpox had been endemic, a Global Commission composed of international experts certified the disease eradicated in December 1979, after they felt confident enough to announce that there had been no cases in the world for two years. This momentous announcement, which many observers had considered impossible, was ratified by the 33rd World Health Assembly gathered in the **World Health Organization’s** headquarters in Geneva, Switzerland, in 1980.

It is generally accepted that the successful **eradication** of smallpox across the world was a result of an unprecedented level of international cooperation—apart from the World Health Organization (WHO), assistance was also provided by other United Nations’ agen-

cies like UNICEF; in addition, countries like the United States and the former Soviet Union provided financial and infrastructural aid on a global scale. Although the WHO played an important role as a manager of resources, directing personnel, vaccine, and money to national and local contexts where this assistance was required, a range of national public health and funding agencies made significant contributions as well. Although workers associated with a range of organizations were regularly posted to the WHO's headquarters or regional offices, several personnel continued to represent formally—and serve—the governments of the countries where systematic smallpox eradication efforts were initiated. All these efforts led to the creation of a series of carefully planned national smallpox eradication programs involving teams composed of international staff and local workers; the dedicated efforts of all these personnel, who came from a range of educational and social backgrounds, over the course of a period of more than a decade made the dream of smallpox eradication a reality.

The calls for the global eradication of smallpox were made relatively early within the WHO. During World Health Assembly meetings held as early as the late 1950s, officials representing the USSR started arguing that such a worldwide campaign was feasible. These calls were not ignored, and some senior officials in the WHO headquarters embarked on a relatively small feasibility study, involving discussions with officials associated with the regional offices and specific national governments. These engagements carried on right through the first half of the 1960s and revealed deep rifts in viewpoint, both within and outside WHO structures, about important elements of the proposed project. These included the shape and the timing of the planned smallpox eradication program, its funding modalities, and, not least, questions of management and leadership. This resulted in weak initial efforts in countries such as India. Although the country's federal authorities agreed to a series of proposals made by the WHO, the implementation of policies was whimsical. As a result, the goal of mass immunization against smallpox, which was generally seen in the early 1960s as the means of achieving eradication, was not met.

These trends resulted in a reexamination of the goals and the structures of the planned global smallpox eradication program. Relevant administrative structures within the



Positive reactions from two vaccinations leave visible scars on the arm of a little boy in Bangladesh. WHO photo. Courtesy of the National Library of Medicine.

WHO were revamped from the mid-1960s onward, leading to a series of personnel changes that would turn out to be crucial to the successful completion of the campaign. **Donald A. Henderson**, who was at that time associated with the U.S. **Centers for Disease Control (CDC)**, was posted to the WHO offices in Geneva and asked to set up a Unit to plan and manage a world program for the smallpox eradication. This went hand in hand with the reform of administrative structures in the WHO regional offices, whose personnel were encouraged to collaborate closely with Henderson and his team. These initiatives were accompanied by negotiations with funding agencies, vaccine donors, and national governments; efforts were consistently maintained to raise money and stocks of reliable smallpox vaccine, which were then promised by the WHO to different national governments in return for their cooperation. National governments and local donor agencies did, of course, also make crucial donations, in the form of vaccine and finance, at important junctures of the campaign. The result was the creation of a reenergized global smallpox eradication program from 1966 onward, straddling Latin America, Africa, and Asia.

Numerous technological and strategic adaptations helped move the eradication program forward. The availability of large stocks of heat-stable, freeze-dried smallpox vaccine proved an enormous boon. These prophylactics were donated in huge quantities by the USSR (to the WHO or to individual countries) and were also purchased from private companies like Connaught (Canada) and Wyeth (United States) for use across the globe; it is, of course, important to note that many of the countries with endemic smallpox also developed the capacity of produce freeze-dried vaccines, with assistance from countries like Denmark, the USSR, the United States, and the United Kingdom, and these stocks were also used to good effect in the program. Another major technological adaptation was the bifurcated needle, which allowed for two extremely important developments: the introduction of less painful immunization methods and the ability to make available stocks of vaccine last much longer. Yet another adaptation, which is generally considered to be crucial to the achievement of smallpox eradication, is the strategy of “surveillance-containment.” Accepting the principle that mass immunization was unnecessary after about 70 to 80 percent vaccinal coverage had been achieved, the strategy was based on the understanding that the main objectives were to find smallpox cases, isolate them, and then vaccinate all contacts. When this was achieved, it was argued and later proven, the chain of smallpox transmission could be broken and the disease eradicated. This strategy was utilized and refined in several contexts by CDC teams working in western Africa, and also by WHO-funded teams of national and international workers in the Indian state of Madras in the 1960s. In practice, surveillance-containment was adapted to the needs of myriad localities by teams of workers, after significant debates with the supporters of mass immunization (who were never completely silenced), in response to the needs and feelings of local collaborators and the civilian populations being targeted. Indeed, it was not unknown for teams of international workers to carry out mass vaccinations in the villages of South Asia in the 1970s; this was often in response to concerted civilian demand for immunization against smallpox, but there were also instances in which entire villages were surrounded and forcibly vaccinated.

These multifaceted efforts paid rich dividends. In countries like Brazil, Pakistan, India, Bangladesh, Ethiopia, and Somalia, smallpox had been endemic, had caused loss of life, and had also been the source of exportations of the disease to the Americas and Europe. Now, one after the other at different points in the 1970s, each was declared free of the errant *variola* virus. See also Measles, Efforts to Eradicate.

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SANJOY BHATTACHARYA

SMALLPOX IN CANADA AND THE UNITED STATES SINCE 1783. By 1783 **smallpox** already had a long history in British North America, but within the next two decades there would evolve a significant medical discovery that could successfully combat the disease. As a result of the work of **Edward Jenner** in England, a far safer and more reliable preventative was developed, one that injected harmless cowpox **virus** into a patient that would provide immunity from smallpox. Because of its source it became known as “vaccine,” and the process “**vaccination**.” After Jenner published his findings, in 1798 the treatment came to North America.

Jenner sent a copy of his report and some of the vaccine to a **physician** friend, the Rev. John Clinch (1749–1819) in Trinity, Newfoundland. He became the first person in North America to attempt vaccination, eventually performing the procedure on several hundred people, including his own child. The technique was lost in Trinity for a few years, but it was picked up in Massachusetts, where another of Jenner’s correspondents, a respected doctor named Benjamin Waterhouse (1754–1846), received both Jenner’s findings and a vaccine sample. In 1800 Waterhouse performed the first vaccination in the United States on his six-year-old son. He also wrote about and promoted Jenner’s system in the United States, and one of his contacts was President Thomas Jefferson (1743–1826), who subsequently began a personal correspondence with Jenner. Jefferson was completely won over to vaccination and became one of its strongest advocates.

Urban Epidemics of the Nineteenth Century. A number of American and Canadian cities experienced smallpox epidemics in the first half of the nineteenth century, including Philadelphia, Quebec City, Boston, and Baltimore. New York City suffered through nine outbreaks, the worst occurring in 1853–1854, that killed nearly a thousand people. Native Americans continued to die in large numbers from the disease, especially those in the Great Plains and on the west coast. There were two major pandemics among the native populations, the first in 1801 and the second in 1836–1840. The areas hit also included Mexican California, Russian Alaska, and British Columbia. Overall, an estimated 300,000 native people died.

Smallpox was a problem during the American Civil War, particularly in the South, which recruited unvaccinated soldiers and which possessed unreliable vaccine stocks. It did not help that new supplies of vaccine were stopped from entering the Confederacy because of the Union blockade of its coastline. By the end of the war, the situation had

become so desperate that variolation—purposeful infection with the variola virus—rather than vaccination had to be used, with very poor results. Smallpox spread to the North carried by freed slaves and by Confederate prisoners of war who were kept in transit camps and prisons in a number of northern states. One of the victims in the North was Abraham Lincoln (1809–1865) who fell ill while returning to Washington after having delivered the Gettysburg Address in November of 1863. Although it proved to be a mild case of the disease, he did develop a characteristic rash within two days and was unable to perform his duties for four weeks. Lincoln, of course, survived, but his black valet caught the disease and died. After the war, smallpox was carried all over the nation with returning soldiers and by a substantial movement of people, both black and white, that occurred in the war's wake.

In the latter nineteenth century, smallpox outbreaks increased in many areas of North America with the growing number of immigrants, particularly those from Europe. The disease could also be spread more expeditiously by the growing network of railroads that crisscrossed the continent. These factors played a role in the epidemics of the early 1870s that seemed to originate from the turmoil of the Franco-Prussian War of 1870–1871 and subsequent population movements spawned by it. Nearly 2,000 died of smallpox in Philadelphia in 1871, and 1,500 in Baltimore in 1872 and 1873. Other urban areas that suffered heavy losses included New Orleans (1872–1875) with 1,400 victims and New York City (1874–1875) with 1,700. Another wave of the disease occurred in 1881–1883 centering on the Midwest, the South, and New England, causing some health officials, especially in the last region, to enforce moribund vaccination regulations.

One reason for the relative failure of vaccination to stem smallpox outbreaks completely during the late nineteenth and early twentieth century was the continuing controversy surrounding the procedure. The growth and influence of anti-vaccination organizations, often led by medical men, had a negative impact on its universal use. There was a fear that vaccination could cause infections from other diseases, a phenomenon that occurred in a small number of cases. Linked to that was the age-old debate involving mandatory vaccination and its violation of **personal liberty** that could result in violent resistance. The problem tended to intensify with the swelling tide of immigrants coming into pre-World War I America and Canada. Many had not been vaccinated before and simply did not trust government encroachment into their lives.

Two famous smallpox outbreaks in the late nineteenth century brought this debate clearly and vividly into focus. Both Milwaukee in 1894–1895 and Montreal in 1885–1886 had to live through not only severe epidemics but also vigorous reaction to public health authorities who tried to combat the disease. In most American and Canadian cities, health officials had established a program of activities to deal with such a situation. They moved to stop the spread of smallpox by the use of mass vaccinations, the removal of victims to isolation hospitals, and the **quarantine** of infected families or businesses. Resistance to these policies first arose over whether the vaccinations were to be enforced by law. The isolation hospitals were unwanted in most neighborhoods, and victims saw them simply as horrible places where no one survived. Quarantines meant the limitation of freedom of movement, and for businesses, a loss of revenue. All these actions could lead to emotional resentment against the boards of health and police.

During the Montreal epidemic of 1885–1886 it was the French Canadian portion of the city's population that harbored doubts about vaccinations. The attempt by public health administrators to enforce necessary vaccinations to prevent the spread of disease

was met in the French wards with rioting and armed violence against police. There was well-publicized resistance to the forced removal of victims to the isolation hospital, especially the separation of infected **children** from their parents. Eventually troops had to be called out to restore order and to enforce the vaccination of over 80,000 people. In the end, within a city of 168,000 residents, over 10,000 had been infected with smallpox, and 3,164 had died. It proved to be Montreal's (and Canada's) last major smallpox epidemic.

A similar dislike of vaccination and isolation hospitals caused a reaction during the smallpox epidemic in Milwaukee in 1894–1895. Again, ethnic divisions motivated events as immigrants from Germany and Poland were vociferous in opposing the health board's policies. Riots broke out, health officers were attacked, and a political battle ensued in city council, where representatives of the ethnic wards successfully challenged the city's health commissioner. In the end, the powers of the health board were cut back, and a victory of sorts for the anti-vaccinationists was won. It was an example of how ethnicity and politics could dominate a smallpox epidemic.

A New Strain of Smallpox. Not all events involving smallpox at the end of the nineteenth century were so demoralizing. A genuine success story occurred in Puerto Rico soon after its capture and annexation by the United States at the conclusion of the Spanish-American War in 1898. A systematic vaccination drive was undertaken, and nearly 80 percent of the population was vaccinated. It meant that the island was one of the first areas of North America to eradicate smallpox from its society. Also, two years earlier, with little initial publicity, a major change emerged in the nature of the disease itself. A weaker strain of the virus, soon to be called *Variola minor*, found its way into mainland North America and would soon be far more prevalent than its virulent relative, *Variola major*. The increasing ubiquity and the uniform mildness of the new strain set the context for how smallpox epidemics would be dealt with into the twentieth century.

Variola minor was first reported in Pensacola, Florida, in 1896. Although it caused many of the signs of smallpox, it often did not cause serious illness. As a result, a person with *Variola minor* often continued to move around, not even knowing at first that he or she was carrying smallpox. Because of this, the strain spread very quickly across the United States and Canada. *Minor* could leave scars, but it was not nearly as disfiguring as *Variola major*. The new strain's mortality rate was approximately 1 percent, as opposed to the old strain's 15 to 30 percent. By the 1920s, *Variola minor* had become the most prevalent form of smallpox on the continent. From 1900 to 1939, the number of reported cases of *Variola minor* grew to 20 times that of *major*. Because of this, the numbers dying of smallpox declined sharply, from 20 percent in 1896 to 4 percent in 1900 to just 0.6 percent in 1906. These figures were reassuring, but they did not mean that the danger from smallpox was over.

The Twentieth Century. Epidemics of *Variola major* did continue to break out. The worst occurred from 1901 to 1903 in a number of large cities including Philadelphia, Boston, and New York. In the last city, a significant number of victims lived in various ethnic wards, and in Boston the outbreak resulted in an important pathological study of those who had died of the disease. Overall, there were 16,000 cases of *Variola major* across America and Canada, with over 3,500 deaths. It was a shocking throwback to the outbreaks of the nineteenth century. In addition, *Variola major* was still active in Mexico, and from its base there, the strain was imported to the United States. From 1915 to 1929, there were 23 occurrences of *Variola major* in the United States, 14 of which had originated in Mexico. Also, it became clear that the two strains could appear at the same time in different regions of the continent.

The last great wave of epidemic smallpox in the United States and Canada took place during the 1920s. Hundreds of thousands of cases of *Variola minor* were reported, and in 1924–1925, 7,400 cases of *Variola major*, especially in cities such as Cleveland, Pittsburgh, and Detroit. The latter epidemic also spilled over the border into Windsor, Canada. During the twenties, a clear pattern for vaccinations became evident. In the face of a *V. Major* attack, the number of vaccinations increased dramatically; with a *Variola minor* outbreak, they increased very little.

In 1926 there were two well-publicized outbreaks of smallpox in the United States with an epidemic of *Variola minor* in Florida and one of *Variola major* in California. In that year, Florida was experiencing a significant decline from the land-boom era of the early twenties. One of the last things that promoters of the state wanted to hear was that a possible smallpox epidemic was afoot. Nonetheless, Florida eventually recorded 2,525 cases, more than any other state in the union during 1926. Still, the Florida epidemic was at least *Variola minor*; California was not so lucky. That state had the second largest number of smallpox cases with 2,432, and unfortunately it was the *Variola major* variety. Only six people had died in the Florida epidemic, but 231 died in California. Therefore, *Variola major* could still strike and still kill, but during and after the 1920s, *Variola minor* continued to dominate, and the number of outbreaks of both strains continued to decline.

In the post–World War II era, smallpox became much less of a threat. There were still outbreaks in Mexico, and on occasion even *Variola major* could be brought into the United States from there. For instance, this happened in 1947 when a businessman arriving from Mexico arrived in New York City carrying *Variola major*. In response, over 6 million residents of the city were vaccinated, and 12 people died. The last reported outbreaks of either strain in the United States or Canada was in 1949. In 1950 the Pan American Sanitary Organization moved to eliminate smallpox from all of the Americas. By the end of 1958, the disease had been eliminated in North America.

In 1980 the **World Health Organization** announced that following a long eradication process the world was now free of smallpox. Previously, in 1972, the United States and Canada had already ended the policy of smallpox vaccination, arguing that it was simply no longer necessary. Thus, after that year, for the first time since Jenner, North Americans would no longer need to procure their own immunity. However, if smallpox ever reappeared, the U.S. and Canadian populations would be nearly as vulnerable to the disease as the native people had been prior to the arrival of Europeans. It was this sobering fact, coupled with the fear of the use of bioweapons by terrorists, that raised concerns during the 1990s. Outside of the two official repositories of smallpox virus in the United States and Russia, were there any other samples that could have gotten into the wrong hands? After 9/11 these fears heightened considerably, beginning a move back to reactivating programs of ring, and even mass, vaccinations.

By 2006 the United States had produced and stockpiled enough smallpox vaccine to vaccinate every person in the country. Also instituted was a policy of vaccinating frontline personnel who would have to deal with an outbreak in an emergency situation. Incredibly, because of the difficult and dangerous milieu of the twenty-first century, the ancient, dreaded disease of smallpox has been placed back into the spotlight once again. See also Biological Warfare; Bioterrorism; Colonialism and Epidemic Disease; Public Health Agencies, U.S. Federal; Race, Ethnicity, and Epidemic Disease; Smallpox Eradication; Smallpox in Colonial North America; Trade, Travel, and Epidemic Disease.

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ERIC JARVIS

SMALLPOX IN COLONIAL LATIN AMERICA. Smallpox, commonly known as *viruelas* in Spanish America and *huitzahuatl*, translated awkwardly by the Spanish as "great leprosy," (*lepra*; measles was "little leprosy") among the Aztecs of Mexico, first appeared on the island of Hispaniola in 1518. From there, the disease spread throughout the Caribbean and onto the Mexican mainland by 1520. During the sixteenth, seventeenth, and eighteenth centuries, major epidemics of smallpox occurred every 10 to 20 years throughout the Spanish and Portuguese colonies. The most severe outbreaks often claimed 25 to 50 percent of those infected, leading to long-term demographic decline among native populations in many areas. The introduction of smallpox and other previously unknown diseases, in conjunction with the violence of European conquest and colonization, ultimately led to drastic cultural, economic, political, and social changes in indigenous societies throughout Latin America.

Historical Record. The nature and scope of the evidence available on epidemics of smallpox in colonial Latin America varies widely by region. In general, the most numerous and detailed accounts, especially for the sixteenth and seventeenth centuries, come from central Mexico and the Andean highlands, areas with the largest indigenous and European populations. Jesuit missionaries in Brazil also recorded detailed descriptions of a number of outbreaks during the second half of the sixteenth century.

The historical record also varies over time, as the number of descriptions and the amount of detail included tended to increase throughout the colonial period. Although a few illustrations by indigenous and European artists survive, almost all of what we know about the history of smallpox in colonial Latin America comes from documents written by Europeans. Some of these documents include eyewitness accounts, whereas others are based on secondhand reports. In some areas such as the Andean highlands of the Inca Empire, the historical record includes transcriptions of oral traditions describing possible epidemics of smallpox that occurred shortly before the arrival of Spaniards in the early 1530s. European explorers, conquerors, settlers, and priests wrote many of the earliest accounts, and, especially in colonial Spanish America, government officials often included information on outbreaks of smallpox and other diseases in their reports.

Some of the earliest accounts are brief and include only vague descriptions of the symptoms of the disease. As a result, confusion often exists as to the exact disease responsible

for some of these epidemics. Similarly, many descriptions contain only vague references to rates of mortality and morbidity, whereas others do not include any references to death rates at all.

The introduction of the smallpox virus to the Americas triggered a series of virgin-soil epidemics that resulted in extremely high rates of morbidity and mortality. Sixteenth-century accounts described skin eruptions that covered the bodies and faces of the sick, and several illustrations also depict the pustules characteristic of the disease. Other symptoms included fever and body pain, and in some areas severe nosebleeds were also common. Most victims died within days of manifesting symptoms. Records indicate that the disease spread rapidly and widely and that the majority of individuals in infected, indigenous communities became ill, with mortality rates averaging between 25 and 50 percent.

Origins and Spread. The first documented appearance of smallpox in the Americas occurred in 1518 when the disease was introduced from Europe onto the island of Hispaniola. According to several witnesses, the disease spread quickly, claiming one-third of the native population. Some Spaniards also became ill, but according to all accounts, none died. The fact that smallpox had not arrived earlier in the New World is not surprising since the *virus* requires three weeks to complete its cycle—a ten- to twelve-day incubation period, followed by the onset of illness, including the appearance of a rash or pustules, that often lasted two weeks. Lengthy transatlantic voyages and childhood immunities already acquired by most Europeans delayed the transfer of the disease to the New World for over two decades. On Hispaniola, this first epidemic of smallpox coincided with the forced resettlement of natives into communities closer to Spanish towns, and the violence and disruption resulting from this policy significantly exacerbated mortality rates once the epidemic had begun.

From Hispaniola, the disease spread to the neighboring islands of Puerto Rico, Jamaica, and Cuba, where it left a similar path of devastation. In 1520 smallpox arrived in Mexico with the expedition of Panfilo de Narvaez (1470–1528), dispatched by the governor of Cuba to arrest Hernán Cortés (1485–1547), the soon-to-be conqueror of the Aztecs. Although some accounts blame the introduction of smallpox in Mexico on an African slave, others argue that the infection arrived with natives from Hispaniola who accompanied the Narvaez expedition. The epidemic, which claimed between 25 to 50 percent of the population according to several accounts, broke out during the Spanish siege of the Aztec capital, Tenochtitlán, claiming the life of the Aztec emperor, Cuitlahuac (r. 1520), and many Indian nobles. The power vacuum that resulted from the deaths of Aztec leaders during the epidemic led to a collapse of political authority and organization, and as a result, many enemies of the Aztecs allied themselves with the Spanish. In addition to the catastrophic loss of life that resulted from both warfare and disease, the collapse of Aztec imperial authority played an important role in Spain's defeat and subjugation of the Aztecs.

From central Mexico, the epidemic spread out, moving south into Central America, where an epidemic, possibly of smallpox, claimed the lives of many Guatemalans in 1520–1521. Whether or not smallpox continued south through Central America at this time is not clear, but one historical account states that the disease was responsible for an epidemic that occurred in Panama in 1527.

The arrival of smallpox in South America is less clearly documented. Some scholars have argued that in the decade following its introduction to the Caribbean, small-

pox became **pandemic**, spreading throughout large sections of the Americas, eventually reaching as far south as the Andes. Both Spanish and Inca chroniclers recorded the impact of an epidemic that occurred several years before the arrival of Europeans. According to these accounts, the disease arrived in the Inca Empire sometime between 1524 and 1530, claiming a significant portion of the population, including members of the Inca royal family. This set off a civil **war** that ultimately weakened the political structure of the empire and contributed to its conquest by the Spanish several years later. In this case, smallpox could have arrived along the coast of Peru on ships coming from Central America; or the infection could have arrived overland from Panama.

Permanent Portuguese settlement of the Brazilian coast began in the 1550s, and the first recorded epidemic of smallpox in Brazil occurred in 1562, although it is possible that the disease may have arrived earlier. Indigenous residents of the missions and those enslaved on Bahia's sugar plantations succumbed in large numbers, leading to severe labor shortages. Labor shortages led to dwindling food supplies, starvation, and further increases in mortality. According to eyewitness accounts, between 25 and 50 percent of the native population died as a result of this initial epidemic.

Because virgin-soil epidemics of smallpox appeared in conjunction with Spanish and Portuguese campaigns of conquest and colonization, the stresses on indigenous populations were extreme. In many cases, basic social services such as the provision of food and **water** broke down completely, increasing morbidity and mortality rates. Throughout the colonial period, major epidemics of smallpox broke out every 10 to 20 years, providing sufficient time between episodes to allow partial recovery of native populations. When the next wave of the disease struck, individuals born since the previous epidemic proved especially susceptible. Although Europeans and Africans also succumbed to the smallpox **virus**, many possessed at least partial immunity to the disease, owing to its presence among Old World populations for many generations. As a result, the infection was often less severe, with correspondingly lower rates of morbidity and mortality.

Individual and Societal Reactions. Both Native Americans and Europeans interpreted epidemics of smallpox and other infectious diseases as divine punishment. But whereas Europeans believed that their Christian god was responsible for sending epidemics of smallpox among nonbelievers, for indigenous peoples the situation was more complicated. Following their conquest by Europeans, two sets of gods, Christian and indigenous, had the power to inflict punishment, and thus both had to be propitiated. Terror, confusion, and despair, all common human reactions to catastrophic events, were frequently noted among Native American populations, especially during the sixteenth and seventeenth centuries. And in several areas, messianic movements appeared in response to the turmoil created by war and disease. When smallpox first appeared in Brazil in 1562, for example, a messianic movement, the *Santidade*, attracted many Indians and slaves with promises of turning masters into slaves and slaves into masters. During this same period, a similar movement appeared in the southern highlands of Peru, posing a serious challenge to Spanish authority in the region. European observers often commented on the tendency of natives to flee in an attempt to avoid infection. This strategy had the consequence, however, of spreading the disease more widely and quickly.

For their part, Europeans responded to epidemics of smallpox in a variety of ways: priests organized religious processions and ministered to the sick and dying, whereas government officials and wealthy citizens often collected donations for charity hospitals. In response to a particularly severe outbreak in 1589, the viceroy of Peru issued a series of specific medical instructions intended to help regional governments mitigate the impact of the epidemic. On the advice of several Lima **physicians**, the viceroy ordered local officials throughout the Andes to **quarantine** all native communities in the hope of preventing the spread of the disease. He also recommended specific medical measures including bleeding and a **diet** of meat as preventative measures, and he urged families to limit contact in order to avoid spreading infection among themselves. Quarantines proved largely unenforceable, however, and as a result, Spanish and Portuguese officials seldom attempted to implement them.

Historical Effects. The introduction of smallpox and other diseases of Old World origin transformed the complex disease environment of the Americas to one of extreme virulence by the middle of the sixteenth century. The devastation wrought by the introduction of smallpox and other diseases from the Old World, in conjunction with the depredations of European **colonialism**, ultimately reduced most Native American populations by 75 percent or more during the course of the colonial period. This demographic catastrophe triggered many wide-ranging alterations in the social, political, and economic order of indigenous life. Waves of native migration throughout Latin America transformed both communities and families. Because adult males often chose to abandon home and family in response to the crushing fiscal and labor demands of colonial settlers, female heads-of-household became more common, and birth rates dropped in many areas. In the wake of major epidemics, labor shortages often materialized, leading to dwindling food supplies and rising prices. In addition, the crisis precipitated by European colonialism also transformed indigenous political structures, as colonial officials replaced traditional native leaders with individuals willing to collaborate with colonial administrators. The long-term impact of the introduction of smallpox and other diseases from the Old World was drastic population decline and traumatic social change within indigenous societies throughout colonial Latin America. *See also* Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Flight; Historical Epidemiology; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria in the Americas; Measles in the Colonial Americas; Religion and Epidemic Disease; Slavery and Epidemic Disease; Smallpox in Colonial North America.

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SUZANNE AUSTIN

SMALLPOX IN COLONIAL NORTH AMERICA. Before 1492, North America was free from **smallpox**. Because the *variola virus* had to be transmitted from an actively ill patient to a fellow human via breath, touch, or material contaminated with the virus, the Atlantic and Pacific Oceans had served as effective barriers to the spread of smallpox from the Old World.

Beginning with Christopher Columbus (1451–1506), however, each shipload of European colonizers and their African slaves to arrive in the Western Hemisphere became a potential vector of the disease. Very soon, the Americans learned to recognize the symptoms so well-known in Europe, Africa, and Asia: an intense fever and headache, pain in the midsection, a thoroughly justified sense of dread, and the characteristic rash of pustules (the pox) that especially attacked the face, palms, soles, back, and the mucous membranes of mouth and nose.

Lacking the genetic resistance common among groups in which smallpox had been endemic for centuries, American native populations constituted “virgin soil” for the virus. They often suffered the disease in its worst forms, and they died in terrible numbers. Although the American-born children of Europeans and Africans were somewhat more likely than Amerindians to survive smallpox (often with disfigurement and blindness), each new generation to grow up without exposure to smallpox represented a large pool of possible victims for the next outbreak.

Smallpox in Fifteenth-, Sixteenth-, and Seventeenth-Century North America. Within 15 years of Columbus’s first voyage, the first recorded American outbreak of *viruela* (the Spanish term) in 1507 proved deadly to the Arawak people of the Caribbean. The 1519–1520 epidemic, carried from Cuba to Mexico by a slave in Hernán Cortés’s (1485–1547) army, enabled Cortés to conquer Mexico City. Two decades later, the Spanish chronicler, Fray Toribio Motolinía (d. 1568) wrote that “in most provinces more than half the population [had] died,” and still more had perished from starvation “because, as they were all taken sick at once, they could not care for each other.” That pattern was repeated in native American communities for centuries to come.

Hernando de Soto’s (1496–1542) 1539 expedition carried smallpox inland to native populations from Florida to the Carolinas, and westward to the Mississippi and Texas. The Spanish slave trade, soon joined by the Dutch, French, and English, was a continuing source of new smallpox infections in the New World.

England’s first attempts at American settlement in the 1580s may have brought smallpox to North Carolina and the Chesapeake Bay: both the English settlers and the Algonquins observed that Indian villages near the Roanoke colony were struck by fatal fevers a few days after visits from the English. Although Jamestown seems to have escaped smallpox until the late seventeenth century, smallpox is often blamed for the death of the most famous figure in Jamestown history, Pocahontas (1595–1617), who was struck down just as she was about to return from London to her native Virginia. John Lawson (1674–1711), the surveyor-general of North Carolina, declared in his *Account of the Indians of North-Carolina* (London 1709), “The Small-Pox and Rum have made such a Destruction . . . that, on good grounds, I do believe, there is not the sixth Savage living within two hundred Miles of all our Settlements, as there were fifty Years ago” (Lawson, 140).

Shortly before English colonists arrived in New England in 1620, an **epidemic** of “sores”—quite possibly smallpox brought by English fishermen—killed thousands of Narragansetts. In 1634, the Narragansetts were further devastated by confluent smallpox, the worst form. Although both the Pilgrims and the Puritans suffered from deadly smallpox

WILLIAM BRADFORD DESCRIBES SMALLPOX AMONG THE NATIVES IN MASSACHUSETTS (1633)

This spring, also, those Indians that lived aboute their trading house there fell sick of the small poxe, and dyed most miserably; for a sorer disease cannot befall them; they fear it more then the plague; for usually they that have this disease have them [pocks] in abundance, and for wante of bedding and linning and other helps, they fall into a lamentable condition, as they lye on their hard matts, the poxe breaking and mattering [suppurating], and runing one into another, their skin cleaving (by reason therof) to the matts they lye on; when they turne them[selves], a whole side will flea of at once, (as it were,) and they will be all of a gore blood, most fearfull to behold; and then being very sore, what with could and other distempers, they dye like rotten sheep. The condition of this people was so lamentable, and they fell downe so generally of this diseases, as they were (in the end) not able to help on another; no, not to make a fire, nor to fetch a litle water to drinke, nor any to burie the dead; but would strivie as long as they could, and when they could procure no other means to make fire, they would burne the woden trayes and dishes they ate their meate in, and their very bowes and arrowes; and some would crawle out on all foure to gett a litle water, and some times dye by the way, and not be able to gett in againe.

From *Bradford's History of Plymouth Plantation, 1606–1646, Vol. 6, Original Narratives of Early American History*, edited by W. T. Davis (Charles Scribner's Sons: New York, 1908), pp. 312–13.

outbreaks (on shipboard and in five major episodes in Boston between 1630 and 1702), they regarded smallpox's continuing mortality among the native inhabitants as a sign of God's blessing on their own colonial enterprise.

In the Mid-Atlantic colonies, settled by the Dutch, Swedes, French Huguenots, Germans, and English Quakers during the seventeenth century, a 1633 smallpox epidemic proved disastrous to the Pequots and Lenape. Pehr Kalm (1716–1779), a Swedish naturalist who visited the Delaware Valley in 1748–1751, ascribed the disappearance of Indians from the region chiefly to smallpox, unknown before the Europeans came. He added the grim detail that wolves devoured the corpses and attacked the survivors.

In New France, smallpox came with French settlers as early as 1616 and quickly spread to the Maritimes, along the St. Lawrence River, and to the Great Lakes. The Hurons associated smallpox with the French Jesuit missionaries and with the nuns who provided care in Québec's first hospital. The French government's plan to

improve relations with the Labrador "Esquimaux" by educating some of their children ended when all the children died from smallpox.

Smallpox in Eighteenth-Century North America. Although figures are uncertain, it appears that the rapid rise in immigration, settlement, trade, and warfare in eighteenth-century North America was accompanied by an increase in the number and geographic spread of smallpox outbreaks. Outbreaks typically began in crowded ports with arrival of a ship carrying someone infected with smallpox. The 10- to 14-day incubation period gave people who unwittingly harbored the virus time to travel many miles by water, road, or trail before the first symptoms struck. For the next two to three weeks of sickness, they, the air they breathed, and everything their bodies touched was a danger to others.

Boston's colonial records show that, out of every 1,000 inhabitants, 37 died from smallpox in an ordinary year. In 1721, the city's worst eighteenth-century epidemic, that rate nearly tripled. Among the approximately 10,000 residents who stayed in the city (1,000 had fled), more than half fell ill, and more than one in seven died: 844 deaths among 5,900 cases of smallpox over the course of a year. Presumably most of those who did not fall ill had survived earlier exposure to the disease.

The 1721 epidemic is notable for the first use of **inoculation** (also called variolation) in North America to prevent smallpox. Of the 244 Bostonians who tried the controversial new method advocated by the minister-scientist **Cotton Mather** and carried out by Dr. Zabdiel Boylston (c. 1677–1766), only six died (anti-inoculation **physicians** disputed Boylston's figures).

The troop movements and battles on the fronts of the French and Indian Wars (1754–1760) brought smallpox inland in the mid-eighteenth century. The British commander-in-chief, Lord Jeffrey Amherst (1717–1797), is notorious for urging the deliberate spread of smallpox among Indians. Both the English and the French used the **biological warfare** technique of introducing infected prisoners or blankets among the enemy at least once.

Despite the increasing use of inoculation as a private and public health measure, smallpox continued to spread through North America. Documenting the 1775–1782 outbreaks that reached much of the North American continent (Mexico to Northern Canada, the Eastern seaboard, the Great Lakes, the Great Plains, and the Northwest coast) in 1775–1782, the historian Elizabeth A. Fenn argued that smallpox was so rampant that the pestilence should be regarded as a pandemic. Moreover, coinciding with the Revolutionary War and propelled by it, the pandemic had an impact on history that was as far-reaching as the war and American independence. Smallpox unquestionably affected the conduct of the American Revolution. British soldiers in the war were either immune or inoculated in England, but thousands of American Indians and slaves recruited to the Loyalist side died miserably from smallpox. General Charles Cornwallis's (1738–1805) inability to draw on these troops was a major factor in his surrender at Yorktown in 1782.

At the outset, the Continental Army had been far more vulnerable than the British to smallpox. The future President John Adams (1735–1826) blamed the failure of the 1776 siege of Québec on the “Cruel small Pox” that had killed an American general and forced the Americans into “precipitate Retreat.” Nonetheless, General George Washington (1732–1799), who had survived the disease as a young man, resisted inoculating his soldiers for fear that the English would descend on the weakened army. Facing a smallpox outbreak in January 1777, Washington declared he had “more to dread from it, than from the Sword of the Enemy.” Even then he did not order his recruits to be isolated for the month required to go through inoculation until harsh winter conditions prevented the British from taking advantage of the situation.

Treatment and Prevention. Neither the Native American healer nor the physician trained in European medicine could offer any effective treatment to smallpox victims. Traditional Indian methods of relieving fever by sweat-baths and cold plunges seemed to increase their mortality from smallpox, European observers felt. In the first medical work published in British North America, *A Brief Rule to Guide the Common-People of New-England How to Order Themselves and Theirs in the Small-Pocks, or Measles* (Boston, 1677), the pastor-physician Thomas Thacher (1620–1687) advised fellow Bostonians during an epidemic to keep patients in cool rooms and give them a simple **diet** of cool drinks, corn-meal gruel, and boiled apples. Adapting the advice of his English contemporary Dr. **Thomas Sydenham** (who in turn had followed the medieval Muslim physician, **Rhazes**), Thacher warned against bloodletting, purges, vomits, and other common European treatments of fevers.

To protect their communities, colonial authorities tried to impose quarantines on incoming travelers and sometimes set guards on households where the disease had struck.

A self-imposed isolation stopped young men from going to European universities where they would be almost certain to encounter smallpox. Colonial Americans understood that smallpox survivors could not catch the disease again or spread it. Consequently, slave-owners paid a premium for African slaves whose pockmarks testified to immunity. (Pockmarks also served to identify runaway servants, slaves, and criminals.)

Early in the eighteenth century, Cotton Mather learned from two very different sources about the **folk** practice of inoculation—the deliberate insertion of a bit of smallpox scab or pus under the skin to induce a mild case of the disease. His slave Onesimus described his own inoculation in Africa, and Mather read reports of successful inoculations in Turkey and Greece, published in the scientific journal *Philosophical Transactions of the Royal Society* in 1714 and 1716. Throughout the eighteenth century, American families, officials, and physicians argued over the risks of inoculation. The hoped-for mild case could turn deadly. The artificially induced case was as contagious as smallpox contracted “in the natural way” and just as dangerous to the susceptible bystander. Inoculation was expensive in doctor’s fees and time lost from work. (Rhode Island’s delegate to the Continental Congress in Philadelphia felt he could not spare the time—and died during Philadelphia’s 1774–1776 outbreak.) To many, inoculation seemed an unnatural, impious challenge to God’s will. Massachusetts, Virginia, and the cities of Charleston and New York severely restricted or banned inoculation. Elsewhere, inoculators set up makeshift isolation hospitals where their patients could “go through” the illness.

These arguments lost force with Dr. **Edward Jenner’s** breakthrough discovery of **vaccination**. North Americans quickly recognized that vaccination was far simpler, safer, and surer than inoculation. Six months after Jenner’s first experiment in 1796, his former schoolmate Dr. John Clinch (1749–1819) received samples of the vaccine and began vaccinating patients in Newfoundland—well before Dr. Benjamin Waterhouse (1754–1846) of Boston read Jenner’s *Inquiry into the Causes and Effects of the Variolae Vaccinae* (1800) and actively promoted vaccination in the United States. As early as 1803, a humanitarian medical mission brought the vaccine to Abenaki communities in Upper Canada, and the Balmis Expedition supplied it to the Caribbean and Mexico. Although smallpox continued to be a major threat to health into the twentieth century, the first step in **smallpox eradication** in the American colonies and former colonies had been taken. *See also* Colonialism and Epidemic Disease; Contagion and Transmission; Latin America, Colonial: Demographic Effects of Imported Diseases; Race, Ethnicity, and Epidemic Disease; Slavery and Epidemic Disease; Smallpox and the American Revolution; Smallpox in Canada and the United States since 1783; Smallpox in Colonial Latin America; Smallpox in Premodern Europe; Trade, Travel and Epidemic Disease; War, the Military, and Epidemic Disease.

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KAREN MEIER REEDS

SMALLPOX IN EUROPEAN NON-AMERICAN COLONIES. The age of European discovery and expansion began in the late fifteenth century, at a time when the dreaded disease **smallpox** was common if not endemic in Europe. Spanish, Portuguese, French, and English explorers and colonists, and infected African slaves, brought smallpox to the New World of the Western Hemisphere with devastating results for the native Americans—north and south—who had no resistance to the virus. **Smallpox in the colonial Americas** defaced, blinded, and killed millions, and it long remained a threat to colonists raised in isolation from the disease. European contact with Africans, South Asians, Australians, and Pacific Islanders also often resulted in the importation of the disease, but the range of effects was much wider and more complex. Some of these regions presented, like the Americas, “virgin soil” for smallpox, whereas others had had long histories with the disease. From at least 1800, colonial authorities attempted to prevent and, to a lesser extent, treat smallpox. These efforts had mixed results in the short run, but they laid the groundwork for the **eradication of smallpox** in the 1970s.

Europe. Europe clearly suffered from smallpox in late antiquity and in the early Middle Ages, but for several centuries before the era of the Crusades, little was reported of the disease. A Danish ship brought smallpox to Iceland for the first time in the mid- or late 1200s—sources disagree on the date—with a (probably exaggerated) death toll of 20,000. The island suffered recorded outbreaks in 1430–1432, 1462–1463 (with 1,600 deaths), and 1472. Iceland’s worst **epidemic**, the “Great Pox,” occurred in 1707–1709, when nearly all of its 50,000 inhabitants (its first census was in 1703) were affected, and between 16,000 and 18,000 died. It took a century to recover. Shortly after 1430, many believe, smallpox struck Greenland from Iceland and essentially wiped out the colonial population. Having been restocked with Danes, the island underwent another epidemic in 1733 when a Greenlander returned from Denmark (probably via Iceland) with the disease. Three-quarters of the white population suffered, and between 2,000 and 3,000 died. Isolation and low population density on both islands generally meant long periods—decades instead of years—between major outbreaks, and thus grew large segments of the population that had not been immunized by previous exposure to the disease. When smallpox hit, the mature as well as the young were susceptible.

Seventeenth-century Russian exploration of and expansion into Asian Siberia brought the **virus** into “virgin soil,” paralleling the American experience. Beginning around 1630, thousands of Ostyak, Tungus, Yakut, and Samoyed natives fell ill, with a mortality rate reported at nearly 50 percent. Further expansion meant further devastation, and in an early example of international public health cooperation, in 1724 the Chinese sent **physicians** to inoculate Siberians during one of the epidemics that recurred every two or three decades. In 1768–1769 Kamchatka lost two-thirds to three-quarters of its native population to *ospa*, and in the later nineteenth century, the Yukaghirs, who had controlled a huge region east of the Lena River basin were reduced to a mere 1,500 souls. Such depopulation allowed for Russia’s rather easy absorption of nearly half a continent.

An epidemic in 1856 killed an estimated 100,000 Russians despite enlightened Imperial laws mandating smallpox **vaccination** from as early as 1812.

India and the Indian Ocean Region. India had had long experience with smallpox when the Portuguese established their colony at Goa in 1510. In many parts of the subcontinent, smallpox was endemic and directly related to the goddess Sitala, who was believed by Hindus to possess the body of the victim. **Inoculation** with smallpox material was thus a ritual, and religious action related more to the goddess cult than to medical prophylaxis. A class of professional inoculators made a good living performing the procedures. Of course, those inoculated could very easily die, and while getting over the infection, they were themselves contagious and needed to be isolated. Inoculation was never systematic, and young children tended to be spared inoculation, which is why most of the 8,000 who died in Portuguese-controlled Goa over three months in 1545 were children.

After the British ran the French out of India and established the ascendancy of the British East India Company in 1764, observers in Bengal noted that smallpox recurred roughly every seven years, in the spring, prompting the colonials to take **flight** to the countryside. In 1769–1770 an epidemic struck the Bengali capital and claimed 63,000 lives, while more widely an estimated third of the Bengali population, or 3 million, died. Bengal was said to have had among the highest regional levels of inoculation: it may well have been that the practice itself helped spread the disease. In 1802 the first **Jenner**-type vaccine arrived in Bombay via Vienna and Baghdad (being transferred arm-to-arm in vaccinated people), and variolation was banned by law in 1804. Though the British saw this as the height of rationality and generosity, native Indians, especially the inoculators and devotees of Sitala, saw the attempt to replace a religious ritual with a rather disgusting secular therapy as demeaning and impious. The fact that the vaccine was a cow product did not help matters. The law was ignored by Indian and colonist alike.

Though vaccination made some inroads, by 1855 a total of about 1.5 percent of the native Indian population had undergone the procedure. Calcutta suffered through smallpox epidemics that killed 11,000 in a population of 350,000 between 1837 and 1850. 1850 saw a pan-Indian epidemic of smallpox and a revival of the previously ignored anti-variolation law. A widespread epidemic around Bombay inspired the regional 1877 Vaccination Act that required all infants to be vaccinated before the age of six months. Bengal followed with the broader 1880 Bengal Vaccination Act, which required the vaccination of all residents and all newcomers. The gradual replacement across colonial India of variolation with vaccination resulted in a drop in smallpox deaths of 75 percent between 1870 and 1930. The colonial Indian Medical Service (established 1887) continued the vaccination program to the end of British rule, vaccinating about 10 percent (4.3 million) of the population annually between 1936 and 1945, and in its last year—1947—a total of 21.3 million. Still, epidemics recurred every five to eight years, and until 1975 India remained the world's main reservoir for the disease. A major reason for this was the unwillingness of either British or Indian authorities to impose strict, compulsory isolation of patients until the 1960s. Though never popular, this measure inhibited the circulation of the disease among the nonimmunized.

The people of Borneo suffered from smallpox for so long that their mythology connected the disease with creation itself. Every 40 years, they believed, the demon was unleashed on the island and took away half of the population. They refused to touch pox-scarred **corpses** and utilized a primitive form of **cordon sanitaire**. Low population densities probably prevented smallpox from becoming endemic, whereas the “40-year cycle”

had to have been marked by sea-borne importations. This cycle was accelerated with colonization, and despite a decades-long program of vaccination, East Java in 1913 suffered an estimated 18,000 cases and 5,000 deaths. A better vaccine, which could be dried and vacuum packed, arrived in Borneo in the late 1920s, and Dutch authorities all but eliminated smallpox from the island by the later 1930s.

As in India, on the largely Muslim island of Ceylon (Sri Lanka) smallpox had long been endemic—and inoculation practiced—when the Portuguese arrived around 1500. A key part of a wide trading network, and factionalized into warring native and colonial social and political groups, the Ceylonese were subjected to regular epidemic outbreaks under both the Portuguese and the Dutch (1658–1800). When British colonial officers assumed authority around 1800, they set up hospitals to isolate the newly inoculated and natural victims. The first vaccine arrived in 1802, and the 1805 peace with the island's Kandy Kingdom led to the vaccination of all residents, a task accomplished by 1818. Colonial authorities believed endemic smallpox had disappeared by about 1821. Fresh importation of the disease caused outbreaks (in the absence of the needed booster shot) in 1819, 1830–1831 (1,000 cases with 257 deaths), and 1836–1837 (303 deaths). By the 1890s, however, smallpox deaths averaged only about 81 per year in a population of 4 million.

Australia and the Pacific. The dense Asian–African trade network that kept smallpox circulating in the Indian Ocean did not extend to the isolated islands of the South Pacific, leaving them “virgin soil” for the disease. The British First Fleet entered Australia's Sydney Harbor in 1788 with some 1,000 colonists. Several months later, a disease—thought by many to be smallpox—began its inexorable destruction of the aboriginal population along the continent's coast and up the major rivers. As in other “virgin-soil” epidemics, people fled the wretched and pustule-covered victims, often carrying the highly contagious disease with them into other fresh populations. Many were left to die unattended, lacking even the strength to feed themselves, and many ended up in mass graves. Tens, perhaps hundreds, of thousands who had never seen a European suffered and died from their “dibble-dibble” in the continent's greatest demographic catastrophe. It may be the case that only the interior and northwestern areas of Australia were spared.

Aborigines and some Europeans suffered again in 1829–1830 and the 1860s, whereas European colonists in Melbourne were struck when smallpox accompanied the *Commodore Perry* from Liverpool in 1857. Up to the year 1900, nine more imported cases broke out in Australia, despite **quarantine** policies and widely applied vaccinations that began shortly after 1800. Between May 1881 and January 1882, Sydney suffered 154 reported cases and 40 deaths, mostly among inner-city residents. The number is probably rather low because many were afraid to report for fear of quarantine and eviction from their residences. A quarantine station was established at North Head, and in December 1881 an isolation **hospital** began operation. In all, some 900 underwent quarantine or isolation. Many of these were Chinese, whose community was boycotted and who were forcibly vaccinated. Indeed, the outbreak led to the Chinese Restrictions Bill, which forced quarantine on, and limited the flow of, all new Chinese immigrants. More reasonably, it also led to the provision of a Board of Health, mandatory reporting procedures, and an Ambulance Corps. In 1886 the smallpox-stricken ship *Preussen*, which sailed from Port Said, Egypt, and landed at Adelaide, Melbourne, and Sydney, had its 112 victims successfully isolated, dropping some at each stop. A stringent program of vaccination from 1900 eliminated *Variola major* smallpox from Australia by

1903, but the much less deadly *V. minor* strain arrived from the United States in 1913. Over four years, there were 2,400 cases but only 4 deaths.

French Polynesia suffered its first outbreak of smallpox in 1841 when introduced by a U.S. ship sailing between Valparaiso, Chile, and Hawaii. Six had died on board, but with no obvious cases active, the vessel was allowed to anchor without quarantine in Matavai Bay, Tahiti. The disease spread rapidly among the islanders, but another American ship that had vaccine material arrived soon after, and a program of vaccination was quickly carried out. Though 200 died, smallpox was confined to the northwest portion of Tahiti. Nonetheless, when the King of Moorea visited Tahiti for treatment by colonial doctors, he contracted smallpox and brought it back to his island, resulting in 57 cases and 29 deaths among the natives. Many islands decided to close themselves to any outside traffic until the outbreaks ceased.

Peruvian slavers carried away some 1,000 islanders in a raid in 1862. Once they landed on the continent, the highly susceptible newcomers contracted smallpox, and many died. The remaining 470 were packed back on a ship and sent home. During the journey, all but 15 died, and these brought the horrors of smallpox to their friends and family. By 1870 a scant 111 people remained on the island, of an estimated 4,500 in 1860.

The Portuguese Ferdinand Magellan (1480–1521) staked the Spanish claim to the Philippine Islands in 1520, but a Jesuit priest reported the first incidence of smallpox in the colony only in 1591. A Spanish ship, the *Nao de la China*, sailing from Mexico is credited with the introduction of the disease that reportedly infected one-third of the Batanga tribe and inflicted a high mortality rate, especially among the older members. Soon the disease was associated with demons, a belief that later made colonial medical intervention difficult. Whether imported from Asia, America, or Europe, inoculation became a popular response by the mid-eighteenth century. Though Spanish colonial authorities in the nineteenth century championed vaccination of the indigenous peoples, a lack of resources, poor quality vaccines and personnel, difficulty in travel, native resistance, and a lack of official compulsion resulted in ineffective efforts. Smallpox claimed annual death tolls around 40,000, as well as causing thousands of cases of residual blindness. After becoming a U.S. territory in the wake of the Spanish-American War (1898), The Philippines underwent an aggressive, military-led vaccination program and the strict banning of inoculation. By 1914, 10 million had been vaccinated, and the death toll had dropped to 700. A year later, only 276 died, but after Filipinos assumed control, the incidence spiked, and in 1918–1919, 64,000 deaths were reported (though many were no doubt related to the **influenza pandemic of 1918–1919**). U.S. intervention and new dried vaccine reduced the death toll to 367 by 1929. The last case considered epidemic occurred in 1931, making The Philippines the first Asian-Region country to eliminate the disease.

Africa. Smallpox arrived in Africa long before Europeans did. At least one Egyptian pharaoh died of it, and Muslim armies and merchants spread it along with the Koran across North Africa and south along the Sahara caravan routes, and along the continent's east coast south of Egypt. Outside of urbanized areas like the Lower Nile, African population densities remained low, and, except along the coasts or established caravan routes, travel and interaction of peoples remained limited. Much of Africa, especially in the south, remained virgin soil even after Muslim traders and slavers in the east and interior and European slavers and colonists along the west and south coastal regions had introduced the disease.

When Portuguese slavers first began collecting and shipping coastal West Africans to the American colonies, they were skimming along the western edge of a region whose

interior had long been in regular contact with Arab merchants, who had moved westward across Central Africa, and with North African caravans, which brought the Mediterranean's goods across the Sahara to trade for gold and black slaves. Regular visits by the Portuguese no doubt sparked epidemics, especially in those areas that remained "virgin," and scholars tend to agree that slaves rather than European colonists first brought the pox to the Caribbean. On the long, wretched voyages, victims who showed any signs of smallpox were tossed overboard in the hope of stunting an epidemic. That any Africans survived such trips suggests that they had been naturally immunized by exposure in their home communities. Even so, low populations and population densities meant that smallpox was probably never endemic and that the dislocations caused by European colonization and slaving spread the disease and accounted for a terrible toll.

The relative isolation of southern Africa kept it free of smallpox until rather late. The Portuguese colony established at Luanda in 1484 may have introduced the disease into Angola and the southern Congo, though the earliest clear evidence for smallpox in the region is 1620. By the 1680s the area was being ravaged by wars and the disease. Rampant smallpox prompted the region's Brazilian slavers to suspend their activities in 1687.

The Dutch first arrived at Capetown, South Africa, in 1652, but the young colony avoided smallpox for six decades. In 1713 a Dutch ship with East Indian passengers dropped anchor in Cape Colony's Table Bay. Laundry contaminated with smallpox was unwittingly given to local Khoi slaves of the Dutch East India Company who began to fall ill and die. By the epidemic's end, whole villages had been emptied, and 15 percent of the white population was dead. In 1755, 2,100 (nearly half white) died in the Cape over six months after a Dutch ship from Ceylon unloaded its deadly cargo. Again the native people suffered worst, and the region's first segregated hospitals were erected. Fleeing natives spread the disease as far north as modern southern Namibia. The effect on the indigenous societies was so profound that tribal identities were eroded or destroyed in favor of the generic "Hottentot." Passengers or cargo in a Danish ship touched off a two-year outbreak in 1767 that killed 179 whites and 440 slaves. This episode saw the first application of arm-to-arm inoculation in South Africa, though whether it derived from a European or an African Bantu source remains unclear.

After the British captured the Cape in 1795, and again in 1815, the largely agrarian Dutch *Volk* migrated inland. British colonists and troops began arriving in large numbers during the 1820s, spreading out from the Cape. Discovery of diamonds at Kimberley, some 400 miles inland, and of gold along the Witwatersrand ridge fueled a rush to South Africa and to these spots in particular. Europeans, Asians, and foreign Africans surged in. Interdicting illegal slave ships could also create problems, as in 1840, when the east African *Escarpa* was seized by the Royal Navy and taken into the Cape's Simon's Bay. Before the ensuing smallpox epidemic died out, some 2,300 Cape residents had succumbed. When smallpox broke out in Cape Town in 1882, Kimberley carefully guarded its southern approaches with a *cordon sanitaire* and a quarantine station 30 miles out, requiring proof of vaccination and burning sulphur fumigation of goods or a six-week quarantine. But when smallpox entered via African migrants from Portuguese territory in 1884, the authorities dismissed the reports or declared the disease chickenpox, rather than generate flight or alienate recruits for the mines. After a three-year bout, 2,300 were infected, and 700—mostly Bantus—died. The epidemic spawned the Cape Colony's 1883 Public Health Act, which mandated vaccination and notification of smallpox cases to medical authorities.

Further north and east, the expanding Ashanti people had their southerly-routed armies stopped by smallpox in 1824, in the 1860s, and in the winter of 1873. Their problems probably arose when smallpox carriers mixed with nonimmune comrades in the early stages of mobilization. Still further north, among the Muslim populations and their neighbors, the annual Hajj **pilgrimage** to Mecca was a consistent source of population mixing and smallpox contagion.

The nineteenth-century European “scramble for Africa” brought the Belgians, French, Germans, and Italians onto the continent and pushed the European presence—and the accompanying native dislocations—further inland than ever before. Otherwise isolated peoples met smallpox, among other diseases, for the first time. The early penetration of railroads made new inroads for disease (the Mombasa to Uganda line stopped short of Masai territory, but between 1896 and 1899, the rinderpest-weakened warrior tribes lost 75 percent of their population to smallpox). Flight and the sporadic African practice of inoculation spread the disease like a shadow preceding the Europeans’ appearance. Colonial wars also mixed populations and drew smallpox across the countryside sparking outbreaks as it went. Portuguese West Africa suffered 25,000 dead of smallpox in 1864–1865 when it raced through the colony, disrupting the mines’ production and trade routes and destroying villages wholesale. In Dahomey the god of smallpox was Sakpata, and ritualized native inoculation continued to be practiced after its ban by colonial authorities. During the Franco-Dahomean War of 1892, smallpox played a significant role in weakening the native army and ensuring its defeat.

Vaccinations began early, but were treated as personal rather than public health prophylaxis. Some mistakenly perceived the procedure to be as dangerous as inoculation. South Africa introduced it before 1812, and it was being employed widely by the 1840s, at least among whites. Madagascar saw its use as early as 1818, and Sierra Leone in 1859. In Egypt and the Sudan, vaccination was compulsory by the early 1820s. But booster shots were needed, and the heat and distances weakened the material until the 1920s, when dried vaccine was made available. Even before then, however, the appearance of *Variola minor*, with its low virulence and immunizing effect, began a natural immunizing process. European colonial troops were usually vaccinated upon induction and again before their theater assignment. But both natural and artificial immunization was sporadic, and large populations remained susceptible. Major outbreaks continued throughout the continent until the concerted efforts to eradicate the disease from the 1960s. Madagascar was the first African region to eliminate the disease, around 1922, but the continent’s incidence rate spiked two decades later when 99,000 cases were reported in 1944–1945, during the crucial stages of World War II. As African states gained their independence from the late 1950s, many underwent political upheavals that created resurgences of smallpox and other diseases as a result of violence, social disruptions, and shifts in resource allocation. See also Colonialism and Epidemic Disease; Smallpox Eradication; Smallpox in Pre-modern Europe.

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JOSEPH P. BYRNE

SMALLPOX IN PREMODERN EUROPE. From the fall of the Roman Empire (c. 476) to the French Revolution at the end of the eighteenth century, **smallpox** gradually emerged to become one of the most significant and deadliest diseases in European history. Smallpox is the common name of the disease in the English-speaking world, derived from the Old English *pocc*, meaning a “pustule.” The prefix “small” was added after the 1490s to differentiate it from the great pox, **syphilis**. Alternative early modern (c. 1500–1800) names of the disease in various European languages include *la petite vérole* (French), *Blättern* (German), and *kinderenpocken* (Dutch).

Smallpox spread throughout the whole of premodern Europe, although the severity and frequency of outbreaks varied widely. These depended primarily upon the size, density, and previous exposure to the disease of the population at risk. In large towns by the seventeenth century, smallpox was endemic, afflicting mainly **children** and leaving survivors immunized. Smallpox could account for up to 10 percent of total deaths. In smaller and sparsely populated settlements, the disease was **epidemic**, with infrequent outbreaks that attacked adults as well as children. People of all social classes succumbed to smallpox, from the lowliest paupers to European royalty. The case fatality rate for the strain of smallpox most likely prevalent in early modern Europe, *Variola major*, was around 25 percent: one in four people infected with smallpox died. Of those who survived the disease, there was a high chance of pockmarks causing permanent disfigurement. Further possible consequences of smallpox included blindness and male infertility.

Regarding changes over the premodern period, the sources indicate an increase in the incidence and mortality of the disease around the seventeenth century with a peak in the eighteenth. Historians have generally accounted for this perceived increase in the virulence of smallpox by either a mutation of the **virus** or the introduction of a new and more virulent strain of *variola* into Europe. Alternative explanations emphasize the changing social and economic conditions of early modern Europe—particularly, the rise in population, **urbanization**, and migration—that led to a disease environment more conducive for smallpox. The eighteenth century saw the dissemination of **inoculation**: a practice that conferred lifelong **immunity** upon the recipient and paved the way for the introduction of **vaccination** (c. 1800).

Historical Evidence. The evidence available for smallpox in medieval Europe (c. 500–1500) is meager and often ambiguous. As with **smallpox in the ancient world**, the first problem is the relative paucity of *all* written records, which were either not created in a largely illiterate society or have not survived to the present day. Secondly, the unspecific nature of disease classification in earlier periods makes identification difficult. To identify a particular disease, therefore, emphasis must be placed upon the descriptions

of symptoms and distinctive epidemiological characteristics. Records improve in the early modern period, although regions of Europe—mainly rural areas—remain either undocumented or underresearched by historians. Evidence for smallpox can be found in a wide variety of sources, including medical treatises, burial registers, legal records, parish account books, and personal documents (e.g., diaries and letters), along with plays, novels, and poems. Quantitative evidence on smallpox mortality is rare and is largely restricted to towns from the early modern period onward: for example, the burial registers in Geneva state the cause of death from 1580, those of London from 1629, and those of Moscow from 1680. Quantitative morbidity data—the number of people who were sick—in this period is almost nonexistent.

Medieval Europe. Two probable smallpox epidemics are documented in the late sixth century. In 573 Bishop Marius of Avenches (Switzerland, c. 530–593) described an epidemic of *Variola* in southern Europe. Seven years later, Bishop Gregory of Tours (France, 538–594) witnessed a fatal disease that struck across northern Italy and southern France. No disease name is recorded, but the detailed description of the symptoms closely resembles that of smallpox. For the next few centuries, very little evidence of the disease exists. It is possible that the Islamic armies of the seventh and eighth centuries spread smallpox into Europe. By the tenth century, a physician-monk called Notkerus, from Switzerland, is reported to have been able to diagnose the disease even before the rash appeared, suggesting familiarity with smallpox. An Anglo-Saxon manuscript from this time contains a prayer to St. Nicaise to defend the suppliant from the disease: Nicaise was the Bishop of Rheims (France) in the fifth century who became the patron saint of smallpox victims.

Into the second millennium, there is the possibility that the Christian armies of the Crusades in the twelfth and thirteenth centuries spread smallpox from the Middle East into Europe. Descriptions of the disease in medical treatises began to appear from this time. For example, Gilbert (fl. 1250), an English physician, compiled a *Compendium Medicinæ* (c. 1240) that included an account of smallpox. By the fourteenth century, a number of smallpox epidemics were recorded in Italian cities: Florence (1335), Naples (1336), Siena (1363), Vicenza (1386), and Bologna (1393). In France, King Charles V (1338–1380) caught and survived an attack of smallpox. By the end of the medieval period, smallpox appears to have spread throughout Europe. However, when compared with those of later centuries, medieval sources give the impression of a relatively mild form of the disease. It is possible that the form of smallpox prevalent at this time was of similar virulence to the *Variola minor* strain of the disease, with a case fatality rate of 1 percent, identified in the late nineteenth century. But this must remain a hypothesis that cannot be verified from the limited historical record.

Early Modern Europe. In Europe and in her colonies around the world, smallpox made the greatest demographic impact during the early modern period. With the rise in urbanization, as more people lived in close proximity to one another, a highly contagious disease like smallpox was able to thrive and survive continually amongst the urban populace. In London by the mid-seventeenth century (population of 400,000), smallpox was an endemic disease, although its death toll continued to fluctuate with epidemic peaks every few years. Smallpox was regularly killing over a thousand Londoners per year, and this increased to a few thousand (or 10 percent of total deaths) at the height of the disease in the mid- to late eighteenth century. Most of the victims were children, because the majority of adults would already have caught smallpox and were thus immunized from

future attacks. This pattern of age-specificity is seen in other European cities. Between 1580 and 1760, nearly half of all smallpox deaths in Geneva were of infants under two years old, and four fifths of victims were under five years of age.

In rural and isolated regions of Europe—where the majority of people lived—the epidemiological characteristics of smallpox were noticeably different. When smallpox could not maintain itself endemically, many years could pass between outbreaks. If it then spread among a population where few people had previously caught the disease, the attack rate would be especially high, affecting adults and children. An extreme example of this occurrence was in Iceland in 1707 when almost all the 50,000 inhabitants of the island caught the disease, and 16,000 to 18,000 died.

Sometimes smallpox epidemics were isolated in time and place, but the disease could also erupt into European-wide pandemics. In 1614, the disease spread throughout France, Germany, Italy, England, Poland, Flanders, Crete, and Turkey. The prevalence and severity of smallpox across Europe is well illustrated in the number of royalty who either survived or succumbed to the disease. In France, King Louis XIV (1638–1715) caught and survived an attack of smallpox in 1647. His great-grandson, who became Louis XV (1710–1774), was not so lucky and died from smallpox in 1774 at the age of 64. Joseph I Habsburg (1678–1711), Holy Roman Emperor and King of Austria and Hungary, died of smallpox. In Britain, King Charles II (1630–1685) survived an attack of the disease, but he lost two siblings, Prince Henry (1640–1660) and Princess Mary (1631–1660) in 1660. England's Queen Mary II (1662–1694) died of smallpox on December 28, 1694, at the age of 32.

Determinants of Smallpox. As a contagious disease that only existed within a human host and had no animal reservoir, smallpox's epidemiology was intimately associated with people's movements and migrational patterns. This applies on a global scale—as in the case of **smallpox in colonial Latin America**—and right down to the local level, as rural–urban migrants had a high chance of catching smallpox the moment they arrived in the city. Factors that encouraged migration therefore helped spread the disease. These included migrants forced to travel for want of food but also those attracted to new areas because of better employment opportunities. **Warfare**, involving the movements of numerous troops, aided the spread of smallpox. The **Thirty Years' War** (1618–1648), in which most of the major European countries played a part, is one such example. Peaks in smallpox mortality have also been correlated with the end of wars, when thousands of soldiers and sailors were demobilized and descended upon friendly cities, either bringing the disease with them or being susceptible to it upon arriving.

Modern clinical evidence suggests that **diet** did not affect an individual's chance of catching smallpox. However, there is an indirect link: inadequate nutrition in pregnancy is known to cause low birth weights in infants and a corresponding increased susceptibility to infectious diseases, including smallpox. The virus is also known to do better in relatively low temperatures and humidity, thereby increasing the likelihood of spreading from one person to the next. In early modern London, there was a slight correlation between smallpox epidemics and low winter temperatures, although the seasonality of the disease remained concentrated in the summer and fall.

Reactions and Responses. Smallpox induced great fear—not only as a cause of death, but also and perhaps more significantly because of the horrific symptoms of the disease and possible permanent disfigurement. Both men and women were pockmarked, but for the latter there was the added dimension of their diminished attractiveness

affecting their chances of marriage. Hence, smallpox discourse in the eighteenth century was partly gendered: for men, the disease spoke of the danger to their lives; for women, it was a danger to their beauty. Specific concoctions aimed at reducing and concealing the scarring appear in numerous early modern recipe books and women's domestic manuals.

Running alongside this fear, however, was a certain degree of acceptance of smallpox—an expectation, especially in towns, that the disease was unavoidable and therefore a rite of passage that all children must endure. Consequently, the flight response to smallpox was mixed: some people hastily left the region during an epidemic, but others stayed. This stands in contrast to **bubonic plague** epidemics, for which the general consensus was to flee if at all possible. Similarly, when compared with plague victims, smallpox patients were rarely quarantined. This was to change with the introduction of inoculation in the eighteenth century, when **quarantine** could be part of the treatment regime.

Physicians treated smallpox patients based upon practices that had developed out of the **Greco-Roman medical** tradition: predominantly alterations in diet and a combination of induced bleeding, purging, vomiting, and sweating to balance the humors. Debates within this tradition included the most appropriate time to bleed the patient, what quantity of blood should be extracted, whether to purge or vomit, and whether to keep the patient hot or cold. One of the most magical treatments of smallpox was the use of red objects, the perceived curative powers being based on color sympathy. This treatment persisted through premodern Europe and around the world, appearing, for example, in Japan. Queen Elizabeth I of England (1533–1603) was wrapped in a red cloth when she caught smallpox in 1562. Because the disease could necessitate intensive nursing, women played an important role in the medical care of smallpox patients. Although vilified in medical treatises for their lack of theoretical knowledge, the **nurses'** depth of practical experience with the disease meant they were arguably more helpful to the smallpox patient than the university-trained male physicians. The theories of smallpox causation ranged from bad **air** (*miasmas*), to various forms of contagion, to the disease being an innate condition derived from menstrual blood.

Inoculation. The most important medical and public health development in the history of premodern smallpox came in the eighteenth century, with the development and wide dissemination of inoculation. Also called variolation or ingrafting, the practice in Europe was to make an incision in the arm of the person to be inoculated and then insert some matter taken from the pustules of an active smallpox case. The inoculee would then develop smallpox, but a considerably milder case than that acquired naturally, while still gaining immunity from future attacks. The origins of inoculation are obscure and developed out of **folk medicine**. Lady Mary Wortley Montagu (1689–1762), the wife of the British ambassador to Turkey, observed the local women carrying out the practice, and is famously attributed with popularizing it in England. She had Charles Maitland (1677–1748), an English physician, successfully inoculate her son and daughter: the latter instance, in 1721, was the first time this practice was carried out in England by a member of the medical profession. Opposition to the controversial practice was vociferous. Religious concerns were raised over interfering with divine providence. People also died from acquiring inoculated smallpox: early statistics were as high as 1 in 60, but this fell to 1 in thousands. Despite the early resistance, confidence in inoculation grew as people accepted the much better odds of surviving inoculated versus naturally acquired smallpox. In England the practice was widespread from the mid-eighteenth cen-

tury onward: consequently, by curtailing smallpox mortality, inoculation might have contributed to population growth at this time. Adoption across the European continent was piecemeal. The French and German medical professions, for example, took longer to accept inoculation than the English. But by the last third of the eighteenth century, it was common practice across Europe, eventually being supplanted by vaccination from the early nineteenth century. *See also* Diagnosis of Historical Diseases; Disease, Social Construction of; Jenner, Edward; Latin America, Colonial: Demographic Effects of Imported Diseases; Smallpox and the American Revolution; Smallpox in Colonial North America; Smallpox in European Non-American Colonies; Syphilis in Sixteenth-Century Europe.

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HENRY MEIER

SMALLPOX IN THE ANCIENT WORLD. Because **smallpox** is caused by a **virus** that induces long-lasting **immunity** in survivors, it required human populations of a certain size (100,000 to 200,000 people) to survive. Consequently it probably did not exist before the development of agriculture in the **Neolithic** period. Research in molecular evolution indicates that within the *Orthopoxvirus* genus the variola virus that causes smallpox is most closely related to the camelpox virus. The variola and camelpox viruses diverged from a common ancestor approximately 6,000 years ago. One scenario for the evolution of smallpox as a human disease is that it was associated with camel domestication in the Bronze Age (c. 3000–1000 BCE) in the Near East or Central Asia. However other scenarios can also be imagined. Smallpox and camelpox may simply share a common ancestor, but the camel need not be the direct source of the human disease. Because the evolution of smallpox was associated with **animal** domestication in Asia during the Neolithic and the Bronze Age, after the migrations to North America, smallpox did not exist in the Western Hemisphere before Columbus.

Ancient Near East and Egypt. The early history of smallpox is shrouded in obscurity, but there are tentative signs that smallpox was present in the civilizations of the ancient Near East. It has been claimed that smallpox is described in the Ebers Papyrus (c. 1500 BCE)

from Egypt, but most medical historians do not accept this. The rash of elevated pustules observed on the skin of three mummies dating to the periods of the XVIII and XX Dynasties in the second millennium BCE (including the mummy of the Pharaoh Ramses V, who died c. 1157 BCE) does resemble the rash of smallpox. Unfortunately, the retrospective diagnosis is not absolutely certain because it was not possible to examine the palms of the hands or the soles of the feet, where the rash would be highly diagnostic of smallpox. Smallpox has also been identified in cuneiform texts from Mari in Upper Mesopotamia dating to the first half of the second millennium BCE. The consistent association of the symptoms described with simultaneous epizootics, however, casts some doubt upon the identification, because by then smallpox had evolved into a purely human disease with no known animal reservoirs—a fact that facilitated its **eradication** in the twentieth century CE.

China. The philosopher and medical writer Ge Hong (283–343 CE) made the first detailed description of the symptoms of smallpox in China in 342. He attributed the disease to bad **air**. Several other early sources suggest that smallpox first reached China in the second half of the third century BCE. It is said to have been introduced to the country by invading nomadic tribes from Central Asia. The movements of armies and merchants often spread early epidemics of smallpox in China. Smallpox has a long incubation period (7 to 17 days), facilitating its spread by people moving around after infection but before clinical symptoms appear. Sometime during the period of the Tang dynasty (618–907), a Chinese physician named Zhao discovered the technique of **inoculation** or variolation, a technique for immunizing people against smallpox that preceded the modern **vaccination** technique. Four different methods of inoculation were devised in China: 1) making a person wear a garment that had previously been used by a sufferer from mild smallpox; 2) introducing into the nose a piece of cotton cloth with fluid from smallpox blisters; 3) blowing dried powder from smallpox scabs into the nose through a blowpipe; 4) drinking water containing dried powder from smallpox scabs.

India and Japan. The classic ancient Indian **Ayurvedic** medical text *Susruta Samhita* gives a very clear description of smallpox. Unfortunately, early Sanskrit texts are difficult to date, but it is likely that smallpox was present in India by at least the second century CE, by which time it had definitely reached both the Near East to the west and China to the east. Eventually India acquired a goddess specifically devoted to smallpox, namely Sitala (the cool one). Having smallpox was interpreted as being possessed by the goddess. Smallpox was introduced to Japan from Korea or China in the sixth century CE along with Buddhism. The new **religion** was initially blamed for the appearance of a new disease, although Buddhism managed to survive in Japan. Over the next few centuries, periodic reintroductions of smallpox caused a series of major epidemics in Japan, because the human population density was not high enough at first for smallpox to become permanently endemic in the country.

The Ancient Greek and Roman Worlds. There is no clear description of smallpox in the texts of the Hippocratic corpus, which pay little attention to epidemic disease in general. Smallpox is one of the more plausible candidates for the identity of the pathogen that caused the **plague of Athens** (430–426 BCE), but there are numerous other theories as well. Moving forward in time, Philo of Alexandria (20 BCE–50 CE) in the first century CE described a **biblical plague** in a way that suggests familiarity with smallpox. However, it is not until the **Antonine “plague”** in the second century CE that the presence of smallpox in the classical world becomes absolutely certain. The Antonine plague started among the soldiers of the Roman army who spent the winter of 165–166 at Seleucia in Mesopotamia during the campaign of Lucius Verus (d. 169) against the Parthians.

According to legend, the epidemic commenced when a demon was released from a golden casket in the temple of Apollo at Seleucia. The disease was then carried back to Rome in 166 by the Roman army. The contemporary physician **Galen** is our main source for the Antonine plague; he observed its effects on a unit of Roman soldiers at Aquileia in Italy in 168–169. The importance of armies for the dissemination of smallpox has already been noted in the case of China. The Antonine plague lasted until about 180, and there was another major epidemic in 189 at Rome described by Dio Cassius (c. 160–229) that might have been another outbreak of the same disease. The historian Ammianus Marcellinus (c. 325–391) stated that the Antonine plague reached Gaul and Germany. Galen described the symptoms of the disease and attempts at treatment in a rather unsystematic manner. The symptoms of the Antonine plague included the characteristic exanthemata, which frequently turned black. Survivors' scabs eventually dropped off the ulcers. Galen's evidence suggests a high frequency of the very dangerous hemorrhagic form of smallpox during the Antonine plague. He also mentions as symptoms upset stomach and diarrhea, followed by black stools in survivors, very strong internal fever (although the skin of patients was cool to touch), vomiting, bad breath, catarrh, and internal ulcerations. The economic and demographic effects of the Antonine plague are the subjects of intense controversy among historians. Unfortunately, the whole period is poorly documented.

Late Antiquity. In late antiquity there are several brief reports of epidemics that resemble smallpox. In 302 Eusebius of Caesarea (275–339) described an epidemic in Syria characterized by a skin rash that spread over the whole body and often resulted in death, or in blindness among survivors. In 451 the invading Huns killed the bishop of Rheims in France. He later became St. Nicaise, the patron saint of smallpox, because he had suffered from the disease the year before his death. Gregory, historian and bishop of Tours (538–594), clearly described smallpox in Italy and France in 580–581. A few years before, Marius (530–594), bishop of Avenches in Switzerland, became the first extant source to use the word “variola” to describe an epidemic disease. Unfortunately he did not describe its symptoms. Such references suggest that during the first few centuries CE, smallpox established itself as an endemic disease in Europe, with periodic epidemics as pools of susceptible individuals gradually accumulated. The patchy record for smallpox across antiquity as a whole may well be a consequence of the inadequacies of the documentary record. However, it may also indicate that smallpox was originally a mild disease, as it is described by **Rhazes** in the tenth century CE, perhaps with the spread of more virulent genotypes from time to time. Research in molecular evolution has shown that the acquisition of immune system genes from their hosts by horizontal transfer has been an important feature of the evolution of poxviruses in general. Consequently, smallpox may originally have been a mild disease, like cowpox, and it may have taken some time to acquire the genes to make it more virulent. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Chinese Disease Theory and Medicine; Corpses and Epidemic Disease; Diagnosis of Historical Diseases; Greco-Roman Medical Theory and Practice; Hippocrates; Historical Epidemiology; Paleopathology; Plagues of the Roman Empire; Smallpox in Premodern Europe; Trade, Travel, and Epidemic Disease; War, the Military, and Epidemic Disease.

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ROBERT SALLARES

SNOW, JOHN (1813–1858). Among **physicians** John Snow is best remembered as a pioneer in anesthesiology and the author of an early textbook on the subject in the 1840s. His enduring fame, however, is based on two landmark studies of **cholera** in London undertaken in the 1850s. Born and raised in a working-class slum in York, England, Snow was aided by a wealthy uncle who placed him as an apprentice with a **surgeon** in London. After two more apprenticeships with **apothecaries** in Newcastle-on-Tyne he returned to study medicine at the Hunterian School in London and the University of London, from which he earned his M.D.

In one of his cholera studies, the Broad Street Study, Snow described a ferocious but localized cholera outbreak in the St. James, Westminster, area of Soho in London, England. The second was carried out simultaneously, and published concurrently, with a more ambitious attempt to determine the cause of cholera in a general **epidemic** in South London. The first stemmed from a single local **water** source, the Broad Street pump, Snow argued. The source of the second was polluted water from the Thames River. In the twentieth century, Snow's cholera studies were lauded as the very essence of the "epidemiological imagination" and the beginning of modern epidemiology, medical geography, and public health.

Cholera is an epidemic disease whose multiple occurrences in the nineteenth century made it the focus of intense study by medical researchers. At that time, most researchers advanced a **miasmatic** theory of disease, believing that epidemic (and some endemic) conditions were generated in the foul airs of the city. Snow, on the other hand, argued that cholera, and by extension other apparently communicable diseases, were water-rather than airborne. Snow first made his argument in an 1849 pamphlet, *On the Mode of Communication of Cholera*. He tested his theory in both the 1854 St. James neighborhood outbreak and, concurrently, the South London registration districts most affected by the epidemic, publishing the results in 1855.

The map Snow drew of the St. James outbreak has become a central icon in both medical geography and cartography. In it, the density of cases proved to be clustered around a single water source, the Broad Street pump. Snow argued this proved a causal relationship between the single water source and the disease. Snow's map of the localized Broad Street epidemic has come to serve as a symbol for a concrete, cartographic approach to the spatial study of disease incidence. For epidemiologists and public health experts, admiration today is focused on Snow's more ambitious (if less conclusive) study of the effect of metropolitan water supplies on the 1854 cholera epidemic in South London.

Although few of Snow's contemporaries accepted his argument as conclusive, in 1883 **Robert Koch** identified the bacterium responsible for cholera as the waterborne *vibrio cholera*. In the twentieth century, Snow's work became a symbol of an approach to disease studies based on a study of the intensity of disease and the location of disease clusters to potential contaminants. See also Farr, William; *Cholera: First through Third Pandemics, 1816–1861; Demographic Data Collection and Analysis, History of; Sanitation Movement of the Nineteenth Century; Water and Epidemic Diseases.*

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TOM KOCH

SOCIAL CONSTRUCTION OF DISEASE. See Disease, Social Construction of.

SOCIAL PSYCHOLOGICAL EPIDEMICS. A variety of social psychological epidemics have been recorded since antiquity. The phenomenon is generally defined as the rapid spread of illness signs and symptoms affecting members of a cohesive group; these unconsciously exhibited physical complaints have no known corresponding organic etiology. Episodes range from examples as diverse as **St. Vitus' dance** mania and Italian tarantism (frenetic dancing thought to be caused by a tarantula bite) during the late Middle Ages to cases of sick building syndrome and **bioterrorism** panics today.

Many agents—demons, **viruses**, witches, chemical toxins, and even society itself—have been attributed as causes of the epidemics. Outbreaks have been viewed as symptomatic of social oppression historically linked to religious persecution, political unrest, cultural intolerance, and economic crisis. Generally, the type of manifestation is contingent upon the cultural preoccupations of certain historical periods, suggesting that outbreaks are socially produced. Episodes thus represent historically specific cultural anxieties.

The first indication of an episode is the collective manifestation of physical complaints without any evident cause. Outbreaks are characterized by medically unexplained physical symptoms such as stomach cramping, dry mouth, uncontrollable twitching or trembling, mild convulsion, irrepressible laughter, or temporary paralysis. They typically occur in small groups situated in enclosed settings such as mills, factories, army barracks, convents, hospitals, prisons, office buildings, and schools. Episodes can last three days to two months.

Little scientific consensus exists on conceptual frameworks and terminology. For example, although the phenomenon has most commonly been referred to as “somatization,” “mass hysteria,” “mass sociogenic illness,” “hysterical contagion,” “epidemic hysteria,” or “mass psychogenic illness,” over 70 synonyms have been identified in the literature. Etiological and epidemiological frameworks are likewise varied and remain inconclusive. Shifting conceptualizations and different historical manifestations make the phenomenon particularly challenging to understand and explain.

Psychological approaches have attributed the occurrence to low IQ scores, childhood trauma, or cognitive dysfunction, whereas other studies suggest a higher preponderance among females and personality types classified as neurotic, extroverted, or paranoid. More recent studies, however, demonstrate neither: given the right set of social conditions, no population is immune; the phenomenon is not correlated to, or caused by, personality or psychological factors. Sociological research suggests that high levels of stress, imitative behavior, or other social strain may be the cause of involuntary psychosomatic reactions within the affected group.

The American Psychiatric Association's (APA) *Diagnostic and Statistical Manual IV (DSM IV)* includes this phenomenon as an hysterical neurosis under the category of Somatoform Disorders subcategory Conversion Disorder. The psychiatric assessment is

based on the absence rather than presence of physical causes making it a diagnosis of exclusion. Contagious psychopathology, fantasy, and mimesis (imitation) have also been hypothesized as psychiatric cause. The term “hysteria,” with its root in the Greek word for uterus (as in “hysterectomy”), has been abandoned for its negative denotation of females as essentially overly emotional, irrational, abnormal, or otherwise deviant.

Although many cases can be shown to have been prompted by actual events, some can arise from rumor of the presence of a **contagion** or other immanent threat. Odor, or the perception of odor, is a common trigger for those situations relating to water, smog, nuclear accidents, or chemical exposure. The fear of **environmental** contagions such as toxic gas from **bioterrorism** or industrial pollution have been known to elicit symptoms such as headache, nausea, breathlessness, weakness, and lightheadedness. The lack of etiological certainty, however, does not detract from the reality of the afflicted, whose complaints should be addressed promptly by health professionals and social authorities.

A thorough investigation upon complaint is imperative to rule out all possible causes to prevent unnecessary social panic and confusion. Environmental analysis and medical tests should be conducted. Occasionally the agent is identified; other times attempts by health authorities to locate and eliminate the source of the problem have failed. Past investigations have been closed prematurely, only to be reopened later upon discovery of causal factors. When all physical explanations are ruled out, investigators may resort to psychological explanations to account for the outbreak and rise in number of cases often leading to resentment amongst the sufferers. Furthermore, economic pressures to reduce emergency services and to resume the work schedule may prevent the exploration of all possible causes and the performance of an exhaustive investigation.

In the heightened “post-9/11” climate, it is highly probable that panic created about bioterrorism may be more dangerous than the actual threat it poses. The consequences of such a panic may result in gross human rights violations. The fear of a threatening agent, increasing numbers of complaints, popular media spectacles and reports, and the legitimating actions of authorities all contribute to tension and thus to the increased probability of symptoms being experienced and reported. All of these factors must be taken into consideration when investigating the source.

Public access to reliable and accurate information is necessary to ensure an educated populace and to avoid widespread social paranoia about unfounded anxieties. Exaggerated media representations and opportunistic government hyperbole, in particular, may contribute to and exacerbate a crisis. Managing the situation thus requires special collaborative efforts by public authorities, health professionals, social experts, and the media.

Psychological epidemics are currently poorly understood. Diagnoses have been—and continue to be—contentious and problematic as a result of classificatory ambiguity, lack of physical/organic evidence, and the highly subjective nature of notions such as threat and risk. The long and controversial history of the concept of hysteria, the lack of theoretical and disciplinary consensus on the mind-body relationship, the political history of its use and implications, the etiological uncertainty, and inconclusive empirical data render the phenomenon a problematic scientific category requiring further attention and research. *See also* Black Death, Flagellants, and Jews; Disease, Social Construction of; Personal Hygiene and Epidemic Disease; Personal Liberties and Epidemic Disease; Poison Libels and Epidemic Disease; Poliomyelitis and American Popular Culture; Religion and Epidemic Disease; Scapegoats and Epidemic Disease.

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HEIDI M. RIMKE

SPANISH INFLUENZA. See Influenza.

SULFA DRUGS. The term sulfa drugs (aka sulfonamides) is a generic term for derivatives of the chemical para-aminobenzenesulfonamide (sulfanilamide). Sulfa drugs act by interfering with the incorporation of para-aminobenzoic acid into the vitamin folic acid, thus inhibiting the growth of susceptible **bacteria**. Organisms that do not require folic acid or that obtain it preformed in their **diet**, such as humans, are not affected by this process.

The discovery of Salvarsan for the treatment of **syphilis** by **Paul Ehrlich** in the first decade of the twentieth century stimulated a search for other chemical agents to combat infectious diseases. Despite some modest successes, progress was slow. By 1930 many investigators were especially troubled by the failure to develop chemotherapeutic agents against the bacteria that were the major cause of disease in nontropical countries. The announcement in 1935 of a chemical agent effective against infections caused by streptococcal bacteria was thus greeted with great enthusiasm.

The German pharmaceutical firm I. G. Farben introduced the compound, a dye named Prontosil. An extensive screening program led by German pathologist Gerhard Domagk (1895–1964) first demonstrated its efficacy against deadly hemolytic streptococci in mice in December 1932. Clinical trials began in the following year, and by early 1935 evidence had accumulated that Prontosil was effective against scarlet fever, childbed fever, and a variety of other streptococcal infections. Dogmagk personally confirmed Prontosil's value in December 1935, when he used the drug to cure his daughter of a serious streptococcal infection following a wound.

Domagk was aware that Prontosil did not kill bacteria in the test tube but worked only in the organism. Researchers at Paris's Pasteur Institute suspected that Prontosil itself was not the active drug, but that it was broken down in the body to produce an antibacterial molecule. They demonstrated in late 1935 that Prontosil was indeed decomposed in the organism, and that one of the resulting products, sulfanilamide, was the active drug. Unlike Prontosil, sulfanilamide was not covered by a patent, and eventually it largely replaced the earlier drug. Both drugs were used together to cure American President Franklin Roosevelt's (1882–1945) son of a life-threatening streptococcal infection in December 1936, an event that helped bring these medicines to the attention of the American public.

It was soon discovered that sulfanilamide could be modified by the addition of various chemical groups to produce a whole series of compounds known as sulfonamides or sulfa drugs. A number of these substances, such as sulfapyridine and sulfathiazole, proved to be effective against such diseases as bacterial pneumonia and **meningitis**. One of these drugs may have saved the life of British Prime Minister Winston Churchill (1874–1965) when he was suffering from pneumonia in late 1943. Domagk was awarded the 1939 Nobel Prize in Medicine or Physiology for his discovery of Prontosil.

Although viewed as miracle drugs at the time, sulfa drugs were largely supplanted by more effective and less toxic **antibiotics** over the next few decades. These historically important drugs still have a small place in therapy today, especially in the treatment of urinary tract infections. *See also* Pharmaceutical Industry.

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JOHN PARASCANDOLA

SURGEON. The role of the surgeon was to treat external diseases and injuries, and the most common treatments in use were bloodletting, tooth pulling, and the cauterizing of wounds and sores. Surgeons performed three major procedures: broken bone setting, limb amputation, and "cutting for stone," which involved slicing into the bladder. Surgeons were not gentlemen, and until the end of the seventeenth century, surgeons in Western Europe were widely seen to be inferior to **physicians**. Like carpenters or barbers, they worked with their hands and sold their services for money. They were generally not university-educated and thus thought to possess no theoretical knowledge of **humoral theory**—the hallmark of intellectual medical authority in this period. Most of all, their trade carried overtones of butchery and torture.

From the early eighteenth century, however, the status of surgery began to rise. Individual surgeons were keen to acquire the social and intellectual eminence of physicians. They began to promote surgery based on new anatomical research of the **Scientific Revolution** rather than on empirical tradition. Innovations in surgical instruments and technique were reflected in the idea of "conservative" surgery, which tried to preserve the function of an injured limb rather than resort to amputation. For the first time, surgeons could become gentlemen and even celebrities. The Scots surgeon William Hunter (1718–1783), for example, opened a private medical anatomy school in London, which became not only a center of surgical teaching and research but also a fashionable place to be seen. In 1745 a group of London surgeons founded a College of Surgeons. In so doing, they made a bid for the same kind of power and prominence as the older Royal College of Physicians.

Developments in medical practice reinforced the new status of surgery. The growth of hospital medical schools in the late eighteenth century brought medical students and apprentice surgeons together, with both "walking the wards" to get experience. Following

the upheavals of the French revolution in the 1790s, a new style of medicine began to be practiced in the large municipal hospitals of Paris. Physicians began to move away from the Classical view of the body, in which disease was seen as a functional problem, treated by restoring the balance of the four humors. They embraced a new model of disease as a localized structural defect, one that could be addressed by physical treatments and surgery.

In the first half of the nineteenth century, surgeons consolidated their power in **hospitals**. By the 1850s they had achieved broadly equal status with physicians, and in the next hundred years the status of surgery rose even higher. Two major developments—**anesthesia** and the “antiseptic method”—dominated surgical practice in the second half of the nineteenth century. Both have become part of surgical mythology, but both were consequences, rather than causes, of the new status and authority of nineteenth-century surgeons. Anesthesia initially emerged in the United States in the 1840s. Agents such as ether, chloroform, and nitrous oxide were initially used in dentistry but rapidly moved into surgery and obstetrics. Surgical practice was already highly invasive before the advent of anesthesia, and its introduction initially made surgery more dangerous as surgeons attempted these ambitious procedures more frequently.

The antiseptic method, meanwhile, was a response to public health reformers, who challenged the new status of hospitals as centers of surgical expertise. By the 1850s most European cities had large hospitals for the poor, and most suffered epidemics of fever and gangrene, known as “hospitalism.” In Britain, sanitary reformers such as **Edwin Chadwick** and **Florence Nightingale** (1820–1910) argued that large hospitals were inherently unhealthy and should be replaced by smaller, rural institutions under the supervision of public health agencies. Surgeons began to look for a scientific response to hospitalism. They hoped to prove conclusively that hospitals were not inherently unhealthy, and in so doing, to preserve and strengthen their intellectual authority.

In 1867 **Joseph Lister** (1827–1912), Professor of Surgery at Glasgow University, began to dress surgical wounds with bandages soaked in carbolic acid. He found that this simple technique slashed the rate of gangrene and fevers. Lister’s work was based on the “germ theory” of the French chemist **Louis Pasteur**. He presented his work as a scientific response to the problem of hospitalism, based on the latest concepts in experimental medicine. Over the next decade Lister expanded his work into an “antiseptic method” of surgery, intended to kill all germs in the operating environment. This included a steam-powered spray to cover patient, surgeon, and nurses in carbolic acid during surgery. In the 1880s and 1890s, the German “aseptic method,” based on the idea of excluding **bacteria** from the surgical environment, gradually replaced Lister’s complex and demanding technique. But Lister’s reputation continued to grow, and in 1900 he became the first British surgeon to be made a lord. Two further technical developments in the 1890s—X-ray diagnosis and blood transfusions—contributed to the eminence of surgery. The surgeon as “hero” had arrived.

By 1900 surgeons were beginning to operate on the brain and abdomen—areas that even a few decades before had been seen as too delicate for surgery. But if surgery grew up in the nineteenth-century hospital, it came of age on the battlefields of the twentieth century. Many of the surgical specialties established by the 1950s—orthopedics, trauma surgery, neurosurgery—had emerged in military hospitals during the First and Second World Wars. With this specialization came even greater reputation. Even in the early twenty-first century, when many aspects of medicine are challenged and contested, surgery has managed to retain its aura of heroism and expertise. *See also* Corpses and

Epidemic Disease; Disinfection and Fumigation; Hospitals and Medical Education in Britain and the United States; Hospitals in the West to 1900; Hospitals since 1900; Medical Education in the West, 1500–1900.

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RICHARD BARNETT

SWEATING SICKNESS. Commonly referred to as the “English Sweat”—*Sudor Anglicanus*—this mystery disease struck England in 1485, 1508, 1517, 1528, and 1551. The first outbreak of the sweating sickness was coupled with Henry VII Tudor’s (1457–1509) invasion of England in August 1485, leading some commentators to argue that the disease was imported from France. There also appears to have been a widespread but short-lived outbreak on the continent, most notably a two-week visitation in Germany in July 1529. At Marburg it interrupted the Colloquy between Reformation leaders Martin Luther (1483–1546) and Huldrych Zwingli (1484–1531) and left 500 dead in Amsterdam and 1,000 to 2,000 in Hamburg.

This disease illustrates the hazards of diagnosing diseases in the past based on symptoms alone, as it has been diagnosed as several different ailments by modern scholars, and by none convincingly. John Caius (1510–1573), the noted English **physician**, provided the best description of the disease’s symptoms in 1552, based on his observation of the 1551 outbreak. The sweating sickness had a sudden onset and ran a 3- to 14-day course. It was characterized by symptoms reputedly more severe than those of **bubonic plague** with a high fever, pain in the extremities and back, vomiting, bleeding, and diarrhea, and it might include multiple organ failure. Most reports of the disease occurred during the summer and early autumn. “The sweat” generally started in rural areas, especially the west of England, but produced higher death rates when it arrived in London and other cities. The disease respected no social class, and nobles as well as peasants died from the sweat. The suddenness of the onset of the disease often led to immediate death, a characteristic described by Caius in *A Boke or Counsell Against the Disease Called the Sweate* (10): “But that immediately killed some in opening their windows, some in playing with children in their street doors, some in one hour, many in two it destroyed.” Those who survived the initial onset of the disease could expect a long convalescence. In sum, contemporaries viewed the sweating sickness as often a killer, feared by all.

The English Sweat has been diagnosed as **influenza**, **typhus**, **Hantavirus**, and spring-summer **encephalitis** among others. A new leading candidate emerged in 1999—Crimean Congo hemorrhagic fever (CCHF)—but it, too, is subject to challenge. CCHF is caused by a **virus**, but other potential diagnoses have **bacterial** agents, and one interesting possibility—**Babesia**—is a **protozoan** disease. From its symptoms, it appears that

the sweating sickness is a vector-borne disease rather than one passed directly from one person to another. The sweating sickness remains a mystery disease with no clearly identified agent of disease, no sure reason for its onset in 1485, and no explanation as to why it vanished in 1551. See also *Diagnosis of Historical Diseases; Hemorrhagic Fevers; Historical Epidemiology; Plague in Britain, 1500–1647*.

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JOHN M. THEILMANN

SYDENHAM, THOMAS (1624–1689). Known as the English **Hippocrates**, Thomas Sydenham was the greatest medical practitioner of his day. A close friend of the **physician** and empirical philosopher John Locke, Sydenham rejected traditional medical practice in favor of firsthand observation and description of suffering patients. Although an avid classifier of diseases, in the spirit of the **Scientific Revolution**, he avoided discussion of ultimate causes of disease and accepted **humoral theory**. He did, however, note that a given disease is the same in "a Socrates or a simpleton" and is not particular to an individual.

The son of a country gentleman, Thomas studied medicine sporadically at Oxford, between hitches with the Parliamentary cavalry during the English Civil War. He was rewarded with a fellowship at All Souls College, which he abandoned in 1655 when he married. Settling in London, he conducted a medical practice among the poor, during which he carefully compiled his observations of symptoms and the courses of illnesses. He fled London during the Great Plague of 1665, though not before observing a case of plague in Westminster, and published his *Method of Curing Fevers* the following year. A second edition, including a section on plague, appeared in 1668, and a greatly expanded version, titled *Medical Observations*, was released in 1676. This earned him a medical doctorate from Cambridge University, though he was never a full member of the College of Physicians or Royal Society, both of which privileged theory over practice and traditional credentials. Sydenham had little use for either, stressing in his works the importance of abandoning incorrect descriptive models for more accurate ones built up from actual experience.

Just as scientists were developing classification systems for rocks and plants, Sydenham sought to differentiate diseases as carefully as possible. This would, he believed, lead to far more effective treatments. He distinguished continual fevers such as **typhus** and **typhoid**

from intermittent fevers like **malaria** and from the diseases whose symptoms included high fevers, plague and **smallpox**. He further distinguished smallpox into two types: the milder “distinct pox” and the very dangerous “flux pox.” His erroneous notion that during an epidemic all other diseases convert to or develop into the epidemic disease, however, retarded advances in epidemiological thought until the development of germ theory in the later nineteenth century. In shorter published letters, he described and made recommendations for treating **measles**, **syphilis**, smallpox, and rheumatic fever. He also updated his *Observations* to include **epidemics** in London from 1675 to 1680.

Despite, or perhaps because of his rudimentary theoretical education in medicine, Sydenham rejected current practices such as medical **astrology** and dependence upon examination of urine and other human waste material, in favor of close attention to the sick human body itself. His descriptions of the symptomatic courses of diseases are thus highly detailed and unambiguous and provide his readers with clear guidelines for diagnosis. His disinterest in theory, however, left him with the **Galenic** model of the human humors, and most of his prescriptions—usually bleeding and inducing vomiting and defecation—directly reflect the limitations of that model. He also ignored the recent advances in human physiology, often made by men he knew. *See also* Plague in Britain, 1500–1647.

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JOSEPH P. BYRNE

SYPHILIS. Syphilis is caused by the **bacterium** *Treponema pallidum*. The infection occurs during vaginal, oral, or anal sexual intercourse with an infected person. The disease is characterized by three stages. The primary infection begins with a painless sore at the site of infection, usually the genital area. If left untreated, the sore heals within a few weeks, and the disease continues into a secondary stage. At this stage, it can mimic a lot of other diseases, which is why it has been nicknamed “The Great Imitator.” After around one to three months, the symptoms usually disappear, and the further course is clinically quiescent. This so-called “latent” stage, during which the infection can only be detected by blood tests, can last a lifetime or, after decades, enter the final, tertiary stage with symptoms appearing on the skin and the in central nervous system, the so called “neurosyphilis.”

Treatment for syphilis is simple. Depending on the stage, one to three shots of the **antibiotic penicillin** are sufficient. Infusions of penicillin are required in every stage whenever the central nervous system is affected.

Biological Agent and Its Effects on the Human Body. Syphilis is caused by *Treponema pallidum*, a spiral-shaped bacterium of the genus *Spirochetæ*. It was identified microscopically as the causative agent in 1905 by two Germans, the dermatologist Erich Hoffmann (1868–1959) and the zoologist **Fritz Richard Schaudinn**. The complete genetic code was sequenced and published in 1998 in the journal *Science*.

The disease is characterized by three distinct stages. After an asymptomatic period of about 21 days, the primary chancre, an almost painless sore, appears at the site of infection and heals spontaneously even when left untreated. A classic chancre is only seen in 60 percent of patients. It is usually located in the genital area, but it may also occur at other sites like the mouth.

In 70 to 80 percent of primary cases of syphilis, the lymph nodes of the groin are enlarged, though usually only on one side. At this stage, an examination in a special dark-field **microscope** can directly prove the presence of the bacteria, which are very motile and characterized by extreme bending in the middle. Blood investigations may yield negative results.

Six to twelve weeks after the onset of the primary chancre the patient enters the secondary stage. At that time, *Treponema pallidum* has been disseminated via the blood stream, and any organ can be affected. The secondary stage usually recedes in 4 to 12 weeks, even without treatment. Almost 60 percent of patients with latent or late syphilis deny a history of secondary disease, as the signs, unless severe, are easily overlooked and forgotten. The skin manifestations are termed “syphilids” and are observed in 80 to 95 percent of patients in the secondary stage. The skin rash, which usually occurs on the trunk, may have different patterns (e.g., spots, nodules, with or without scales). Spots and nodules on the palms and soles are very characteristic and strongly suggestive of syphilis. The face can be involved, especially the mid-face and the hairline, giving a crown-like pattern. Hair loss includes two types: hair thinning throughout the scalp and patchy, so-called moth-eaten, alopecia. Another skin sign is the so-called Condylomata lata in 20 to 70 percent of patients in the secondary stage. They are moist, flesh-colored nodules of the genital and anal area, full of *Treponema* bacteria and extremely infectious. In the mouth, flat sores may appear, and the patient can suffer from a sore throat. In over 85 percent of cases, the lymph nodes of the neck, axles, and groin are swollen.

Nearly all organs can be involved during secondary syphilis (e.g., mild swelling of the spleen, reduction of red blood cells, and acute inflammation of the kidneys, liver, and gut with bellyache); acute vision and hearing complications are typical clinical signs for the involvement of the central nervous system. Even bone and muscular symptoms are described.

Most of our knowledge of the natural course of syphilis is derived from the classical Oslo study, which was carried out in the pre-antibiotic era. It was conducted in Oslo, Norway, between 1891 and 1910, when 2,181 cases of syphilis were left untreated and the records of almost 1,000 patients were traced, analyzed, and reported in 1955. According to this study, an untreated patient usually becomes noninfectious as early as six months after the disease has been contracted.

If untreated, the asymptomatic latent stage follows the secondary stage in which the infection can only be proven by positive blood tests. This stage is called late latent syphilis and may continue for the rest of the lifetime in an asymptomatic form in about two-thirds of untreated patients. The other third develops tertiary syphilis, which becomes manifest as skin granulomas (called “gummas”) (16 percent), or heart (9.6 percent) or central nervous system (6.5 percent) disease. The last is termed “neurosyphilis”

Transmission. *Treponema pallidum* is transmitted by an infected person via vaginal, oral, or anal sexual intercourse. If the sore occurs in the mouth, transmission by open mouth kissing is possible. In rare cases, it may be transmitted by nonsexual contact in communities living under conditions of poor **personal hygiene**. Importantly, *Treponema*

bacteria are very fragile, and infection can only occur through direct body contact and not by daily activities (e.g., touching toilet seats, using hot tubs, sharing cutlery).

A very special situation is the primarily infected pregnant woman in whom the *Treponema* bacteria can cross the placenta to infect the unborn child. **Children** born with “congenital syphilis” suffer from severe mental and physical disabilities, which is the reason why all pregnant women need to be screened for syphilis infection. A coinfection with other genital diseases such as genital cold sores eases and therefore may mask the discomfort associated with undiagnosed syphilis.

Epidemiology. Though it first appeared in Western Europe in the later 1490s, syphilis is not only a disease of historical interest. Over the past 60 years, syphilis infection has fluctuated in the United States, as in other developed countries. Syphilis rates peaked during World War II, followed by a dramatic decrease, particularly as a result of the introduction of penicillin. Syphilis has been regarded as a typical example of a sexually transmitted infection that can be controlled by public health measures. There are several characteristics of *T. pallidum* that enhance prospects for control and eventual regional elimination: *T. pallidum* is an exclusively human pathogen and has no animal reservoir, and penicillin is still the treatment of choice without problems of antimicrobial resistance. Worldwide, penicillin mass treatment programs in most “hot spots” in the 1950s and 1960s were some of the most successful health programs of the **World Health Organization (WHO)**.

However, syphilis remains a public health problem worldwide, and the WHO estimates that 12 million new cases of venereal syphilis occur worldwide annually, mainly in the developing countries, but also in the major urban areas of the United States and western Europe. In the latter, the infections have shifted to particular risk groups (e.g., outbreaks among male homosexuals and abusers of illegal drugs). In Russia and in much of eastern Europe, the reemergence of syphilis is contributing to the **HIV/AIDS epidemics**. Syphilis infection facilitates acquisition and transmission of the human immunodeficiency virus (HIV).

Control of the Disease. Blood tests are carried out for screening in asymptomatic individuals as well as in patients with clinical symptoms to prove syphilis infection (e.g., in the second and third stages). A presumptive **diagnosis** is possible with the use of two types of blood tests for syphilis. The first is a nontreponemal test, which detects the patient’s immune response (antibodies directed against the bacteria’s membrane) and are used for monitoring syphilis activity and treatment response. These tests have their limitations because they may yield false positive results in patients not infected with *T. pallidum*. The second type of test, a treponemal specific test, provides evidence of infection.

There is no vaccine for the prevention of syphilis infection. Therefore, the disease has to be treated whenever it is diagnosed. Penicillin is the preferred drug for treatment of all stages of syphilis. Primary and early secondary syphilis is treated with one shot; latent syphilis and tertiary syphilis are treated with three shots of penicillin. Whenever the nervous system is involved, penicillin infusions for 10 to 14 days are required.

Current State of the Disease. As infection rates in the developed world have been low for decades, most physicians in the developed world are no longer familiar with the symptoms of syphilis. The recent outbreaks of syphilis in urban areas in the United States and western Europe since the beginning of the millennium have completely changed the situation. Awareness in the medical community as well as the public about the possibility of infection with *Treponema pallidum* has had to be reestablished through education

and health campaigns. In patients with symptoms pointing at treponemal infection, blood tests for syphilis should be performed deliberately. Screening schedules for syphilis in asymptomatic patients should be maintained and reestablished, respectively. Risk groups at focus are HIV-positive men who have sex with men, prostitutes, and illegal drug abusers.

Because of limited financial resources, there is a different attitude and medical approach in the developing world, where most new infections occur. Screening in these countries can only be focused on the identification of newly infected patients in the primary and secondary stages of syphilis, who can transmit the disease to their sexual partners and, in the case of pregnancy, to unborn children. In these countries, routine screening with at least a non-treponemal test that is cheap but unspecific for syphilis should be performed on a wide scale. *See also* Disease in the Pre-Columbian Americas; Fracastoro, Girolamo; Gonorrhea and Chlamydia; Human Immunity and Resistance to Disease; Paracelsus; Sexual Revolution; Syphilis in Sixteenth-Century Europe; Venereal Disease and Social Reform in Progressive-Era America.

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STEFAN WÖHRL AND ALEXANDRA GEUSAU

SYPHILIS IN SIXTEENTH-CENTURY EUROPE. The virulent irruption of previously unknown **syphilis** in Europe at the end of the fifteenth century introduced a very significant health problem. This was the first known epidemic of a sexually transmitted disease in the West, though there is no consensus on the reasons for its surge at this time.

At the end of the fifteenth century, several authors from Germany, Italy, and Spain discussed a strange, new disease. The German Joseph Grünpeck (c. 1473–1532) published his *Treatise on the Flowing Pestilence, or the French Disease* (Augsburg, 1496) in both Latin and German. In it he explained the emergence of this **epidemic** as a function of celestial causes, as a divine punishment against an immoral world carried out through means of an adverse celestial conjunction. This conjunction of planets, he believed, provoked the pestilential corruption of **air** that poisoned its victims. In this and other ways the era's **physicians** followed the pattern set for explaining and dealing with the plague. The physician Niccolò Leonicensi (1428–1524) participated in the medical dispute at the court of Ferrara, Italy, in the spring of 1497 over the nature of this mysterious sickness. He claimed that syphilis was not new but had been known to and described by classical medical

writers. He published his thesis in *Booklet on the Epidemic that Is Commonly Called the French Disease* (Venice, 1497), but despite thorough research, he was not able to prove this assertion.

Avoiding **astrology** and humanism, Spanish physician to the Papal Court Gaspar Torrella (1452–1520) approached the novel disease in a more clinical way. He composed the *Treatise with Advice Against “Pudendagram” or the French Disease* (Rome, 1497). Torrella based his book on a study of 16 case histories, revealing the fruits of careful observations of the pathologic phenomenon but staying within the traditional framework of medical interpretation and explanation. Another Spanish doctor, Francisco López de Villalobos (1473–1549), published *A Summa on Medicine, with a Treatise on the “Bubas” Pestilence* (pox) (Salamanca, 1498). The appended treatise on pox (syphilis) is considered one of the best of all works on the subject in the fifteenth and sixteenth centuries.

Several books written during the first third of the sixteenth century contain carefully drawn verbal pictures of the effects of syphilis. One example is Grünpeck’s second book, *Booklet on Mentulagra, Otherwise Known as the French Disease* (1503). Another is the text of German Ulrich von Hutten (1488–1523; *On the Medicine Guaiacum and the French Disease, Book One* [Mainz, 1503]), in which he recorded the benefits he personally received from the use of the new drug guaiacum—derived from South American trees. In a similar vein, the Spaniard Francisco Delicado (c. 1475–1535) wrote *How to Use the Wood of the West Indies: A Healthful Remedy for Every Injury and Incurable Illness* (Rome, 1525).

Undoubtedly, the best work on syphilis, because of its clinical excellence and its literary quality, is the poem *Syphilis, or the French Disease* (Verona, 1530), by the famed Italian physician **Girolamo Fracastoro**. Originally a pastoral character in this work, Syphilis soon became synonymous with the disease itself. In poetic form, Fracastoro summarized his era’s knowledge of the disease and imputed sexual transmission to syphilis (“most obscene,” he says). In the first of the poem’s three books, Fracastoro describes a terrible and new malady that is the result of a fatal conjunction of the planets Jupiter, Mars, and Saturn (a specific conjunction elsewhere blamed for plague). He also links the appearance of the disease in Italy to the French invasion of the 1490s and later military campaigns—from which it received its original popular name, the “French disease.” The second book deals with treatment. He prescribed a classical regimen of health and medication but also praised the curative properties of mercury. A good humanist, Fracastoro wraps this in a fable of one Ilceus, on whom Apollo inflicted this disease. The lad is thrice dipped in a stream of mercury (“living silver”) by a wood nymph and cured. In the third, Fracastoro praises the glory of the transoceanic discoveries and presents another myth. In the New World, a Spanish army discovers a village of natives whose skins are covered by disgusting ulcers. Their chief explains that the shepherd Syphilis abandoned worship of the sun and received this tremendous scourge from on high, as will all infidels thereafter. The helpful nymph America, however, transplants to this land the beneficent tree, the guaiacum, which will heal them (as it did Von Hutten).

Though modern specialists still argue about the ultimate source of syphilis, most early German, Italian, and Spanish writers blamed its origins and spread on the French, during whose aggression in Italy the disease first clearly appeared. By the 1520s, however, the idea of an American origin emerged, as reflected in Fracastoro’s poem. Gonzalo Fernández de Oviedo (1478–1557) clearly sustains this opinion in his *Summary of the Natural History of the Indies* (1526). The first doctor who supported this idea with data was Rodrigo Ruiz Díaz de Isla (1462–1542), in his *Treatise on the “serpentine” disease* (Seville, 1539; composed in 1520). This surgeon explained that an unknown disease, neither seen nor described

before, had its origin in Haiti and appeared in Barcelona in 1493. Chroniclers claimed that syphilis was a very common, light, benign, and cutaneous affliction in Indians that caused severe problems for the Spaniards. The “American thesis” explains that the infection was brought back to Spain by Columbus’s crews and carried to Italy by Spanish troops. During the siege of Naples, the disease was transmitted to French soldiers of Charles VIII: hence the French name, *mal de Naples*. When the war ended, the troops went back to their respective countries spreading the disease.

But there is **paleopathological** evidence suggesting the existence of syphilis in Europe before Columbus’s voyage. Current epidemiological theories maintain that the disease was in existence on all continents before 1492, and certain changes in conditions provoked an increase in the severity of syphilis at roughly that time.

The symptoms of syphilis were acute and dramatic: rashes, eruptions, and ulcers of the skin and mucous membrane of the pharynx, complete alopecia, severe articular pain, and quick organic consumption. From the beginning, its contagious character was patent, but doctors discovered only belatedly its venereal origin. Therefore, the preventive measures were generally those for the plague (**personal hygiene** and appropriate **diet**, public sanitation and **quarantine**). Special preparations of mercury, however, were soon employed as a specific and useful treatment. Though highly toxic to the body as well as to the pathogen, its successes supported the new, iatrochemical approaches of **Paracelsus** and the **Paracelsians**. Another medication also appeared in the epidemic’s early stages: the ingestion of large quantities of the decoction of the American guaiacum wood (*Guaiacum officinale*). Though it had little effect, doctors believed the treatment for a disease was to be found naturally in the disease’s place of origin.

Both medications were expensive, and the social problem was how to attend to all poor victims of the disease. Special **hospitals** for this duty were set up in Italy during the sixteenth century: the *incurabili* (incurables) hospitals. The Genoese Hospital of the Ridotto is probably one example. The Ridotto accepted the syphilitic poor because they were rejected by the other hospitals because of their incurable disease. Bologna and Ferrara established hospitals for the treatment of syphilis, and in Milan and Orvieto portions of the general hospitals were devoted to syphilitic patients. During the 10 years between 1515 and 1526, another seven *incurabili* hospitals were founded, and three more included special wards in existing hospitals in several Italian cities. *See also* Astrology and Medicine; Colonialism and Epidemic Disease; Contagion Theory of Disease, Premodern; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Historical Epidemiology; Humoral Theory; Medical Education in the West, 1100–1500; Plague and Developments in Public Health, 1348–1600; Plague in Europe, 1500–1770s; Poverty, Wealth, and Epidemic Disease; Religion and Epidemic Disease; Sexuality, Gender, and Epidemic Disease; War, the Military, and Epidemic Disease

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JUSTO HERNÁNDEZ

T

TB. See Tuberculosis.

THEILER, MAX (1899–1972). Epidemiologist Max Theiler is best known for developing the first **vaccinations** that could immunize humans against **yellow fever**. He received the Nobel Prize for Physiology or Medicine in recognition of this achievement in 1951.

Theiler was born in Pretoria, South Africa, the son of Sir Arnold Theiler (1867–1936), a veterinary scientist who did research in veterinary **immunology**. Max began his medical education at the University of Cape Town Medical School, but in 1918 he transferred to London to study at St. Thomas Hospital and the London School of Tropical Medicine. He received his medical degree in 1922 and became a Licentiate of the Royal College of Physicians and a Member of the Royal College of Surgeons. After graduation, Theiler took a post in the Department of Tropical Medicine at the Harvard Medical School in Boston, Massachusetts, where he studied a number of infectious diseases, including amoebic **dysentery**, rat bite fever, and yellow fever. In 1930 he joined the International Health Division of the **Rockefeller Foundation** in New York City, where he continued his research on yellow fever. He accepted a position as professor of **epidemiology** and microbiology at Yale University in 1964 and remained there until his retirement in 1967.

In the 1920s, scientists sought to identify the specific factor that caused yellow fever. By 1927 Theiler had proven that the disease was caused not by a **bacterium** but by a filterable **virus** that he hoped to cultivate in the laboratory. At the time, rhesus monkeys were the only animals known to be susceptible to yellow fever, but they were expensive as laboratory animals, so Theiler searched for a less expensive alternative. By 1930 he discovered a means of infecting mice with the yellow fever virus by injecting pieces of infected monkey liver into their heads. Using this procedure, Theiler isolated a strain of the virus that was extremely deadly in mice but that would barely produce a fever when

injected into monkeys. Furthermore, he proved that when this strain, which was attenuated, or weakened, in monkeys, was introduced under the skin of humans, it provided immunity to the disease. There were complications associated with this early **vaccination** in some patients, however, so Theiler tried to isolate a safer strain to use in a vaccine. In a new series of experiments, he cultivated the yellow fever virus in chick embryos and by 1937 had managed to develop a safer attenuated virus, named "17D," which was more suitable for use as a vaccine. Thereafter, the Rockefeller Foundation mass-produced 17D vaccine and distributed it without cost to 33 tropical countries from 1940 to 1947. *See also* Yellow Fever in Latin America and the Caribbean, 1830–1940.

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WILLIAM H. YORK

THIRD PLAGUE PANDEMIC. *See* Bubonic Plague in the United States; Plague in Africa: Third Pandemic; Plague in China; Plague in East Asia: Third Pandemic; Plague in India and Oceania: Third Pandemic; Plague in San Francisco, 1900–1908.

THIRTY YEARS' WAR. The Thirty Years' War (1618–1648), fought in the area of modern Germany and its neighbors, is the classic example of a "military mortality crisis," in which war drives a dramatic increase in civilian mortality.

The war was, on one level, a conflict between Catholics and Protestants. As it proceeded, however, almost every major European power, from Spain to Sweden, became involved at one stage or another, and the war became a struggle for European hegemony in which religious differences were secondary. It evolved into the largest war that had been seen in continental Europe since at least Roman times.

The epidemic disease environment of the time was hostile. **Bubonic plague** was an ordinary hazard of life; the major German city of Augsburg had suffered plague in 17 of the 100 years prior to the outbreak of the war. Reports of significant epidemics of other diseases such as **typhus**, dysentery, and **smallpox** were comparatively rare, however. Dearth and famines caused by adverse weather conditions were by no means unknown; there was a sequence of poor harvests in Germany between 1622 and 1628, and a Europe-wide harvest failure occurred in 1635.

During the Thirty Years' War, the population of Germany declined by perhaps a third in urban areas and 40 percent in rural areas. Because the urban population was very small, the key figure is the latter. Although a decline in the birth rate and net emigration played a part in this decline, the major factor was an increase in mortality caused largely by plague and starvation. The classical view is that the exceptional mortality was caused by an unusually rapid geographical spread of epidemic disease, itself caused by troop movements and civilian **flight** from areas affected by war, and by nutritional stress caused by troops who requisitioned and plundered food from the peasantry.

Recent research has deepened this account, emphasizing the “socioeconomic relations of warfare.” It focuses on the nature of the relationship between soldiers and the civilians on whom they depended for food, fodder, and shelter. In the Thirty Years’ War these relationships gradually became marked by disorder, wanton destruction, violence, and atrocity. By the mid-1620s in some areas, and the 1630s in others, civilians had learned to dread the soldiery and to flee their villages at the first sign of the soldiers’ approach. It was these hostile and highly violent relations between the soldiery and civilians that undermined the ability of civilians to feed themselves and led to the frequent and widespread civilian flight of the classical account. *See also* Diet, Nutrition, and Epidemic Disease; Plague in Europe, 1500–1770s; Religion and Epidemic Disease; Typhus and War; War, the Military, and Epidemic Disease.

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QUENTIN OUTRAM

TRADE, TRAVEL, AND EPIDEMIC DISEASE. The role of trade and travel in the spread of infectious diseases is an ancient one. Wherever humans travel, microbes accompany them. The mobility of humans, ground **animals**, birds, and **insects** has been a continuing influence on patterns of infectious disease occurrence. The speed, volume, and reach of today’s trade and travel are unprecedented in human history and offer multiple potential routes for microbial spread around the globe. **HIV/AIDS**, with its primate origins in central Africa, has spread quickly around the world in the past quarter-century. In 2003, **severe acute respiratory syndrome** (SARS) migrated out of the Chinese mainland and then radiated rapidly from Hong Kong to Vietnam, Europe, and Canada.

Vectors such as mosquitoes can travel with trade and transport. In the past several decades, a major mosquito vector for the **Dengue** fever **virus**, *Aedes albopictus* (the “Asian tiger mosquito”), has greatly increased its geographic range between continents. This has occurred, particularly, via the inadvertent intercontinental exportation of mosquito eggs in used car tires into Africa and the Americas. There have been countless other such episodes of geographic spread via trade and travel, over many centuries. The **Black Death** of the fourteenth century, which killed around one-third of the European population, is a well-known example. This dreaded bacterial infection, **bubonic plague**, entered Europe via infected black rats that had spread from the Asian steppes and then westward along the traders’ Silk Road toward the Black Sea, an eastern portal to Europe, where it unleashed its devastation over the ensuing half-decade. Recurrences of plague in the European and Islamic worlds are often attributed to humans carrying the necessary rats and fleas along communication routes from reservoirs of endemic plague.

Historically, there were great equilibrations between the regional infectious disease pools across Eurasia during the millennia immediately before and after the time of Jesus Christ. These exchanges of microbes, often with devastating **epidemic** consequences, resulted from the various forms of intensified human contact—trade, travel, military

incursions, and conflict. For example, the bubonic plague **bacterium**, *Yersinia pestis*, apparently accompanied Roman legions returning to Constantinople from the Middle East. Indeed, this mirrored the dissemination of the respiratory infection, **tuberculosis**, by Roman legions as they fanned out around the Roman Empire.

Trade. Advances in the ease and speed of transportation, first at sea and then on the land, created new and tighter networks of contact that widened and quickened the spread of epidemic disease and prompted new thinking about it. In mid-nineteenth-century London, Dr. **John Snow** noted that epidemics of cholera followed major routes of commerce between Asia and Europe, consistently appearing first at seaports when entering a new region. Outbreaks of cholera occasionally appeared beyond its natural “homeland.” Although this occurred on a localized scale several times during the seventeenth century, it did so more substantively in 1817 as British military and colonial activity in India increased. In 1854 Snow observed that “cholera began to spread to an extent not before known; and, in the course of seven years, it reached, eastward, to China and the Philippine Islands; southward to Mauritius and Bourbon; and to the northwest as far as Persia and Turkey. Its approach towards our own country [England], after it entered Europe, was watched with more intense anxiety than its progress in other directions.”

Indeed, cholera provides an excellent example of the role of travel, trade, and human migration (including troop movements) in the localized and, then, distant spread of infectious disease. The disease appears to be ancient: descriptions in ancient Hindu, Chinese, and Greek texts from 2,000 to 3,000 years ago refer to severe outbreaks of cholera-like dehydrating diarrheal diseases. Cholera’s ancestral homeland appears to have been along rivers and estuaries in India, particularly in the populous basins of the Ganges and Brahmaputra rivers. Cholera epidemics, however, appeared outside south and east Asia with the acceleration of trade and European colonization in the region during the nineteenth century. Discrete epidemic waves over the course of the century challenged early epidemiologists to identify the spatial and temporal factors connected to epidemics, and led to International Sanitary Congresses in which national delegates debated the best ways of containing epidemics without undermining trade.

In the twentieth century, advances in epidemiology have accompanied the even more dramatic evolution in transportation and continue to clarify the relationship of human movement and disease. The still-continuing seventh pandemic of cholera is the largest and longest ever. It began in 1961 and has engulfed Southeast Asia, the Middle East, Russia, Europe, much of Africa (where it has now become endemic for the first time), and the Americas. In 1991 it entered Latin America, where it subsequently caused over 1 million cases and around 12,000 deaths. This distant spread has been attributed to the dumping of cholera-contaminated ship’s ballast water off the Peruvian coast—and that at a time when coastal waters were unusually warm (during an El Niño meteorological event) and conducive to the amplification of the cholera *Vibrio* in plankton and its subsequent entry into the local marine food chain, leading to human consumption.

Inadvertent epidemic-related biological introductions through trade also underscored the importance of surveillance of nonhuman activity. The vector mosquito of African **malaria**, *Anopheles gambiae*, entered Brazil for the first time in 1937. The mosquito migrated on the mail boats from western Africa that crossed the Atlantic in just three to four days. This same mosquito species then spread along the Brazilian coastal region and inland and caused up to 50,000 malaria deaths. Fortunately, an extraordinary campaign,

led by the American Fred Soper (1893–1977), eliminated this mosquito species from Brazil in the early 1940s.

In recent times, the globalization of food production and distribution has amplified the movement of pathogens from one region to another. For example, an outbreak of cholera in the 1990s in Maryland was traced to the importation of contaminated frozen coconut milk. Alfalfa sprouts grown from contaminated seeds sent to a Dutch grower-and-shipper led to outbreaks of Salmonella food poisoning in both the United States and Finland.

Regional free trade agreements have both caused and brought to light various examples of how intensified, deregulated market competition can heighten the risks of infectious diseases in disempowered and poorly educated workers. For example, in the 1990s there were several outbreaks of **hepatitis A** and cyclosporiasis (a protozoan infection) in the United States caused by fecally contaminated strawberries and raspberries imported from Central America. The North American Free Trade Agreement had eroded environmental and labor standards (such as providing toilet facilities for workers) in the face of the demands of open competition and profitability. This, plus modern rapid air-transport, meant that within two days of the berries being picked, upmarket diners in New York would acquire the same fecally transmitted infections as the dispossessed farm workers in Guatemala.

Travel. From its points of origin in central and western Africa, **HIV/AIDS** burst on the world scene in the 1980s. Long-distance travel had a great deal to do with its rapid spread. It is widely thought that Cuban troops sent by Fidel Castro to Africa, to assist the quelling of a local conflict, acquired this sexually transmitted disease and took it back to the Caribbean, from whence its subsequent spread was aided particularly by gay sex tourism. In the last 50 years, soldiers, tourists, businesspeople, and even **pilgrims** have all unwittingly contributed to the spread of infectious disease. *Neisseria meningitidis* is a pathogen that has long caused seasonal epidemics of **meningitis** in parts of Africa: the so-called “meningitis belt.” The disease has recently spread more widely. Studies with molecular markers have shown how Muslim pilgrims who brought an epidemic strain of *N. meningitidis* from southern Asia to Mecca in 1987 then passed it on to pilgrims from Sub-Saharan Africa—who, after returning home, were the cause of strain-specific epidemic outbreaks in 1988 and 1989.

West Nile Virus disease (WNV), newly introduced to North America, further illustrates the impact of long-distance trade and travel. The disease has its origins in Africa, and it occurs sporadically in the Middle East and parts of Europe. It was unknown in North America until it arrived in New York in 1999, via an infected *Culex* mosquito on an airplane. There were apparently favorable conditions for the virus to survive and spread within New York City. Early season rain and summer drought provided ideal conditions for *Culex* mosquitoes. July 1999 was the hottest July on record for New York City. Suburban/urban ecosystems supported high numbers of select avian host and mosquito vector species adapted to those conditions. Furthermore, large populations of susceptible bird species existed, especially crows. Suburban/urban ecosystems were conducive for close interactions among mosquitoes, birds, and humans.

West Nile Virus affected birds first; then, as temperature and rainfall changed, the birds left town, and humans became the preferred target for the vector mosquitoes. The disease subsequently spread across the United States and established itself as an endemic virus in a majority of states, harbored by animals (including birds and horses) and transmitted via culicine mosquitoes. There was a marked increase in the number of human cases of

WNV disease during 2002–2003, involving many U.S. states. Today, the disease is well established in a majority of U.S. states.

In July 2003, Mexico declared a state of emergency when West Nile Virus arrived in that country. There had been concern that the disease could spread more rapidly in Central and South America than in North America. Latin American countries could be ideal breeding grounds because of their warmer climate, large bird populations, and year-round mosquito activity. Ecologists have anticipated an increasing range of adverse effects of the WNV infection on domesticated horses and on the diverse animal and bird life in the tropics.

Trade and Travel Combined: Severe Acute Respiratory Syndrome. SARS emerged from Guangzhong Province in southern China in late 2002, and by year's end, 25 persons in the capital Guangzhou had developed this severe respiratory disease. Soon the disease reached adjoining Hong Kong, where both hospital "super-spreading" and defective sewerage design in high-rise housing amplified the spread. By March–April 2003, cases began to be reported more widely, especially from Canada. Propelled by modern air travel, SARS extended to all continents and 31 countries. Its rapid dissemination to dozens of countries in the first half of 2003, infecting over 8,000 persons and killing one-tenth of them, and its ominous pandemic potential, captured headlines for months.

The actual zoonotic source of the SARS coronavirus, for a while uncertain, is now thought to be a rainforest bat. The evidence suggests that, from this natural animal source, the virus reached humans via the long-distance trading of live wild animals, themselves incidentally infected by the bat virus. Infection of palm civet cats with the SARS virus has been reported. Surveys have shown that the live markets and restaurants in Guangzhong sold various species of small carnivores (e.g., civet cat, raccoon dog, and ferret badger) that were captured in China, Laos, Vietnam, and Thailand, transported to markets (often across national borders), and thereby brought into close proximity with one another.

This type of unregulated trade, and the conditions of the wet markets with live animals for sale, means that infectious agents have great opportunities to move between edible species. Further, the recent popularization and intensification of what was previously a restricted and local practice has escalated urban demand for exotic animal foods in Southern China, and this has greatly amplified the health risks of what previously were localized cultural practices in rural settings.

Dengue Fever. Dengue fever is numerically the most important vector-borne viral disease of humans. The Dengue virus causes almost 100 million cases of infection each year, with high fatality rate in young **children**. This **hemorrhagic fever** is a good example of how patterns of trade, travel, and settlement can all influence infectious diseases.

Dengue evolved as a specialized human infectious disease sometime during the past three centuries in Asia, apparently from a progenitor zoonotic (animal-to-human) virus that had originated in Africa. The disease then spread in a leisurely fashion between continents. Although details are not known, four different strains of the virus subsequently evolved, in relatively separate geographic regions.

Although Dengue, by its origins, is primarily a tropical disease, its extension in recent decades into various temperate countries reflects both the introduction of the disease's main mosquito vector species, *Aedes aegypti* (which is behaviorally adaptable to both a cooler climate and to an urbanized **environment**), and the increase in imported cases of Dengue resulting from increased travel. The disease was brought under substantial control

in the 1930s and 1940s, via mosquito spraying programs, but reestablished itself widely after World War II with the aid of troop movements, increases in travel and trade, and premature relaxation of control programs. This increase in the range of Dengue also reflects the distinctive capacity for rapid evolutionary adjustment of the *Aedes aegypti* mosquito species to coexistence with urban-dwelling humans, having originated in the forests of Africa. Indeed, this mosquito species has followed humankind on its migrations around the world.

Conclusion. As the diversity and intensity of human activities increases, with the growth of human numbers and wealth, so is there the likelihood that travel and trade will continue to fuel the emergence and spread of infectious diseases. The microbial world is protean in its diversity, strategies, and genetic flexibility, and this, in conjunction with continual changes in human ecology and behavior, ensures that there will be continuing unexpected infectious disease outbreaks. A recent example from the escalating international trade in exotic pets is illustrative: the monkey pox virus was recently introduced into the United States in imported African rodents, bought as illicit pets, with subsequent transmission of the virus to prairie dogs—some of which were then sold in pet shops; from them the virus passed to other pets and to their human owners.

There are, of course, many other permutations to these patterns and determinants of ever-changing infectious disease risks and ecological relationships. One important consideration is that the cross-species transmission of microorganisms can operate in both directions. That is, it can also entail nonhuman primate species and other wildlife being infected by human pathogens. There is speculation, for example, that the demise of the great mammoths of northern America around 13,000 years ago could have been, in part, a result of their infection by germs introduced by the newly arrived proto-Amerindians or their dogs. In modern times, the enteric pathogen, *Giardia* has been inadvertently introduced into the Ugandan mountain gorilla population by humans via contacts that have occurred during ecotourism and conservation activities. Similarly, nonhuman primates have acquired **measles** from ecotourists.

The grand and colorful narrative of microbial traffic among species continues. Indeed, it does so at an ever-faster pace, in a world in which human numbers are growing and human activities are intensifying. *See also* Animal Diseases (Zoonoses) and Epidemic Disease; Black Death, Flagellants, and Jews; Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1862–1947; Cholera: Seventh Pandemic, 1961–Present; Colonialism and Epidemic Disease; Contagion and Transmission; Cordon Sanitaire; Early Humans, Infectious Diseases in; Epidemiology; Flight; Geopolitics, International Relations, and Epidemic Disease; Irish Potato Famine and Epidemic Disease, 1845–1850; Latin America, Colonial: Demographic Effects of Imported Diseases; Personal Liberties and Epidemic Disease; Plague: End of the Second Pandemic; Public Health Agencies, U.S. Federal; Quarantine; Slavery and Epidemic Disease; War, the Military, and Epidemic Disease.

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ANTHONY MCMICHAEL

TRANSMISSION OF DISEASE. See Contagion and Transmission.

TRAVEL. See Trade, Travel, and Epidemic Disease.

TRYPANOSOMIASIS. See Sleeping Sickness.

TUBERCULOSIS. Tuberculosis (TB) is a very contagious, often lethal, bacterial disease resulting from the infection of the lungs and other tissues by the bacillus *Mycobacterium tuberculosis*. Mummified human remains found in both Egypt and Peru demonstrate that tuberculosis has been afflicting humankind for at least several thousand years. Over its history, the illness has been known by the Greek term *phthisis* (pronounced tee-sis) as well as the more general term "consumption," both of which refer to the way that tuberculosis victims seem to waste away, or be "consumed" by the illness. Its highly contagious nature makes tuberculosis an **epidemic** disease in industrializing societies where populations are densely packed and live in poor sanitary conditions. Currently, it is among the most widely spread microbial diseases in the developing world, infecting an estimated one-third of the world's population (more than 2 billion people) and causing between 2 and 3 million deaths per year. Strains of tuberculosis **bacteria** that are resistant to many, if not all, forms of **antibiotic** treatment are becoming more common—a fact which greatly complicates treatment. Overall, tuberculosis presents one of the greatest infectious disease challenges affecting humankind today.

Agent and Effects. *Mycobacterium tuberculosis* is a rod shaped, Gram-positive bacillus that grows in a highly oxygenated (aerobic) environment. For this reason it grows preferentially in the lungs, but in about 15 percent of cases it infects other tissues such as the bones and lymph nodes, resulting in different disease symptoms. Tuberculosis infections begin when airborne bacteria contact the tissue of the lungs and are engulfed by macrophages (white blood cells). The bacteria have a waxy coating that resists digestion, allowing them to replicate inside the macrophages. More and more macrophages respond to the infection and are themselves infected, resulting in a hard lump of bacteria and dead tissue, called a tubercle (lump or knot), from which the disease takes its modern name. In most cases, the disease is halted at this stage and lies latent, with patients suffering few ill effects, although they will carry the bacteria with them for the rest of their lives. Such latent carriers of tuberculosis are always at risk of the disease becoming active. In approximately 5 to 10 percent of infections, the disease progresses to active tuberculosis, destroying the lungs through the creation of more tubercles and spreading throughout the body in a manner similar to the metastasis of cancer. Patients become weak and waste away; they cough severely, putting those around them at risk for infection. When tubercles form near blood vessels, the result

is hemorrhaging in the lungs, causing the patient to cough up blood. Prior to antibiotic treatment, more than half of active tuberculosis cases resulted in death within five years.

Transmission. Although it takes only a small amount of bacteria to lead to infection, in reality, prolonged exposure to a patient with active tuberculosis is usually necessary for transmission. Numerous variables including age, health, **nutrition**, and **environmental** conditions determine the overall susceptibility of an individual. **Heredity** also seems to play a role in individual susceptibility to tuberculosis. The overcrowded, unsanitary conditions of industrializing cities and prisons were ideal breeding grounds for tuberculosis in eighteenth- and nineteenth-century Europe and America; in England, mortality peaked in 1780 at 1.25 percent of the entire population per year. These conditions prevail in the expanding cities and badly managed prisons of poorer nations today, so that there are more people, in absolute numbers, sick and dying from tuberculosis in the twenty-first century than at any time in the past.

Tuberculosis and Society. Inevitably, tuberculosis claimed the lives of many of the literary and artistic elite of industrial Europe and America. Among nineteenth-century victims, perhaps the most famous is the poet John Keats, who died of the illness at the age of only 26, but tuberculosis also ended the lives of American author Henry David Thoreau (1817–1862), Russian novelist Fyodor Dostoyevsky (1821–1881), the Polish composer Frédéric Chopin (1810–1849), and several members of the Brontë family. Notable twentieth-century victims include Russian author Anton Chekhov (1860–1904), Czech writer Franz Kafka (1883–1924), and English novelist George Orwell (1903–1950). Brilliant youth cut down in the prime of life is a theme that easily lent itself to drama and Romantic tragedy, and consequently tuberculosis became a fixture in literature and the theater in the nineteenth century. The romanticizing of tuberculosis was taken to such extremes that the physical appearance of individuals in the later stages of the disease—gaunt, pale, delicate—was celebrated as the aesthetic ideal for feminine beauty.

Research and Treatment. In 1882 the German **physician Robert Koch** definitively identified *Mycobacterium tuberculosis* as the causal agent for consumption (for years thereafter, the bacillus was referred to as Koch's bacillus). This still ranks as one of the most profound achievements in the history of medicine, for not only did it provide a unifying theory and explanation for the various forms of tuberculosis, but it also helped usher in the **germ theory** of disease more generally and helped to establish a path toward more effective treatment.

Prior to Koch's work, the treatment of tuberculosis was a chronicle of applied superstition. For example, scrofula, a form of the disease in which the bacteria infect the lymph nodes of the neck, was believed to be curable by a touch from royalty; English monarchs upheld this tradition until the early 1700s. By the mid-nineteenth century, rest and fresh air were commonly prescribed, leading to the creation of **sanatoria** for the treatment of tuberculosis. Often built in isolated locales, sanatoria offered a retreat where the tubercular patient could partake of rest and fresh air while under the strict supervision of a medical staff. The association between tuberculosis and rest was carried to the tissues of the lung themselves; for years, physicians believed that "relaxation" of the lung was also an effective form of therapy. This relaxation of the tissue was achieved surgically, by collapsing one of the lungs. Today, surgery is sometimes used to remove portions (or all) of a tubercular lung in cases in which the disease is extremely advanced and aggressive.

The most effective treatment for tuberculosis is the use of antibiotics, but even this form of treatment is problematic. The tuberculosis bacillus replicates very slowly; because antibiotics affect bacteria during replication, it takes a very long time to treat



A boy or young man, suffering from pulmonary tuberculosis, sits in a Bath chair in front of his chalet, accompanied by a woman (presumably his mother). The chalet contains a bed and a chair, and is open, possibly to allow fresh air to circulate for the benefit of the inhabitant. Wellcome Library, London.

a tubercular patient. Therefore, antibiotic therapy ordinarily requires six months of disciplined and regular medication. In addition, tuberculosis can go dormant or remain inaccessible to drug treatment deep within diseased tissues. Patients often feel better and end their drug routines prematurely, contributing to the emergence of antibiotic resistant strains of the disease. Because tuberculosis is such a challenge, the **World Health Organization** currently recommends a comprehensive treatment strategy called Directly Observed Therapy (DOTS), which consists of a treatment regimen composed of several different drugs as well as outpatient care and observation to ensure patient compliance.

Vaccination. Since the 1920s, a vaccine for tuberculosis, called Bacille Calmette-Guérin (BCG) vaccine, named after its developers, has been available, but its effectiveness is still unclear. In the production of the vaccine, multiple strains of bacteria were used, resulting in inconsistent results. Many vaccine trials also suffered from a lack of rigor—in some, patients were not screened for latent tuberculosis before receiving the vaccine, and overall the dosage of the vaccine varied from trial to trial. It appears as though the vaccine is effective in preventing some of the more severe forms of the illness and is effective in protecting certain age groups, such as very young children. In other age groups, it seems to offer no protection at all.

Complicating matters is the fact that usage of the vaccine on a large scale makes diagnosis more challenging. Exposure to tuberculosis is usually determined by reaction to a test in which a protein derivative of the bacillus is injected under the skin. A positive reaction indicates infection, either latent or active. However, all patients who receive the BCG vaccine respond positively to the skin test, making it ineffective as a diagnostic tool. This undesirable side effect, coupled with the vaccine's general unreliability, has led the United States to reject the BCG vaccine as a preventive measure. After World War II, combinations of streptomycin, isoniazid, and para-aminosalicylic acid (PAS) proved so successful as an outpatient treatment that most sanatoria worldwide closed down by the 1980s. More recently, isoniazid has been coupled with rifampin and fluoroquinolones, but new challenges have emerged.

Future Research. Improved **diagnostic** tools are very badly needed, especially those that would allow physicians to distinguish quickly whether or not a patient is infected with

drug-resistant strains of the bacillus. Here, rapid identification of specific genetic sequences via the technique known as polymerase chain reaction (PCR) is very promising. New drugs are needed as well, for two major reasons. The first is to combat extremely resilient forms of the bacillus. There are currently strains of tuberculosis known as XDR-TB (extremely drug-resistant) that defy treatment with virtually all known antibiotics. These strains have established themselves in vulnerable populations, such as those with HIV/AIDS, and are a serious threat to tuberculosis control. The second reason is to shorten treatment times. If new, more effective drugs can be developed that cut treatment time down from six months, patient compliance is likely to increase, improving the overall success rate of the therapy, reducing costs, and lowering the chances for the emergence of resistant strains. Research also continues on a more effective, consistent vaccine. See also Air and Epidemic Diseases; Contagion and Transmission; Drug Resistance in Microorganisms; Industrialization and Epidemic Disease; Industrial Revolution; Tuberculosis and Romanticism; Tuberculosis in England since 1500; Tuberculosis in North America since 1800; Tuberculosis in the Contemporary World; Urbanization and Epidemic Disease; Vaccination and Inoculation; War, the Military, and Epidemic Disease.

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JEFFREY LEWIS

TUBERCULOSIS AND ROMANTICISM. Tuberculosis had long been prominent among Europe's poor and displaced, but as the eighteenth century drew to a close, a mushrooming **urbanization** brought about by the **Industrial Revolution** created an **epidemic** within Europe's upper and middle classes. Among the victims were some of the most creative figures of the Romantic era—writers John Keats (1795–1821), Percy Shelley (1792–1822), Emily (1818–1848) and Anne (1820–1849) Brontë, Branko Radečević (1824–1853), Johann Wolfgang von Goethe (1749–1832), Novalis (Friedrich Leopold von Hardenberg, 1772–1801), and Friedrich von Schiller (1759–1805); painters Franz Pforr (1788–1812) and Philippe Otto Runge (1777–1810); and musicians Frédéric Chopin (1810–1849), Niccolò Paganini (1782–1840), and Carl Maria von Weber (1786–1826). The unbridled passion these writers and musicians brought to their art in spite of their physical limitations soon led to the notion that the disease bestowed a heightened spiritual awareness and creative energy to its sufferers. The Romantic Movement to which these

artists belonged was a revolt against the formal and rigid aesthetic standards of the period and emphasized a brooding quest for artistic inspiration, a reckless engagement with life, and an idyllic pursuit of the natural world. The idea that aesthetic genius could literally drain the life from an artist was just one more facet in the movement's understanding of the artistic enterprise. Over time, in spite of the vast number of **poverty**-stricken people who suffered from the disease, tuberculosis came to be considered a disease primarily of the upper and middle classes and of sensitive types such as writers and musicians, giving the disease an air of fashion during this period.

Limited scientific knowledge regarding disease pathology opened the door to inductive speculation that tuberculosis might be caused directly or indirectly by the emotion, imagination, and creativity so obvious in its most famous victims. Tuberculosis was the most common of many serious lung diseases called "consumption" for its capacity to emaciate and waste away its victims. That consuming quality of the disease served as a physical manifestation of the psychological and emotional exhaustion associated at that time with creative activity. Keats, who studied medicine before turning to poetry and soon thereafter succumbed to consumption, assumed such a connection when he wrote: "I feel from my employment that I shall never be again secure in robustness." Romantics, like many in the medical community of the time, considered disease to be a part of the process of life itself, an internal quality of the individual, so a predisposition to tuberculosis—called "consumptive diathesis"—might well be indicated by other traits such as artistic talent or romantic sentimentality. Samuel Taylor Coleridge (1772–1834) claimed to have felt Keats's tuberculosis in a handshake long before the disease manifested itself. Prevention and, if necessary, treatment consisted of attempting to moderate or even avoid items or behaviors that could inflame the dormant disease, such as "bad **air**," crowds, a poor **diet**, sexual desire and sexual activity, and occupations that would accentuate an individual's emotional sensitivity—lawyer, minister, teacher, musician, poet. In his elegy on Keats's death, *Adonais* (1821), Shelley suggested even that the despondency and stress brought on by a harsh review of Keats's poem *Endymion* (1818) contributed to his death. Treatment strategies were complicated by unpredictable relapses, which served as a reminder of how little control sufferers had over the disease. Chopin exhibited such frustration when he wrote from Majorca of his prolonged infirmity in spite of the warm weather, a generous supply of tropical fruits, and the close attention of three famous **physicians**, all of whom disagreed on his prognosis.

The perceived link between tuberculosis and genius led not only to speculation that creative activity might bring on the disease, but also the inverse: that the disease gave its victims an enhanced sense of artistic passion and creative talent. Artists of the Romantic era generally believed that consumption stimulated the brain in much the same manner as opium or alcohol. Later attempts to explain the increased artistic insight and creative output of Romantic writers and musicians, however, have focused on the possibility that such artists acquired a new and profound understanding of life in the face of impending death, accentuated by a physical debilitation that forced the victims to spend more time inside their own imaginations. Certainly, writers from the Romantic era exhibited a deep fascination with life and death, evidenced perhaps most pointedly by Edward John Trelawney's (1792–1881) description of Shelley's cremation. The reverential account ends in Trelawney's stunning confession to finding Shelley's heart untouched by the flames and surreptitiously removing it as a keepsake. On the other hand, the beauty and insight of Romantic poetry was not simply the result of idle time and a sense of desper-

tion. Poems such as Shelley's "Ozymandias" (1817), Keats's "Ode on a Grecian Urn" (1819), and Lord Byron's (1788–1824) "And Thou art Dead, as Young and Fair" (1812) demonstrate a profound concern with the fragile nature of life, as well as the power of artistic achievements to survive centuries after their creators have died. When Keats described his tuberculosis to friends and family, he spoke in terms of a heightened psychological and emotional capability, writing at one point that his imagination had grown to such a degree that he no longer lived in just one world, but a thousand. He left no doubt, as well, of his belief that his creativity was killing him, telling a friend that his life was but a choice between two poisons—spending a few years in India or spending a "feverous life alone" writing poetry.

In spite of Keats's reference to India as a poison, consumptives of the Romantic era traveled widely in search of improved health. Their belief in "balance" as a source of vitality—an outgrowth of **humoral theory**—led them to consider both tropical and bleak wintry climates especially dangerous, but the temperate climes and curative "sea-air" of the Mediterranean made Italy, Majorca, and the Greek islands inviting destinations for those seeking relief. Throughout Italy and the Mediterranean, where draconian administrative measures for isolating **bubonic plague** victims had been in place as early as the fourteenth century, attitudes regarding tuberculosis proved to be dramatically different from those across northern Europe—fearful, judgmental, hysterical—and in spite of their renown, the artists quickly became pariahs. People would refuse to enter carriages in which they had ridden, Paganini was thrown out of his house in Naples, Keats's Italian landlady was afraid to be in his presence, and Chopin was shunned during his stay in Majorca. By contrast, Chopin was greeted personally by Queen Victoria (1819–1901) on a trip to England (though the weather had a devastating effect on his health), and Weber was mobbed and embraced by adoring European crowds, even though both were in the final stages of their diseases. Forced to choose between returning home to a climate thought to be destructive to their health or living with the rejection and isolation their disease brought them in the more temperate locales, most preferred the comfort of home and friends. As a result, Romantics often spent extended periods in the English and European countryside as refugees from the city and its "foul air," as with Chopin's summers at George Sand's (1804–1876) home in Nohant.

Consumption was often used in Romantic literature and beyond as a metaphor for the melancholia and consuming romantic passion so prevalent during the period. Keats's poetry played perhaps the most significant role in fostering the romantic sentimentalism through which tuberculosis came to be viewed. His poems "Ode to a Nightingale" and "La Belle Dame Sans Merci" are particularly effective in romanticizing the connections between consumptive illness, love, and death. By the emergence of Victorian literature around the middle of the nineteenth century, tubercular characters began to appear regularly in novels and dramas, frequently possessing qualities associated with eroticism, beauty, and mystery, as in Henri Murger's (1822–1861) *Scenes of the Bohemian Life* (1848), and later Giacomo Puccini's (1858–1924) *La Bohème* (1896), Charles Dickens's (1812–1870) *David Copperfield* (1849–1850), Victor Hugo's (1802–1885) *Les Misérables* (1862), Alexandre Dumas fils's (1824–1895) *The Lady of the Camellias* (1848), and Giuseppe Verdi's (1813–1901) *La Traviata* (1853). Around the same period, Pre-Raphaelite painters became known for the moody medieval eroticism in their works, achieved through an exaggerated paleness and thinness in their female subjects, for which they hired tubercular models. One such model, Elizabeth Siddal (1829–1862), later even

ENCOUNTERING TUBERCULOSIS IN THE ROMANTIC AGE

. . . [*Jean Valjean, known as M. Madeleine*] entered Fantine's chamber, approached the bed, and drew aside the curtains. She was asleep.

Her breath issued from her breast with that tragic sound which is peculiar to those maladies, and which breaks the hearts of mothers when they are watching through the night beside their sleeping child who is condemned to death. But this painful respiration hardly troubled a sort of ineffable serenity which overspread her countenance, and which transfigured her in her sleep.

Her pallor had become whiteness; her cheeks were crimson; her long golden lashes, the only beauty of her youth and her virginity which remained to her, palpitated, though they remained closed and drooping. Her whole person was trembling with an indescribable unfolding of wings, all ready to open wide and bear her away, which could be felt as they rustled, though they could not be seen.

To see her thus, one would never have dreamed that she was an invalid whose life was almost despaired of. She resembled rather something on the point of soaring away than something on the point of dying.

The branch trembles when a hand approaches it to pluck a flower, and seems to both withdraw and to offer itself at one and the same time.

The human body has something of this tremor when the instant arrives in which the mysterious fingers of Death are about to pluck the soul.

M. Madeleine remained for some time motionless beside that bed, gazing in turn upon the sick woman and the crucifix, as he had done two months before, on the day when he had come for the first time to see her in that asylum. They were both still there in the same attitude—she sleeping, he praying; only now, after the lapse of two months, her hair was gray and his was white.

From Episode 1, Book 8 of *Les Misérables*, by Victor Hugo.

became the wife of prominent Pre-Raphaelite artist Dante Gabriel Rossetti (1828–1882). Over time, consumption became so fashionable that women began to wear whitening powder rather than rouge and white muslin clothing designed to make them appear more emaciated.

By the end of the nineteenth century, after the **epidemiology** of the disease had been discovered, tuberculosis came to be considered a result of individual degeneracy and social conditions, and perhaps as a consequence of that, associated with ethnic and racial minorities. Nevertheless, the Romantic idea that tuberculosis endowed writers, artists, and musicians with extraordinary creativity lingered well into the twentieth century. This was fueled by a steady stream of creative artists from the late nineteenth and early twentieth centuries who continued to suffer from the disease, including Robert Louis Stevenson (1850–1894), Thomas Mann (1875–1955), and Franz Kafka (1883–1924). Psychologist Havelock Ellis (1859–1939) noted in *A Study of British Genius* (1904) that 40 of his subjects suffered from tuberculosis, and psychologist Arthur Jacobson (1872–1958) wrote in *Genius: Some Revaluations* (1926) that a sure recipe for producing the highest form of the creative mind was to combine a spark of genius with tuberculosis. In fact, Jacobson considered the creative influence of tuberculosis on the human brain to have a biological connection. Such a position was not inconsistent with broader medical opinion at the time. A 1932 article in the *Journal of*

the American Medical Association reported that toxins from tuberculosis stimulated the brains of patients so as to produce restlessness, apprehension about death, and general agitation, which, given the limited physical capabilities of the patients, led to an enhanced mental development. In the twenty-first century, with tuberculosis still one of the world's

most virulent diseases and no reliable empirical evidence of its connection to genius or creativity, the Romantic views of the disease have largely been relegated to mere historical interest. See also AIDS, Literature, and the Arts in the United States; Cinema and Epidemic Disease; Disease, Social Construction of; Literature, Disease in Modern; Plague Literature and Art, Early Modern European; Popular Media and Epidemic Disease: Recent Trends; Sanatorium; Tuberculosis in England since 1500.

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DEVON BOAN

TUBERCULOSIS IN ENGLAND SINCE 1500. Tuberculosis (TB) is an infectious disease caused primarily by *Mycobacterium tuberculosis*, a bacillus discovered in 1882 by the German bacteriologist **Robert Koch**. The disease has been associated with various names such as scrofula or struma indicating swellings of the neck glands, phthisis, or consumption for tuberculosis of the lungs; Pott's disease for spinal infection; and lupus vulgaris for TB of the skin. In the 1930s it was shown that tuberculosis is mainly transmitted by airborne particles (droplets) during talking, coughing, sneezing, and so forth. The exception is *Mycobacterium bovis*, the only **animal** tuberculosis able to infect humans. Here, the bacillus is usually transmitted by ingesting infected milk or meat.

During the sixteenth century, deaths from tuberculosis increased considerably in countries undergoing **urbanization** because the disease is associated with poor and overcrowded living conditions. In England, it caused about 20 percent of all deaths at mid-century, but the greatest concentration of tuberculosis was in London. The London Bills of Mortality, recorded from 1562–1837, show high death rates from consumption, especially in the seventeenth century. Richard Morton (1637–1698), a London **physician**, published the first Western medical text on tuberculosis, entitled *Phthisiologia: or, a Treatise of Consumptions* (1689). Consumption, typified by fever and weight loss, was generally an adult disease, whereas scrofula commonly afflicted children. Scrofulous glands, which sometimes subsided spontaneously, were nevertheless believed to be cured by a monarch's touch through God's grace rather than by medical treatment, and the disease was known as the "King's Evil." Royal touching, instigated by thirteenth-century French and English kings, was particularly revived by Tudor monarchs as a symbol of their divine right to rule. Applicants, vetted by court physicians, were ceremoniously touched during a church service, after which they received gold tokens. Mary I (1553–1558), Elizabeth I (1558–1603), and James I (1603–1625) all touched for the King's Evil. The last monarch

to perform the ceremony was Queen Anne (1702–1714). The writer Samuel Johnson (1709–1784) was touched by her in about 1712 but was not cured. On the Hanoverian succession in 1714, the practice was scorned as medieval and superstitious.

Epidemics of tuberculosis during the eighteenth century were associated with the **Industrial Revolution** and its occupations such as coal and tin mining, iron smelting, textile production, and pottery manufacture. Autopsies on Londoners revealed that most had developed TB during their lives, though they might have died of something else. Victims were fearful of tuberculosis and clamored for cures. Resins such as amber and myrrh formed bases for TB medicines, as did turpentine, gold, copper, and phosphorous. Lungwort (*Pulmonaria officinalis*), a plant with leaves similar in appearance to tuberculous lungs, was a specific herbal remedy. Physicians such as **Thomas Sydenham** and George Bodington (1799–1882) recommended fresh air, country living, and horseback riding. Explanations of the disease's cause were rooted in **humoral theory**, which related individual constitution to lifestyle and environment. Later, as tuberculosis developed its own mythology, medical practitioners constructed the "TB diathesis," whereby a tuberculous "taint" was inherited and then brought to fruition through exposure to a cold damp climate, dusty trades, **poverty**, improper **diet**, and so forth. Its stigma was such that family physicians often refrained from diagnosing tuberculosis because of social and employment consequences to patients and their families. Sufferers did not seek treatment for the same reasons. As late as 1912, a prominent English lung specialist, Herbert de Carle Woodcock, described it as a coarse, common disease, attacking failures, the depressed, alcoholics, and lunatics. In this context, he was arguing against the nineteenth-century portrayal of consumption as romantic or "poetic." In truth, it was a common disease, and it carried off many young talented individuals including the English poets Lord Byron (1788–1824), John Keats (1795–1821), and Percy Shelley (1892–22), and writers Anne (1820–1849) and Emily Brontë (1818–1848), Robert Louis Stevenson (1850–1894), and D. H. Lawrence (1885–1930).

During the nineteenth century, tuberculosis killed more people, especially young adults, than any other disease, depriving the economy of a labor force at its most productive age. Thirteen percent of all deaths in England and Wales from 1851 to 1910 were from TB, but of those aged 20 to 24, almost half died of the disease. Consumption accounted for 60 to 80 percent of TB deaths. The disease claimed a larger proportion of women's than men's lives at mid-century, partly because of pregnancy and inferior nutrition in cases in which working men in poor households were given the best food. England's worst areas for tuberculosis were the northern and midland industrial-urban areas of Lancashire, the West Riding of Yorkshire, Northumberland, and Birmingham. Despite these shocking statistics, a steady fall in TB deaths was established by 1870, which coincided with a rise in real wages and improvements in housing, hygiene, and diet. People lived longer with the disease, and others seemed able to overcome initial infection.

After Koch's discovery of the bacillus, procedures to deal with tuberculosis as an infectious disease were established. The National Association for the Prevention of Tuberculosis was founded in 1898 to educate the public in preventive measures, to promote the establishment of **sanatoria**, and to campaign for elimination of the disease from cattle. Tuberculosis had been described in slaughterhouse cattle from the early 1800s, but the discovery, in 1890, that 87 percent of Queen Victoria's (1819–1901) cows were infected with *Mycobacterium bovis* was a sharp indicator of its prevalence. In Manchester, for example,

18 percent of the milk supply from local herds was infected, yet it was not until 1929 that the danger of animal-to-human transmission of tuberculosis received government debate. By 1931 over 1,000 children under the age of 15 were dying of bovine TB in England and Wales each year. During the 1930s, tuberculin testing (for TB) was introduced in British cattle, and 40 percent were found to be reactors. Pasteurization, introduced initially to preserve milk, helped control the transmission of bovine disease to humans, resulting in a decline in deaths from 1931 to 1937. However, it was 1960 before all British milk was required to be pasteurized. In Britain, the real battle for tuberculosis control in the animal world is in its transmission from wildlife, principally badgers, to cattle. By 1986 TB had infected 88 herds, but in 2005 over 5,500 herds carried *M. bovis*. Similarly, the incidence in culled badgers rose from 5 percent in 1972 to about 38 percent in 2002–2004. In 2004 there were only 22 identified cases of bovine TB in humans, yet during the following year, 30,000 cattle were slaughtered to prevent the risk of transmission, causing significant economic harm to many farmers.

Tuberculosis bacteria are destroyed by ultraviolet light, a discovery that inspired the Danish physician Niels Ryberg Finsen (1860–1904) to treat TB of the skin with light therapy. During the 1890s, he constructed a powerful carbon arc electric lamp containing rock crystal lenses to focus ultraviolet rays. Finsen's success in treating this disfiguring condition, commonly affecting the face, earned him a Nobel Prize (1903). In 1898 Alexandra (1844–1925), Princess of Wales, who was Danish by birth, donated a Finsen Lamp to the London Hospital. Nurses, wearing dark protective glasses, held rock crystal against the patient's skin to ensure sufficient light penetration. By 1908 the hospital had 13 lamps treating over 1,000 patients a week, and hospitals throughout the country established light therapy departments, which were important up to the 1930s.

The sanatorium movement, based on open-air treatment and education in self-care, was well established by the beginning of the twentieth century. By 1920 there were 176 sanatoria in England. One of the most interesting was Papworth Village Settlement near Cambridge, founded in 1917 by Dr. (later Sir) Pendrill Varrier-Jones (1883–1941). Varrier-Jones believed that TB was incurable, and so his institution was committed to permanent holistic treatment. Papworth was a traditional sanatorium where patients in all stages of tuberculosis were received, but it also included a “settlement” where selected ex-patients (mostly male) were employed and lived with their families in a self-supporting rural community. Papworth Industries, which included cabinet-making, luggage manufacture, printing, poultry farming, and horticulture, was a successful commercial enterprise, expanding from a turnover of £410 in 1918 to over £100,000 by 1938 with about 300 workers. The total population at Papworth in 1938 was 1,000, including staff, 400 patients, and 142 families with 368 children. It was, nevertheless, an institution in an isolated part of the countryside where entertainment and social activities were supervised. Settlers did not rebel. They were generally grateful to be there during years of economic slump.

The results of sanatorium treatment were generally poor. For example, of the 3,000 patients discharged from London County Council sanatoria in 1927, only 24 percent were still alive by 1932. The 1930s and 1940s witnessed the routine use of surgical therapies such as artificial pneumothorax, whereby the diseased lung was collapsed for a period of rest and healing, and thoracoplasty, which collapsed it permanently. There is little evidence that surgical procedures influenced survival rates and, indeed, before the advent of

antibiotics, the course of the disease was totally unpredictable. Furthermore, by 1948 mass miniature radiography of 3 million people had revealed an active-case rate of 4 per 1,000 among those previously unsuspected of having tuberculosis. This created additional pressures on institutional accommodation and required the services of 2,900 more nurses.

Streptomycin, isolated by Selman Waksman (1888–1973) in 1943 in the United States and marketed in 1946, seemed to be the first real hope of a cure for tuberculosis. Postwar Britain could only afford to purchase 50 kilograms, enough to treat about 200 people. Professor (later Sir) Austin Bradford Hill (1897–1991), at the Medical Research Council, designed a fair test by randomly allocating patients to receive some of the limited supply of streptomycin. The results were impressive with 51 percent of the streptomycin patients improving by the end of six months compared to 8 percent of the controls. The problem of streptomycin resistance was solved by combining it with another new drug, para-aminosalicylic acid (PAS). By the 1960s, standard treatment for TB consisted of streptomycin for three months, followed by PAS and isoniazid (discovered in 1952) for up to two years. At the end of the 1970s, a multidrug regimen for eight months had become accepted. The Bacille Calmette-Guérin (BCG) vaccine, developed in 1920 by Albert Calmette (1863–1933) and Camille Guérin (1872–1961) in France, was not assessed in England until 1959, but by 1963 it was said to offer 79 percent protection against the infection.

During the 1960s and 1970s, tuberculosis in England came largely under control after centuries of being a major killer. However, since the mid-1980s, there has been a worldwide increase in TB of about 1 percent per year. In the United Kingdom, the increase has been nearer to 2 percent. Tuberculosis in England increased by 25 percent from 1994 to 2004 and continues to rise. Two out of five cases of TB are in London. The incidence in one London borough exceeds 80 per 100,000 a year, comparable to that of a developing country. Three-quarters of people with tuberculosis in England come from an ethnic minority, mainly the Indian Subcontinent and Sub-Saharan Africa. At least 3 percent of people with TB are estimated to be **HIV** positive, although the number is higher in London. About 350 people die of tuberculosis each year. In 2004 the Chief Medical Officer, Sir Liam Donaldson, produced an action plan for stopping tuberculosis in England, which some tuberculosis experts consider impossible to implement because of a lack of resources. See also Tuberculosis and Romanticism; Tuberculosis in North America since 1800; Tuberculosis in the Contemporary World; Vaccination and Inoculation.

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CAROLE REEVES

TUBERCULOSIS IN NORTH AMERICA SINCE 1800. Tuberculosis is a chronic, infectious disease, transmitted by **bacteria** called tubercle bacilli and *Mycobacterium tuberculosis*. Tuberculosis was the leading cause of death among North Americans for most of the nineteenth century. The epidemic is believed to have peaked there in the 1850s. In 1839 the German physician Johann Lukas Schönlein (1793–1864) coined the term “tuberculosis,” but the disease was more commonly known as “consumption” or “phthisis” throughout the nineteenth century. Tuberculosis afflicted all socioeconomic classes. Nevertheless, nineteenth-century **urbanization** and **industrialization** produced crowded living and working conditions that particularly fostered the spread of disease among the poor. In 1882 the German bacteriologist **Robert Koch** discovered the bacteria responsible for tuberculosis’s transmission. His theories challenged previous medical understanding, which conceived of **environment** and **heredity** as underlying causes. In the late 1800s, North American voluntary **Non-Governmental Organizations (NGOs)** and governments intensified tuberculosis control and prevention. **Sanatoria**, or rest hospitals, became a common therapy for middle and upper classes, whereas visiting nurses and outpatient dispensaries offered care to the urban working class. Even with increased public health interventions, tuberculosis killed approximately one in seven North Americans by 1900. Although the Bacille Calmette-Guérin (BCG) **vaccination** helped prevent tuberculosis in Canada, it was not until the Second World War that reliable pharmaceutical cures were discovered. The North American tuberculosis death rate fell dramatically after the 1940s but resurged in the mid-1980s, thanks in part to **drug resistance** among certain strains.

Before 1882. In the nineteenth century, **physicians** and civilians understood consumption as unavoidable, the result of an individual’s constitutional weaknesses. Although the causative bacterial agent was unknown until 1882, diagnostic and therapeutic innovations in the early nineteenth century affected patients’ experiences.

Clinical diagnosis of consumption became easier in the 1820s and 1830s, when the French pathologist Rene Laennec (1781–1826) published descriptions of its characteristic lesions and symptoms. Laennec introduced the concept of consumption as a specific disease. He also pioneered the method of auscultation of the lungs with the stethoscope, simplifying physical diagnosis. Many North American physicians studied medicine in Paris in the early nineteenth century and brought Laennec’s methods home.

Laennec doubted that consumption was contagious, and many North Americans agreed with him. Massachusetts doctor Henry I. Bowditch (1808–1892), for example, understood consumption as primarily hereditary in nature. Such beliefs relied on empirical observations of the disease. From physicians such as Pierre Louis (1787–1872) in Paris and sanitary reformers such as England’s **Edwin Chadwick**, North American doctors became acquainted with clinical and **demographic** statistics in the 1830s. These armed physicians with quantitative methods to analyze tuberculosis’s incidence.

As diagnostic and observational methods changed, new public health responses and therapies emerged. Consistent statistical collections revealed the extent of tuberculosis and helped to generate demands for reform. Many North Americans supported a **sanitation movement** that encouraged the ventilation of homes, slum clearance, and urban cleanups. Sanitarians also advocated for behavioral changes, including looser clothing for women, exercise, and temperance. Cities and states established permanent boards of health, beginning with the New York City Metropolitan Board of Health in 1866 and the

Massachusetts State Board of Health in 1869. Although all of these responses focused on public health more generally, tuberculosis was of particular concern.

More specific therapies included changes in climate, rest, fresh air, and hardy **diets**. Florida and Cuba attracted many North Americans in the earlier part of the nineteenth century. Dry climates such as Minnesota, Colorado, and the U.S. Southwest began to draw consumptives later. Some physicians used drugs such as iodine or creosote, but most favored behavioral change and physical improvement.

In 1865 the French physician Jean-Antoine Villemin (1827–1892) demonstrated the transmission of tuberculosis and argued that it was contagious. However, many North American physicians disputed his findings and clung to hereditary, behavioral, or environmental explanations.

1882–1943. Biomedical understandings of tuberculosis changed substantially in 1882, when Robert Koch identified its causative microorganism. Koch experimentally inoculated lab animals with material cultured from established tuberculosis cases. He also stained the tissues, making the disease's rod-shaped bacilli visible. His published results announced to the world what some physicians already suspected: tuberculosis was a contagious disease, transmissible between people. The cause and nature of tuberculosis would be reconceptualized according to this **germ theory of disease**.

Koch's ideas spread rapidly to North America but did not win immediate acceptance. Physicians and public health professionals debated how contagious tuberculosis really was. It did not appear as communicable as other infectious diseases. Some medical professionals recognized the obvious correlations between **poverty** and working conditions and tuberculosis incidence, and believed that environment must play at least a complementary role in infection. Theories of tuberculosis's hereditary nature also continued to influence medical professionals. By the early twentieth century, many North American **physicians** began to incorporate newer germ theories with older understandings of consumption. Although they admitted its infectious nature, for example, they argued that some individuals were predisposed by **heredity** to infection.

Tuberculosis's infectious nature raised questions about prevention. Incorporating new ideas about biological inheritance popularized by the period's eugenics movement, some medical professionals saw tuberculosis as linked to poor breeding. Some eugenicists argued that the state could slow transmission by restricting marriage between infected individuals. Others promoted more positive solutions, such as improved maternal and child health programs.

Starting in the late nineteenth century, many cities passed legislation against behaviors believed to facilitate tuberculosis's transmission. Public health leaders such as Hermann M. Biggs (1859–1923), a major figure in the New York City and State Boards of Health, attacked tuberculosis aggressively and demanded greater power to control it. Municipalities demanded that landlords clean up tenements and ventilate buildings and established new offices to inspect milk and meat for tuberculosis. By the 1910s, many health departments required physicians to report tuberculosis cases. New laws increasingly targeted individuals. Many North Americans were forbidden from spitting in public, for example. Advocates for anti-tuberculosis legislation thus prioritized public health over **personal liberties**.

Newly established voluntary associations supported the campaigns for increased interventions. In 1892 Doctor Lawrence Flick (1856–1938) organized the Pennsylvania Society for the Prevention of Tuberculosis, the first such **private agency** in the United States. Medical professionals and interested citizens established many similar associations

at the city and state level. In 1900 the Canadian Tuberculosis Association was established, followed by the U.S. National Association for the Study and Prevention of Tuberculosis in 1904. These associations promoted education about tuberculosis transmission and prevention. They also raised funds and awareness.

Public understanding of tuberculosis and its infectious nature increased by the early twentieth century, but the disease continued to infect many. By 1900 approximately one in seven North Americans died from tuberculosis, second only to pneumonia and **influenza**. The search for effective therapies remained important.

Climate and physical improvement continued to influence treatment. These methods were institutionalized in the late 1800s in sanatoriums, specialized hospitals that treated tuberculosis with rest, diet, fresh air, medical supervision, and education. Edward L. Trudeau (1848–1915), a physician and consumptive himself, became interested in them after recuperating in the Adirondacks. Influenced by German sanatorium models and methods, Trudeau opened the Adirondack Cottage Sanatorium in Saranac Lake, New York. Trudeau's institution gained national attention and established an example for others. Trudeau and other sanatorium directors required patients to spend most of their time outdoors or in open buildings, even in winter. The standard treatment included both prolonged rest and guided exercise. Generous diets rounded out the regime, with patients fed large quantities of eggs and whole milk to regain strength. Whereas proponents of sanatoriums argued that they offered genuine cures, some critics saw them as merely a way to isolate infected individuals.

The sanatorium movement grew quickly in North America. The first Canadian institution opened in 1897. Because treatment was expensive, patients tended to belong to the middle and upper classes. In 1905, however, the Canadian Senate and House of Commons passed legislation for the construction of public sanatoriums in each province. The same year, Hermann Biggs established the first public municipal tuberculosis sanatorium in the United States, in Otisville, New York.

State support increased the number of beds available, but many patients continued to recuperate in their homes. At the turn of the century, visiting nurses and tuberculosis dispensaries supplemented home care. Both of these strategies targeted indigent populations, educated patients about transmission and prevention, and registered new cases. Visiting nurses taught patients how to change their behaviors, and encouraged families to isolate tubercular members and to ventilate their homes.

Many scientists also experimented with biomedical therapies. An early hope for a tuberculosis cure materialized with Robert Koch's 1890 development of tuberculin, a substance made of sterilized culture in which tubercle bacilli had grown. Koch's experiments with tuberculin on guinea pigs and humans elicited a physiological reaction, which he hoped demonstrated tuberculin's potential as a treatment. In spite of early excitement and testing, tuberculin failed to cure. Nevertheless, the tuberculin reaction did represent an important phenomenon—a positive reaction to the injection of tuberculin indicated tubercular infection. In 1907 the Austrian physician Clemens von Pirquet (1874–1929) presented his research on the tuberculin skin test, offering medical professionals a more exact diagnostic procedure.

In 1908 the French bacteriologist Albert Calmette (1863–1933) and the veterinarian Camille Guérin (1872–1961) began to experiment with a vaccination created from a weakened strain of *M. bovis*, the bovine form of tuberculosis. The pair spent years at the Pasteur Institute in Paris cultivating a strain of bacilli that were not virulent enough to

infect humans but that would confer immunity. After refining their inoculation on animals, Calmette and Guérin tested it on humans in 1921 and produced the BCG vaccine. International acceptance was initially slow. In North America, the Canadian National Research Council first experimented with BCG in 1925 and tested it extensively over the next two decades. The majority concluded that the vaccine was safe and fairly effective, providing immunity in approximately 80 percent of cases. In the United States, physicians proved more skeptical of BCG and doubted its safety and efficacy. Through the 1930s and 1940s, the U.S. Public Health Service instead invested in hygiene reform and the development of pharmaceutical cures.

By the 1920s, tuberculosis had waned among North Americans, in spite of the lack of effective therapies. In the 1920s and 1930s, surgical treatment offered some hope. Physicians in both Canada and the United States experimented with pneumothorax, a procedure in which physicians collapsed a patient's lungs and pumped air into the chest cavity. Others preferred thoracoplasty, a surgery that involved removing ribs to give the lung more space. Both procedures were supposed to let the lung rest and repair. Although surgeries increased in the 1930s, they involved many hazards and their efficacy remained debatable. The brief surgical era in tuberculosis treatment declined with the introduction of effective chemotherapies after World War II.

1943–Present. The Second World War marked a turning point in tuberculosis management in North America. With the introduction of antibiotics, sanatoria and surgical treatments declined. However, the early faith in pharmaceutical eradication would prove premature by the century's end.

In the early 1940s, tuberculosis rates continued to decline in North America, but at a slower rate than previously. In the United States, the physical examinations required of military recruits revealed that a significant proportion of American men had latent or active tuberculosis. This generated a demand for greater federal government involvement. In 1944 the U.S. Public Health Service established a Tuberculosis Control Division, which adopted **vaccination** with BCG on a wider scale.

Biomedical developments offered new cures. In 1943 Selman Waksman (1888–1973), a microbiologist at Rutgers University, identified an organism named *Streptomyces griseus*. From it, he and his graduate students isolated a potent antibiotic, which they named streptomycin. Streptomycin proved remarkably effective at killing tubercle bacilli. Waksman's research caught the attention of researchers at Minnesota's Mayo Clinic, who experimented with the drug on humans in 1944.

Streptomycin was effective, but many patients relapsed and developed resistance. In the 1950s, researchers in Germany and the United States discovered an antimicrobial drug, named isoniazid, which surpassed streptomycin in its effectiveness. By the late 1950s, the United States and Canada had largely adopted the two-drug regimen, given to most patients for 18 months to two years.

The rise of antibiotic therapy stimulated the decline of older strategies. Saranac Lake closed in 1954, symbolizing the end of the sanatorium era. While the number of sanatorium beds in Canada actually peaked in 1953, the number had declined by half 10 years later. More patients remained at home for treatment. Voluntary associations changed their missions as tuberculosis cases dropped. The U.S. National Tuberculosis Association became the American Lung Association in 1973, shifting its emphasis to all lung disorders.

The seeming triumph over tuberculosis masked its persistence in certain populations. Tuberculosis continued to plague patients without access to regular medical care, such as

chronic alcoholics, immigrants, and the urban poor. The decline in state and voluntary commitment to tuberculosis control eroded the social services available to tubercular patients. The perception that it had disappeared in North America led many to disregard it globally.

North America's indifference to tuberculosis unraveled in the 1980s with the appearance of **HIV/AIDS** and multidrug-resistant strains of tuberculosis (MDR-TB). These health issues led to an upsurge in tuberculosis cases. In 1985, the first time that century, the United States recorded a national *increase* in cases. In 1990 MDR-TB appeared in New York. Simultaneously, HIV case rates soared, and researchers recognized tuberculosis as a common AIDS complication. The growing visibility of tuberculosis as a national and international health problem led to renewed public interest. New strategies such as Directly Observed Therapy (DOTS) programs combined drug regimens with regular patient visits to ensure that patients completed the course of pharmaceutical treatment. In 2002 the **World Health Organization** adopted this strategy as a global treatment paradigm.

At the start of the twenty-first century, it became clear that tuberculosis was not an historic ailment, but a very contemporary problem. Tuberculosis was no longer a North American disease, but rather a global **pandemic** that required international efforts to combat. *See also* Human Immunity and Resistance to Disease; Tuberculosis and Romanticism; Tuberculosis in England since 1500; Tuberculosis in the Contemporary World.

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JULIA F. IRWIN

TUBERCULOSIS IN THE CONTEMPORARY WORLD. The **antibiotic** revolution of the 1940s and 1950s led a range of leading public health campaigners, scientists, and **physicians** confidently to predict the eradication of **tuberculosis** by the year 2000. By

the early 1980s, TB appeared to be largely a disease of historical interest in the West, a consensus that indicated a dangerous complacency in the face of the continuing high prevalence of the disease in many developing countries. As recently as 1987, for example, the *Oxford Textbook of Medicine* predicted the virtual eradication of tuberculosis in “most technically advanced countries” before the year 2050. Yet those who considered TB in a global context—especially in impoverished parts of the global South or among the rising homeless populations of the global North—were far less optimistic.

The turning point in global efforts to control TB can be traced to the United States in the mid-1980s. There, a sudden increase in cases was observed in urban areas: between 1985 and 1992 there was a rise in TB cases of over 20 percent. Cities such as New York faced a rapid and unexpected spread of TB that quickly escalated into a public health emergency. This surge in reported cases can be attributed to increases in **poverty** and homelessness during the 1980s combined with the effects of **HIV** infection and the spread of TB strains showing **drug resistance**. The emerging public health crisis facing deprived inner-city neighborhoods represented a microcosm of the changing global incidence of the disease. It soon became apparent that the problems facing inner-city America were surfacing on a global scale in response to the combined effects of drug resistance, HIV, and poverty.

The development of drug resistance is thought to be responsible for around 10 percent of new TB cases worldwide. The problem of drug resistance was encountered soon after the discovery of streptomycin and other anti-TB drugs and led to the gradual emergence of multidrug treatment programs. Factors involved in the emergence of drug resistance include the poor supervision of therapy, the use of badly prepared combination preparations, the existence of inconsistent prescribing practices, the problem of erratic drug supplies, and the lack of regulation of over-the-counter sales of drugs. The most commonly encountered resistance in a microorganism is to a single drug, usually streptomycin or isoniazid, and most TB bacteria with such resistance respond adequately to a multidrug treatment program. The emergence of resistance to rifampicin is much more serious, however, as this is the most powerful anti-tuberculosis drug, with the ability to sterilize lesions by destroying near-dormant “persisters” bacilli. Furthermore, most rifampicin-resistant strains are also resistant to isoniazid; by convention, a case of tuberculosis that results from strains resistant to these two agents, with or without additional resistances, is said to be multidrug-resistant. The use of standard short-course treatment becomes not only ineffectual but may even be harmful, as resistance to other drugs such as pyrazinamide and ethambutol also develops as part of the so-called “amplifier effect.” In Russia and other states of the former Soviet Union, mutant forms of TB, variously referred to as multidrug-resistant tuberculosis (MDR-TB), have been rapidly spreading in response to chronic overcrowding in the prison system and severe cutbacks in primary health care. The problems and costs of managing each case of MDR-TB are enormous. Successful therapy requires prolonged courses of less effective, more expensive, and more toxic drugs, under long-term supervision. In the case of New York, the spread of MDR-TB was facilitated by reductions in public health expenditures during the 1980s, but the city ended up having to spend 10 times more than it saved in order to bring TB under control. And more recently, the spread of extensively drug-resistant TB (XDR-TB), which is even more virulent than MDR-TB, threatens to disrupt all current efforts to contain the disease: in poorer countries with high proportions of immuno-suppressed individuals, the impact of XDR-TB is potentially lethal. A recent survey reveals that XDR-TB is now present in 17 countries worldwide, and the

absence of a coordinated health-care strategy could lead to a shift into the “post-antibiotic era” of TB control.

The AIDS **pandemic** is now estimated to contribute around 10 percent of TB cases worldwide. In Africa, however, HIV is responsible for at least 20 percent of TB cases. Given that one-third of the world's population carries quiescent TB infection, the effects of immune system damage can be expected to have devastating consequences. For example, the most recent data suggest that in parts of Sub-Saharan Africa, more than one-quarter of the adult population is now infected with HIV, and rates of infection are now rising quickly in South Asia and many other regions. Infection by HIV is currently the most important predisposing factor for the development of overt TB in those infected before or after becoming HIV positive. By the late 1990s, there were estimates of at least 10 million coinfecting persons. The increasing recognition of links between TB and HIV among patients has had the adverse effect of adding to the stigma of TB symptoms and has hindered cooperation among patients, health-care workers, and local communities. The return of tuberculosis has also exposed tensions between different conceptions of medicine and **personal liberty**. In the United States, for example, the threat of MDR-TB and coinfection with HIV has led to calls for punitive public health strategies based on mandatory screening and treatment, case notification to public agencies, aggressive contact tracing, and the use of **quarantine**. Such measures are reminiscent of early twentieth-century approaches to public health. They are in conflict with contemporary conceptions of individual liberty, though the recent emergence of new “bio-security” agendas, sometimes linked with reactionary political programs, may alter the direction of public health policies.

A further dimension to the contemporary resurgence of TB is the effects of global social and economic change. Mass movements of people in response to **war**, increased economic insecurity, community breakdown, and other factors have been involved in the spread of TB and other infectious diseases associated with overcrowding, makeshift housing, and poor public sanitation and **personal hygiene**. In London, for example, the overcrowding and stress experienced by recently arrived immigrants have contributed to the spread of the disease, though media reports often misleadingly claim that the disease is being spread by the migrants themselves. In addition to short-term disruption, it is important to consider the longer-term social and economic shifts that have emerged since the early 1970s. There is now increasing evidence that growing poverty, infrastructural decay, and declining health services have facilitated the spread of TB, **diphtheria**, **sleeping sickness**, and other preventable diseases. Similarly, the spread of TB and other preventable diseases in the so-called “de-developing enclaves” of urban America and the poverty-stricken cities of the former Soviet Union can only be fully understood with reference to the dynamics of global political and economic change since the Second World War. With the advent of more diffuse patterns of **urbanization** and the greater mobility of capital investment, it has become far easier for public health crises to be effectively ignored where they present no generalized threat to the overall well-being of an increasingly globalized economic system.

Over the last 30 years, the historical synergy between health reform and social justice has been displaced by an increasing emphasis on the individual patient or consumer rather than on the wider social and political context of disease. The profit-driven restructuring of global health care has led to widening health inequalities, as the world's poor find themselves unable to benefit from the latest biomedical advances. In comparison with other major health afflictions, TB remains relatively neglected, and most **pharmaceutical**

research is devoted to the more lucrative markets for drugs in developed economies rather than to providing remedies for diseases of the less developed global South. Research is also being skewed by the current emphasis on **bioterrorism** and the planning for hypothetical scenarios rather than existing health conditions. Although new scientific advances may play a useful role in the treatment of TB, the eventual eradication of the disease will rest on a political commitment to tackle problems of poverty, inequality, and inadequate access to health care. *See also* AIDS in Africa; Capitalism and Epidemic Disease; Human Immunity and Resistance to Disease; Medical Ethics and Epidemic Disease; Popular Media and Epidemic Disease: Recent Trends; Public Health Agencies, U.S. Federal; Tuberculosis in England since 1500; Tuberculosis in North America since 1800.

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MATTHEW GANDY

TYPHOID FEVER. *See* Enteric Fevers.

TYPHOID FEVER IN THE WEST SINCE 1800. For centuries, fevers were regarded as natural disease processes resulting from humoral imbalances, were treated according to the principles of **humoral theory**, and were classified according to seasonality, severity, and duration. By the early nineteenth century, however, most British physicians followed the view of William Cullen (1710–1790), that fever was a general disease showing a range of inflammatory complications. In France, where pathological anatomy was pioneered, Pierre Bretonneau (1798–1862) identified characteristic intestinal lesions in those who died during an 1816 "continued fever" **epidemic**. These lesions were also seen by Pierre Louis (1787–1872), who published a study of 138 cases in 1829. The disease observed by Bretonneau and Louis, known as dothiënteritis or **typhoid fever**, was assumed to be similar to British **typhus**. It typically attacked young migrants to Paris and lasted 28 days. Louis's American students were able to identify typhoid when they

returned home, among cases formerly diagnosed as “autumnal” or “remittent” fever, but by 1835 one student, William Wood Gerhard (1809–1872), had clearly distinguished between typhoid and typhus. The latter was of shorter duration, displayed no intestinal abnormalities, and was accompanied by a distinctive rash.

The differences between typhoid and typhus, however, were not generally accepted until William Jenner (1815–1898) published his studies of cases at the London Fever **Hospital** in 1849. He reasoned that if the diseases were distinct, they must have specific causes, and the identity of those causes was of great concern. According to one estimate, each year 20,000 people died of typhoid in Britain, and 100,000 survived the disease. From 1856 William Budd (1811–1880), another student of Louis, argued that drinking **water** contaminated by sewage containing an infective agent was the means of transmission, an idea repeatedly reinforced by outbreak studies during the 1860s and 1870s. Epidemics spread by milk were also described, usually involving impure water used for washing dairy equipment. In 1880 Carl Eberth (1835–1926) described a bacillus found in typhoid, which was named *Eberthella typhosa*. Also known as *Bacillus typhosus* and later as *Salmonella typhi*, it was obtained in pure culture in 1884. Given the impossibility of **animal research** (typhoid only infects humans) it was difficult to prove that the bacillus *caused* typhoid, but in 1896 it was shown that that serum from typhoid patients caused the clumping and precipitation of the bacillus in broth cultures, the basis of a test devised by Fernand Widal (1862–1929).

Typhoid affected all classes and occurred sporadically or as small epidemics in villages and towns as well as cities, arising most regularly in late summer. One famous victim was the father of U.S. president Herbert Hoover (1874–1964), a blacksmith, who died in 1880. Another death ascribed to typhoid was that of Prince Albert (b. 1819), husband of Great Britain’s Queen Victoria (1819–1901), who died in 1861, although the diagnosis has recently been challenged.

The decline in typhoid correlates broadly with sanitary reform and improvements in plumbing. In 1880 there were 261 deaths from typhoid per million of population in England and Wales, and 358 in Scotland, where the pace of **sanitation** reform was slower. By 1940 there were only three deaths per million in both countries. Hospitalization in fever hospitals, recognition of the role of carriers, and chlorination of water all played important roles. In 1897–1898, Almroth Wright (1861–1947) developed a vaccine, which was first deployed on a mass scale by the British Army First World **War**. Although the efficacy of the **vaccinations** has been questioned, the British anti-typhoid measures were altogether remarkably effective. Typhoid became an almost negligible problem, whereas, during the South African (Boer) War (1899–1901) there had been 59,750 cases among the British and, during the Spanish-American War (1898), 20,926 cases among the Americans.

As sanitary reform reduced waterborne typhoid, epidemiological interest shifted toward foodborne typhoid, especially shellfish, but the realization that outbreaks were often caused by healthy carriers dominated policy in some countries in the early twentieth century. In 1902 **Robert Koch** published a paper on typhoid carriers and began a campaign to prevent typhoid in southwestern Germany. It seemed that 2 percent of infected individuals became carriers. In the United States, the theory was confirmed dramatically in 1906, when a family outbreak in Oyster Bay, near New York, was traced to the cook **Mary Mallon**, who was shown to be linked with outbreaks in seven homes in which she had worked previously. She was also responsible for later outbreaks, despite promising not to take further employment handling food, and was subsequently detained for the rest of

her life. The “Typhoid Mary” affair had a profound impact upon American public health, shifting the focus from the environment toward the control of dangerous individuals. Apart from restrictions on employment and, as a last resort, incarceration, surgical treatments for typhoid carriers were also devised, usually involving the removal of the gall bladder, the usual site of continued infection.

In Britain the carrier theory was less influential. The identification of carriers was less proactive, and the powers given to public health officials less extensive. Typhoid had ceased to be endemic, and outbreaks were generally blamed on temporary loss of vigilance with regard to traditional public health measures. Some officials began to consider typhoid a disease of the past. But this view came under strain in the light of the milk-borne Bournemouth outbreak (1936) and the waterborne Croydon outbreak (1937). The former resulted from cows drinking from a river containing sewage from a cottage of a carrier, whereas the latter was probably linked to a carrier among the workmen who repaired a well while chlorination was suspended. Senior British health officials, however, continued to stress sanitation, rather than focusing on carriers as the key to prevention, the chief lesson taken from Croydon being the need for universal chlorination.

During the 1930s there were important developments in the science of typhoid. Arthur Felix (1887–1956), in England, devised a modified Widal test, for an antibody to a particular *Salmonella typhi* antigen, the V_i or “virulence” antigen, which he had discovered in 1934. This led to a new “improved” vaccine (which was later shown to be useless) but, importantly, to phage typing, which was devised by James Craigie (1899–1978) and a colleague in Canada. During the Second World War, the value of phage typing was demonstrated, allowing, for example, sporadic cases to be traced to sources many miles away.

After the war, the British Emergency Public Health Laboratory Service became permanent, with Felix as director of its Central Enteric Reference Laboratory. In 1947 Felix and Craigie published a standardized method of phage typing, and the International Congress for Microbiology recommended that it be adopted universally. An International Committee for Enteric Phage Typing was formed, and Felix’s laboratory became the international reference facility. The laboratory supported investigations of outbreaks. Phage typing became the basis of many remarkable detective stories. Notifications of typhoid dropped from 396 in 1948 to 90 in 1960 in England and Wales. For the remaining cases, an effective **antibiotic**, chloramphenicol, became available in 1950; it reduced the mortality rate to around 1 percent. Trials of the drug in the treatment of carriers, however, were inconclusive.

Compared to most other European counties, Britain had the advantage of not having been occupied during the war, facilitating postwar progress in controlling the threat of typhoid. Soon, a large proportion of the remaining cases in Britain were contracted abroad, mainly in continental Europe or on the Indian subcontinent. The hazards of overseas travel were dramatically illustrated in 1963 by the large waterborne outbreak at the ski resort of Zermatt, Switzerland, which led to cases among vacationers from many countries, including the United Kingdom. The large outbreak of typhoid in Aberdeen, Scotland, the following year, which hospitalized over 500 people, was also the result of imported infection, in this case via a surprising route: in a large can of corned beef. An official enquiry concluded that the infection had entered through a defect in the can during manufacture in Argentina using unchlorinated cooling water. The role of overseas **trade and travel** as the source of the majority of the remaining typhoid cases in Western countries reflects the continued prevalence of the disease in less developed regions. See

also Contagion and Transmission; Diet, Nutrition, and Epidemic Disease; Disinfection and Fumigation; Enteric Fevers; Personal Hygiene and Epidemic Disease; Public Health Agencies in Britain since 1800.

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DAVID F. SMITH

TYPHOID MARY. See Mallon, Mary.

TYPHUS. Typhus, from the Greek word for "smoky" or "hazy," which describes neurological symptoms of the disease, is the designation for an illness caused by infection with rickettsial organisms and characterized by a fever and a rash. Typhus is usually divided into two major categories: classic **epidemic** typhus and its recurring form known as "Brill-Zinsser disease," and murine typhus or "tabridillo."

Biological Agent and Its Effects on the Human Body. Both types of typhus are caused by rickettsiae, very small bacterial organisms that share with **viruses** the habit of living inside the cells of the infected host. Because they exhibit characteristics of both **bacteria** and viruses, they were for some years thought to be a separate category of infectious microorganism, but in the late 1960s, they were demonstrated to be true bacteria. The name "rickettsiae" for these organisms was derived from Howard Taylor Ricketts (1871–1910), a **physician** who lost his life to typhus in 1910 while conducting some of the earliest studies on these pathogens.

Epidemic typhus is caused by *Rickettsia prowazekii*, and murine typhus by *Rickettsia typhi*. Both epidemic and murine typhus exhibit an incubation period varying from 5 to 15 days, after which the onset of the disease is abrupt. A rapidly rising fever is accompanied by headache, loss of appetite, and general malaise. Chills, nausea, and prostration may ensue during the first week. After the fourth day, a widespread noneruptive rash appears under the skin. After a week, the fever usually subsides, and recovery is rapid. In fatal cases, however, prostration becomes more marked, with increasingly severe neurological symptoms including deafness, stupor, delirium, and symptoms of circulatory collapse preceding death. For classic epidemic typhus, the death rate in untreated cases usually varies from 5 to 25 percent and occasionally reaches 40 percent. In cases of murine typhus, the disease is almost never fatal, with a mortality rate of only about 2 percent.

Since the introduction of broad-spectrum **antibiotics** in the late 1940s, death need not result from either form of typhus if the disease is recognized early and treated promptly. A case of typhus produces a long **immunity**, but under certain circumstances, epidemic typhus may recur. The observation of typhus-like symptoms without the existence of an

epidemic was originally noted in 1910 by Nathan Brill (1860–1925) and hypothesized in 1934 by Hans Zinsser (1878–1940) to be a recurrence of typhus in persons who had suffered a previous attack. When experiments in the 1950s confirmed that typhus could recur years after the initial infection, the condition was named Brill-Zinsser disease.

Transmission. *Rickettsia prowazekii* is transmitted by an insect, the human body louse *Pediculus humanus corporis*. The body louse spends its entire lifetime in the clothes of humans. Lice take four to six blood meals a day from hosts, and human blood constitutes their only food. *R. prowazekii* in the blood of an infected person are ingested by feeding lice and multiply rapidly in louse intestines. They are secreted in the feces of infected lice and transmitted to new hosts by contact of infected louse feces with skin abrasions caused when the human host scratches the unpleasant itch caused by the lice as they feed. The vector louse also dies from its infection with *R. prowazekii*.

Rickettsia typhi is a natural infection of rats and is transmitted by the rat flea, *Xenopsylla cheopis*. The name “murine typhus” reflects the disease’s relation to rats, and humans living in areas where rats are abundant are most susceptible. Like epidemic typhus, murine typhus is transmitted when a human host rubs infected rat feces into the abrasion caused by a flea bite. Neither the rat nor the rat flea suffers ill effects from the infection.

Epidemiology with Specific Factors. Classic, epidemic typhus has long been known as a disease of cold weather and of crowds. Its various names—jail distemper, ship fever, camp fever, famine fever—suggest the poor hygienic conditions characteristic of groups of people confined to close quarters in cold weather without access to clean clothes or bathing facilities. Epidemics peak in winter and taper off in the spring.

Murine typhus, in contrast, is more often associated with warmer climates and human living conditions where rats are abundant. Local names for the disease reflect the human-rat **environmental** connection: shop typhus, urban typhus, and “tabridillo” in Mexico.

History. The first account of typhus by a contemporary described a disease that occurred during the 1489–1490 **wars** in Granada, Spain. It killed 17,000 Spanish soldiers—six times the number killed in combat. In the early sixteenth century, another typhus epidemic may have altered European history. The French army was at the point of a decisive victory over the Italians and Spaniards in Naples when the disease struck down 30,000 French soldiers, forcing a withdrawal of the troops that ended the French threat. In 1548 **Girolamo Fracastoro**, who had observed this epidemic in Italy, published the first clear description of what he termed a “lenticular or punctate or petechial” fever. By the end of the sixteenth century, typhus—presumably epidemic typhus introduced by Europeans—was also recorded in Mexico, where it killed over 2 million Native Americans.

In the nineteenth century, the incidence of typhus increased dramatically. In 1812 typhus plagued Napoleon’s (1769–1821) invasion of Russia. Between 1816 and 1819, a great epidemic struck 700,000 people in Ireland. Confusion of typhus with **typhoid**, which also produces a rash, muddled the clinical understanding of the disease. In 1837 William Gerhard (1809–1872) described specific intestinal lesions that characterized typhoid but not typhus. Gerhard’s work, however, was not immediately accepted. Even into the twentieth century, some confusion continued in nomenclature between typhus and typhoid. In 1848 European revolutions spawned typhus epidemics. A particularly severe outbreak in Silesia prompted German physician **Rudolf Virchow** to observe that typhus primarily afflicted the poor, the uneducated, and the unclean. He



Typhus rash on the face and neck of a woman in the Fever Hospital, Abbassia, Egypt, 1943. Courtesy of the National Library of Medicine.

called for democracy, education, and public health measures as proper “treatment” for the epidemic.

During the last quarter of the nineteenth century, the advent of the **germ theory** of infectious disease led bacteriologists to search for a microbial cause of typhus. In 1909, **Charles Nicolle**, director of the Institut Pasteur in Tunis, Tunisia, demonstrated that the body louse transmitted typhus. In 1910 Howard Taylor Ricketts, working in Mexico City, described tiny microorganisms in the blood of typhus victims, in infected lice, and in lice feces. Before he could confirm his observations, however, he became infected with typhus and died. In 1916 Brazilian Henrique da Roca Lima (1879–1956) described similar organisms, which he named *Rickettsia prowazekii* after Ricketts and Stanislaus von Prowazek (1875–1915), a researcher who had also died from a laboratory-acquired typhus infection.

In the 1920s, American epidemiologist Kenneth Maxcy (1889–1966) described a widespread form of typhus fever that was endemic. He postulated that some **ectoparasite** of the rat was its vector. By 1931 infected fleas had been found in nature that confirmed Maxcy’s hypothesis. In 1932 the Swiss pathologist Herman Mooser (1891–1971) proposed the name “murine typhus” for the disease to indicate its relationship with the rat. Mooser also distinguished in the laboratory the causative organism *Rickettsia typhi* from *Rickettsia prowazekii*.

Research, Prevention, and Therapeutic Efforts. After rickettsiae were identified as the causative agents of typhus, many paths were explored to prevent or treat the infections. During World War I, the only effective approach was vigilance in keeping soldiers and civilian populations free from body lice. This was accomplished largely through showers for people and steam-cleaning of clothing. The result was not highly effective.

During the interwar period, a number of candidate **vaccines** against *R. prowazekii* were developed. The most promising grew the large concentrations of rickettsiae needed for vaccine production in the yolk sacs of fertile hens' eggs. The yolk sac typhus vaccine was administered to all U.S. servicemen at the beginning of World War II, but it was never completely evaluated. The reason for this was the development of the highly effective **insecticide** dichloro-diphenyl-trichloroethane (DDT). A "blowing machine" was developed to blow DDT under clothes so that people did not have to disrobe to be treated. When a typhus epidemic struck Naples, Italy, in the winter of 1943–1944, the outbreak collapsed with astonishing speed once DDT was brought into use. Within two decades, however, the adaptive resistance of lice to DDT was documented, and its ecological hazards were documented so that is no longer widely used.

In 1948 broad-spectrum **antibiotics** were discovered to be effective treatments for all rickettsial diseases. Since then, little research has been conducted on vaccines to prevent typhus. Civilian and military physicians have relied almost completely on the use of antibiotics to cure rickettsial diseases.

Current State of the Disease. In the twenty-first century, typhus poses little threat in populations in which Western medicine makes antibiotics widely available to treat infections. The principal locales where *R. prowazekii* is still likely to be contracted because of infestations of body lice in local populations are the cool, mountainous regions of Africa, Asia, and Central and South America. In addition, recent molecular and genetic screening techniques have shown that fleas that live on flying squirrels can transmit *R. prowazekii*. Campers, inhabitants of wooded areas, and wildlife workers may be vulnerable to typhus if they come in close contact with flying squirrels, their ectoparasites, or their nests. Murine typhus still exists worldwide and may be contracted anywhere rats are prevalent and humans may be bitten by their fleas. *See also* Colonialism and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Irish Potato Famine and Epidemic Disease, 1845–1850; Personal Hygiene and Epidemic Disease; Poverty, Wealth, and Epidemic Disease; Typhus and Poverty in the Modern World; Typhus and War; War, the Military, and Epidemic Disease.

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VICTORIA A. HARDEN

TYPHUS AND POVERTY IN THE MODERN WORLD. “The history of typhus,” wrote German physician August Hirsch (1817–1894) in his classic nineteenth-century study of disease, “is written in those dark pages of the world’s story which tell of the grievous visitations of mankind by war, famine, and misery of every kind” (1883; p. 35). Hirsch’s formulation is a poetic shorthand for the past, present, and, most probably, future, of a particularly dreaded disease. For there is a repetitive quality among typhus stories, each of which seemingly takes Hirsch’s formula of “war, famine, and misery” as a guiding theme, masking—at least from a distance—the distinctiveness of individual outbreaks and personal suffering. Whether we are visiting instances of “war,” “jail,” “ship,” or “spotted” fever in the sixteenth to eighteenth centuries, “hunger” fever in the nineteenth, or “typhus fever” as presently defined, we witness similar stories of human suffering. No wonder, then, that many a student of typhus has come to see the disease as a kind of moral barometer of civilization.

It should be noted that these stricken civilizations tended to dwell in temperate zones. Similar living conditions in more tropical climes might set the stage for the free play of a host of other diseases—but not of typhus. This geographic constraint was well known, long before it could be effectively explained. It was one of the disease’s great mysteries.

Origins. Mystery has similarly shrouded typhus’s origins. There are those who believe that the unknown epidemic (430–426 BCE) known as the **Plague of Athens** was typhus. Of course, efforts to diagnose early epidemics are notoriously difficult. Earlier diagnosticians classified diseases in different ways. Moreover, “typhus” was only clearly differentiated from “typhoid” in the nineteenth century—and, from “murine” typhus in the 1930s. Despite these redefinitions, historians of disease generally agree that classic typhus was striking down Europeans by the latter part of fifteenth century. Thereafter, great numbers of individuals displayed its characteristic fever, rash, searing headache, and delirium. Typhus followed the ever-present course of military conflict over the next couple of centuries, spreading throughout Europe and into North Africa and remaining long after those wars had ended. (It even, as Hans Zinsser [1878–1940] demonstrated, influenced the outcome of more than one of those conflicts.) It also struck residents of the “New World.”

Nineteenth-Century Patterns. After the **Napoleonic Wars** ended, typhus began to settle among populations already suffering from the darker side of the **Industrial Revolution**. Consequently, those studying the conditions of the laboring poor began to study typhus more closely. **Rudolf Virchow**’s celebrated examination of the typhus epidemic in Upper Silesia (1848) was in fact preceded by investigations into the connections of **poverty** and disease by men such as Scotland’s William Pulteney Alison (1790–1859). Alison, a politically and philosophically inclined professor at Edinburgh’s medical school, argued in 1841 that pauperism was the “great and general disease of the body politic”—and that the causal chain leading from economic hardship to deprivation to disease was evident. Typhus, which persisted in poorer sections of Scotland and Ireland even when it was growing less common in more opulent locales, offered an illustrative example. (Still, Alison believed that typhus was caused by particular morbid agents.) The apparent pervasiveness of typhus during the **Irish Potato Famine** of 1846–1849 lent further credit to his arguments. Virchow noted the influence of Alison and others on his interpretation of the Silesian outbreak.

At the time typhus struck in 1847, Upper Silesia, an area now split between Poland and the Czech Republic, was an economically depressed province of Prussia with a large

Catholic Polish population. According to Virchow's later report (1848), the Prussian government had essentially ignored the growing epidemic—and the locally influential Catholic clergy were inclined to preach that the people's wretchedness was a means of their salvation. Virchow was finally sent to the typhus-ridden area in February 1848. There, he quickly compiled materials for his classic study. Relying on the case histories and autopsy records of doctors—who played the forward-thinking heroes (and, more than occasionally, martyrs) in his narrative to the villainous forces of church and state, Virchow presented a striking and moralizing picture of typhus. Typhus was, fundamentally, the product of the near-feudal state that persisted in Upper Silesia. The rich were no longer bound by an older mentality of *noblesse oblige* and instead “indulge[d] in the luxury and the follies of the court, the army and the cities.” The poor, on the other hand, were kept in their poverty by ignorance and neglect. Whatever the specific causes of typhus, its cure could only be found in the overturn of feudal oppression by “full and unlimited democracy” (pp. 89–90). The synchronicity of Virchow's conclusions with Karl Marx (1818–1883) and Friedrich Engels's (1820–1895) *Communist Manifesto* (1848) was no coincidence—despite distinct differences in their ideologies.

The broad outlines of misery that shaped Virchow's typhus story were also evident in any number of mid-century typhus epidemics. In many of these instances, misery had opened the door to typhus, but what followed *after* typhus often had regionally specific, and occasionally broadly national, consequences. The effects of Ireland's mid-century famine tend to be well known. Disease and hunger combined to provide a strong motive for mass emigration. A number of those immigrants took ship for America, arriving in eastern port cities that in turn became (relatively circumscribed) hubs of typhus. The impact of typhus in Tunisia is less well known. During the nineteenth century, Tunisia's leaders had made a number of questionable financial decisions, largely in an effort to keep up with their Western neighbors to the north. Then, in the 1860s, the already-burdened country was plagued by drought, crop failure, and two “classic” plagues: **cholera** and typhus. By 1869 the country was officially declared bankrupt, and, with that, the stage was set for its eventual appropriation by France as a “protectorate.”

Still, when August Hirsch wrote his revised disease geography in the early 1880s, “typhus” was being written on far fewer of western Europe's “dark pages.” Hirsch was not the only doctor to be perplexed by the disease's sudden retreat. By the century's end, typhus had been constrained to a veritable “ring” around the United States and western Europe: in Eastern Europe, North Africa, and Mexico (with occasional incursions into American seaports and more persistent outbreaks in Ireland). It seemed to have been domesticated. Yet in this ring around the West, it continued to be perceived as a threat—and as a mystery.

The Twentieth Century: Explaining Mysteries. By the start of the twentieth century, much had been learned about the cause and spread of many diseases. The so-called **germ theory** of disease—roughly, that one specific microbe caused one specific disease—had been effectively demonstrated and disseminated as the new bacteriological gospel. Knowledge of the microbial causes of such diseases as cholera, **tuberculosis**, and **bubonic plague** was in hand; the complications caused by “vectors,” such as mosquitoes for **malaria**, were also understood. Laboratory studies had been central to these successes. Typhus proved resistant to the prying of laboratory methods. Consequently, neither the disease's causal agent nor its mode of human-to-human transmission had been identified. Without a known microbial agent, diagnosis, too, remained difficult. In 1898 one of America's top

diagnosticians, Nathan Brill (1860–1925), published a paper on an apparent “typhoid fever” epidemic among recent immigrants into New York. Only when he returned to the problem over a decade later did he determine that his patients had been suffering from typhus, not typhoid. In 1900 typhus remained, as Hirsch had described it, a mysterious disease of human misery. Ultimately, its connection to human misery helped guide efforts to unravel those mysteries.

In the first decade of the twentieth century, French researchers in Tunisia and American researchers in Mexico, began to make progress in the longstanding effort to understand the disease. The “answer” was first demonstrated in Tunis—earning **Charles Nicolle** the Nobel Prize (1928) and relegating the Americans in Mexico to the role of providing confirming evidence. Nicolle was well familiar with the history and reputation of typhus, but, until he moved from France to Tunisia, he had not encountered the disease in a patient. As director of Tunisia’s Pasteur Institute, Nicolle was soon faced with a typhus epidemic that took the lives of the two doctors with whom he had intended to visit patients. During subsequent outbreaks, Nicolle set his colleague, Ernest Conseil (1879–1930), to work on the disease’s epidemiology. Conseil followed outbreaks back to laborers in the countryside, who moved to the city in early spring to find work. Their numbers increased dramatically in years of drought—such as 1909—when they could find no agricultural work. In the city, they lived in squalor. Conseil discovered that the epidemic tended to spread only to those in close proximity to them: innkeepers, doctors, and others who cared for them in the hospital. Later, Nicolle would describe his discovery of typhus transmission as a “eureka moment” arising from Conseil’s Hirschean observations. Typhus, he reasoned, must be spread by something close to the body: something that was removed by a thorough scrubbing and change of clothes: “It could only be the louse!” Nicolle quickly turned to the laboratory to demonstrate his hypothesis.

Longstanding mysteries of typhus had been illuminated. Why did typhus follow human misery and movement? Why did it shun areas that were either too frigid or too hot? The louse provided the answer. Where the body louse thrived, typhus could take root. Yet even this new insight did not dispel all the mystery or overturn all the moral judgments attached to the disease. The perception of lice as filthy creatures would have done little to overthrow these assumptions. Indeed, the association of typhus with lice made the tragedy of its continued existence more dramatic still. Typhus could—should—be controlled; but it was not. As Nicolle’s good friend Hans Zinsser wrote, “Typhus is not dead. It will live on for centuries, and it will continue to break into the open whenever human stupidity and brutality give it a chance, as most likely they occasionally will” (1963, p. 301).

In the meantime, typhus, in its classic, louse-borne form, continued to be further differentiated from disease varieties once thought identical to it. Typhus outbreaks in Mexico during the late 1920s and early 1930s attracted researchers from around the world. They determined that the typhus of Mexico was different. Maintained in rats and transmitted to humans by fleas, it was milder than the epidemic variety—and was evolutionarily distinct. (This realization led Nicolle, Zinsser, and others to press for further study of the evolution of infectious diseases.) With this knowledge, Zinsser returned to study Nathan Brill’s mildly ailing immigrant population. Strangely, most of these patients had been in the United States for decades, safely outside active typhus centers. Zinsser determined that the immunity conferred by typhus was durable, but not absolute. Decades after a typhus victim had recovered, the disease could reappear—or, “recrudesce.” If conditions were right—that is, if body lice were abundant—typhus might erupt.

The discovery that the louse acted as a necessary link between human misery and typhus encouraged an all-out war on the louse. That lice tended, particularly as the twentieth century progressed, to be found on the poor certainly did little to discourage the aggressiveness of those campaigns. Whether among laborers at the border of the United States and Mexico, black populations in South Africa, or nomadic laborers (or colonial troops) in North Africa, typhus was kept away from more affluent neighbors by aggressive attacks on lice. It can hardly be surprising that these campaigns often seemed to shade imperceptibly into campaigns against the poor people harboring the lice.

The Persistence of Typhus. Typhus epidemics appear far less frequently today. This is, in part, the result of developments in vaccines and **antibiotics** from the mid-twentieth century. Despite these advances, however, the story continues. In the 1990s, for example, typhus ravaged the higher and relatively cool regions of Burundi in Africa, underscoring the misery that had resulted from civil war, mass dislocation, and relocation in refugee camps.

The persistence of typhus and its continued coupling with human misery despite the advances of science and the efforts of global health workers support history's judgment of the disease as a window onto the often-tragic "health" of civilization. As Nicolle noted in *Naissance, Vie, et Mort des Maladies Infectieuses* (1930; pp. 195–196):

Typhus presents itself to us as both a plague and a moral lesson. It tells us that man has only recently emerged from barbarity, that he still carries on his skin a disgraceful parasite such as brutes themselves carry, and that, when man conducts himself like a brute, this parasite . . . will prove, in effect, that he is merely a brute. The disappearance of typhus will only be possible on that day when, wars having disappeared, the work of a collective hygiene will suppress the louse. Humanity will only know this immense progress when it merits it. Will we ever merit it?

See also Diagnosis of Historical Diseases; Ectoparasites; Environment, Ecology, and Epidemic Disease; Historical Epidemiology; Insects, Other Arthropods, and Epidemic Disease; Personal Hygiene and Epidemic Disease; Pesticides; Sanitation Movement of the Nineteenth Century; Typhus and War.

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KIM PELIS

TYPHUS AND WAR. Since at least the sixteenth century, epidemic **typhus** has been one of the most common and deadly **epidemic** diseases to accompany armies on campaign. Typhus in general is caused by **bacteria**-like microorganisms known as rickettsia, which are spread by wingless body lice, rodent fleas, mites, or ticks. There are three variants of typhus: flea-borne endemic (murine), louse-borne epidemic, and mite-borne scrub. Researchers developed vaccines against endemic and epidemic typhus in the early 1930s, but none yet exists for scrub. Early typhus symptoms include headache, acute fever, and small pink spots on the skin; vomiting and prostration may follow.

Louse-borne Epidemic Typhus. In epidemic typhus—also known as **war fever**, ship fever, camp fever, jail fever, and the Hungarian disease—delirium and deafness often precede the final stage of circulatory collapse (toxemia) that brings on death in anywhere from 5 to 40 percent of untreated cases. Full recovery confers limited **immunity**. The body louse *Pediculus humanus corporis* that transmits the pathogenic *Rickettsia prowazeki* lives in human clothing and feeds on human blood. The pathogenic bacteria are deposited on the victim's skin in powdery louse feces and enter when the skin is abraded by the victim's scratching. Lice will migrate from one human to another, thus spreading the rickettsia from dying or immune hosts, but they thrive on bodies whose clothing is undisturbed and unlaundered for long periods. Low levels of **personal hygiene**, so common in pre-contemporary armies, were the louse's best friend. When combined with cold-weather campaigning, exposure to the elements, forced exertion, and poor **diet**, the infected louse and its tiny parasite could cripple the most valorous of soldiers and the greatest of history's armies. Before the twentieth century, disease—especially typhus—invariably killed more soldiers than action in battle, sometimes four or five times as many. The 1906 Russo-Japanese War was the first major conflict whose battle casualties outnumbered those from disease.

Early Appearances. Typhus symptoms are close enough to those of **measles**, **malaria**, and **typhoid fever** to make undoubted **historical diagnoses** a real problem. Medical pioneer Hans Zinsser (1878–1940) noted that murine typhus was known to Western medicine since at least the eleventh century CE, though the early sixteenth-century Italian physician **Girolamo Fracastoro** considered epidemic typhus a new disease (though louse transmission was not discovered until 1909 by **Charles Nicolle**). The earliest clearly recorded military outbreak was during the last phase of the five-century *Reconquista*, the Christian Spanish siege of Muslim Granada during the winter of 1489–1490. Fracastoro echoed contemporary claims that the disease had been brought into Iberia by Spanish soldiers who had been fighting alongside the Venetians against the Turks in Cyprus. At Granada, epidemic typhus is said to have accounted for 17,000 of the Spanish casualties, whereas the Moors accounted for 3,000. Final Christian victory was postponed until the fateful year 1492.

Fracastoro noted cases in Spanish-dominated southern Italy as early as 1505, but its earliest Italian outbreak was at the French siege of Naples in 1528, in the midst of the Habsburg-Valois Wars. Typhus, plague, and desertion had cut Emperor Charles V's (1500–1558) Spanish and German garrison down to around 11,000 disheartened men who found themselves surrounded by a proud French army of some 28,000. In early July, disease began to pick off the French, soldier and commander alike. Typhus is considered to have been the principal killer, as disease reached deadly epidemic levels. With much of his army sickly or expired, the new French commander, the young Marquis de Saluzzo (1490–1533), raised the siege on August 29 and began the long march back north. Imperial troops and allies harried the slow-moving columns mercilessly, and Charles's victory

was complete. Twenty-four years later his fortunes were reversed, however, when his army of Spaniards, Germans, and Italians besieged the well-defended, French-held fortress city of Metz. This was to be the first step in a final, victorious Habsburg counteroffensive against his perennial enemy. Ill-advisedly opening the siege in October, in a single month he lost 10,000 of his 75,000 men to typhus (and other diseases including **dysentery**), which then spread across the countryside. Charles raised the siege in January, and his defeat helped persuade him to retire as Emperor in favor of his brother Ferdinand (1503–1564).

Typhus had checked an Imperial army a decade earlier, in 1542, when Joachim II Hektor von Brandenburg (1505–1571) organized an international force against the Turks who had just occupied the Hungarian city of Buda (Budapest). In his history of the campaign, surgeon Thomas Jordanus von Klausenburg (1540–1585) left a clear picture of the effects of the Christian army's lack of good food, water, and beer, and of the filth and heat of the march. Dysentery, enteric fevers, and, above all, typhus dissolved away the war machine even before it reached the city. The resulting peace left the Muslim Ottomans in command of the Hungarian Plain.

Early Modern Trends and Examples. Seventeenth-century armies fighting the **Thirty Years' War** (1618–1648) and the English Civil War (1642–1648) were no cleaner or better fed, and thus no less susceptible to lice and rickettsia than their predecessors. Whether Catholic Imperial, Protestant German, French, Spanish, Danish, English, or Swedish, soldiers shared typhus among themselves and the civilian populations through whose countryside and city streets they trudged. Armies marched, countermarched, and fought relatively rarely, spending much of their time foraging for food and needed supplies. Germany provided most of the battlefields and foreign armies with little concern for the local civilians spread disease with abandon. Reinforcements, new recruits, and fresh national armies kept the fires of war and pestilence stoked, whereas the disease-ridden were often taken in by, or forced upon, local households. Rural refugees crowded besieged cities and suffered from typhus alongside defenders, further blurring distinctions between soldier and civilian. As the Swedes approached Nuremberg in the summer of 1632, Imperial Habsburg forces interposed themselves, remaining outside the city. By September scurvy and typhus had ravaged both armies, and both moved on, littering their paths with the sick, dying, and newly infected. By war's end, typhus may have killed more than 10 percent of the total German population, and disease in general accounted for 90 percent of Europe's casualties. Peace treaties led to demobilization, first in 1635 and finally in 1648: troops returning home took typhus with them in every direction. Thereafter, as biologist R. S. Bray put it, "Typhus went on to affect the outcome of every war on the European continent up until the Second World War."

During the early stages of the English Civil War, the Parliamentary army led by the Earl of Essex marched toward Royalist Oxford. In mid-April 1643, his 18,000 men stopped and surrounded the town of Reading for two weeks in mid-April. In an odd reversal, townspeople transmitted typhus to the Roundheads, who broke camp and quickly relocated to Buckinghamshire. Though no record of casualties exists, the toll was enough to dissuade Essex from attacking Oxford, which was well enough, because the King's army was in the process of rapidly passing the disease along to Oxford's residents and to the villagers beyond. The following July, Essex and his men marched west and occupied Tiverton, Devonshire, which raised the townspeople's mortality rate by nearly 10 times

normal according to burial records. Though less spectacularly, this pattern of typhus dissemination continued for much of the war.

The eighteenth century produced few peaceful years, and national armies became larger than ever before. The aggressive and protracted territorial wars of France's Louis XIV and Frederick the Great of Prussia, and then the French Revolutionary and counter-Revolutionary campaigns of the 1790s, mobilized hundreds of thousands of men and sent them streaming across Europe time and again. Central Europe north of the Alps and from the Rhine to Silesia (modern western Poland) hosted most of the military activity and suffered most from the diseases it spread. In every army, typhus took its inevitable toll among the ranks, and every army spread the disease as it marched and foraged. Conditions in sedentary army camps grew especially squalid, and cities and fortresses were often targets. Burdened with refugees, defending garrisons, and enemy troops, towns became focal points for typhus outbreaks. During the War of Spanish Succession (1702–1714), Bavarian Augsburg suffered in 1703–1704, first when occupied by friendly French and Bavarian troops and then when captured by the English and Austrians. Burial records show interments more than tripling between 1702 and 1704, and returning to normal in 1705. Dresden was wracked twice during the Seven Years' War (1756–1763), in 1757 and 1760, and in 1758 Breslau in Silesia matched 9,000 local military deaths from typhus and related diseases with those of 9,000 of its own citizens.

The Modern Era. The **Napoleonic Wars** between 1796 and 1815 dwarfed those of earlier rulers, as did Napoleon's armies and those sent against him. After the Battle of Austerlitz in December 1805, Napoleon left 48,000 wounded French and allied troops in various forms of shelter in Brno. Of these, 12,000 died of typhus. In June 1812, Napoleon led 650,000 French and allied troops into Russia. Thanks to typhus exposure as they crossed Polish territory, only 130,000 remained fit to fight at Borodino (September 7), and fewer than that entered Moscow a week later. The horrors of the French midwinter retreat resulted in fewer than 40,000 reentering Central Europe in 1813. Nevertheless, Napoleon returned to France and raised another army of half a million men. Of these 105,000 were lost in battle in Germany (Dresden and Leipzig) in August and October 1813, but an estimated 219,000 died of disease within less than a year.

In spring 1813, Bavarian authorities wisely established sanitary stations along their eastern border to intercept French stragglers from the Russian campaign. Those who were diseased, generally with typhus, were isolated in lazarettos or other isolation facilities such as military hospitals. This kept the region free of epidemic typhus until October brought the new French army, its diseased troops, and its battle casualties. The diseased and wounded, prisoners and the abandoned, and, increasingly, diseased civilians flooded **hospitals** and other care facilities. These were transformed into filthy hellholes reminiscent of the worst medieval **pest houses**. According to Bavarian records, between October 1813 and June 1814, civilians suffered 18,427 cases of typhus, of which 3,084 were fatal, numbers that are undoubtedly very low given the chaotic conditions. The retreating French army continued to fill hospitals with its diseased and dying, but by June or July the typhus epidemic in Germany had ended.

Nineteenth-century wars tended to be on a smaller scale and more quickly decided than those of the previous century. This generally meant fewer potential typhus carriers, less time on campaign, and less impact on civilian populations. The American Civil War (1861–1865) seems to have produced very few cases of typhus. When France and Britain

sent armies to aid the Ottoman Turks against the Russians in the Crimean War (1854–1856), they were repeating an old pattern. The allies bottled up the Russians at Sevastopol in September 1854 and established siege camps around the city. Cholera, dysentery, and typhoid established themselves and horrified the early newspaper war correspondents and their readers. British reformers, including the nurse Florence Nightingale, saw to it that British conditions were improved, including the regular laundering of clothing, which helped discourage the body louse. When the French contracted typhus in the fall of 1855, suffering over 17,000 deaths, the British remained largely unaffected, with only 62 fatalities. At war's end, soldiers spread both typhus and **cholera** outward from the battleground. The French took the precaution of quarantining returning troops—primarily on the Isles d'Hyere near Toulon—who thus carried neither disease home. British military leaders, however, allowed unfettered return, which resulted in local epidemics back home.

At the southern tip of the Ottoman Empire, Egyptian troops with Sudanese allies invaded Ethiopia in 1876 and promptly contracted typhus. Attempts to isolate cases merely resulted in the spread of the disease to military camps and other Egyptian units. Ethiopian units also caught typhus—some thought from Egyptian **corpses**, others from the **miasma** that had rendered the corpse—and carried it into their towns, such as Aduwa, which lost over 60 percent of its people.

Nicolle's 1909 discovery of the role of lice prompted the use of hot baths and steam cleansing of clothing as prophylactics by some armies in World War I (1914–1918). The realities of the front, however, made such niceties rare. When Austrian troops invaded Serbia in late 1914, many contracted typhus, and huge losses forced their early withdrawal. They left behind some 60,000 prisoners, most of whom were diseased. The Serbs spread these about the countryside in camps, and typhus spread with them. A third of Serbia's 350 physicians succumbed to the fever, as did fully half of the Austrian POWs. Though typhus was rare in the Western trenches, perhaps as a result of cross-immunization by the common rickettsial trench fever, it swept through armies on the Eastern Front. During the seven years between 1916 and the end of the Civil War, an estimated 30 million Russian soldiers and civilians suffered from typhus, and 10 percent of these died. About 1930, Austrian-born Pole Rudolf Weigl (1883–1957) developed the earliest typhus vaccine.

Though military personnel during World War II (1939–1945) generally went on campaign having been vaccinated against epidemic typhus, civilians whose environments were disrupted by the war often suffered. In Poland typhus was nearing elimination (between 2,000 and 4,000 annual cases) when the German army invaded in September 1939. Nevertheless, the Nazi authorities began rounding up Polish Jews under the false pretext that they were carriers of exanthematous typhus whose relocation aided public health. In fact, the horrendous conditions of the Nazi death camps only fostered disease among the living. Destructive Nazi policies and activities also led to malnutrition and reduced levels of health care and hygiene in conquered Jewish communities throughout occupied Europe, which led to outbreaks of typhus and its spread through mass resettlement.

With the German conquest of France in 1940, life in French Algeria and Morocco underwent rapid and jarring change, including shortages of soap, insecticides, and new clothing. In 1942 the disruption was accelerated, and epidemic typhus appeared among the native Arab and Berber peoples as well as European civilians and refugees. Dissemination was widest and fastest in more densely populated areas including major cities. A larger percentage of native North Africans than Europeans contracted typhus, though death rates

were much higher among the less naturally immune Europeans. Moroccan authorities acted quickly to immunize and to isolate known cases, which helped reduce the annual number of cases from 25,000 in 1942 to 4,000 the following year. Cases spiked again in 1945, but with ample use of DDT—first developed as an insecticide in 1939—they fell to 126 in 1947. All told, at least 50,000 and perhaps a quarter-million Algerian residents fell ill, and 12,840 died between early 1942 and mid-1944; from 1942 to 1945, an estimated 40,200 Moroccans fell ill of typhus, and 8,040 died.

In British-controlled Egypt, the war effort required the **migration** of workers from typhus-ridden areas to northern cities such as Cairo and Alexandria. Incidence rates rose dramatically, and by war's end, authorities recorded an additional 110,000 typhus cases and 20,000 fatalities. Imperial Japan's occupation of Korea resulted in many typhus-carrying Korean laborers being shipped to wartime Japan, reintroducing the disease for the first time since 1914. When the war ended, many of these laborers were repatriated to Korea, bringing their disease with them. Many Japanese returning home from Korea also carried typhus, sparking epidemic outbreaks in Osaka, Tokyo, and Yamagata. In Algeria, Egypt, and Korea, late- or postwar immunizations and extensive use of the **pesticide** DDT for fumigation brought the epidemics to a close.

Allied occupiers paid less attention to typhus cases in Japan. Immunizations for scrub typhus have never been developed, and both Japanese and Allied forces fighting in the Southwest Pacific islands and in Ceylon and Burma suffered from the harvest mite-borne disease. Whereas no Japanese figures are available, an estimated 18,000 Allied troops came down with the disease and a few percent died of it. Careful ground-clearing at new facilities sites and application of pesticides on clothing and blankets tended to keep the mites at bay.

Though typhus is rarely encountered today, African civil and regional wars still spawn sporadic reports of the disease from isolated refugee camps, or more widely as in war-ravaged Burundi in 1997 (24,000 cases reported). It has also been reported that typhus has been weaponized into an aerosol biological warfare agent. Though rickettsiae are in some ways perfect candidates for this use, it is very difficult to maintain virulence during production, and the disease is not directly passed on by human contact. *See also* Diagnosis of Historical Diseases; Historical Epidemiology; Napoleonic Wars; Thirty Years' War; Typhus and Poverty in the Modern World.

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JOSEPH P. BYRNE

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URBANIZATION AND EPIDEMIC DISEASE. The origins of city development date back to the late **Neolithic** period. The adoption of agriculture and the advent of sedentary living led to worldwide population increase and settlements of ever-higher density. Human susceptibility to **epidemics** of infectious diseases has its origins among the dense populations of the earliest cities. Some diseases—for example **schistosomiasis** and **malaria**—are transmitted to humans via an animal vector, whereas others are passed by human-to-human **transmission**. The latter—for example **typhoid fever**, **leprosy**, or amoebic **dysentery**—may be caused by a microorganism that renders the host infective for a prolonged period of time, thus enabling its survival even in smaller communities. However, the most rapidly spreading acute infections, such as **cholera**, **smallpox**, mumps, **measles** (rubeola/rubella), and chickenpox, rely on large concentrations of people available for infection.

The Beginnings. Our nomadic ancestors did not settle down long enough in one place to suffer the ill effects of pollution, for example by contaminating **water** sources with human and animal wastes. Nor did they come into close and prolonged contact with animals, and thus they were spared the zoonotic diseases picked up by their sedentary successors. As a result of the more abundant food supplies agriculturalists enjoyed, their populations increased rapidly when compared to the smaller bands of hunter-gatherers. On the other hand, the diet of sedentary populations would have been less varied, with heavy reliance on cereals. In years of crop failure or animal diseases, famine was an unavoidable reality. It can be assumed that zoonotic diseases were contracted through close contact with domesticated animals, such as dogs, goats, and cattle, but another source of infectious diseases was rodents and insects attracted by accumulating waste and stored foodstuffs in permanently settled habitations. Because these settlements were usually situated along watercourses, waterborne diseases such as schistosomiasis (bilharzia), a disease that is still prevalent today throughout the Nile valley, could have established

themselves among these sedentary populations. Another waterborne disease, typhoid fever, might also have originated in these early settlements. Population numbers were probably not large enough, however, to sustain the ravaging epidemics experienced in the centuries leading up to the modern era. In addition, many survivors of illnesses would have built up temporary or permanent **immunity**, and many infectious diseases might have become less virulent over time and eventually have become endemic, minimizing the chances of epidemic outbreaks among early urban populations.

Early Cities. During the later part of the Neolithic period (c. 5000–3000 BCE), the Bronze Age (c. 3000–1000 BCE), and the subsequent Iron Age, increasing population numbers and advances in technology led to the foundation of new urban centers and the enlargement of existing cities in Egypt, Mesopotamia, South Asia, China, and South America. Hand in hand with an increase in populations, food demands increased, and many of these settlements thrived because of innovations such as irrigation systems. They also domesticated a wider range of **animals** and increased the possibility of the transmission of new zoonotic diseases. Egyptian medical papyri of the second millennium BCE and texts found in the capital of the Hittite empire (modern Turkey) describe epidemic outbreaks, though of which diseases remains unclear. Viral diseases such as smallpox and measles possibly originated in these densely populated cities, but the scientific evidence is inconclusive. The skin lesions observed in the mummified remains of Pharaoh Ramses V, who died in 1157 BCE, are often attributed to smallpox, but a number of other diseases are equally likely, and analysis of ancient DNA has thus far not confirmed the diagnosis. Other clues come from the writings of Mesopotamia and China, as well as the recorded **biblical plagues**.

A number of factors made early cities the perfect places for epidemics: high population density; crowded and often squalid living conditions; poor public sanitation; water supplies of questionable purity; food supplies that attracted rodents and other disease vectors; regular trade connections with other cities and the regular arrivals of travelers and merchants, especially by ship; **war**; and the housing of refugees. Greek historian Thucydides (460–395 BCE) survived and described in detail what is now regarded as the first recorded epidemic in antiquity, the **Plague of Athens**. In 430 BCE, at the outset of the Peloponnesian War, an outbreak of an infectious disease hit the city-state of Athens. The Athenian army and inhabitants of the city and the surrounding countryside were sheltering behind the city walls, and this concentration of people provided the necessary number of hosts for the unidentified disease to spread and kill at least one-third of Athenians. Further epidemics occurred in the following years, also afflicting the enemy city-state of Sparta, as well as the eastern Mediterranean more widely. The Plague of Athens has been attributed to **bubonic plague**, measles, smallpox, and **hemorrhagic fevers**, among others, but recent ancient DNA analysis of teeth from putative victims of the epidemic has identified the causative agent as typhoid fever. According to historical accounts, the disease spread from Ethiopia to Egypt and Libya, and it probably arrived by ship in the harbor of Athens before it spread through the overcrowded city.

Though lagging behind the Greek city-states in urban development, Rome, capital of the Roman Republic and later Empire, housed enough people to sustain epidemic diseases from early in its history. From 165–166 to 185 CE, Rome and other Roman cities were ravaged by an epidemic outbreak brought back to the capital by troops returning from Northern Mesopotamia. Named the **Antonine Plague** after the Roman emperor who fell victim to the disease, its signs and symptoms were described by the Greek physician

Galen, and it appears that it may have been smallpox. From 251 to 266, Rome was again the scene of a devastating disease outbreak, known as the Plague of Cyprian, after the bishop of Carthage, whose city was equally affected by the epidemic, with thousands of people dying each day. The Plague of Cyprian has been tentatively identified as measles. The high number of deaths during these outbreaks might indicate that there had been no prior exposure to this disease or to the previous Antonine plague. It also attests that population numbers were large enough to sustain epidemic outbreaks of infectious diseases.

Although previously described epidemics claimed large numbers of lives much worse was to come. The Byzantine Empire and its capital, Constantinople, were hit by what is known as the first plague pandemic, the **Plague of Justinian**. The origins of the disease have been traced to Egypt, from whence it was transported to Constantinople by ships delivering grain to the metropolis in 541–542 CE. Rats living in large granaries within the city could have easily spread the disease identified as bubonic plague from contemporary descriptions—a disease that recurred regularly over the next 200 years, spreading throughout the Byzantine Empire and well beyond and killing probably more than half of the entire population.

The Era of the Black Death. Although urban life had remained vital throughout the Middle Ages in the Islamic world and what remained of the Byzantine Empire, the Latin West was underdeveloped until the later thirteenth and fourteenth centuries. Rising populations everywhere fed burgeoning cities that offered new occupational opportunities and freedoms. Wealthy classes independent of the older nobility and church built trading networks and rudimentary industrial concerns. These same classes established independent or semi-independent civic governments following the ancient Roman Law, seizing, buying, or negotiating their freedom of action from their sovereign lords. Cities were crowded warrens where rich and poor lived cheek-by-jowl and little effort was directed to sanitation. Drains were choked with refuse and rivers served as sewers. Ships plied ancient coastal routes, and powerful port cities like Genoa and Venice stretched trading tentacles as far as the Crimea. It was along these trade routes and into these urban centers that plague rats traveled in the later 1340s, bringing a scythe-like pestilence for which no one was prepared. From towns and cities, the disease moved outward into rural areas as people fled the horrors so graphically depicted by the literate urban classes. Returning in 10-year and then longer cycles, the plague eventually settled in cities, the brisk commercial traffic of which refreshed the supply of infected rodents, and the filth of which promised a large reservoir of native rats.

Though populations dropped throughout the West, by the sixteenth century many cities had either reemerged or had grown up to house high concentrations of people and had begun to serve as links in maritime chains that stretched ever further across the globe. Older diseases like measles and smallpox became endemic amid population concentrations heavy enough to sustain them. New ones like **syphilis** and **yellow fever** found “virgin soil” in densely packed port cities and military camps. Because no Christian, Muslim, nor Jew understood the microscopic pathogens that caused these maladies, neither physicians nor public health efforts were of much value. Some measures, like **quarantine** and **cordons sanitaires**, could limit exposure at least somewhat, but most efforts were in vain.

European Expansions and Early Modern Cities. With the activities of European explorers and colonists Old World diseases were unintentionally introduced to the Americas. Tenochtitlán, present day Mexico City, was an enormous urban center and capital of the Aztec Empire. Within a few years of the arrival of the first Spanish ships in 1521, however,

the city's inhabitants were massacred by smallpox, enabling the Spanish conquistador Hernándo Cortés (1485–1547) to conquer the Aztec Empire. Further smallpox outbreaks occurred in the Incan Empire of modern Peru, killing most of the native inhabitants of the capital Cuzco. Other new diseases such as measles, typhoid, and **influenza** swept colonial cities of both urban natives and native-born colonists.

As in the Old World, urbanized civilizations like those of Peru and Mexico featured cities in which concentrations of people fed the epidemics, which then spread into the countryside and from region to region along trade routes linking these centers. Because the civilizations' economy, culture, and political life were focused on the cities, they became the target of European predation. With populations and garrisons weakened by disease, the Spaniards had little trouble seizing control, especially when they were immune.

In both Europe and the colonial world, cities grew in size and importance. Sanitation and water supply remained problems, and travel and trade continued to introduce and reintroduce dangerous pathogens. Personal cleanliness was rare, so fleas, ticks, lice, and mites found comfortable homes on human bodies. As administrative centers, cities invited foreigners and natives to mix and mingle with the capitals' citizens. Increasingly industrialized towns and cities brought folks from the countryside into the wretched and growing slums—people who then added to the filth and demand for water. Close quarters meant easy transmission of pulmonary diseases. Plague slowly disappeared giving way to smallpox in the eighteenth century and then cholera and **tuberculosis** in the nineteenth. Yet smallpox prompted **inoculation** early in the century and **vaccination** later on, and worldwide cholera pandemics in the 1830s and 1840s spawned new and very fruitful thinking and action regarding urban sanitation and general cleanliness. The **Sanitation Movement of the nineteenth century** was an urban movement dedicated to cleaner living and fresher water. Tubercular patients were removed to sanatoria from pollution-hazed cities, and municipal water supplies were separated from polluted upstream sources. Urban **hospitals** began to provide more sophisticated treatments, and the emerging acceptance of **germ theory** from the 1870s meant a growing number of effective treatments developed using the new science of bacteriology. New understandings of **insect** vectors revealed that plague could be limited by killing rats and their fleas, and that drainage could control the yellow fever that scourged American cities and the malaria that killed in Europe and Africa.

Reemerging and New Diseases of the Modern World. Although modern medicine enables most of the world's population to lead relatively healthy and long lives, reemerging and new infectious diseases present an increasing threat. This is especially true in the huge cities of the developing countries in Asia, Africa, and South America. As centuries before in Europe, the large cities and suburbs of the modern world attract uneducated and unskilled newcomers seeking accommodation, work, and food, leading to the development of largely unsanitary and crowded areas where the economically less successful congregate. The constant influx of new residents into cities and suburbs across the globe taxes infrastructures such as water and sewer provision and can also introduce both new and old diseases, whereas spreading urban development opens previously uninhabited areas and can bring people into contact with new diseases. The reemergence of tuberculosis (TB) is a good example of the return of an old infectious disease. By the mid-twentieth century, TB was considered nearly eradicated, but recently the disease has been making a comeback in the troubling form of new drug-resistant strains. New cases are reported on a regular basis, and it is the large metropolitan areas that are most affected. Furthermore, the **Human**

Immunodeficiency Virus (HIV/AIDS), an infection of epidemic proportions since its emergence in the United States in the 1980s, is largely transmitted within the male homosexual and drug cultures of large cities. In addition, the rise and spread of prostitution and the practice of casual sexual encounters within urbanized areas throughout the world helps to spread the virus. Other sexually transmitted diseases such as syphilis and **gonorrhea** are also once again on the increase. Reemerging infectious diseases include urban yellow fever, which occurs in the cities of South America and Africa, where the mosquito vector has adapted to breed in water containers, discarded car tires, open sewers, and flower pots. **Dengue** hemorrhagic fever is also reaching epidemic proportions in the cities of Southeast Asia and South America.

Childhood diseases, such as measles and **diphtheria**, which were once well controlled by immunization programs, are also returning. With the decline in vaccination programs and the availability of large numbers of susceptible people, cities are a major resource for these reemerging viruses. Furthermore, air travel enables infectious diseases to cover vast distances, moving from city to city, emerging in unlikely parts of the world.

In 2003, **Severe Acute Respiratory Syndrome (SARS)**, caused by a highly infective pneumonia **virus**, was stopped short of becoming a major threat after it spread from southeastern China to Hong Kong, Beijing, and eventually Toronto, Canada. Live animals kept in crowded conditions and close contacts between humans and animals may enable viruses to jump the species barrier. The **Avian influenza** virus, which first reemerged in birds in the Far East in 2004, is feared to cross the animal-human border eventually because of its ability to change genetically, and human deaths caused by the virus have already been reported worldwide. However, if the virus is able to pass from human to human, a major pandemic outbreak is likely, which could spread rapidly within cities and from one urban center to the next. *See also* Colonialism and Epidemic Disease; Contagion and Transmission; Diagnosis of Historical Diseases; Disease in the Pre-Columbian Americas; Drug Resistance in Microorganisms; Environment, Ecology, and Epidemic Disease; Historical Epidemiology; Hospitals and Medical Education in Britain and the United States; Industrialization and Epidemic Disease; Personal Hygiene and Epidemic Disease; Plague in Britain, 1500–1647; Plague in Europe, 1500–1770s; Plague in San Francisco, 1900–1908; Plagues of the Roman Empire; Plagues of the Roman Republic; Poverty, Wealth, and Epidemic Disease; Religion and Epidemic Disease; Sexual Revolution; Yellow Fever in North America to 1810; Yellow Fever in the American South, 1810–1905.



Disease, in the form of a skeleton on a skeleton crow, flies into a city, threatening death. Early twentieth-century drawing. Courtesy of the National Library of Medicine.

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TINA JAKOB

V

VACCINATION AND INOCULATION. Inoculation and the later practice of vaccination entail the introduction of disease-related biological material under the skin in order to produce an immunizing reaction in the human body. The term inoculation comes from the Latin word *inoculatio* (*in*: into; *oculus*: bud), and it means to graft. In the field of medicine, inoculation is the introduction of microorganisms, disease agents, infective material, serum, and other substances into tissues of living plants, animals, people, or culture media.

Because the smallpox (*variola*) virus was involved in one of the first inoculations of a European, the procedure is also called variolization. It had long been known in the East Asia, having been employed in China from the tenth century by means of introducing into the nose dust of variolic scrapings. From the time of the seventeenth-century emperor K'ang (1654–1722), the Chinese used the practice very widely, especially on soldiers and children. In the twentieth century, this practice was still being used in some regions of China. Indians also practiced variolization from ancient times. They would puncture the distal part of the deltoid muscle with a needle moistened in variolic pus. The technique spread as far as Istanbul, Turkey.

In 1714 the Greek doctor Emmanuel Timonis, who lived in Istanbul, presented an article outlining his success with variolization to the Royal Society in London. This was published in the Society's *Philosophical Transactions*. The scientific community did not acknowledge Timonis's findings immediately, but the intervention of Lady Mary Wortley Montague (1689–1762) proved invaluable. She arrived in Turkey in 1717 with her husband, who had been appointed ambassador. She had suffered with smallpox in the past, and as soon as she learned of the technique, she ordered her son to be variolized by the ambassador's physician, Dr. Charles Maitland (1677–1748). After the family's return to Britain in 1717, Lady Montague spread the news of the value of inoculation. Because several epidemics of smallpox had occurred during those years, people willingly followed Lady Montague's advice, and

ON EARLY ATTEMPTS TO INOCULATE FOR MEASLES (1774)

Attempts have been made to communicate the measles, as well as the small-pox, by inoculation, and we make no doubt but in time the practice may succeed. Dr. Home of Edinburgh says, he communicated the disease by the blood. Others have tried this method, and have not found it [to] succeed. Some think the disease would be more certainly communicated by rubbing the skin of a patient who has the measles with cotton, and afterwards applying the cotton to a wound, as in the small-pox; while others recommend a bit of flannel which had been applied to the patient's skin, at the time of the disease, to be afterwards laid upon the arm or leg of the person to whom the infection is to be communicated. There is no doubt but this disease, as well as the small-pox, may be communicated various ways; the most probable, however, is either from cotton rubbed upon the skin, as mentioned above, or by introducing a little of the sharp humour which distils from the eyes of the patient into the blood. It is agreed on all hands that such patients as have been inoculated had the disease very mildly; we therefore wish the practice were more general, as the measles have of late become very fatal.

From *Domestic medicine; or, The family physician: being an attempt to render the medical art more generally useful, by shewing people what is their own power both with respect to the prevention and cure of diseases. Chiefly calculated to recommend a proper attention to regimen and simple medicines.* By William Buchan, M.D. of the Royal College of Physicians, Edinburgh . . . *The second American edition, with considerable additions, by the author.* Philadelphia: Printed by Joseph Crukshank, for R. Aitken, at his book-store, opposite the London Coffee-House, in Front-Street., MDCCCLXXIV. [1774]



Freeze-dried smallpox vaccine being prepared from virus grown on the skin of a calf in Bangladesh. WHO photo. Courtesy of the National Library of Medicine.

in 1721 and 1722 a significant number were inoculated.

The Scots **surgeon** John Hunter (1728–1793), pioneer in experimental surgery, carried out the first self-inoculation of pus from a patient suffering with venereal disease in 1767. Hunter intended to determine whether **syphilis** and **gonorrhea** were the same disease. But the patient had both syphilis and gonorrhea, and Hunter was convinced that it was the same disease.

The English surgeon **Edward Jenner** coined the term *vaccination* in 1798 for his technique of producing in human beings the disease called cowpox (*Variolae vaccinae*). After observing carefully and proving that people who had suffered from cowpox never contracted smallpox, he concluded that artificially inducing a mild variety of *Variolae* through vaccination was a way to protect against the far more deadly **smallpox**. Jenner's technique was based on a **folk** practice that he experimentally confirmed but could not fully explain. Now we know that the smallpox **virus** (*Variola virus*) is genetically related to the cowpox virus (*Cowpox virus*). Due to this genetic resemblance, each is able to produce a cross-defense against the other in the human body.

In 1877 the French chemist **Louis Pasteur** broadened the definition of vaccination to include any medical procedure using a vaccine—a small amount of attenuated or dead pathogen agents that cause a certain disease—to induce in people protection against diseases. Through **animal research**, he discovered that by gradually giving animals small doses of the germ of a specific disease, he could make them immune to that disease. He started by administering doses of weak germs, followed by more active germs, and finally one dose of the most active ones. After the full course, the animal was protected against that disease.

The Spanish doctor Jaime Ferrán (1851–1929) was the first to use a vaccine against a bacterial infection in human beings in 1885, during a severe **epidemic** of **bacterial cholera** in Valencia, Spain. The vaccine, which included dead germs of cholera, proved to be effective. Three months later, Pasteur successfully employed a vaccine against rabies. It was the first time a killed-pathogen vaccine was used against a viral disease. During the following years, several vaccines were developed.

During research on the vector of **yellow fever**, in the first years of the twentieth century, several volunteers allowed themselves to be bitten by the *Aedes aegypti* mosquito, which they thought was the carrier of the causal agent of yellow fever. Because they

SOME EARLY SUCCESSFUL VACCINATIONS, BY DISEASE

- 1796: Smallpox**, by English physician **Edward Jenner**
- 1897: Bubonic Plague**, by the Russian doctor **Waldemar Mordechai Haffkine**.
- 1912: Pertussis**, by the Belgian doctors Jules Bordet (1870–1961) and Octave Gengou (1875–1957).
- 1923: Diphtheria**, by the French doctor Gaston Léon Ramon (1886–1963).
- 1927: Tuberculosis** (BCG: *Bacillus Calmette-Guérin*), by the French veterinaries Léon Calmette (1863–1933) and Camille Guérin (1872–1961).
- 1927: Tetanus**, by the French doctor Gaston Léon Ramon (1886–1963).
- 1935: Yellow Fever**, by South African doctor **Max Theiler**.
- 1955: Injectable Polio Vaccine (IPV)**, by the American doctor **Jonas Edward Salk**.
- 1961: Oral Polio Vaccine (OPV)**, by the Polish-born American doctor **Albert Bruce Sabin**.
- 1964: Measles**, by the American doctor **John Franklin Enders**.
- 1967: Mumps**, by the American doctor Maurice Ralph Hilleman (1919–2005).
- 1970: Rubella**, by the American doctors Stanley A. Plotkin (1932–) and colleagues
- 1981: Hepatitis B**, by the French doctor Philippe Maupas (1939–) and the American doctor Maurice Ralph Hilleman (1919–2005).

developed the disease, they proved it was the vector of yellow fever, but unfortunately, some of them died. Because vaccination introduces pathogens—whether living or dead—into the human body, there was both professional and popular resistance to its use at various points in its development. This was especially true when the popular media reported experiments on large numbers of people that resulted in many contracting the disease. This occurred after 1902 in the Indian Punjab with a **bubonic plague** vaccine, and in the United States following the development of the live **polio** vaccine.

By the twenty-first century, safe and effective vaccines have been developed for a wide range of diseases, and these have proven to be invaluable tools in the medical battle against epidemic disease. *See also* Chinese Disease Theory and Medicine; Pharmaceutical Industry; Plague in India and Oceania: Third Pandemic; Poliomyelitis, Campaign Against; Sabin, Albert; Salk, Jonas E.

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JUSTO HERNÁNDEZ

VENEREAL DISEASE AND SOCIAL REFORM IN PROGRESSIVE-ERA AMERICA. The early twentieth century is frequently referred to as the Progressive Era in America. In reaction to changes brought about by industrial **capitalism**, Progressive reformers wanted government to intervene more than ever before in American economic and social life. Under President Theodore Roosevelt (1858–1919), Progressives undertook national efforts to break up large trusts, regulate railways, ensure pure foods and drugs, and enact various other political and economic reforms. The Progressive movement, however, was as much a cultural, and even a religious, phenomenon as a political one. Early on and for several distinct reasons, reformers tackled the sex trade and its role in spreading the social ill of sexually transmitted diseases.

Progressive leaders, who largely represented the middle class, were as concerned as many other middle-class Americans about the changes that immigration and **industrialization** were effecting on the nation, resulting in a more diverse culture. Moralism was an important part of their agenda. Progressives tended to be especially concerned about the leisure patterns and morals of the working class. Men of the working class were often viewed by the reformers as sexually lascivious and uncontrolled. Working-class women were sometimes stereotyped as being ignorant and promiscuous.

Issues of sexual morality easily fit within the Progressive framework. Some reformers preached education as the means to slow the spread of sexual vice and disease, whereas

others called for repressive measures, such as the eradication of prostitution. There was, however, a continued hesitancy to discuss sexual matters in the early twentieth century, as reflected in the terminology used in newspapers and other popular media. For example, the term “social evil” was consistently used in reference to prostitution, which is generally not mentioned by name. Similarly, **syphilis** and **gonorrhea** were referred to as “social diseases.” And the effort to combat these problems was referred to as the “social hygiene” movement.

Prince Morrow (1846–1913), a New York **physician**, is generally regarded as the “Father of Social Hygiene.” Morrow was born in Kentucky and received his medical training in Europe. In 1901 Morrow chaired the Committee of Seven of the New York County Medical Society on venereal disease. It was apparently his attendance in 1902 as a U. S. delegate at the International Conference on Prophylaxis of Syphilis and Venereal Disease in Brussels, however, that stimulated him to become a crusader against venereal disease. Upon returning from this meeting, he immediately began to speak and write on the subject.

In 1904 Morrow published a book on *Social Disease and Marriage*, in which he emphasized the toll that syphilis and gonorrhea took on marriage and family life. He told of sterility among women, congenital blindness in infants, insanity, and other problems that these infections could introduce into the family. He spoke of the “innocent victims,” the wives and unborn children, who might contract the disease because of the indiscretion of the husband and father. And he traced these infections ultimately back to prostitution. Morrow agreed, however, with a group of nineteenth-century reformers who had placed the blame on the male client rather than the female prostitute, who had usually been viewed as the main culprit.

Morrow also opposed the “conspiracy of silence” about venereal disease, believing that ignorance and prudishness were responsible for the high incidence of syphilis and gonorrhea. He complained that social sentiment held that it was a greater impropriety to mention venereal disease publicly than to contract it privately. The New York physician also argued that the public should be made fully aware of the consequences of contracting a venereal infection.

Convinced that there was a need for an organization to deal with the problems of prostitution and venereal disease, Morrow formed the American Society for Sanitary and Moral Prophylaxis in 1905. The professed aim of the Society was to prevent the spread of diseases that had their origin in the “social evil.” Twenty-five physicians attended the organizational meeting at the New York Academy of Medicine. Believing that venereal disease was not strictly a medical issue, Morrow soon reached out to clergy, educators, journalists, and others to expand his organization, which grew to a membership of nearly 700 by 1910. In that same year, similar groups that had been founded in a number of cities, such as Philadelphia and Detroit, came together with Morrow’s organization and under his leadership to establish the American Federation for Sex Hygiene.

At about this time, most large American cities had also begun to organize vice commissions to combat prostitution. These commissions emphasized that prostitution was a particular problem in cities. Young men looking for work migrated to urban areas, where they were away from the watchful eyes of family and neighbors and were often lonely. The cost of living was high, and wages were low, and so young bachelors frequently postponed marriage. The cities also offered more opportunities for social contacts between the **sexes**, at dance halls, movie theaters, and other amusement venues. As more women entered the

workplace, the vice commissions noted, social contacts between the sexes also increased. Some observers pointed out that women who had to earn their living sometimes turned to prostitution because it offered more lucrative earnings than many low-wage jobs. And single young women who lived apart from their families were subject to the same loneliness and temptations as young men in that position.

Although most social reformers agreed on a strategy of combating prostitution through education or through repression, there were still advocates of the view that prostitution would never be eliminated and that it was therefore best for the state to regulate it. Some physicians, in particular, continued to argue that licensing and inspecting prostitutes were the only sure means of controlling venereal disease. In 1910 the debate reached a climax when the State Legislature of New York passed the act popularly known as the Page Law. The act established a night court for women, required the fingerprinting of convicted prostitutes, and provided for the medical inspection of prostitutes. If a woman was found to be infected with a venereal disease, she could be detained for treatment. Opponents were outraged, as they believed the law essentially established state-regulated prostitution. The New York Court of Appeals ended the debate over the law in 1911 when it found the section dealing with medical inspection and detention of prostitutes to be unconstitutional because it violated due process by making the diagnosis of the physician binding on the court.

The battle over the Page Law seems to have served to unite the various social hygiene and anti-vice groups. Social hygienists tended to believe that sex education and public enlightenment were the best strategies for dealing with the problems of prostitution and venereal disease. They were especially concerned with the health aspects of the problem. The anti-vice organizations, on the other hand, focused more on so-called white slavery (forcing women into prostitution) and the repression of prostitution. Although Morrow recognized the advantages of combining forces, it was not until after his death in 1913 that these forces came together. Before his death, however, Morrow had persuaded a leading philanthropist to raise most of the funds needed to form a federation.

Several months after Morrow's death, leaders of his American Federation for Sex Hygiene and of the American Vigilance Association, an organization formed in 1912 that focused on eliminating the traffic in women, met in Buffalo to discuss a merger. The representatives voted to consolidate as the American Social Hygiene Association. John D. Rockefeller Jr. (1874–1960), who attended the Buffalo meeting, provided the greatest financial assistance to the new organization in its early years. In the previous year, Rockefeller himself had created a Bureau of Social Hygiene for the scientific study of prostitution and venereal disease. Charles W. Eliot (1834–1926), President Emeritus of Harvard University, agreed to serve as the first president of the American Social Hygiene Association. Operation began on January 21, 1914, with the responsibility for management of the Association initially shared by James Bronson Reynolds (1861–1924), an attorney experienced in vice investigations, and physician William Freeman Snow (d. 1950), a professor at Stanford University and a California public health official. The Association's office was at first located in New York City.

Snow, who soon became the Association's first executive director, discussed the origin and meaning of the phrase "social hygiene" in a 1916 report. He related that the term apparently originated in 1907 with the Chicago Society for Social Hygiene, a group that at the time was primarily concerned with sex education. He went on to define the term as follows: "Its present meaning is largely due to the necessity for some descriptive activities

directed toward sex education, the reduction of venereal disease, and the repression of prostitution.” Thus, the new Association’s name and its goals incorporated the concerns of the different groups of reformers that came together to found it. See also *Disease, Social Construction of; Non-Governmental Organizations (NGOs) and Epidemic Disease; Personal Hygiene and Epidemic Disease; Personal Liberties and Epidemic Disease; Public Health Agencies, U.S. Federal; Religion and Epidemic Disease; Sanitation Movement of the Nineteenth Century; Scapegoats and Epidemic Disease; Sexuality, Gender, and Epidemic Disease.*

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JOHN PARASCANDOLA

VIRCHOW, RUDOLF (1821–1902). Prussian physician Rudolf Virchow, the father of cellular pathology and a critical researcher on social determinants of disease, was born in 1821 in Pomerania. A leading figure in the Revolution of 1848, he made singular contributions to clinical medicine, medical theory, and theories of the social context of disease.

After receiving his medical degree in 1843, Virchow served as an intern at Berlin’s Charité Hospital where he worked under pathologist Robert Froriep (1804–1861). There he became the first to describe leukemia (1845) and, in 1846, to detail the process by which blood clots cause thrombosis and embolism. Also in 1846, Virchow literally redefined health and disease. Most believed sickness was a condition foreign to normal tissues, a type of parasite on the healthy body. Virchow argued that disease resulted when healthy tissues were transformed by disease, their functions impaired as a result. Health was the absence of disease, disease the transformation of healthy tissue.

With others of his era—such as **Edwin Chadwick** in Great Britain—Virchow was a leader in describing the social context in which disease took hold. In 1848 the Prussian government sent Virchow to investigate a violent **typhus** epidemic in Upper Silesia, an area undergoing a famine. His report publicly blamed the government for the social realities he argued created an environment in which the **epidemic** could flourish. “It was a failure by the government to allow autonomous self-rule, to provide proper roads, agricultural improvements, and support of industry that had led to present conditions,” Virchow argued. The root cause of the typhus epidemic, in other words, lay in the conditions of systemic poverty, social degradation, and a lack of adequate sanitation. What made Virchow’s argument unique, and uniquely powerful, was its combination of the clinical, including autopsy, and the social into a single argument.

When a series of popular uprisings for social change swept across much of Europe in 1848, Virchow proved to be a firebrand as a public speaker arguing for political change that many believed would result in better social conditions. Briefly disciplined by the government, Virchow was later named to a chair in pathology at the University of Würzburg where he wrote the landmark text *Cellular Pathology* (1859). That work focused disease studies on the chemical and physical events occurring at the cellular level. Virchow's interests in physical anthropology and archeology led him to form the German Society for Anthropology, Ethnology, and Prehistory in 1869. He remained a publicist for public medical matters, founding and/or editing *Reform of Medicine (Mediscinische Reform)*, *Archive for Pathological Anatomy and for Clinical Medicine*, *Journal of Ethnology*, and *Virchows Archiv*. Virchow was a member of the German Reichstag from 1890 to 1893 and functioned as a liberal critic of Chancellor Otto von Bismarck (1815–1898), who challenged him to a duel. Nonetheless, Virchow's renown as a researcher of infectious diseases and pathology garnered him the presidency of the First International Congress on Leprosy, held in Berlin in 1897.

Twentieth-century social epidemiologists best remember Virchow as the founder of cellular pathology and for his argument that the state is responsible for conditions that promote epidemic diseases. Ever since, proponents of social medicine and social reformers have invoked his name in arguing that social factors such as **poverty**, poor sanitation, and inadequate medical infrastructure contribute to epidemic and endemic disease. See also Contagion Theory of Disease, Premodern; Demographic Data Collection and Analysis, History of; Environment, Ecology, and Epidemic Disease; Epidemiology, History of; Sanitation Movement of the Nineteenth Century.

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TOM KOCH

VIRUS. Prior to the 1930s, "virus" was general term for any microbial agent of infectious disease. Since then, however, the term has been restricted to such agents that pass through filters that retain **bacteria** and other larger microbes, appropriately called "filterable viruses." The simple term "virus" is now used.

Viruses are obligate intracellular parasites that can exist as potentially active but inert entities outside of cells. Viruses can infect many animal, plant, and protist cells with effects ranging from unapparent infection to lethality. All virus infections have an entry phase; an intracellular phase of multiplication, integration, or latency formation; a virus release phase; and usually some type of host response. These host responses usually appear as signs and symptoms of the infection. Well-known virus diseases include **measles**, chicken pox, rabies, **hepatitis**, the common cold, **influenza**, **yellow fever**, and **AIDS**.

Initial Entry and Local Virus Multiplication. All viruses have some structural features in common: a core of nucleic acid (either RNA or DNA) that acts as the viral genome and encodes the viral functions, and a coat of protein that may or may not be surrounded by a lipid membrane. At the cellular level, a virus first must enter the cell, often by adsorption or attachment to a specific receptor on the surface of the target cell. A virus receptor may be a molecule or group of molecules that the cell uses for other purposes; for example, one of the lymphocyte cell recognition molecules is used by the human immunodeficiency virus (HIV) as its attachment and entry site. In some cases, only the viral nucleic acid enters the cell, but in other cases, the entire virus is taken into the cell, and the viral genome is exposed after a process of “uncoating.” If virus proteins enter along with the genome, the proteins often regulate expression and replication of the viral genes. Some viral proteins may function to suppress host gene expression to help the virus subvert cellular processes to its own advantage. Some genes of the virus are expressed immediately after infection, and their translation into proteins starts the intracellular virus replication phase. Once a large number of viral genomes have been produced, and a sufficiently large pool of virus structural proteins has accumulated, virus assembly takes place.

The Virus Release and Viremic Phase. The cell then ruptures or is lysed from within by specific enzymes. Hundreds to thousands of new infectious virus particles burst forth from each infected cell, each one available to spread the infection. Some viruses, however, do not undergo this “lytic cycle” but have evolved a symbiotic relationship with the host cell. They integrate their genomes into the host cell chromosome in a “repressed” or latent state by a complex process that differs for RNA- and DNA-containing viruses.

Common routes of infection of **animals** are through the respiratory tract, the gastrointestinal tract, directly into the blood stream, by sexual contact, or by the bite of an infected insect vector. After the local infection of susceptible cells, the initial viremia (virus in the blood) transports the progeny virus to target cells or tissues in the body where the virus may replicate further, adding more virus to the blood (secondary viremia). Often, the immunological responses of the individual are provoked only by the secondary viremia because the primary viremia may be inadequate in duration or intensity to do so.

Immunological Responses in the Host. Most virus infections are asymptomatic or, at most, cause such common and inconsequential symptoms that the infection passes unnoticed. Analysis of the antibodies in normal human serum shows that we have many antiviral antibodies that indicate a history of prior unrecognized encounters with many viruses.

The viremic phase of infection allows the cells of the immune system to respond to the presence of virus. If the virus is sufficiently immunogenic, a primary antibody response occurs in about a week. This response results in the production of long-lasting memory–B cells that can be activated later by subsequent exposure to the same virus to provide a rapid and intense secondary immune response. This immunological memory is the primary reason for lifelong immunity once a person has survived a particular viral infection.

The specific antibodies produced by the primary immune response can combine with the virus in the blood and result in circulating immune complexes that facilitate the destruction and clearance of the virus from the body, but also result in activation of some processes such as the production of fever.

Some viruses that enter into a latent or symbiotic state within the host cell can provoke abnormal cell behavior. Many such viruses carry extra genes that regulate cell division and can result in the malignant transformation of the cell to produce a cancer.

These cancer-causing (oncogenic) viruses are a special group of viruses that are of great current interest because of both their special biology and their practical importance.

Effects on the Host. The usual outcome of a viral infection is recovery of the organism with long-lasting immunity. After the initial local virus multiplication, viremic phase, and immunological responses, the virus is eliminated from the body. The immune memory cells provide for long-term protection against another infection. If this sort of immunity is produced by deliberate infection, usually with a weakened strain of virus, the process is called **vaccination** (more accurately, immunization). If, however, the immune system is compromised, if the virus replication overwhelms the immune system, or if the virus enters cells or tissues that are hidden from the immune system, the virus may destroy critical tissues or organs and result in illness or death.

The classic mode of prevention of viral diseases is by artificial immunization with whole attenuated viruses or parts of virus particles. This approach was first used in the case of **smallpox** when it was observed that infection with viral material from a mild case often resulted in a mild case of smallpox (so-called inoculation or variolation) that then conveyed lifelong immunity. Later, a related but nonlethal virus, the cowpox virus was used to induce immunity to smallpox.

Some viruses, after the primary infection, enter into a latent form and remain asymptomatic until later reactivation. The herpes group of viruses is especially prone to such latent infections. Initial infection, for example, with the chicken pox virus (actually a member of the herpes group) produces viremia and generalized skin rash. The virus then latently infects the dorsal root ganglia of the spinal cord and later, at times of lowered immunity, the virus reactivates producing skin lesions along the distribution of the spinal nerve, resulting in a case of “shingles.” Chicken pox and shingles are different manifestations of the varicella-zoster virus. A few viruses (e.g., HIV) are known to replicate at such a low level and to remain relatively benign initially, yet to escape the immune system and establish a true persistent infection.

Host cell proliferation may result from latent virus infections resulting in local, limited growths such as viral warts and the small skin lesions caused by the virus of *molluscum contagiosum*. Other latent infections can lead, in ways not yet fully understood, to malignant diseases such as Burkitt’s lymphoma, nasopharyngeal carcinoma, Kaposi’s sarcoma, and **cervical cancer**.

Virulence and Transmission. Viruses are called virulent if they have a high propensity to cause disease or other evidence of infection. This principle has been widely exploited to produce vaccine strains of viruses. Virulence may be related to the interaction of essential viral functions with related host cellular functions. In certain cases, the virulence genes of the virus can be deleted or modified to make avirulent variants. A virus strain may be virulent for one host species and avirulent for another. Repeated selection for virulence in one host species may select for mutations that render the virus less virulent (attenuated) in another. The transmissibility of the virus is an important factor in the spread of infections and is often a genetic property of a specific viral strain. Highly transmissible strains of the influenza virus and of the common cold virus are much more likely to cause epidemic outbreaks than virus strains of lower transmissibility.

Because viruses are intracellular parasites that depend on many cellular processes for their growth and replication, there are few unique, virus-specific pathways that can be targeted with antiviral drugs without interfering with the uninfected host cells. The very simplicity of viruses and their nearly total dependence on cellular functions have been

major reasons why there are few effective antiviral drugs and why viral chemotherapy remains a stubborn challenge. *See also* Contagion and Transmission; Hemorrhagic Fevers; Human Immunity and Resistance to Disease; Human Papilloma Virus and Cervical Cancer; Immunology; Poliomyelitis.

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WILLIAM C. SUMMERS

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W

WAR, THE MILITARY, AND EPIDEMIC DISEASE. The relationship between military activity and **epidemic** disease is an ancient and complicated one. Disease is met with at every stage of an army's life: its formation from raw recruits, its training, its off-duty pleasures, its encampments, its travel through its own territory and then the enemy's, its engagements with the enemy, its treatment of the wounded, its advance after victory or retreat after defeat, its ravaging of the enemy's countryside and towns between battles, its sieges, its transport and housing of prisoners, and its return home and demobilization.

Wars have involved thousands, tens, and even hundreds of thousands of soldiers at a time. Recruits from distinct disease ecologies intermingle and share their diseases and those of their new home until they are "seasoned." On campaign, soldiers bring their own diseases and encounter new ones. Fatigue, malnutrition, wounds, and stress lower immune responses, whereas camp life in crowded and unsanitary conditions encourages the spread of contagious diseases and creates ideal ecological niches for both native and imported parasites. Civilians also play various roles in these processes as sources of disease, victims of diseased soldiers and their parasites, healers and caregivers, medical researchers and innovators, and refugees. War disrupts societies in manifold ways, from forced quartering to destruction of homes and hospitals, from sparking local and regional epidemics to the voluntary and forcible displacement of large populations whose squalid new living conditions invite wholesale death by disease. This entry presents a few contemporary and historical examples of the many ways in which war and disease intersect.

Mobilization and Training of U.S. Armed Forces. Though an army may be gathered only from among local populations, as when city-states fought one another in ancient Greece or medieval Italy, armies have historically brought men together from near and far. Pathogens of many types arrived at camp with them, and many of these could spread quickly, especially among those who had never encountered them before.

Prior to the U.S.-Mexican War (1846–1848) and Europe’s Crimean War (1853–1856) few armies kept records that fully detail personnel deaths. During America’s Civil War (1861–1865), many Confederate records were lost when Richmond was burned, but Federal (U.S.) records remain intact. They show that recruiting in 1861 and 1862 brought urban and rural men, often from far-flung regions, together in very close quarters for training, and that this led to an immediate spike among them of the typically childhood diseases of **smallpox**, scarlet fever, erysipelas, and **measles**. The last was especially contagious, striking a third to a half of recruits in epidemics lasting as long as two months. When African Americans were first inducted in 1863, the effects of congregating were even greater, though the initial high incidence of diseases slid downward very rapidly.

In April and May 1898, 150,000 American men were recruited to serve in the Spanish-American War. Many volunteers battled measles, mumps, and even **meningitis**, but **typhoid fever** struck most widely and severely. Because survivors gained immunity, typhoid struck hardest at induction and training camps. Endemic in much of the United States, *typhi* bacilli were deposited by carriers in their feces. This material was then spread by incidental contact or by houseflies that were attracted to feces, horse manure, and other organic material. Flies walked and fed on contaminated waste, then landed or defecated on people, food, and other objects commonly handled. At a large camp, a million or more flies could hatch daily. Eventually, 24,000 cases resulted in 2,000 deaths, peaking in late August and early September. Men were first brought together in state basic training camps, then concentrated in four so-called national camps that brought men from across America together. The mixing of these men with those from other camps, and the continued routing of the volunteers among camps, served to spread the disease even more widely, accounting for fully half of the typhoid cases.

This experience, the research into typhoid by **Walter Reed** and the Typhoid Board, and the conclusions made by the Dodge Commission, led to routine typhoid vaccination of U.S. recruits from 1911 and to much greater attention being paid to camp sanitation and **personal hygiene**. Between America’s entry into World War I (1914–1918) in April 1917 and December 1918, 3,700,000 recruits underwent training in camps that ranged in quality from long-established bases to tent cities. Although only 244 contracted typhoid fever, over 92,000 suffered from mumps, almost 61,000 from measles, 16,236 from **tuberculosis**, and 15,488 from rubella, scarlet fever, or meningitis. As during the Civil War, most cases occurred early in the mobilization process. The huge exception was the “**Spanish**” **influenza**, which struck U.S. camps in September and October 1918 with 327,480 cases.

A range of immunizations, several of which had been developed by the military, was available to the World War II inductees. Only after the war, however, was a full range of **vaccinations** developed. The vaccines currently given to U.S. trainees include measles, mumps, rubella; **hepatitis A**; hepatitis B; influenza vaccine; polio vaccine; **diphtheria**, acellular pertussis, tetanus; meningococcal conjugate vaccine; and, if warranted, varicella and **yellow fever** vaccine. Still others are provided if deployment is into disease-ridden environments.

Camp Conditions and Life. A study published in 2005 theorized that the great **influenza pandemic of 1918–1919**—which killed an estimated 40,000,000 people—had its origin in a huge rear area British military camp in northern France (Etaples) in the winter of 1917–1918. The authors note that this installation contained dangerous toxic gas supplies that were mutagenic, as well as large numbers of swine, fowl, and horses—all

associated with **animal** forms of influenza. Typically 100,000 men were housed here, but turnover was great as they transited to and from the frontlines and back and forth from Britain. Leakage of gas could have altered swine, avian, or equine flu **viruses**, allowing them to lodge with the hoards of transient soldiers and spread to friend and foe alike. If true, then this is certainly the most egregious example of unsanitary camp conditions affecting the history of human disease.

Troops barracked at home also suffered from the influenza. Fort Riley, Kansas, has the distinction of being the known point of origin of the pandemic in the United States (March 1918), and the flu clearly spread through the network of military bases and camps and to the neighboring communities and beyond. These installations suffered one death per hour at the pandemic's height, or about 200 per week, whereas British home camps lost 2,000 per week. Despite good sanitation and nutritious food, living conditions were still crowded and allowed the virus free reign. Though an extreme case, this was by no means a unique experience: in 1950, a modern Israeli military facility near Tel Aviv suffered a bout of **West Nile Fever**, for which 636 of the resident 1,000 soldiers had to undergo treatment.

Before the advent of germ theory and the emphasis on sanitation, military camps, bases, and forts tolerated poor quality food and **water**, lax standards for waste removal, and substandard personal hygiene—all of which fostered the growth and spread of pathogens and disease. For military personnel, flight was not an option, unless insightful commanders took the lead. When **bubonic plague** struck the enormous Russian Black Sea fortress of Ochakov in the spring of 1739, the Russian commander eventually decided to relocate the garrison to Ukraine, but not before some 30,000 had fallen victim. **Cholera**, too, could sweep through military bases, as it did in July 1830 at the Russian Caspian Sea port city of Astrakhan. Because of the regular relationships, commercial and otherwise, between soldiers and civilians, the disease spread quickly through the city of 37,320, causing 3,633 cases with a mortality rate of 91 percent. At the same time, Moscow lost 3,102 to cholera, its garrison taking a quarter of the fatalities. But progressive commanders who sought to stanch the epidemic sometimes paid a price, as when Russian Novgorod's barracks erupted in riot against harsh sanitation measures being implemented at the base.

With the development of European **colonialism** in the eighteenth and nineteenth centuries, European troops and sailors often found themselves in tropical ports and bases where local diseases could—and did—run rampant. The British military first encountered endemic cholera in the early 1780s in Ganjam, India, when 1,143 soldiers in a garrison of 5,000 fell ill. Another thousand cases soon weakened the Madras garrison, and the disease spread to Britain's Indian allies. The origins of the first cholera pandemic are also found among the British in northwest India, in 1817. An especially virulent epidemic in 1861 in Delhi and Lahore, in which 457 cases resulted in 261 deaths over 10 days, threatened to topple the regime and prompted the imperial government immediately to establish the Indian Sanitary Commission.

Africa earned its nickname as the white man's grave. Military occupation of ports and forts always accompanied colonization, and troops sent to serve needed several weeks—sometimes more—to acclimate their bodies to the weather and disease **environment**. Yet even the best “seasoning” might not prepare a unit, as in 1778 at the Senegalese Fort St. Louis. Apparently Senegal had not known yellow fever, but it arrived with a slave ship from Sierra Leone, where, as elsewhere, it had long been endemic. The British colonists and soldiers as well as local natives dropped from the disease, suffering a mortality rate of

60 percent in what some consider Africa's first epidemic of yellow fever. It continued to affect colonial armies in much of West Africa, and Sierra Leone itself suffered 15 epidemics between 1815 and 1885. In similar ways, European and U.S. colonial armies in the Caribbean, Southeast Asia, and the Philippines suffered far more from disease than hostile action.

The First Gulf War (1990–1991): Protecting Coalition Troops against Disease. In the summer and fall of 1990, over half a million Coalition troops from 40 countries shipped out to Saudi Arabia and other friendly nearby states to force Iraqi dictator Saddam Hussein (1937–2006) to abandon his military occupation of Kuwait. Coalition war planners expected to encounter the diseases and perhaps case rates experienced in the region during World War II. The predominant participants—U.S., British, and Canadian soldiers and marines—were carefully vaccinated against childhood diseases such as diphtheria and **polio**, as well as influenza, yellow fever, hepatitis A, and tetanus, and many were also vaccinated against anthrax and plague. Military planners employed a sophisticated regimen of prophylaxis to insure that serious infectious diseases remained in check. Desert camps and staging areas were kept sanitary, ample potable water was provided, and food was continually inspected for tainting or parasites. **Insecticides** and repellents were applied lavishly, inspection and surveillance for disease was constant and careful, and an infectious disease diagnostic laboratory was included along with state-of-the-art field medical facilities. Along with standard theater diseases, planners feared Iraqi biological weapons use. During the build up from July 1990 to January 1991, 60 percent of U.S. service personnel experienced predictable and nonacute gastrointestinal ailments such as diarrhea and mild colds and other respiratory ailments that accompany close living quarters. They reported only 32 cases of leishmaniasis (caused by a **protozoan** carried by sandflies), 7 cases of **malaria**, and 1 of West Nile fever. Only one U.S. serviceman died of an infectious disease, a case of meningococcal meningitis. Very limited contact with local residents and general lack of privacy kept rates of venereal disease far below the norm for troops in theater. Many veterans of the nine-month campaign have long complained of a variety of chronic ailments generically labeled Gulf War Syndrome, though no single cause has been widely accepted.

Disease and Military Opportunism. An outbreak of epidemic disease may so debilitate a military force that its misfortune tempts its enemies. The **Plague of Justinian** that began in the sixth century CE so weakened both the Persian and Byzantine empires and their armies that the upstart Muslim forces from Arabia had little trouble conquering the first and devouring much of the second in the middle of the seventh century. When the English army positioned in southern Scotland near Selkirk contracted the plague in 1349, the Scots thought that their hour had arrived. In the course of their advance, the clansmen shared the English fate, and before long 5,000 Scots had succumbed to the Black Death. In the Western Hemisphere the diseases that accompanied the Europeans and Africans from the late fifteenth century mowed down the indigenous peoples and opened doors for conquest. The Aztec capital of Tenochtitlán, praised for its size and wealth by the Spaniards who first encountered it, lost half of its population to smallpox and lay prostrate before the victorious Spanish conquistador Hernán Cortés (1485–1547) in 1521. Within only a few years the disease had penetrated to Peru and killed the Inca emperor Huayna Capac (1464–1527) and his wife, an event that precipitated a civil war. The Incan losses to both violence and imported disease opened the door to Spain's Francisco Pizarro (1471–1541), who smashed the Incan empire in 1532. In 1706 an outbreak of yellow fever in English Charleston, South Carolina, tempted the French and Spanish naval squadron in

St. Augustine, Florida, to sail north to make an easy conquest. The colonial militia, which had stayed outside the fevered city, remained healthy and staved off the small fleet, which retired to its base.

Disease on Campaign. Epidemic outbreaks rarely started or ended conflicts, but, as at Selkirk, they often played roles in determining battles and even campaigns. Debilitating diseases did not have to kill combatants to cripple an army; they could simply take so many off active duty as to blunt its effective force. Early in the American Civil War, the Confederate forces in western Virginia were halted (September 13, 1861) during an otherwise successful campaign when a combination of measles, dysentery, typhoid fever, and pneumonia struck the men with a biblical fury. In 1722 Czar Peter the Great of Russia (1672–1725) was forced to halt his campaign of expansion in the Caucasus during the Russo-Persian War because of *ergot*-tainted rye bread. It was said he lost 20,000 men to the disease. In the later sixth century CE, the Christian Ethiopian prince Abraha (r. c. 525–553) controlled a considerable portion of the Arabia Peninsula. The prince's military campaign to convert Arabians to Christianity in 569–571 was halted abruptly when smallpox or measles broke out among his troops as they approached the important trading center of Mecca. So weakened were the Ethiopians that they lost what they had controlled in Arabia, an event celebrated in the Koran's Sura 105. Had Mecca been converted, the life story of Muhammad (579–632), Prophet of Islam, might have been very different. The Black Death brought hostilities between France and England to a standstill in 1349; in 1691 yellow fever felled 3,100 British sailors on 18 British warships bound from Barbados to French Martinique, forcing the fleet to return to England, and it was probably malaria that forced Attila the Hun (406–453) to halt his horde's advance through Italy to Rome in 452. Tropical campaigns could be especially deadly before troops could undergo vaccination.

But armies were not merely victims of disease: they were often responsible for spreading it, among enemy as well as friendly populations, and sometimes at long distances. In 1643 English Royalists were engaged in civil war with Parliament's army, and both were maneuvering across the English landscape. The problem was that both armies were suffering from typhus, and both spread it liberally among the people along their routes. During the cholera pandemic of 1831, the Czar sent Russian troops into Russian Poland from Volhynia to confront revolutionary students and other liberals. The freedom-loving Poles were met not only with Russian bayonets but also with the cholera that accompanied the regiment. The Boer War in South Africa broke out in the early stages of the Third Plague Pandemic. Between 1899 and 1902, British cargo vessels bringing military supplies from ports in South America brought plague to South African ports, and from there, military transport trains carried it inland, where it readily spread among the civilian population. In 1936 smallpox broke out among unvaccinated Ethiopians who were fighting Benito Mussolini's (1883–1945) Italian army in Somalia. Somali nomad tribes came into contact with the Ethiopians, and over a six-week period 1,142 cases developed among civilians, with 471 fatalities. During the early stages of American involvement in the Vietnam War, bubonic plague broke out in several South China Sea provinces. It moved along the coast and then inland. U.S. military activity in the region disrupted the rodent populations—largely bandicoots—among which the *Xenopsylla cheopis* flea made its home. Average annual reported cases of plague among the South Vietnamese were 15 from 1956–1960 and 4,000 from 1965–1970. After the U.S. military withdrawal, annual cases dropped to around 2,500. During the War, 25,000 cases of plague were reported,

though estimates run as high as 250,000 throughout Vietnam. Unreported cases probably meant untreated cases, which would have meant a very high mortality rate.

Siege. Siege warfare entailed one army surrounding a second army or garrison within a city or other well-fortified defensive position. Given the stagnant nature of a siege, living conditions in both the attackers' camp and the defensive position would deteriorate as weeks and often months would pass. Food and clean water were vital for both parties, and though the besieged were often in the worse position, the attackers were often little better off. Typhus, dysentery, and venereal diseases could run rampant through either or both armies. During the supposedly "bloodless" Glorious Revolution in 1688–1689 King James II's (1633–1701) troops besieged a Protestant garrison in the northern Irish city of Derry. Troops and civilians numbering 37,000 suffered a 105-day siege and 10,000 deaths largely as a result of typhus and dysentery. James's Catholic army suffered also, however, from dysentery and typhus as well as syphilis, and the siege was broken. The famous **Plague of Athens** occurred as the Spartan army hemmed the city in. As was often the case with sieges, many people from the countryside had flooded into the city, putting a greater strain on food supplies and other necessities and creating the kind of crowded conditions in which epidemics can thrive.

Armed Forces, War, and Venereal Diseases. Traditionally all-male organizations, armies have contracted and spread venereal diseases such as syphilis and gonorrhea in numerous ways. During training or while barracked at home, soldiers may have access to prostitutes or other willing sex partners, including one another. "Camp followers," who included prostitutes (Union Civil War General Joe Hooker's [1814–1879] "hookers"), often trailed premodern armies on campaign, and while on duty in foreign noncombat zones or on leave from an active zone, military personnel may take advantage of local sex professionals. In cities such as Saigon during the Vietnam War, Paris during World War II, or Tokyo during the Korean War, many sex workers were displaced young women, often from rural areas and with little or no access to health care or physical protection. Although modern armies have long provided "hygiene" education to enlighten the unsophisticated recruit, drugs, alcohol, peer pressure, loneliness, and the stress of battle may override even the most graphic warnings. Finally, venereal diseases may be contracted or spread during rapes, which may occur in the wake of battle or in the depths of boredom accompanying a campaign in or occupation of enemy territory. Rape is far from unknown as a means of degrading a defeated enemy population or venting frustration by brutalizing the enemy's women sexually. This was especially feared by German civilians as Soviet troops approached Adolf Hitler's (1889–1945) Reich in early 1945. Before and during World War II the Japanese armed forces compelled thousands of Korean women into sexual service as military prostitutes, effectively institutionalizing their continuous rape.

Napoleon Bonaparte (1769–1821) mandated licensing and medical examination of French prostitutes, and those in British naval ports were subjected to the Contagious Diseases Acts of the 1860s, which also required regular screening for venereal diseases. In Australia during World War II, press and civic groups such as the Women's Christian Temperance Movement and the newly formed Australian Society for the Eradication of Venereal Diseases unduly whipped up popular opinion against women who entered the wartime workforce and the contrived epidemic of sexually transmitted diseases (STDs) that accompanied it. Public voices flatly blamed and stigmatized liberated women—their healthy inhibitions dulled by "strong drink"—for catering to servicemen's lusts (including those of 1 million transiting American GIs). City governments hired

additional policewomen to handle the supposed influx of “promiscuous amateurs” who needed to be screened for disease for the public’s and military’s protection. Though during World War I, 1 in 10 Australian soldiers contracted an STD, in the early 1940s, only 1 percent did.

In the United States, mobilization in 1942 prompted a coordinated state, local, and federal Public Health Service effort to deal with the potential problem. Like the Australian programs, it targeted women. Within two years, 47 “rapid treatment centers” had been established to isolate women (and some men) who had venereal diseases and were thus deemed public health threats. Military authorities also created prostitute-free zones around military bases and training facilities, an activity sanctioned by the May Act of 1941. The War Department pressured mayors and urban police chiefs to close down brothels, but local interests often outweighed federal influence and threats. The military also tried to reduce the demand for commercial sex: films and posters stressed the horrors of STDs, public relations campaigns enlisted celebrities to extol the virtues of sexual abstinence, and the United Service Organization (USO) worked to entertain and distract troops.

Returning Troops and Refugees. There are many cases in the historical record of armies or military units returning home and bringing with them diseases of all kinds. As troops are demobilized, they spread their diseases deep into the population of their home states. The **Antonine Plague** of the mid-second century CE that struck the Italian peninsula and western Mediterranean was either smallpox or measles carried by Roman troops returning from duty in Mesopotamia. When the novel disease hit the “virgin soil” in the west, it did tremendous damage. In 570 Byzantine troops on campaign near Mecca (Saudi Arabia) contracted a similar disease and, upon return, spread it about the eastern Mediterranean. As the remnants of Napoleon’s Grande Armée completed their retreat from Russia in 1812 and 1813, they carried typhus, dysentery, malaria, and influenza with them. They infected and killed thousands in the German lands they passed through and thousands more in France. At the end of the Crimean War, typhus had been a problem for the British and French armies in the Black Sea region. In 1856 returning French troops were quarantined on an island off the southern French coast, averting any outbreak at home. British troops, on the other hand, returned directly and sparked an outbreak of typhus in the British Isles.

Refugees fleeing a victorious enemy can also spread disease. One of the most significant cases was that of French smallpox carriers fleeing the advancing Prussian army in 1870. Conditions in and around Paris were frantic as new troops were being mustered, existing units repositioned, and thousands packing and fleeing. Smallpox had been rampant in the area since 1868, and it began to spread in every direction. Between 60,000 and 90,000 French are thought to have died in 1870–1871. French prisoners of war (723,500) brought the disease to Germany, and by spreading the prisoners around the new country in 78 prisoner facilities, the military authorities spread the disease. In 1871–1872 an estimated 162,000 were reported dead of the disease. Fleeing French carried smallpox into England (42,000 deaths), Belgium (21,315 deaths) Switzerland, and northwestern Italy, prompting outbreaks, and even New York City suffered 3,084 cases and 805 deaths connected with these refugees. The French army of 1 million had 125,000 cases of smallpox, of whom 23,500 died. The German army, on the other hand, had vaccinated its troops every seven years since 1834, and it only recorded 8,500 cases among its 1.5 million soldiers, of whom 460 died. All told, an estimated 500,000 Europeans—mostly children—succumbed

to smallpox. This prompted England and Germany to make vaccination compulsory in 1871 and 1874, respectively.

Contemporary conflicts also produce refugee emergencies, especially in war-torn parts of Africa. In 1994 civil war in Rwanda displaced 1.2 million refugees who established camps outside the Eastern Zaire city of Goma. Living in filth with little or no fresh water, these people suffered greatly from cholera as well as malnutrition. In 1999 Mozambique's civil war sent thousands into northern South Africa, where epidemic malaria quickly broke out. This spread to tourists in the Kruger National Park, and eventually 50,000 cases were reported.

Epidemics in Postwar Conditions. The social, economic, and physical disruptions caused by war, especially among the defeated, have often left openings for serious outbreaks of deadly diseases. Returning soldiers and prisoners of war, displaced and homeless people, refugees, and occupying soldiers all bring with them their various pathogens. Infrastructural elements such as hospitals, suppliers of medicines, and freshwater delivery systems are often simply gone, as are medical specialists and even primary care providers. The attitude of the victor is often key: if vengeful, it may carry off what it can and damage the ability of the defeated society to care for itself for decades; if magnanimous, it may provide extensive resources to repair, rebuild, and restructure.

Between the 1770s and 1918, Poland had been divided among Germany, Austria-Hungary, and Russia. With the defeat of Germany and Austria and the collapse of Russia in the First World War (1914–1918), international treaties reconstituted Poland as a republic. The country's three regions had been tramped across by armies advancing and retreating, reinforcements traveling to the fronts, prisoners heading to camps, wounded returning for care, demobilized divisions redeploying westward, repatriating Poles, and Russian and Ukrainian refugees first from the War and then from the violent birth pangs of the Soviet state. The new Polish government established a Ministry of Health whose initial duty was to stem the tide of infectious diseases that had been ground into the Polish people. By the summer of 1919, it had established 44 mobile epidemic disease units with 2,400 beds, 103 local hospitals with a total of 4,400 beds, and 35 disinfection units. Twenty-three epidemic medical specialists helped coordinate the efforts of local physicians and other health-care providers. Limited funds, infrastructure, and supplies undermined efforts to tackle the wide array of diseases and huge number of cases encountered.

War and Reemergent Epidemic Disease. From the early 1990s, wars, civil wars, and endemic regional violence in portions of central Africa have created the social disruption, destruction of medical and public health infrastructure, and forced migration on which epidemic diseases thrive. In war-swept villages and overpopulated refugee camps, poor sanitation, malnutrition, tainted water, stress, and unavailability of needed drugs and other medical supplies affect all involved, but especially the most vulnerable, not least the children. Between 1990 and 1993, crude death rates (CDR) of refugees in countries like Kenya, Ethiopia, and Zimbabwe were 5 to 12 times higher than back home before the violence. Those who were displaced and remained in their home countries fared far worse, with CDRs 12 to 20 times higher those before the disruption. Most common were deaths of infants and children from preventable diseases. A study of Lacor Hospital in war-torn Uganda from 1992 to 2002 demonstrated that almost 80 percent of admissions were of infants, children, and women, and that the most common complaints were typical childhood diseases easily preventable under normal circumstances. Ebola, HIV/AIDS, malaria,

and tuberculosis came next, with violence-related injuries and wounds fluctuating with the local level of fighting.

Sleeping sickness is endemic in most of Africa between the Sahara and the southernmost regions and was brought under control by successful efforts to control the tsetse fly vector and livestock infections. These efforts flagged as political turmoil turned to open conflict in Uganda in the mid-1970s. As a result, sleeping sickness rebounded, leading to a reported 40,000 cases over two decades and a suspected number 10 times as high. Treatment is expensive and complicated, but without it, the disease is virtually always fatal. In Sudan, civil war led to sleeping sickness's reemergence in 1997, and soon its prevalence rates in some areas rose to between 20 and 50 percent. By 2007 it ranked beside AIDS as the top regional killer. In Uganda the epidemic occurred when war disrupted living conditions, increased the likelihood of human exposure to the infected tsetse fly, decreased the likelihood that victims would have access to treatment. The cessation of insect control efforts and the movement of displaced people into swampy, fly-infested areas increased transmission rates, while the closure of clinics and blocking of relief efforts denied access to lifesaving services. The Sudanese civil war effectively halted the medical surveillance of populations, especially of refugees, in which the disease was rampant. But even if needful populations had been identified, poor and dangerous transportation infrastructure, roadblocks, official corruption, and the desire of each faction to murder its enemies would have seriously hampered relief efforts.

Military Research on Infectious Disease, Prophylaxis, and Treatment. During World War II, German units serving along the Metaxis Line in Greece and in the southwestern USSR suffered heavily from malaria. Hitler's Army Medical Academy, as well as pharmaceutical companies such as Bayer and I. G. Farben, searched for new malaria drugs and a vaccine and for new means of insect control. Correct dosing of Plasmochine and Atabrine, the two standard drugs, remained elusive, and ruthless experimentation on prisoners and the mentally disabled took many lives. Armies have always had a huge stake in developing the ability to curb the effects of disease, but only since the development of smallpox inoculation in the eighteenth century could they effectively do so. Military researchers, often under combat conditions, have worked diligently to defeat disease, and the ranks of the disease fighters are rife with military careerists. They include the work of Walter Reed and **William Gorgas** in fighting yellow fever, as well as the efforts of **Alphonse Laveran** and **Ronald Ross** to understand malaria and its transmission. The current protocols for treating malaria were developed and tested by U.S. military researchers in Vietnam.

Biological or Germ Warfare. From at least 1347, when Mongol warriors hurled bubonic plague corpses into the Christian outpost of Kaffa hoping to spread the pestilence, belligerents have sought to use disease as a means of weakening the enemy forces. Advances in germ theory and microbiology in the later nineteenth and early twentieth century unlocked the secrets of dangerous pathogens, allowing scientists to "weaponize" a range of biological agents. The second Gulf War ignited when Iraqi dictator Saddam Hussein (1937–2006) refused to disavow or allow inspection of biological weapons development sites, and these remain a grave concern to diplomats and military planners worldwide.

In the early 1930s, the Empire of Japan began a concerted effort to develop effective weapons using a score of different pathogens. Though outlawed by the Geneva Convention of 1925 (not ratified by Japan), the program was initiated and led by the racist microbiologist Dr. Shiro Ishii (1892–1959). As Japanese militarists gained power and

influence in the government during the 1930s, they saw the value of germ warfare, and Ishii was provided with laboratory facilities first in Tokyo and then in Manchuria. At Pingfan, near Harbin, Ishii's infamous Unit 731 built a research city housing some 400 human laboratory subjects, including political and military prisoners. By the end of World War II, 20,000 Japanese military and personnel had worked for Unit 731's facilities at Pingfan and scattered across the Empire. Inmates were given many diseases, including anthrax, dysentery, diphtheria, hemorrhagic fevers, smallpox, typhoid, and yellow fever. Autopsies and vivisections were performed, vaccines tested, and the remaining corpses incinerated in crematoria. An estimated 20,000 people died under these conditions. Pathogens in powder form were placed in bombs and shells, and in August of 1942, 80 victims in Jiangshan Province, China, died of purposely cholera-tainted fruits, rice cakes, and well water. At the same time, an estimated 200,000 died of weaponized cholera in Shangdon Province, and an equal number succumbed to the same in Yunnan Province. By the end of 1942, 1,700 Japanese soldiers who had entered contaminated zones had died of these diseases. Between medical experiments and "field tests" perhaps as many as half a million people perished at the hands of Ishii and his scientists. *See also* Cholera: First through Third Pandemics, 1816–1861; Malaria and Modern Military History; Measles in the Colonial Americas; Napoleonic Wars; Poverty, Wealth, and Epidemic Disease; Race, Ethnicity, and Epidemic Disease; Smallpox and the American Revolution; Smallpox in Colonial Latin America; Thirty Years' War; Typhus and War; Yellow Fever Commission, U.S.; Yellow Fever in Latin America and the Caribbean, 1830–1940.

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JOSEPH P. BYRNE

WATER AND EPIDEMIC DISEASES. Water plays a vital role in transmitting several deadly epidemic diseases, the most notable being **cholera**, **typhoid**, and **dysentery**. The three main pathogens for these waterborne diseases are *Vibrio*, *Shigella*, and *Salmonella* genera. Epidemics are most apt to spread in urban areas by the contamination of drinking water by human feces that contain the microorganisms of each disease. Waterborne epidemics have played an important part in shaping modern public health policy. The epidemiological link between infected water supply and epidemic disease was first made in mid-nineteenth-century Britain, and projects to reform municipal water supplies have followed since that time. Despite the fact that waterborne epidemics have virtually been eliminated in most Western countries, they continue to threaten widespread disaster among populations whose systems of public sanitation and health remain underdeveloped.

Although waterborne epidemics are a serious threat to human health, a host of other illnesses are water related. Water is a breeding ground for **insects** and other parasites that spread deadly epidemics such as **malaria** and **Dengue**. Other health threats spread by water include intestinal worms, anemia (a nutritional deficiency), schistosomiasis or Bilharzia, leptospirosis (an infection that occurs through direct contact with the urine of infected animals), and **Legionnaires' disease**. Interdisciplinary research on emerging infectious diseases has shown that the variety of water-related microbial diseases is increasing. Since 1970 several new species have been identified, including cryptosporidium, *Escherichia coli* 0157, rotavirus, **hepatitis E** and **A** viruses, and norovirus. Industrial pollution of water with substances such as arsenic and lead also contributes to water-related death tolls, as does the addition of excess fluoride (which can lead to fluorosis). According to the **World Health Organization** (WHO), as of 2004, water-related diseases remained the leading cause of morbidity and mortality worldwide.

Drinking Water, Sanitation, and Waterborne Diseases. The pollution of drinking water is the principal factor in spreading waterborne disease. Since antiquity there has been a concern for the quality of drinking water. Although there was no direct recognition of the role of water acting as a medium in spreading epidemics, the ancients viewed water as central to individual health. The seminal public health document in the classical Greek **Hippocratic Corpus**, *Airs, Waters, Places*, considered water as a vital component of the maintenance of health and contributor to disease. The Hippocratic author stated, “the effect of water on the health must not be forgotten. Just as it varies in taste and when weighed, so does its effect on the body vary as well.” The Hippocratic theory of epidemic disease causation, or miasma theory, had direct implications for public health in the ancient world. Following miasma theory, the ancients believed that epidemics were transmitted through the putrefaction of the **air** by rotting animal or vegetable material. As a result, public health efforts focused on preventing bad smelling air, fumigating unpleasant spaces, and producing general environmental cleanliness. Water only contributed to epidemic disease if it smelled bad and helped corrupt the atmosphere. The importance of water in the ancient world can also be seen in the expansive and intricate water supply for the city of Rome, which began around 313 BCE. The association of epidemics and stagnant water also led the Romans to begin massive drainage projects, which was perhaps the first intervention against vector-borne diseases such as malaria. The ancient Greeks also took great care to obtain clear, fresh water, as they supplemented local city wells with mountain spring water. Although water played a role in distributing disease in the ancient world, historical epidemiologists have not fully examined mortality trends during water-related epidemics.

Throughout the Middle Ages (c. 500 CE–c. 1500 CE) and into the early modern period (c. 1500–1800), the scarcity of water became an important factor in European communal life. In most areas, people spent much of their time gathering water from streams, rivers, and wells. Water continued to be associated with disease, as medieval governments feared that stagnant water and marshes were the source of plagues and fevers. In Valencia, Spain, for example, a law was passed that sentenced any farmer to death who planted rice too close to villages or towns. The deliberate pollution of water in spreading epidemics was also feared. The best example of this is the major epidemic of the **Black Death**, between 1348 and 1352, as social groups such as Jews were accused of **poisoning** wells and were sentenced to death. By the sixteenth and seventeenth centuries, water companies in some European urban centers began to supply water to the houses of private customers. In 1613 wealthy Londoners could be supplied with water from either The London Bridge Water Company or The New River Company. By the end of the seventeenth century, many European cities had followed. The first municipal waterworks supply in the United States was the Fairmount Waterworks Company, which operated in Philadelphia from 1819. However, improved water-related technology still lagged behind the growing problem of up-stream pollution, which was intensified by urbanization and industrialization. In places such as the Ganges River Valley in India, long distance pilgrimages along what has been called the “epidemic highway” clearly fostered the pollution and spread of water-related epidemics. What is clear is that before the twentieth century, the distribution and access to water in households was insufficient and largely uneven. More common sanitary technology consisted of cesspits or chamber pots, where refuse was stored until horse drawn carts would collect the offensive matter. Even costly private water supplies were unpredictable and intermittent. By the early nineteenth century, water filtration

became increasingly seen as important to health. The first municipal filtration system was built in Paisley, Scotland, in the early 1830s.

Although water clearly played a role in the distribution of certain diseases throughout history, low population density and inadequate water supply systems probably kept the threat of widespread waterborne epidemics at bay. Intense and rapid **urbanization** and **industrialization** in Europe during the eighteenth and nineteenth centuries increased population densities and environmental pollution, adversely affected living conditions for many, and expanded the threat of disease. Concurrent improvements in water supply exacerbated the threat: once contaminated, pumped and piped water is a highly efficient medium for the transmission of epidemic disease. Indeed, as population densities rose, waterborne epidemics replaced plague as the primary hazard to urban populations. Cholera, **typhoid fever**, **dysentery**, and various conditions of diarrhea all contributed to the staggering mortality rates witnessed by nineteenth-century populations. The dominance of miasma theory and anticontagionism deflected attention from direct person-to-person spread of disease and further hindered effective responses until the full development of **germ theory**. The medical understanding of the specificity of disease and the role of water in spreading epidemics began to change first with epidemiological and bacteriological studies conducted in western Europe in the second half of the nineteenth century.

Establishing the Link between Water and Epidemics. The London anesthetist and epidemiologist **John Snow** was the first to discover that cholera was a waterborne disease. Conducting epidemiological investigations in London in the 1840s and 1850s at a time when cholera was devastating Europe, Snow argued that cholera was a singular disease with a singular route of transmission. Only a previous case of cholera could give rise to another, and the causative agent had to be introduced into the body by swallowing the dejecta of a previous case. Under Snow's model, water became the central vehicle for transmitting the epidemic over large metropolitan areas. Snow's famous investigation of the relationship of cholera incidence to neighborhood use of the water pump on Broad Street, where cholera had struck particularly hard, led authorities to disable the pump and greatly reduced the disease's local incidence. In a larger metropolitan investigation of two London water companies, Snow mapped the relationship of cholera deaths to water suppliers and demonstrated that the mortality rate for the residents supplied by the Southwark and Vauxhall Company was between eight and nine times greater than for those supplied by the Lambeth Company, which had moved its water source upstream to a less polluted area of the Thames River. Snow's theory of disease transmission was as important as his epidemiological investigations. Although few contemporary physicians and public health reformers believed Snow, his research influenced the direction of public health throughout the second half of the nineteenth century.

Between 1860 and 1880, epidemiological investigations in Britain by John Simon (1816–1904), head of the Medical Department of the Privy Council and Local Government Board, and his inspectors provided the substantial evidence that typhoid, diarrhea, dysentery, and cholera were spread by contaminated water—a conclusion many consider the greatest achievement of nineteenth-century epidemiology. The most important of these epidemiologists were George Buchanan (1831–1895) and John Netten Radcliffe (1826–1884). Radcliffe's studies were particularly significant, especially his investigation of the cholera epidemic in East London in 1866. Here, Radcliffe joined with statistician **William Farr** and chemist Edward Frankland (1825–1899) to demonstrate that the East

London Waterworks Company had been drawing its water from an unfiltered source, thus fostering the spread of the epidemic. By the early twentieth century, the growing discipline of bacteriology had isolated the agents of the major epidemic diseases, thus confirming what half a century of epidemiological work had sought to prove. Once the theory of waterborne transmission was universally accepted, however, private institutions, governments, and scientists constantly argued over the policies needed to reform and safeguard water supplies. What was clear by the twentieth century, however, was that the provision of safe water was the responsibility of government. By the end of the nineteenth century, most Western countries had begun massive projects to construct safe and clean water supply systems.

Throughout the twentieth century, water standards and infrastructure made clear progress in the developed world. Although changes in water supply had clearly been made in most Western countries, the control of standing water as a breeding ground for insects was virtually unresolved. One important example is the experience of the United States in the 1930s and 1940s. The creation of the Tennessee Valley Authority by President Franklin D. Roosevelt (1882–1945) in 1933 marked the beginning of a massive drainage campaign in the southern United States against environments conducive to malaria and **yellow fever**. Although malaria affected around 30 percent of the region's population when the TVA began, by the 1950s, the diseases were virtually eliminated. Worldwide, however, malaria remains the most important parasitic infectious disease. Although the **World Health Organization** (WHO) began a malaria eradication program in 1955, many areas of the world, most notably Sub-Saharan Africa, are still rife with the disease.

Current Problems. The prevention of water-related disease in developed countries through elaborate systems of water filtration, water analysis, and public health infrastructure has led to dramatic improvements in health. In part because of improved water supply, most western countries have experienced increased life expectancy, lowered infant mortality, and the virtual elimination of the major epidemic waterborne diseases. One recent achievement is the U.S. Safe Drinking Water Act of 1974, through which the federal government regulated drinking water for the first time. However, as a result of ineffective systems of waste disposal and improper hygiene, even in some developed countries access to safe drinking water in low-income communities is still a major threat to health, as the standard of treatment and **disinfection** of drinking water is often inconsistent. In developing countries, waterborne diseases constitute around four-fifths of all illness. The leading cause of childhood death worldwide is infantile diarrhea. Often, the installation of adequate public sewage systems is deterred by political instability and marred by the high cost of such projects. Across the world, the collection of reliable data on water supply and disease is lacking. Furthermore, the detection and epidemiological investigation of water-related epidemics is generally inadequate in most countries worldwide. Statistics gathered by the United States between 1991 and 2000 have shown that the etiological agent of around 40 percent of water-related outbreaks was not identified. Because of different approaches in recording disease outbreaks, the exchange between central and local public authorities, waterworks companies, and international organizations is often poor.

International campaigns to secure clean water are currently being waged. The leader is the JMP (Joint Monitoring Program), a WHO and United Nations Children's Fund (UNICEF) co-sponsored program that has conducted a series of global water-related reports worldwide since 1991. Using national censuses and household surveys, the JMP has made clear that monitoring problems are most acute in urban slums, small towns, and

rural areas. In 2002 the JMP reported that about 2.6 billion people live without even the most basic sanitation facilities.

Epidemiological and ecological studies have only recently begun to examine the full picture of the relationship between water and epidemic disease. This relationship involves a complex host of factors, including competitive environmental advantages for hosts and pathogens, host immunity, microbial virulence, and evolution. However, with the emergence of new water-related infectious diseases such as the new strain of cholera, *El Tor* Serotype, and the reemergence of other salmonellas and *E. coli* species, more research is crucially needed. Another example is **schistosomiasis**, a chronic debilitating disease spread by water that affects more than 200 million people worldwide. Cholera epidemics still are prevalent in parts of Africa and India. Millions of people throughout the world are at risk of contracting waterborne epidemics because of limited access to safe water and lack of public health infrastructure.

Victims of waterborne epidemics are usually treated by oral rehydration therapy (ORT), a simple and cost-effective solution. When provided quickly after symptoms appear, ORT virtually eliminates mortality from waterborne pathogens that kill through massive dehydration. The major problem worldwide is access to this therapy, particularly in rural areas. ORT also does not protect sufferers from tissue damage that results from the invasion of waterborne pathogens in the intestinal lining. Clearly, more long-term assessments need to be made both on effective therapies and on changes in the virulence of waterborne pathogens.

The importance of water in the transmission of illness is being continually assessed as new tools become available through advances in science, medicine, technology, and epidemiology. The emergence of new species, as well as the reemergence of previously known pathogens poses continual threats to human health. Universal access to safe drinking water and effective sanitation is of primary concern to public health. The United Nations considers a reliable and clean source of drinking water a fundamental basic human right and argues that it should be the highest priority of any country. If clean water is seen by the international community as a universal right, its provision worldwide is desperately lacking. *See also* Biological Warfare; Bioterrorism; Capitalism and Epidemic Disease; Cholera: First through Third Pandemics, 1816–1861; Cholera: Fourth through Sixth Pandemics, 1862–1947; Cholera: Seventh Pandemic, 1961–Present; Colonialism and Epidemic Disease; Ectoparasites; Environment, Ecology, and Epidemic Disease; Latin America, Colonial: Demographic Effects of Imported Diseases; Malaria in Africa; Malaria in Medieval and Early Modern Europe; Malaria in the Americas; Malaria in the Ancient World; Pesticides; Poison Libels and Epidemic Disease; Poliomyelitis; Poverty, Wealth, and Epidemic Disease; Protozoan, –zoa; Sanitation Movement of the Nineteenth century; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in North America to 1810; Yellow Fever in the American South, 1810–1905.

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JACOB STEERE-WILLIAMS

WEST NILE FEVER. West Nile **Virus** is transmitted to humans primarily by mosquitoes. For most people the disease is mild, but for some people the disease can cause paralysis, **encephalitis**, or death. In nature, the virus cycles between songbirds and mosquitoes. West Nile Virus is originally from the Old World, but it has become successfully established in the New World.

Biological Agent and its Effects on the Human Body. West Nile Virus (WNV) is an arbovirus (short for arthropod-borne virus) in the family Flaviviridae, which includes some of the most important arboviruses infecting humans (e.g., **Dengue fever virus**, **yellow fever virus**). WNV resembles a tiny (50-nanometer) sphere with small spikes. WNV contains a single central strand of RNA as its genetic component, surrounded by a protein-containing envelope. When an infective mosquito bites, a highly variable number of virus particles (3 to 200,000) are deposited into the skin along with the mosquito's saliva. It is believed that WNV particles first invade and replicate within dendritic cells (immune cells in the skin), then spread to regional lymph nodes, and finally move into the blood where they are distributed throughout the body. In most people, WNV infections are asymptomatic. However, about 20 percent of people get West Nile fever, accompanied by fatigue, headache, muscle ache, and sometimes a rash. Rapid onset of symptoms occurs within 3 to 14 days after being bitten by a WNV-infected mosquito, and symptoms generally last a few days. In severe cases, symptoms can last up to a month. Recovery is mediated by neutralizing antibodies produced in response to WNV infection. In a small proportion of people (around 1 percent, mostly elderly), antibodies fail to halt the infection, and WNV invades the central nervous system. This is a grave situation and can lead to serious and sometimes fatal **meningitis**, **encephalitis**, ocular complications, or a flaccid, **polio**-like paralysis. Neurological symptoms persist for months, even for life. There is no cure.

Transmission. WNV is a zoonotic disease. These are diseases that normally cycle among wildlife but can also infect humans. WNV is primarily a disease of songbirds and is transmitted from bird to bird by mosquitoes, particularly in the genus *Culex*. Songbirds are more important than other types of animals in the **transmission** cycle because songbirds produce very high concentrations of WNV in their blood. This is important because there is a threshold amount of virus (around 10^4 to 10^5 plaque-forming units per milliliter of blood) necessary to infect mosquitoes. Although humans (and horses) may be severely affected by WNV, they are considered "dead-end" hosts because they do not produce enough WNV in their blood to infect mosquitoes and therefore cannot contribute to the transmission cycle. Indeed, WNV levels in some songbird species (e.g., crows) get so high that healthy birds can sometimes contract WNV infections from pecking at sick birds that are shedding lots of WNV from their mouths and cloacae. People contract WNV primarily via mosquito bites. In the early 2000s, however, it was recognized that, as with many

other types of blood infections, some people have acquired WNV infections through blood transfusions, organ transplantations, or breastfeeding.

Epidemiology. Like many arboviral diseases, West Nile fever has a seasonal pattern. Most human cases occur in late summer. At the beginning of each mosquito season, transmission is usually low, and so the risk of being bitten by an infectious mosquito is also low. WNV requires several rounds of mosquito-bird-mosquito transmission in order to gain intensity. This is known as viral amplification. The intensity of WNV amplification within a given locality depends on the local species of birds and mosquitoes present and their respective susceptibilities to WNV. The more susceptible the bird or mosquito species, the greater will be the WNV amplification within that locality. Similarly, the intensity of WNV amplification during a given year depends on local meteorological conditions. More than any other environmental factor, temperature plays a role in driving WNV amplification. Warmer temperatures accelerate both mosquito and virus development. Thus, production of infectious mosquitoes can happen quickly. Cooler temperatures prolong these processes, and the virus has less time to undergo multiple rounds of amplification. Thus, the intensity of WNV amplification (and incidence of human cases) tends to be less when summers are cool.

Because WNV is found in northern latitudes where mosquito activity ceases during the winter months, there is some uncertainty as to how WNV transmission in these areas is reinitiated at the beginning of each mosquito season. Theories include 1) influx of WNV-infected birds migrating northward, 2) influx of WNV-infected mosquitoes blown northward on prevailing winds, and 3) persistence of over-wintering mosquitoes infected with WNV. The last theory has gained support from studies demonstrating that WNV-infected mosquitoes can, at low levels, pass the virus on to their progeny through a process known as transovarial transmission. This is crucial to the “over-wintering mosquito theory” because in temperate latitudes, *Culex* mosquitoes spend the winter hibernating in protected places as mated, non-blood fed females. Because they do not feed on blood before initiating hibernation, the only way that over-wintering *Culex* mosquitoes can be infected with WNV and thus initiate transmission the following spring is through transovarial transmission.

History of Major Outbreaks. *West Nile Story* is a modern-day classic about how a relatively minor and little-known disease, when introduced into a new **environment**, suddenly erupted into a continent-wide **epidemic**. WNV was first isolated in 1937 from the blood of a febrile patient in the West Nile district of Uganda, Africa. Other isolates were made in the early 1950s from apparently healthy **children** in Egypt. Initially, WNV was considered a minor arbovirus that caused little illness in humans. But that assessment changed when cases of WNV encephalitis in humans and horses appeared in Israel and France during the 1960s. Since then, sporadic outbreaks of encephalitic WNV infections have occurred throughout the Mediterranean region, eastern Europe, India, and Australia. In August 1999, a virulent Middle Eastern strain of WNV caused a sudden outbreak of encephalitis among residents of New York City. How WNV crossed the Atlantic Ocean is unknown; perhaps it arrived via infected mosquitoes in shipping containers or airplanes, or via the importation of infected, exotic birds. WNV first took root in the Bronx Zoo, where zookeepers noticed unusually high sickness and mortality among both captive exotic birds and free-ranging native birds. After some initial confusion, the link was made between bird die-offs in the zoo and the appearance of encephalitis in humans. An intense mosquito control operation was rapidly implemented by New York City to quell the spread of the disease. Despite these efforts, WNV reappeared the following spring, and by the end of

summer 2000, it had spread to several mid-Atlantic states. Expansion of WNV during the next three summers was amazing. By the end of 2004, WNV was present in all 48 contiguous states of the United States, in areas of southern Canada, and in parts of the Caribbean and Latin America. As WNV moved across North America, a pattern emerged. During its initial introduction into an area, WNV transmission was generally low. But during the second year, WNV transmission exploded, often producing extensive bird die-offs and high incidences of human disease. By the third year, WNV transmission generally subsided. For many parts of eastern North America, WNV transmission has remained low, perhaps because of the development of immunity in bird populations and the presence of a marginally susceptible urban vector species (*Culex pipiens*). Curiously, WNV transmission has remained intense in the upper Great Plains, despite the short transmission season. Apparently, the ecology of northern prairies, with their large songbird populations and presence of a highly susceptible vector species (*Culex tarsalis*), favors the continued transmission of WNV. Despite fears to the contrary, WNV has not caused major epidemics or bird mortalities in the Caribbean and Mexico.

Current Situation of the Disease. There is no treatment for WNV disease. Therefore, public health policy has stressed prevention. Prevention can be done in three ways: **vaccination**, traditional mosquito control, and avoidance of mosquito bites. There are two types of WNV vaccines available for horses, and several vaccine candidates for humans are undergoing development. Until these become available, recommendations on WNV prevention focus on community mosquito control and on avoidance of mosquito bites. Peak transmission occurs during late summer, and the primary vectors (*Culex*) are nocturnal. Therefore, it is recommended that during late summer, one should either avoid being outdoors after dark or wear **insect** repellent on skin and clothes when out at night. *See also* Pesticides.

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JEFFERSON VAUGHAN

WHITE PLAGUE. *See* Tuberculosis.

WHOOPIING COUGH. Whooping cough, also known as pertussis, is a highly contagious and life-threatening respiratory infection. Its common name comes from the most characteristic sign, a prolonged series coughs followed by a loud "whoop" of in-rushing

breath. Whooping cough has historically been considered a childhood disease; although its threat is greatest for young children, however, it can occur at any age.

It is possible that a passage by **Avicenna** in 1010 CE may be the first reference to a disease that can be recognized as whooping cough. The initial description of whooping cough is attributed to Guillaume de Baillou (1538–1616), an early epidemiologist and **physician** in Paris, who described the characteristic cough during an **epidemic** in 1578. He likened the cough to a dog's barking, and so the disease was termed "the dog cough." English physician Thomas Willis (1621–1675) provided a more definitive description of the disease in 1675. That same year, **Thomas Sydenham** gave the disease its current common name.

Since its early descriptions, and likely well before that, epidemics of whooping cough have occurred at about three- to five-year intervals. This period of time allows for a new group of susceptible **children** to be born and exposed to scattered individuals in the community who are infected. Currently, about 30 to 50 million cases of pertussis occur per year worldwide. Annually, as many as 300,000 people die from whooping cough. This mortality rate makes pertussis one of the most frequently fatal diseases for which we have a means of prevention by **immunization**. People who recover from pertussis generally have lifelong immunity to reinfection. On the other hand, medical immunization does not provide permanent protection. As a result of decreasing immunity over a person's life, there has been a shift in the age of people affected by pertussis, with increasing numbers of teens and adults and decreasing numbers of younger children becoming infected.

Whooping cough is caused by *Bordetella pertussis*, a Gram-negative coccobacillus. The **bacteria** travel easily in droplets coughed out by infected individuals and inhaled by others nearby. The ease of aerosolizing large numbers of the bacteria during severe coughing spells contributes to the very high degree of **contagion**. When the bacteria are inhaled into the trachea and bronchi, they produce a hemagglutinin that helps them bind to the surface of the epithelial cells that line the airways. As they multiply, the bacteria make and release toxins that contribute to the severity of the infection. Pertussis toxin and tracheal cytotoxin cause destruction of the cilia that propel infected mucus, contributing to additional bacterial growth. These toxins also destroy the epithelial cells lining the airways, leading to the severe cough of pertussis. A related disease, parapertussis, is caused by *B. parapertussis*, which lacks the toxins produced by *B. pertussis*. Because of the lack of destructive bacterial toxins, parapertussis is much less severe and less protracted than pertussis. Both *B. pertussis* and *B. parapertussis* appear to be limited to humans as their hosts. Another related bacterium, *B. bronchiseptica*, causes pneumonia and other respiratory infections in **animals**, especially dogs, but rarely in humans.

The manifestations of pertussis are most severe in children, especially young infants. In children, the disease typically has three stages: the catarrhal, the paroxysmal, and the convalescent.

The initial, catarrhal, stage begins about seven to ten days after exposure to an infected person, and appears much like a common cold or other mild upper respiratory infection. During this stage the child typically has a runny nose, a mild cough, and little if any fever.

Over the next week or two, the cough gradually grows more severe, and the child develops the typical paroxysmal coughing bouts of pertussis. Each paroxysm consists of a string of 10 to 30 barking, staccato coughs that may last a minute or more. Finally, the child takes a deep breath in, causing the whooping sound that gives the disease its name. These paroxysms are terrifying both to the child who cannot breathe and to bystanders who are powerless to aid the child. During each paroxysm, the child will turn first red, then blue for lack

of oxygen; he will stream tears, mucus, and saliva; at the end he will collapse in fatigue and may even have a seizure as a result of lack of oxygen. This will happen as often as 20 times a day and can be precipitated by attempts to eat or drink, or by any activity. As this paroxysmal phase goes on for up to a month, the child can become progressively exhausted and even malnourished because of the inability to eat. Especially in small infants, these paroxysms can cause severe enough respiratory difficulty to cause sudden death.

Finally, after weeks of violent paroxysms of cough, there will be a gradual decrease in the frequency and severity of these episodes as the child enters the convalescent phase. The convalescing child may continue to have coughing spells for as long as six months after the onset of the illness.

Because of the degree of damage done to the cells lining the trachea and bronchi and the compromised nutrition of the child, secondary infections, especially pneumonia, are frequent. The pressure waves of the cough itself can also cause complications, ranging from hernias to pneumothorax (rupture of a lung as a result of over-expansion) to bleeding into the brain or spinal cord. Whether because of this hemorrhage or because of oxygen deprivation to the brain, as many as 1 percent of infants who survive whooping cough have permanent neurologic damage, ranging from seizures to mental handicaps, blindness, deafness, paralysis, or coma.

Pertussis is most hazardous when it occurs during the first six months of age. In young infants, the diameter of the trachea is much smaller, and its cartilage rings are much less stiff than later in life. Because of this, respiratory failure during a paroxysm of cough is much more likely. Younger infants also have a less well-developed immune system and nutritional reserve and so are more likely to develop pneumonia or other secondary infections.

Teens and adults who have pertussis usually have a much milder course of the disease. The catarrhal stage is mistaken for a cold; the paroxysms of cough are usually not as severe as they are in children and are rarely accompanied by the whooping noise. The adult with pertussis will usually seek medical help and finally be diagnosed because the cough lasts for weeks to months without improvement. Despite the less severe nature of the disease in adults, they can also develop secondary infection. During coughing spells, they may faint, pass urine involuntarily, and even cough hard enough to break a rib.

During both the catarrhal and paroxysmal stages, the patient with whooping cough is highly contagious and can easily pass the disease on to others near him. Because of their milder disease and the likelihood that it will not be diagnosed promptly, teens and adults are a more likely source of contagion than young children are.

The **diagnosis** of whooping cough can usually be made easily in children based on the severity and duration of their cough and the absence of fever. In teens and adults, the diagnosis is usually thought of during epidemics of disease in the community or because of the prolonged persistence of the cough. In any age group, the diagnosis is confirmed by culturing *B. pertussis* from secretions obtained by a nasal swab or by examining secretions with immunofluorescent stains. However, these techniques may be positive in as few as 80 percent of cases. Polymerase chain reaction studies may offer a faster and more sensitive way to confirm the diagnosis.

The bacterium that causes pertussis is quite sensitive to erythromycin. Treating a patient with the **antibiotic** erythromycin during the catarrhal phase may shorten and make less severe the paroxysmal phase. Unfortunately, because of the mildness of the catarrhal phase, it is unlikely that a patient will be recognized unless there is a history of

recent contact with someone who has active pertussis or there is a community epidemic. Giving antibiotics during the paroxysmal phase is not likely to influence the severity of disease in the patient, but will make him less contagious after about five days of treatment.

Pertussis is a disease that can be prevented by immunization. In the 1940s a combined immunization against **diphtheria**, pertussis, and tetanus (DPT) became widely available. Infants were immunized at two, four, and six months of age, with booster doses before starting school. Prior to the availability of this preventive measure, as many as 147,000 cases of pertussis occurred in the United States annually, and about 8,000 children died of it. The incidence of the disease dropped to only a few thousand per year as a result of immunization. There were side effects associated with the original agent, a derivative of whole bacterial cells. Most children had redness and soreness at the site of injection for a few days; about 1 percent developed fever and irritability. Rarely, some children even developed seizures and other neurologic problems. These severe reactions were estimated to occur about once in 100,000 immunized children. In the 1990s, a more purified acellular product became available that provides the same degree of immunity with far fewer side effects. Unfortunately, because of concerns that some parents have about the safety of the immunization, they withhold it from their children. This subjects the children to a much higher risk of complications and even death from the now-preventable disease. See also Human Body.



A female Indonesian child suffering from malnutrition and whooping cough. WHO photo. Courtesy of the National Library of Medicine.

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CHARLES V. BENDER

WORLD HEALTH ORGANIZATION. See International Health Agencies and Conventions.

WU LIEN TEH (WU LIENDE OR WU LIANDE, 1879–1960). Wu Liende, plague expert and Chinese public health pioneer, was born in Penang in the Straits Settlements (now Malaysia) on March 10, 1879. While at the Penang Free School, Wu decided to become a **physician** because as an Asian he was barred from the civil service but not from a profession such as medicine. He matriculated at Emmanuel College, Cambridge, in 1896 for the natural science course. After his three-year course, he spent the summer of 1899 studying with a prominent English bacteriologist and pathologist, Dr. German Sims Woodhead (1855–1921).

Earning his degree in medicine at St. Mary's Hospital in London, Wu became house physician at the Brompton Hospital for Consumption and Diseases of the Chest to learn more about **tuberculosis**, a major disease in the Straits Settlements. Subsequently he studied with **Ronald Ross** at the new Liverpool School of Tropical Medicine, with Karl Fraenkel (1861–1901; former assistant to **Robert Koch**) in Halle, Germany, and with Ukrainian Elie Metchnikoff (1845–1916) at Paris's Pasteur Institute.

After a short period as a researcher and private practitioner in Penang, he accepted an offer from Yuan Shih-kai (1859–1916), Grand Councillor of China, to become vice-director of the Imperial Medical College in Tientsin, a school recently established to teach Western Medicine.

An outbreak of **plague in China's** region of Manchuria in 1910 gave Wu a new direction in his work. There he investigated the nature of plague, the organism, and its mode of spread. His modern European training provided him with approaches that were universally admired, and for the first time, Western medicine was learning from a Chinese physician about modern medicine.

An International Plague Conference, held in Mukden during April 1911, was the first international scientific meeting held in China. Wu was the president of the conference, the proceedings of which became a major reference on **pneumonic plague**.

Wu did not return to Tientsin but continued to study plague in Harbin. In one of its final acts before the Republican Revolution in October 1911, the Imperial regime established Western medicine as official state policy with the establishment of the North Manchurian Plague Prevention Service under Wu's direction. This service continued until 1931 as China's main defense against plague as well as **cholera**. Wu became the authority on pneumonic plague, and his 1926 monograph is still a standard reference.

Wu Liende was an effective organizer and administrator: a founding member of the China Medical Association in 1925 and of its successor, the Chinese Medical Association in 1932, and an advocate for uniform standards in Chinese medical education and health promotion groups such as the National Anti-Tuberculosis Association. Wu had an active interest in the medical culture of China and coauthored *History of Chinese Medicine* (1932, 1936).

As events led up to World War II, Wu resumed general medical practice in Penang after a hiatus of some 30 years. After the War, Wu used his international contacts and

stature to advocate for improved public health measures in Malaya. To the end of his life, he worked to end one of Asia's major health problems, opium use and addiction.

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WILLIAM C. SUMMERS

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Y

YELLOW FEVER. Yellow fever is an acute, infectious disease characterized by frontal headaches, fever, prostration, muscular pain, proteinuria (excess protein in the urine), jaundice, and, in the final stages, internal bleeding, kidney failure, delirium, and convulsions. Vomiting partly digested blood from stomach hemorrhages—called “black vomit”—is a particularly ominous sign. In the eighteenth and nineteenth centuries, yellow fever’s unpredictability, rapid course, and horrifying outcome (death seven to ten days after onset) created mass panic and paralyzed commerce. Even though **typhoid fever** had a higher fatality rate, it failed to arouse a similar public reaction. Yellow fever was indisputably “the single most dreaded disease in the Americas.”

Yellow fever was known by 150 synonyms, most of which were based on a single terrifying symptom (*vomito negro*), geographical location (Boullam fever), season of prevalence (autumnal **epidemic fever**), or severity (malignant bilious fever). “Yellow Jack,” its most familiar name, originated from the **quarantine** flag that adorned suspect ships in harbor.

Etiology. Yellow fever became the first viral disease experimentally proven to exist in humans when, in October 1901, James Carroll (1854–1907), of the U.S. Army Yellow Fever Board in Cuba, demonstrated that yellow fever was caused by a living organism smaller than any known **bacterium**. Carroll filtered serum from confirmed yellow fever patients through a sterilized porcelain filter, and the bacteria-free filtrate produced the disease when injected into nonimmune volunteers. Importantly, blood taken from yellow fever patients whose illness had been caused by the ultrafiltrate produced the disease in a third individual.

The causative agent, an arbovirus (transmitted by arthropod vectors) of the *flaviviridae* family, which includes the **West Nile** and **Dengue fever** viruses, was isolated in 1927. A decade later, **Max Theiler**, a medical researcher at the **Rockefeller Foundation** Yellow Fever Laboratory in New York City, developed a live, attenuated vaccine derived from the 17D **virus** strain. Mass immunizations of U.S. military personnel in **World War II**

GRIFFITH HUGHES'S DESCRIPTION OF YELLOW FEVER IN BARBADOS (1715)

The Patient is commonly seized with a shivering Fit, as in an Ague, which lasts an Hour or two, more or less; and the Danger is guessed at, according to the Severity and Continuance of the Ague.

After the shivering Fit, a violent Fever comes on, with excessive Pains in the Head, Back, and Limbs, Loss of Strength and Spirits, with great Dejection of Mind, insatiable Thirst and Restlessness, and sometimes too with a Vomiting, attended with pains in the Head, the Eyes being red, and that Redness in a few days turning to Yellowness.

If the Patient turns yellow too soon, he hath scarce a Chance for Life, and the sooner he does so the worse.

The Pain in the Head is often very great, when first seized with this Fever.

After some Days are past, this Pain abates, as well as the Fever; and the Patient falls into a breathing Sweat, and a temperate Heat, so that he appears to be better; but on a narrow [closer] View, a Yellowness appears in his Eyes and Skin, and he is visibly worse.

About this time he sometimes spits Blood, and that by Mouthfuls; as this continues, he grows cold, and his Pulse abates till at last it is quite gone; and the Patient becomes almost as cold as a Stone, and continues in that state with a composed, sedate Mind.

In this Condition he may perhaps live Twelve Hours without any sensible Pulse or heat and then expire.

Such were the Symptoms and Progress of this Fever in the Year 1715 . . .

After Death, the Corps of such appear livid in some Parts or other; or else marked with pestilential Spots, Carbuncles, or Buboës.

From Griffith Hughes, *The Natural History of the Barbados* (London, 1750), p. 38.

(1939–1945) proved the vaccine's benefits: not a single vaccinated serviceman contracted yellow fever during the conflict. The 17D vaccine is still the gold standard and provides decades-long, and possibly lifelong, immunity.

Transmission. In the aftermath of the Spanish-American War (1898), U.S. occupational forces in Cuba faced a more lethal foe than the vanquished Spanish army: yellow fever. In response to this crisis, Army Surgeon General George Sternberg (1838–1915) established the U.S. Army Yellow Fever Board in May 1900 with follow-up instructions to “give special attention to questions relating to the etiology and prevention of yellow fever.” In a remarkably short time, the board, headed by Major **Walter Reed** and comprised of contract surgeons (civilian physicians) James Carroll, Jesse Lazear (1866–1900), and Aristides Agramonte (1868–1931), discredited the prevailing etiological theories (bacteria, noxious **air**, filth, soiled clothing/bedding). Their everlasting contribution to modern medical science was the demonstration that yellow fever was not contagious, but

was spread from human to human solely by means of the bites of infected female *Aedes aegypti* mosquitoes.

The **insect-vector** theory did not originate with Reed and his coworkers. In 1881, Cuban physician Carlos Finlay (1833–1915) had postulated a relationship between the mosquito now known as *A. aegypti* and yellow fever. He was never able to prove his hypothesis, however, despite carrying out more than 100 mosquito inoculations in 90 subjects over a 20-year period. The Reed board succeeded because it discovered the keys to infectivity that had eluded Finlay. First, the mosquito could acquire the yellow fever germ from a donor only during the first two or three days of the disease, when the virus titer was high in the bloodstream. Second, the imbibed virus needed a two-week incubation period within the mosquito's body before the insect could infect a healthy recipient—a process termed *extrinsic incubation*. During this time, the virus multiplied and traveled from the mosquito's stomach to its salivary glands.

Epidemiology. Yellow fever evolved first in the swampy and riverine regions of Africa, and natives developed a high tolerance. When Africans were brought to the Americas as slaves, slavers brought the disease with them in shipboard water supplies. In the Western Hemisphere, yellow fever epidemics usually began in July, peaked in September, and ended with the first hard frost. An attack conferred lifetime immunity against the disease. *A. aegypti*, known as the “household” mosquito because of its preference for human habitations, breeds in standing water found in roof gutters, ditches, cisterns (principal foci), horse troughs, tanks, water barrels, and other rainwater receptacles. Swarms of newly hatched mosquitoes, the presence of yellow fever carriers (undiagnosed mild cases) to which these insects had access, and warm and humid conditions combined to provide ideal conditions for the propagation of the disease among a susceptible population. In numerous instances, the seeds of destruction were unwittingly imported into maritime cities in the form of infected newcomers and mosquito-infested cargoes.

From 1702 to 1879, the English colonies and the United States experienced at least 113 yellow fever epidemics. The most notorious outbreaks decimated Philadelphia in 1793 (4,044 deaths, 10 percent of the population), New Orleans in 1853 (about 9,000, 9 percent), and Memphis, Tennessee, in 1878 (5,150, 10 percent). The 1878 epidemic was a stupendous calamity. It started in New Orleans and spread by rivers and railroads to Memphis and to 200 other towns throughout the Mississippi and Ohio River valleys, leaving in its wake an estimated 100,000 cases and 20,000 fatalities. The economic cost to the country ranged up to \$200 million. Is it any wonder then that a contemporary Memphis newspaper personified yellow fever as “The King of Terrors”?

Social Impact. What set yellow fever apart from other diseases was its staggering social impact—most noticeably in the semitropical climate of the American South. Once the disease became entrenched in a community, people shunned others and seemed moved only by the instinct of self-preservation. Those who could afford it fled to safer locations. As the dead piled up, shops, businesses, and trading houses closed. Countless acres of fertile farmland lay idle. The resulting economic disaster fueled public health reform. Whereas northern sanitarians focused on pure food, milk, and drinking water, their southern counterparts formed health departments explicitly to fight yellow fever. Their concern was more with saving business losses than with saving lives. Any lives spared could be attributed to improved sanitation systems (drainage, sewerage, and water) that unintentionally reduced mosquito breeding areas.

The Reed board's findings revealed that yellow fever was not an inscrutable pestilence to be feared, but a comprehensible mosquito-borne disease that could be prevented. Only after laypersons—who lagged behind the medical profession in acceptance of the mosquito menace—understood this, could the blind panic that had been an enduring feature of eighteenth- and nineteenth-century epidemics subside.

Public Health. Throughout the nineteenth century, yellow fever was central to debates on public health practice. In this regard, the importance of the Reed board's elegant, foolproof discoveries cannot be exaggerated, for they provided a scientific rationale for redirecting yellow fever control efforts. Old approaches included such absurd methods as burning pine tar in the streets to dispel poisonous air; twentieth-century procedures focused on systematically destroying adult mosquitoes and their larvae, eradicating breeding sites, and preventing mosquitoes (netting and screens) from biting anyone with the disease.

By instituting sanitary regulations based exclusively on the mosquito doctrine, Major **William Gorgas**, the chief sanitary officer of Havana, rid the Cuban capital of yellow fever for the first time in two centuries. From 1853 to 1900, there were 36,000 deaths from yellow fever in Havana; by October 1901, not a single case of the disease was reported in the city. This was the first example in history of ending an epidemic by controlling its vector. Applying the same techniques in 1904 that had proven so successful earlier in Havana, Gorgas—now a colonel—and his sanitary team preserved the health of the labor force constructing the Panama Canal. From May 1906 until the canal opened in 1914, there were no cases of yellow fever in the Canal Zone. Gorgas estimated that 71,000 lives were saved in the process.

Current Status. As we enter the twenty-first century, yellow fever is found only in South America and Africa. Despite the availability of a safe and effective yellow fever vaccine, large populations in these countries remain unvaccinated. In Africa, where only 6 percent of the people have been immunized, yellow fever epidemics have recurred in every decade of the twentieth century, with the most severe in Ethiopia in the 1960s (about 30,000 deaths). Thousands died of the disease in Ghana in the 1970s, Nigeria in the 1980s, and the Sudan in 2003. Smaller outbreaks occurred during the 1990s.

The last yellow fever epidemic in North America occurred in New Orleans in 1905 (3,402 cases; 452 deaths); it was aborted by quick implementation of mosquito suppression measures. Since then, only a handful of unvaccinated U.S. citizens have become yellow fever victims, all having contracted the disease during international travel. See also Yellow Fever Commission, U.S.; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in North America to 1810; Yellow Fever in the American South, 1810–1905.

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VINCENT J. CIRILLO

YELLOW FEVER COMMISSION, U.S. **Yellow fever** devastated American troops occupying Cuba during and after the Spanish-American War (1896). In May 1900, Army Surgeon General George Sternberg (1838–1915) created a medical board to investigate infectious diseases prevalent on the island, particularly yellow fever. Major **Walter Reed**, a career army **surgeon** then completing a study of **typhoid fever** in U.S. army camps, headed the new Yellow Fever (or Reed) Commission. The three other members of the Commission were temporary wartime surgeons. James Carroll (1854–1907) worked with Reed in army laboratories in Washington, Cuban-born Aristides Agramonte (1868–1931) was an experienced yellow fever investigator, and Jesse Lazear (1866–1900) was a brilliant young researcher from Johns Hopkins Medical School in Baltimore.

The Mosquito Hypothesis. Assembling in Havana in June 1900, the Commission quickly demonstrated that the **bacterium** *Bacillus icteroides*, suspected by several other researchers, did not cause yellow fever. Two other theories, however, did capture their attention. Havana **physician** Carlos Finlay (1833–1915) was convinced that the female *Culex fasciatus* mosquito (now *Aedes aegypti*) transmitted yellow fever. Despite two decades of experimentation, Finlay never succeeded in transmitting yellow fever to nonimmune immigrants through the bite of infected laboratory mosquitoes. Immigrants, mostly Spanish nationals, had agreed to participate because they fully expected to contract yellow fever naturally after arriving in Cuba. The second theory had been developed by Henry Rose Carter (1852–1925) of the U.S. Public Health Service. In 1898 he analyzed detailed house-by-house and day-by-day observations of a yellow fever outbreak in two isolated towns in Mississippi. He concluded that there was a gap of approximately two weeks—the “extrinsic incubation period”—between the identification of the first case in a community and the appearance of subsequent cases. It was probably Lazear who combined the two theories, hypothesizing that yellow fever was transmitted by a mosquito that had incubated the infectious agent for approximately two weeks.

Human Subjects Experiments. Commission members agreed that experimentation on human beings, including themselves, was necessary to prove the mosquito hypothesis. Mosquitoes raised in Lazear’s laboratory were fed on the blood of active yellow fever cases at the Las Animas Hospital near Havana. After several days, these “loaded” mosquitoes, were allowed to bite military volunteers as well as Carroll and Lazear. Carroll and one soldier developed yellow fever and recovered. Lazear died following a violent attack. Agramonte, assumed to have acquired immunity in childhood, was not an experimental subject. Reed, who had left Cuba temporarily to complete his typhoid report, considered these cases

suggestive but not conclusive, because the subjects had not been strictly isolated from sick patients or random mosquitoes.

With Sternberg's approval, Reed designed his now-famous human experiments at a mosquito-free site, named Camp Lazear, near Havana. Subjects were recruited from non-immune Spanish immigrant laborers. Each was offered \$100 to participate and an additional \$100 plus the best care available from American medical officers if he developed yellow fever. American soldiers also volunteered. Some refused the money, avowing that they volunteered "in the interest of humanity and the cause of science." Reed insisted on written informed consent in English or Spanish from all volunteers, a revolutionary concept in human experimentation.

The experiments were conducted between November 1900 and January 1901. Several carefully isolated volunteers became ill after being bitten by loaded mosquitoes. Reed thus confirmed the mosquito theory. In another experiment, healthy volunteers were housed in a mosquito-free cabin with screened windows. For 20 nights, they slept on bed linens and wore nightclothes soiled with the vomitus and excrement of hospitalized yellow fever victims. Despite the revolting conditions, these men remained well, disproving the popular theory that contaminated nonliving objects (fomites) transmitted yellow fever. A second group stayed in a partitioned cabin with a screened opening between the two rooms. The men in one room were bitten by loaded mosquitoes and some developed yellow fever. The volunteers in the second room remained well, thus disproving the theory that contaminated air in a building transmitted yellow fever.

Application of the Commission's Work. The usual sanitation and **quarantine** measures had failed to halt yellow fever in Cuba. U.S. army physicians, who followed the Commission's work closely, quickly recognized the importance of destroying mosquitoes and their larvae. Havana sanitary officer, Major **William Gorgas**, despite lingering personal doubts about the mosquito theory, initiated a military-style campaign against the mosquito and the eggs it laid in standing **water**. Gorgas's "mosquito brigades" went house to house, covering or applying a thin layer of oil to cisterns and draining standing water. Within months, Havana was free of yellow fever, a remarkable demonstration of the application of scientific medicine to public health.

Reed returned to Washington and was considered for the post of Army Surgeon General. He died of appendicitis in 1902. Carroll, with Reed's support, returned to Cuba in late 1901, where he demonstrated that yellow fever was caused by an organism smaller than a bacterium. He died in 1907, possibly from cardiac complications of yellow fever. Lazear is remembered as a martyr to medicine. Agramonte continued medical research at the University of Havana and later in New Orleans, dying in 1931. Within a few years, Gorgas successfully applied the mosquito theory to yellow fever (and malaria) as chief medical officer of the Panama Canal project. In the century since the successful work of the Yellow Fever Commission, medical historians and other interested parties have argued over the perceived slighting of Finlay as the discoverer of the mosquito vector of yellow fever, the issue of Walter Reed's failure to participate personally in human experiments, the impression of some participants that Reed received disproportionate acclaim for the Commission's work, and the ethics of medical experimentation on military volunteers. *See also* Colonialism and Epidemic Disease; Environment, Ecology, and Epidemic Disease; Human Subjects Research; Insects, Other Arthropods, and Epidemic Disease; Medical Ethics and Epidemic Disease; War, the Military, and Epidemic Disease; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in the American South, 1810–1905.

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SANDRA W. MOSS

YELLOW FEVER IN COLONIAL LATIN AMERICA AND THE CARIBBEAN.

Yellow Fever or, as it was called by early modern Iberians, *vomito prieto* (black vomit), was one of the most important factors in the shaping of the social, cultural, political, and economic states of the Spanish and Portuguese colonies of the "New World." In the Americas, **epidemics** of yellow fever defeated armies and decimated Indian and European populations, while sparing African slaves. The works of the *flavivirus* causing *vomito prieto* shaped the Latin America that emerged after the European conquest and colonization.

In 1648 yellow fever paid its first recorded visit to the Spanish colonies when epidemics shook Yucatán (Mexico) and Cuba. Three factors explain the relative delay of the appearance of this disease in the Western Hemisphere: the yellow fever **virus's** short life cycle, its endemic state in most of West Africa, and the characteristics of this germ's vector.

Once in a human body, the yellow fever virus's life cycle is particularly short. In seven to ten days the host is either killed or becomes immune to the disease. Yellow fever induces an effective and life-lasting immune response in its victims and runs a relatively mild course when it is first acquired during infancy. Thus, enslaved African Americans, having lived in close contact with the virus since childhood, were ineffective as a means of transport for the virus. Its transfer from the "Old" to the "New" World needed a large nonimmune population; one that would allow for the virus to pass from host to host during the 12-week trip from Africa to the Americas. In addition, like the virus itself, the vector for the **transmission** of yellow fever, the *Aedes* mosquito, adapted to human populations and settlements and breeds, almost exclusively, in shallow clay pots or other containers of undisturbed water, both of which were common elements on slave trading ships.

Although delayed, the arrival of yellow fever on American shores was not silent. Yellow fever quickly presented itself with terrifying epidemics. Thousands of Europeans died in the midst of high fever, palpitations, muscular cramps, exhaustion, and jaundice from liver failure. Victims suffered profuse bleeding from skin wounds and body orifices, including the upper intestinal track, from which digested blood—which turns black—was vomited. This black body emission gave the name to the disease in the Spanish realm, *vomito prieto*.

Colonial Latin American statistics of yellow fever's impact are, at best, unreliable, since only nonimmune guests presented yellow fever's classic symptoms. Mild cases, especially in Africans and **children** of all races, went unrecognized as merely *calenturas* (high fevers). Thus, only severe cases of yellow fever were recorded as such, while mild cases were not accounted for. Such bias explains, at least partially, the high mortality rates (deaths/cases of illness) recorded by chroniclers of the royal Spanish medical corps, the *protomedicato*—rates as high as 70 percent). Modern mortality estimates are around

10 percent. Because yellow fever virus induces a permanent immunity in survivors, it became a disease of the immune-naïve European residents as well as of visitors, foreigners, newcomers, and invaders, such as the 1,500 soldiers sent by France to invade St Lucia in 1655.

“Brazen Jack” (as yellow fever was called by many Britons) also helped Spaniards defend Cartagena de Indias (Colombia) when in 1741 British Admiral Edward Vernon (1684–1757) launched the largest amphibious military assault before the Second World War. Of the 22,000 men assailing Cartagena, at least half died of *vomito prieto* during the unsuccessful three-month campaign.

The disease also played a major role in the fates of the two most powerful armies of the late eighteenth century, when they attempted to invade St. Domingue, the northern portion of the island of Hispaniola (present-day Haiti and the Dominican Republic). By 1775 St. Domingue had grown to be the most lucrative colony in the world, thanks to its sugar plantations. The ubiquitous plantations on the island provided the perfect breeding grounds for *Aedes* mosquitoes and made *vomito prieto* equally omnipresent. After the French Revolution brought turmoil even to the more distant French colonies, the black slaves on St. Domingue armed themselves, ousted the colonial government, and in 1804 established the first free black republic (in the Western Hemisphere second only to the United States in declaring independence). The chain of events that finished in the foundation of Haiti was stalwartly influenced by “Yellow Jack.”

With the excuse of preventing further slave rebellions in the rest of the Caribbean, British Prime Minister William Pitt (1759–1806) sent a 20,000-man army to invade St. Domingue. The French were not willing to lose their most precious overseas possessions without a good fight and sent around 35,000 soldiers to subdue both Britons and the rebellious slaves led by Toussaint L’Ouverture (1742–1803). Between 1793 and 1798, both armies arrived in the yellow fever-infested northern portion of Hispaniola. Although some historians refute the number of deaths attributed to yellow fever and malaria in St. Domingue as exaggerated by contemporaries, it is undeniable that yellow fever played a major role in shaping the events in the former French colony. By 1798, 12,500 Britons had died either at the hands of L’Ouverture’s followers, or of yellow fever or malaria. The French contingent did not fare much better; only 6,000 of them returned home. Haiti has retained both its liberty and its population of predominantly African extraction.

Brazil received the lion’s share of the African diaspora to the Americas. Common sense suggests that the gigantic Portuguese colony should have been the place in which most yellow fever epidemics occurred during Latin America’s colonial period. To the contrary, however, after the first big yellow fever epidemics between 1685 and 1696, Brazil did not suffer another bout with the disease until 1845. At this time Europeans were lured to join the predominantly immune African population living in Brazil in “whitening” campaigns carried out by the Creole government. It was only then that the mild variant of yellow fever that had thrived endemic in the Brazilian cities and plantations for two centuries suddenly found plenty of susceptible victims. Yellow fever epidemics struck Salvador, Rio de Janeiro, and other Brazilian cities, killing thousands. Almost all of them were recent immigrants. By 1860, in Rio de Janeiro alone, 60,000 people had died of *vomito prieto*. But, if in Brazil yellow fever’s absence in 1807 lured exiled Portuguese King João VI (1767–1826) to establish his court in Rio de Janeiro, after the Napoleonic invasion of Portugal the same year, in Cuba, “Jack’s” presence became an irresistible excuse for invasion.

By the late nineteenth century, Cuba was the only remaining Spanish colony in the Western Hemisphere. The United States, however, was interested both in the riches of Cuba's sugar plantations, and in establishing hemispheric hegemony. Americans found in the epidemics that ravaged their southern neighbors the perfect excuse to invade Cuba and put an end to the four-century-long colonial enterprise of Spain in the Americas. American warmongers promoted the Spanish-American War, at least in part, as a way to defend Louisiana and Florida from the successive visits of "Brazen Jack." According to American officials, these epidemics generally originated in Cuba. The U.S. army ousted from Cuba Spanish colonists, the *Aedes* mosquito, and with it yellow fever. All this was to the great amusement of the Cubans, who had become immune to yellow fever thanks to many earlier outbreaks.

Yellow fever killed thousands of French workers struggling to build a canal in Central America in the late nineteenth century and made the French enterprise fail, thus paving the way for American intervention. In the wake of the Spanish-American War Theodore Roosevelt (1858–1919) became president of the United States and successfully secured the secession of Panama from Colombia. The U.S. government effectively controlled mosquito-breeding fields in the Panamanian jungle and avoided the fate of the French. American engineers created the Panama Canal, which would be crucial to the consolidation of U.S. hegemony over the former Iberian colonies and to its rise as a world power. *See also* Latin America, Colonial: Demographic Effects of Imported Diseases; Slavery and Epidemic Disease; War, the Military, and Epidemic Disease; Yellow Fever Commission, U.S.; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in North America to 1810; Yellow Fever in the American South, 1810–1905.

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PABLO F. GOMEZ

YELLOW FEVER IN LATIN AMERICA AND THE CARIBBEAN, 1830–1940.

Yellow fever in postcolonial Latin America and the Caribbean region was largely endemic where present. It presented essentially a mild **childhood** disease, but it could and did flare into **epidemics**, usually because of its importation into port cities by ships from other, infected seaports. It played a part in U.S. southern expansion in 1847, and a half-century later, this latter conflict—the Spanish-American War—led to the research that finally allowed for control of the disease. International concern with yellow fever in the Western Hemisphere also led directly to the formation of organizations that helped to eradicate

smallpox and are still working to eradicate infectious diseases such as measles and tuberculosis.

The Mexican-American War (1846–1848). U.S. notions of Manifest Destiny dictated that the young republic seize southern border territories—now Texas, Arizona, Southern California, and New Mexico—from Old Mexico. American strategists envisioned a strike deep into Mexican territory at Mexico City itself, the success of which would provide the leverage necessary to wrench away the northern provinces in a peace treaty. They designed an amphibious landing at Veracruz by General Winfield Scott (1786–1866) and an army of 10,000. Planners were careful to set dates that avoided the area's storms and the mainland's spring yellow fever season, a factor for which Scott had great respect. U.S. plans went awry, however, and the landing took place almost two months late and dangerously close to yellow fever season. The U.S. forces besieged Veracruz as the first cases of yellow fever began to appear. By March 29, the city had surrendered and the Mexican garrison had evacuated. Scott moved in quickly and marched out on April 2 en route to Mexico City via the Sierra Madres and the fever-free zone. He had narrowly bypassed one of the Mexicans' most effective allies, and few U.S. troops had fallen ill to *Il vomito*. Scott's capture of the Halls of Montezuma in September all but ended the conflict. By war's end, over 13,000 U.S. servicemen had been killed, though about seven fell to disease, predominantly yellow fever, for every battle death.

Brazil, Panama, and Cuba to 1903. Brazil had suffered yellow fever epidemics in the late seventeenth century but was free from major outbreaks until the mid-1800s. An American ship docking at Bahía in the fall of 1849 is said to have carried fresh, infected mosquitoes from New Orleans and Havana. These may have infected Danish crewmen who went ashore in Rio de Janeiro and began spreading the disease through the city as native mosquitoes feasted on their tainted blood. The disease disseminated linearly through the streets until most of the capital was affected, some four months after their arrival. By the end of 1850, 90,658 cases had been reported, of which 4,160 proved fatal. But this was just the beginning. Once reestablished, the fever flared again and again, especially among the newly arrived and the younger whites who had had little or no immunity-conferring exposure. In the 1850s, 10,173 died; in the 1860s, only 1,815. The 1870s saw a resurgence with 13,140 yellow fever deaths. This decade's increase in yellow fever was shared by much of South America. In Argentina, for example, Buenos Aires alone suffered some 15,000 deaths. In the next decade, the toll in Rio dropped to 9,563, though 2,115 died in 1889 alone. The early 1890s doubled that annual rate, and by late 1894 the city had lost 14,944. Another 5,722 died between 1885 and 1900, bringing the toll since 1850 to nearly 60,000. Like much of Africa, Rio gained the reputation of the "white man's grave," and immigration from Europe dropped off. Because of the variety of theories of causation (fomites, *miasma*, insects, interpersonal *contagion*) officials took few actions to address the situation before 1903.

The utility of—indeed the need for—a sea passage across Central America linking the Atlantic and Pacific Oceans had long been recognized. The British held the Isthmus of Panama with a vague plan for shortening the distance between India and England with a canal, but the native mosquitoes and fever finally forced them to relinquish their claims to Colombia. Following their success with the Suez Canal, the French De Lesseps Panama Canal Company obtained rights from Colombia to dig across the 50-mile wide, jungle-encrusted strip of land. Work proceeded from 1882 to 1889; the costs were enormous. The firm went bankrupt because of cost overruns, poor and corrupt management, and yellow

fever. Managers maintained a steady flow of nonimmune workers, and the mosquitoes provided a death rate of 176 per 1,000 in 1886. After nearly seven years, some 22,000 laborers and engineers had succumbed to the disease, reflecting mortality rates that fluctuated wildly from 12 to 70 percent depending on the season.

In Cuba, yellow fever may have been endemic as early as the 1760s, and it clearly was in Havana and other coastal cities by the mid-nineteenth century. Yellow fever was endemic in many of the coastal and low-lying regions of the island, but higher, interior areas remained virgin soil. In 1895 a major insurgency broke out, and over the next three years Spain sent thousands of its troops to reinforce the colonial garrisons. Whereas the new forces brought and spread **smallpox**, they contracted yellow fever in epidemic proportions. While on maneuvers against guerrillas in the island's hills, they carried the disease with them, introducing it among the defenseless civilian populations. At the same time, unimmunized Cuban civilians who had been "reconcentrated" by force from the countryside to huge urban camps shared the Spanish soldiers' fate. Overcrowded and unsanitary habitations, barracks, and hospitals facilitated the spread of the fever, along with many other diseases. By the end of the Spanish-American War in 1898, 53,440 Spanish soldiers, or over a quarter of the total Spanish forces, had died of disease, with yellow fever predominating. Over the same four years, over 200,000 Cubans died of smallpox and other illnesses that accompanied the Spanish counter-insurgency and military activities.

Havana suffered an epidemic when victorious but susceptible U.S. troops entered the capital. Chief Sanitary Officer for the U.S. Army **William Gorgas** headed an effort to sanitize the city of filth, removing what were believed to be the sources of the disease. Over a year into the program, the fever was still rampant, well above its usual endemic incidence levels. In 1900 **Walter Reed** and his **Yellow Fever Commission** joined Gorgas and confirmed the theory presented 19 years earlier by U.S.-educated Havana physician Carlos Finlay (1833–1915) that mosquitoes—and neither contagion nor corrupted air—transmitted the responsible microbe. Gorgas again went to work, this time against open and standing water pools in which the mosquitoes bred. Swampy areas were drained, ditches and watercourses screened off, and oil sprayed on still water. The city that had reported 1,400 active cases in the summer of 1900 reported only 37 in 1901 and no cases by the end of summer 1902.

Rio and Panama and after Gorgas's Success. A delegation of French scientists including **Paul-Louis Simond** of the **Pasteur** Institute arrived in Rio in 1900 to study yellow fever *in situ* and to benefit from the recent insights gained by the Americans in Cuba. Over the course of five years, the crew developed important information about the life of the mosquito, transmission of the disease, and means of countering it. In 1903 Rio's young Dr. Oswaldo Cruz (1872–1917) convinced the Brazilian legislature to establish a Yellow Fever Service, despite fervent popular and media skepticism and opposition. Service officers attacked mosquito breeding grounds as Gorgas's men had but concentrated on fumigating against the adults and went beyond them in reporting cases and isolating victims (a major reason for opposition). In less than a year, the Service's efforts had paid off, however, and the incidence of the disease fell off dramatically. Rio eliminated epidemic yellow fever by 1906, and within two or three years the disease itself was eliminated.

Following the Spanish-American War, the U.S. Congress authorized the purchase of the French canal and already-established railroad right-of-way in Panama, but the Colombians balked, refusing to sign the necessary treaty. With French and U.S. support,

Panamanians rebelled and gained their autonomy from Colombia in late 1903. Almost immediately the new government ceded the Canal Zone to the United States with the Hay-Bunau-Varilla Treaty. Gorgas was dispatched to the Zone with the mission of eliminating the mosquitoes and the threat of yellow fever, which he did in about two years; the last death from the disease in the region occurred in 1906. Work on the canal began in 1907 and continued into 1914, unhampered by yellow fever.

In 1913 the American non-governmental **Rockefeller Foundation** established its International Health Commission (IHC) with the goal of eliminating threats to human health in the Western Hemisphere. Yellow fever and malaria were specifically targeted for elimination in 1915. Yellow fever was believed to be a predominantly urban and coastal disease, which meant that depriving the mosquitoes of their breeding grounds in a few highly populated locations would do the trick. Guayaquil, Ecuador, was the first battleground. William Gorgas arrived in 1916 to find that urban environmental factors such as stagnant drinking water sources were directly linked to the mosquito problem, but the IHC wanted nothing to do with improving the infrastructure. U.S. entry into World War I (1914–1918) delayed Gorgas's project, but in November 1918 it began in earnest. Within two years, it had proven successful and was handed over to the Ecuadorian government in 1920. The IHC next targeted towns along the coasts of Mexico and Peru, and between 1921 and 1924 efforts were rewarded with success.

Four coastal regions of Brazil had long been on the IHC list, but as states rather than the federal government controlled Brazilian public health machinery, the Foundation had no leverage. In addition, Oswaldo Cruz had established programs for local **fumigation**, and neither he nor most Brazilians desired foreign intrusion. This changed in 1928 when yellow fever again broke out in Rio de Janeiro, for the first time in two decades. The federal authorities agreed to work with state public health authorities and complemented Cruz's fumigation with Gorgas-style draining and oiling. Results were disappointing, but a change of government in October 1930 meant unhampered federal initiative along IHC lines. This outbreak forced the scientists to realize that there were also rural animal reservoirs of the disease ("jungle yellow fever"-carrying monkeys), and that simply targeting the coastlines would never be enough. The International Health Division (name changed in 1927) shifted its efforts to the development of a vaccine.

Yellow Fever and Hemispheric Health Organization. The international epidemic of the 1870s that struck Argentina, Brazil, Paraguay, and Uruguay jumped northward by sea into the Mississippi Valley, resulting in a major outbreak of yellow fever in 1878. This prompted the United States to offer to host the Fifth International Sanitary Conference in 1881 in Washington, D.C. The conference was attended largely by diplomats and a few medical specialists, and an attempt was made to organize the kind of international reporting and communication that could stop the cross-border passage of disease. Participants also heard from Dr. Carlos Finlay about his theory of yellow fever's vector. By the end of the decade, the movement for hemispherical cooperation over issues of trade had resulted in the First International Conference of American States, held in Washington, D.C., in 1890. This body created the International Union of American Republics, which later became the Organization of American States. Delegates to the Second International Conference, in Mexico City in 1901, organized the First General International Sanitary Convention of the American Republics (Washington, D.C., 1902), which was to generate "sanitary agreements and regulations" to halt the spread of disease across the hemisphere. Also established was a permanent board for executive oversight, the International Sanitary

Bureau—later the Pan American Health Organization (PAHO)—the world's oldest continuing international health agency. Later in the century, it would be directly involved in the **World Health Organization** disease (smallpox, tuberculosis, measles) eradication programs. Yellow fever remained at the center of concern of these organizations, but by the time the Second International Convention convened, in Washington in 1905, the successes of Reed and Gorgas had borne fruit, and a pattern of international cooperation and action had begun to develop. The Third Convention (Mexico City, 1907) called for organized infectious disease information collection and communication by each member nation to the Bureau and urged the European powers with American colonies to join the Convention's efforts, especially with regard to yellow fever.

The successes of international cooperation and national efforts are evident in such cases as that of Bolivia, which established a Yellow Fever Service only in 1932. Since then about 10,000 cases have been reported, roughly evenly split between mosquito-borne and jungle types. 1936 saw the last mosquito-borne epidemic, and the *Aedes aegypti* mosquito itself was eliminated from the country in 1943. The existence of reservoirs of jungle yellow fever and continuing incursions into the previously undisturbed natural wilderness will ensure a flow of yellow fever cases. See also Environment, Ecology, and Epidemic Disease; Latin America, Colonial: Demographic Effects of Imported Diseases; International Health Agencies and Conventions; Sanitation Movement of the Nineteenth Century; Trade, Travel, and Epidemic Disease; Yellow Fever Commission, U.S.; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in the American South, 1810–1905.

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JOSEPH P. BYRNE

YELLOW FEVER IN NORTH AMERICA TO 1810. Between 1693 and 1810, **yellow fever** was one of the most dreaded of all **epidemic** diseases to afflict the American colonies and United States. It has not been possible to determine positively that yellow fever was present in this country before 1692. Although **smallpox** and **tuberculosis** had higher death rates, yellow fever struck so quickly and was so devastating that mortality

rates from 10 percent to 70 percent were not uncommon during epidemics. These factors and the disease's unknown cause helped spread fear and panic throughout the country. It was not until the beginning of the twentieth century that researchers found the cause to be a **virus** transmitted to humans when bitten by an infected *Aedes aegypti* mosquito. This explained why the disease was not contagious and why it occurred only during the summer months: the mosquito that carries the disease dies when cold weather arrives.

Yellow fever symptoms usually appear within six days of infection and range from very mild to so severe that death results. Classic cases are characterized by fever, headache, yellowish discoloration of the skin and body tissues, and bleeding into the stomach and intestinal tract. Individuals who recover from yellow fever have lifetime **immunity**. Because of the wide range of symptoms, yellow fever has always been difficult to diagnose and has been confused with many other illnesses such as **malaria**, scurvy, **typhoid**, and **typhus**.

The disease has been known by some 150 names. The yellowish color of affected skin caused it to be labeled yellow fever, while other names included "bleeding fever" and "Yellow Jack" (because of the yellow **quarantine** flag flown by ships). The black blood-laden fluids vomited by the victims provided the name "black vomit." It was first identified as "yellow fever" by Griffith Hughes in his *Natural History of Barbados* (1750).

Infected African mosquitoes probably accompanied to the New World ship-borne **slaves** who were immune to the disease's effects. The first recognizable epidemic in the Western Hemisphere struck Barbados in 1647 and then spread to other areas of the Caribbean. By the late 1600s, yellow fever had begun to be reported in the English colonies on the continent, chiefly in the major cities along the east coast that conducted **trade** with the Caribbean.

Charleston, South Carolina. The first yellow fever epidemic in Charleston began during the late summer of 1699 and killed nearly 200 individuals. The disease afflicted many government officials and caused great concern among the residents. Government and business activity nearly ceased until cold weather came, and the epidemic ended. Although physicians recognized the disease by its symptoms, its cause was not understood, and it was believed to be a contagious disease.

In 1706, French and Spanish armies stationed at St. Augustine, Florida, believed they could seize Charleston because yellow fever was once again ravaging the city. They were unable to overcome Charleston's fortifications and the spirited defense of its militiamen, while the yellow fever killed nearly 5 percent of the city's population of about 1,300 people. This epidemic also created havoc with government and commercial affairs and raged into October. But when cold weather arrived, Charleston was freed from its grip.

The city experienced an epidemic in 1728 and again only four years later. The 1732 epidemic reached its height in July with as many as 12 deaths daily. There were so many funerals each day that the city prohibited the tolling of funeral bells, and wealthier residents fled to country plantations to escape the disease. This epidemic killed 130 individuals, and all government and commercial affairs ceased until the cold winter weather began.

Charleston also experienced major epidemics during 1739, 1745, and 1748. The disease did not reach epidemic proportions again, however, until the summer of 1792 and each summer thereafter from 1794 to 1799.

Because it was believed that yellow fever was a contagious disease, quarantine laws were imposed, and a board of health was established in 1796. As the eighteenth century

came to a close, physicians began to realize that the disease was not contagious because those in close contact with yellow fever victims did not get the disease nor did it spread into the countryside.

New Haven, Connecticut. A severe outbreak of yellow fever occurred at New Haven in 1794 and killed about 70 percent of those who were infected. A ship from the West Indies arrived in June, and within days members of a nearby family came down with the dreaded disease. They had come in contact with clothes belonging to a sailor on the ship who died from yellow fever, and the clothes were thought to have brought the disease to New Haven. Noah Webster (1758–1843), of dictionary fame, observed and wrote about this epidemic. He believed that certain atmospheric conditions, such as the cleanliness of the **air**, determined whether or not the disease would spread in a certain geographical area. In this case, he theorized that some fish cleaned near the family's home may have contaminated the air and caused the family to become ill.

New York City. Yellow fever struck New York City during the summer of 1702. Twenty people died daily during this outbreak, and the final death toll reached nearly 600 persons or about 10 percent of the estimated population. City authorities spread quicklime and coal dust in the streets and lit bonfires in order to clean and sanitize the supposedly "corrupted" air.

Outbreaks of yellow fever ravaged New York City in 1743 and again in 1745. A 1795 epidemic killed 732 persons of an estimated population of about 50,000. The cause of this epidemic was greatly disputed, but most observers believed that the disease arrived aboard a ship. Another severe epidemic occurred in 1798, causing more than 2,000 deaths.

Philadelphia, Pennsylvania. The yellow fever epidemic of 1793 infected 17,000 people with 5,000 deaths (10 percent of the population). During the summer of 1793, thousands of French refugees came to Philadelphia from St. Domingue with news of the French Revolution and the yellow fever that raged in the Caribbean islands. The city was also in the grip of a lengthy drought, and the **water** was so low and drainage so poor in the waterways and marshes that rotting animals, dead fish, and sewage caused stagnation and horrible odors. Although unknown to anyone at that time, ideal conditions existed for the mosquito population to expand rapidly and spread the disease.

Philadelphia was then serving as the nation's capital while the city of Washington was being constructed, and the severity of the epidemic caused all government operations to cease. As the deaths began to mount, the mayor of Philadelphia asked the medical community and government officials to consider how the contagion might be controlled. It was at first deduced that hygiene and climate were responsible for causing the disease. Coffee beans brought by a ship from St. Domingue and left to rot on a wharf were also blamed for having caused the epidemic. A controversy about whether the disease was contagious or was caused by bad air added to the city's general fear and panic.

By September, those who could left the city. Among them were George Washington (1732–1799), other government officials, business people, and ordinary citizens. In all, some 12,000 people left the city to escape the dreaded pestilence. However, news of the Philadelphia plague was known throughout the region, and some refugees were robbed whereas others were quarantined at isolated locations. In Philadelphia, victims were often turned out by their own families, and the poor were left to die in the streets. Because the cause of the disease was unknown, all manner of preventive methods were tried, such as bonfires, sprinkling vinegar on clothing and household furnishings, and firing guns so that the smell of gunpowder would permeate the air.

As civil unrest and chaos spread through the city, the mayor was able to enlist volunteers to help run the government and take action to control the disease. **Hospital** care was improved so that people could successfully recover, an orphanage was established, the dead were properly disposed of, and relief was provided for the poor. Their work went so well that donations of money, food, and supplies began arriving. By November the disease had weakened, and the city was returning to normal. *See also* Colonialism and Epidemic Disease; Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Disinfection and Fumigation; Environment, Ecology, and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Latin America, Colonial: Demographic Effects of Imported Diseases; Public Health Agencies, U.S. Federal; Rush, Benjamin; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in the American South, 1810–1905.

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RICHARD EIMAS

YELLOW FEVER IN THE AMERICAN SOUTH, 1810–1905. Although **yellow fever** continued to afflict the United States during the 1800s, it was during this period that the disease eventually receded in the central and northern Atlantic coast regions. Nonetheless, it became an increasingly serious problem for the southern states into the early twentieth century.

The last significant yellow fever **epidemics** to strike the northeastern United States were in 1805 when major outbreaks occurred in both Philadelphia and New York. Although the disease appeared infrequently in succeeding years, another epidemic did not occur until 1819, when it struck Baltimore, Philadelphia, and Boston. It lingered for the next three summers in Philadelphia and Baltimore and made one final visit to New York in 1822. After that time, yellow fever was no longer a major problem for the states north of Virginia.

Although infected individuals continued to arrive at northern coastal cities, strict **quarantines** helped keep the disease from spreading. The shorter northern summers also limited the activities of the disease-carrying *Aedes aegypti* mosquito and contributed to the elimination of yellow fever in the central and northern Atlantic coast regions.

As the country grew and expanded south to the Gulf Coast states, profitable **trade** relationships developed with the West Indies, Africa, and South America. Sailing vessels frequently stopped for food and water at ports in the West Indies where yellow fever was common. Disease-carrying mosquitoes as well as infected passengers and crew often arrived on slave or trade ships from Africa or South America. As a result, yellow fever continued to be carried to the southeastern Atlantic coast and along the entire gulf shore

from Florida to Texas where the warm, damp climate was an ideal habitat for the *Aedes aegypti* mosquito.

Fortunately, when cooler winter weather arrived in late November or early December the mosquito population was greatly reduced, and yellow fever ended for that particular year. Nonetheless, yellow fever continued to return year after year, and it was rare that more than two or three years passed without a minor outbreak. Periodically the disease assumed major proportions, often destroying from 5 to 10 percent of the population.

Although it is now known that yellow fever is spread by the *Aedes aegypti* mosquito, its cause was still as great a mystery during the 1800s as it had been since it was first encountered 200 years earlier. Yellow fever was difficult to diagnose because early symptoms of the disease could easily be confused with other diseases. The medical community was aware that a diagnosis of yellow fever was certain to cause economic upheaval, possibly lead to panic and mass exodus and cause nearby towns to institute quarantines and blockades against the infected city. Therefore, they seldom dared make this pronouncement without first consulting their colleagues. Even then there was no assurance that the question was settled, for the findings were almost certain to be questioned. As a result, presence of the disease was rarely made public before the situation was beyond control.

As yellow fever became a serious threat to public health, it touched off a decades-long public debate concerning whether or not yellow fever was an imported contagious disease or a noncontagious fever generated in filth and decaying substances. The public tended to believe that it was a contagious disorder, whereas the medical profession generally felt that it was not a contagious disease.

Depending upon the severity of the epidemic, preventive measures included **disinfection** by spreading quicklime in gutters, sewers, and outhouses as well as in the graveyards and on the **corpses** of victims. Rooms and buildings where the sick had died were thoroughly cleaned and fumigated. Cannons were fired at sunrise and sunset, and barrels of tar were placed at street corners and burned during the night to fight the **miasma**. Since the cause of yellow fever was unknown, the effectiveness of these measures was questionable, though fumigants may have kept mosquitoes at bay.

New Orleans. New Orleans was the largest city on the Gulf Coast in the early 1800s with a population of 10,000. Although the city had experienced mild outbreaks of yellow fever in the late 1700s and early 1800s, it was not until 1811 that a more severe epidemic claimed 500 lives. In 1817 the disease claimed more than 800 victims. There was a minor outbreak the following year followed by a major epidemic in 1819. By 1820 the population exceeded 27,000, and 20 years later the city had over 100,000 inhabitants. Three successive epidemics from 1853 to 1855 claimed 14,000 lives. Following the 1858 epidemic, almost 5,000 yellow fever victims were counted among the dead. New Orleans experienced relatively few cases from 1859 to 1867, in large part because of the Union blockade and martial law during the Civil War. In the latter year, however, a major epidemic took 3,100 lives. A few scattered cases appeared in 1868 and 1869, and in 1870 the disease again flared up in epidemic proportions, killing almost 600 citizens. Throughout the 1870s cases appeared every summer, but only in 1873 and 1878 did the disease reach epidemic proportions. In 1873 the death toll was just over 200, but the 1878 epidemic resulted in over 4,000 deaths.

Although yellow fever cases continued to be diagnosed almost every summer, New Orleans had experienced the last of the great epidemics. The disease flared up once more in 1897, and on this occasion there were about 300 deaths. The disease struck again with

epidemic force in 1905. However, by this time, the role of the *Aedes aegypti* mosquito was more clearly understood, an effective program for mosquito **eradication** was implemented, and the epidemic was over before the end of August. Even so, this last outbreak of yellow fever in the United States brought death to 452 residents.

Other Southern Cities before the Civil War. Because of its size and role as the major southern port, New Orleans bore the brunt of these onslaughts, and the pattern established by the disease there was duplicated in dozens of other cities and towns. Charleston, South Carolina, only a third as large as New Orleans, experienced a similar pattern of outbreaks. A series of epidemics arrived in the late 1790s and early 1800s. Major epidemics struck the city again in 1817 and 1819, and after that time there was a succession of epidemics, with the peak being reached during the 1850s.

North Carolina also suffered several outbreaks of yellow fever. Wilmington was afflicted from 1796 to 1862, and New Bern and other towns were also affected. Georgia's major port, Savannah, suffered a series of yellow fever epidemics from 1800 to 1858. Because the Atlantic coast of Florida was sparsely settled and had no major ports, it largely escaped the disease. Even so, St. Augustine and Jacksonville suffered occasional epidemics in the years prior to the Civil War. Key West, off the tip of the Florida peninsula, and Pensacola, on the Gulf Coast, however, were frequently visited by the disease. The history of yellow fever in Pensacola is a repetition, on a smaller scale, of what happened in New Orleans and along the entire Gulf Coast.

In 1839, when yellow fever struck the city of Galveston, Texas, its population was just over 2,000, and the outbreak claimed 200 lives. For the rest of the 1800s, with only a few minor exceptions, whenever a major yellow fever epidemic broke out in New Orleans, it almost always afflicted the cities of Galveston and Houston.

The most northerly ports to suffer from yellow fever epidemics were Norfolk and Portsmouth, Virginia. Norfolk, which bore the brunt of the attacks, endured a series of epidemics starting in the 1790s and then experienced one final devastating blow in 1855. At the time of this epidemic Norfolk and Portsmouth had a combined population of between 25,000 and 30,000, and the number of deaths was close to 3,000.

During and after the Civil War. With some exceptions, yellow fever was not a major problem during the Civil War years 1861 to 1865. The effectiveness of the Northern blockade of Southern ports and the disruption of normal trade relations undoubtedly played a role in keeping yellow fever to a minimum. The chief epidemics of the war years occurred in Charleston, in Wilmington and New Bern, North Carolina, in Pensacola and Key West, Florida, and in Galveston, Texas. Following the war, the disease appeared infrequently during 1866 and then broke out in many places along the Gulf Coast in 1867, one of the major yellow fever years. From Pensacola to Brownsville, Texas, almost every town was affected. After a four-year lull, the pestilence returned in 1871 and again in 1873. In neither of these years, however, was it as widespread or as severe as in 1867.

During the 1870s, cases were reported nearly every summer in many of the Gulf Coast towns, but the disease did not generally become epidemic until the summer of 1878, a momentous year in the annals of yellow fever. The distinguishing characteristic of this outbreak was that it swept far up the Mississippi River. Almost from the beginning of the century, riverboats had carried yellow fever from New Orleans to many river towns in Louisiana and Mississippi. Natchez, Mississippi, more than 200 miles up the river from New Orleans, was first attacked in 1817 and suffered repeatedly in the succeeding years. Vicksburg, Mississippi, further north, witnessed its first outbreak in 1841.

By the 1870s railroad expansion and the development of faster steamboats, coupled with the gradual spread of the *Aedes aegypti*, made it possible for yellow fever to reach as far north as St. Louis. The 1878 epidemic struck first at Baton Rouge and Vicksburg, then at Memphis and Cairo, Illinois, eventually reaching St. Louis. At the same time, the disease moved up the Tennessee River to Chattanooga, Tennessee, and traveled up the Ohio River as far as Louisville, Kentucky. Memphis, Tennessee, which had a population of about 35,000, was hit the hardest with some 15,000 yellow fever cases and about 3,500 deaths. Vicksburg, another town to feel the full impact of the epidemic, reported more than 3,000 cases and over 1,000 deaths in a population of about 12,000.

Although the fever returned to New Orleans, Memphis, and a number of other cities in 1879, no serious epidemics developed. Throughout the 1880s and early 1890s, the United States enjoyed relative freedom from yellow fever. Scattered cases appeared here and there, but with the exception of an outbreak in Florida in 1888, the disease did not reach major epidemic proportions. The Florida epidemic was centered around Jacksonville on the Atlantic Coast and ranged inland as far as Gainesville. Before cool weather halted the disorder, the cases numbered in the thousands, and deaths in the hundreds.

The beginning of the end of yellow fever's seemingly endless attacks on North America came just three years after the disastrous yellow fever year of 1878, when Carlos Finlay y Barres (1833–1915) of Cuba theorized that the *Aedes aegypti* mosquito transmitted the disease. In 1900 the U.S. Army Commission on Yellow Fever in Havana headed by **Walter Reed** confirmed his theory with human volunteers at the cost of three additional lives.

There is no question that yellow fever slowed growth and development throughout the South, but the widespread epidemic of 1878 hastened the development of state and local health boards and was also responsible for the first attempt to create a national health department in the United States. Yellow fever played an important role in focusing attention on public health needs and in bringing pressure to bear upon legislative bodies to institute the necessary reforms to protect the health of its citizens. *See also* Contagion Theory of Disease, Premodern; Corpses and Epidemic Disease; Disinfection and Fumigation; Environment, Ecology, and Epidemic Disease; Insects, Other Arthropods, and Epidemic Disease; Public Health Agencies, U.S. Federal; Rush, Benjamin; Yellow Fever Commission, U.S.; Yellow Fever in Colonial Latin America and the Caribbean; Yellow Fever in Latin America and the Caribbean, 1830–1940; Yellow Fever in North America to 1810.

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YERSIN, ALEXANDRE (1863–1943). Swiss physician and microbiologist Alexandre Yersin is credited with having discovered the *Yersinia pestis* plague bacterium. He began his medical studies in his native Switzerland at Lausanne, followed by further studies at Marburg, Germany, in 1884, and at the Hôtel Dieu hospital in Paris in 1885–1886. He wrote his medical thesis on tuberculosis in 1888 while working on vaccinations against rabies at the Pasteur Institute in Paris. In the summer of 1889, he completed Robert Koch's course in bacteriology in Berlin, giving him exposure to the two leading—and competing—approaches in the new science. Returning to Paris later the same year, he worked with Emile Roux (1853–1933) on diphtheria and became a naturalized French citizen.

On the verge of a promising scientific career, the reclusive Yersin in 1890 suddenly fled the Pasteur Institute to travel to Indochina where, in 1892, Albert Calmette (1863–1933) was able to persuade him to join the French colonial health service. When news of the Hong Kong bubonic plague outbreak of 1894 reached Saigon, French health officials immediately despatched Yersin to the beleaguered British port.

Yersin arrived three days after a Japanese team headed by Shibusaburo Kitasato, who had studied under Koch in Berlin. The two men have been jointly linked to the discovery of the plague bacillus. Yersin, however, was the better scientist, and much later, his more accurate results eventually resulted in the taxonomic naming of the bacillus *Yersinia pestis* after him in 1971. Its earlier denomination had been *Pasteurella pestis*. Yersin's original description of the plague bacillus was concise and correct, whereas Kitasato's contained errors. In addition, only Yersin suggested that rats were a major factor in the transmission of the disease. Finally, only Yersin persisted in plague research, returning to Emile Roux's Paris laboratory in 1895 to develop an anti-plague serum from the blood of horses to boost human immune systems. Following his stint in Paris, Yersin returned to Indochina where he also developed a preventative anti-plague vaccine from a live but attenuated organism in 1896. It proved of limited value because it only afforded protection for two weeks. Later that year, Yersin traveled to plague-infected southern China to test the Pasteur Institute's anti-plague serum. In 1897 he appeared in Bombay for the same purpose, but the results in both China and India proved disappointing.

Yersin rarely returned to Europe after 1900. He helped found the Medical School of Hanoi in 1902 and was its first director. He also pioneered in the cultivation of rubber trees imported from Brazil. From 1904 until his death in 1943, he served as Director of the Pasteur Institute at Nhatrang, Vietnam. His burial site there later became a venerated pilgrimage site, and his memory is honored by the Vietnamese state. See also Pasteur, Louis; Third Plague Pandemic related articles.

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MYRON ECHENBERG

Z

ZOONOSIS. *See* Animal Diseases (Zoonoses) and Epidemic Disease.

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Glossary

Abscess: An inflammatory, pus-filled pocket created by the immune system to isolate a foreign object; the purpose is to contain the infection in this location and quickly remove the invader

Acute: Proceeding quickly and/or lasting a short time

Adsorption: The attachment of a virus to a cell

Aerosol, -ize: Small particles suspended in the air, such as small drops of liquid; to create small droplets spread into the air (i.e., through sneezing aerosolized droplets containing bacteria)

Agar: A chemical obtained from red algae or seaweed that forms a jelly-like consistency at room temperature; it is often used as a growth medium for bacterial or fungal cultures or as part of a method to separate parts of proteins and DNA

Agent: A substance or organism that has a specific and predictable effect on a cell or organism; an infectious disease used as a biological weapon

Alopecia: Loss of hair as the result of an autoimmune disease in which the body attacks hair follicles, preventing hair growth

Animalcule: An historic term used to describe microscopic organisms (single- or multi-celled)

Anthrax: A bacterium *Bacillus anthracis* which can cause a severe infection and, in some cases, death; transmission usually occurs through spores (the dormant form of the bacterium)

Antibacterial: A chemical applied to living tissue to prevent the growth of bacteria

Antibody: A protein produced by the immune system for the detection, and ultimately destruction, of foreign microbes

Antigen: A molecule (foreign or self) against which the body produces an immune response

Antimicrobial: A chemical that prevents growth of microorganisms, typically disease-causing microbes

- Antisepsis, -tic:** The use of antimicrobials on tissue to kill bacteria and prevent infection
- Antiserum:** Fluids passed from one organism to another, containing specific antibodies for the purpose of passing on immunity (i.e., acquired immunity)
- Arbovirus:** A virus transmitted to humans by an arthropod (short form of “arthropod-borne virus”)
- Arenavirus:** A genus (or large group) of viruses that exist in animals; often they are transmitted to humans by rodents
- Armamentarium:** The total collection of resources and equipment used by physicians or a hospital
- Aseptic:** The technique used to prevent contamination by foreign microbes when working with either bacterial cultures or sterile objects
- Aspirates:** Objects removed by aspiration, or the collection of a sample that has been aspirated (suctioned up) into a dispensing tube or pipette
- Asymptomatic:** Without symptoms of a disease; occasionally a disease is present with no symptoms, hindering diagnosis
- Attenuated:** Weakened; referring to a less virulent form of a virus used in vaccines to allow for immunological resistance to that virus
- Autoimmune:** The inability of the immune system to recognize parts of the body as self, resulting in the body attacking itself
- Avirulent:** Not disease-causing
- B cell:** A cell of the immune system that produces antibodies
- Bacillus (pl. bacilli):** A rod-shaped bacterium; a member of the genus *Bacillus*
- Bacteriology, -ist:** The study of bacteria and scientific applications; one who studies bacteria
- BCG vaccine:** Bacille Calmette Guerin vaccine made from a bacterium related to tuberculosis to immunize individuals against the disease
- Benign:** A disease that is not progressing; a noncancerous tumor
- Bezoar Stone:** A “stone” found in the intestines made from undigested food, such as salts
- Bills of Mortality:** Mortality counts reported weekly by causes of death and parishes of Londoners, compiled by local parish officials and published as pamphlets; began in Italian cities in the fifteenth century and in England in the early sixteenth century; lasted into the nineteenth century
- Bioinformatics:** The study of biology using mathematics and computer science for modeling and organization of molecular biology information
- Biopsy:** A procedure used to diagnose cancer in which a piece of tissue is removed and examined or analyzed
- Biovar:** A bacterial strain that differs from others (of the same species) in biochemical or physiological characteristics
- Bleeding:** Also “bloodletting” or “phlebotomy”; the premodern medical practice of opening a patient’s vein with a sharp lancet and letting blood flow in a controlled manner; according to humoral theory, this helps balance the body’s humors for good health or healing
- Bloodletting:** See “bleeding”

- Broad-spectrum:** Referring to an antibiotic's ability to target a wide range of bacterial classes of pathogens, as compared to narrow spectrum antibiotics
- Bubo:** A visible swollen lymph node at the armpit or groin, characteristic of the bubonic plague, gonorrhea, syphilis, or tuberculosis
- Caravanserai:** A stopping place for caravans, usually provided with food, water, shelter, and a wall around the site
- Carrier:** An individual who has either an infection or genetic trait with the ability to transmit it to another; may not display characteristics
- Case fatality rate (CFR):** The proportion of individuals who die from a disease
- Catarrh:** A runny nose; mucus drainage
- Cell:** The basic unit of life that contains elements necessary to reproduce, metabolize, and maintain homeostasis, or internal consistency; cells can be specialized to form a tissue or they can exist as single-celled organisms
- Chemoreceptor:** A type of cell that converts a chemical signal (from a protein or other chemical) into an electrical signal within the cell, which allows for fast responses
- Chemotherapy:** Any treatment for a disease using a chemical, most often refers to treatments for cancer that stop cell multiplication
- Chromosome:** A compact piece of DNA that forms in a dividing cell; humans have 23 pairs
- Chronic:** Lasting a long time or recurring frequently
- Chronic disease:** A long-lasting, continuous disease; typically refers to a disease with symptoms that are apparent for more than three months
- Cilium (pl. cilia):** An extension of a cell that either provides movement or is used for sensing the environment
- Clinical:** Referring to the treatment or observation of patients in a controlled setting
- Clone:** An organism that has the same DNA as another
- Commensal, -ism:** A type of symbiosis, a relationship between two organisms such that one benefits from the relationship and the other is not significantly affected
- Constitution, -al:** The total of an individual's physical makeup; relating to an individual's well-being
- Culture:** n. A mass of microbes; v. To create such a large group of cells by spreading them over agar to allow them to grow quickly—a technique used largely for identification of disease
- Dejecta:** Feces or excrement
- Delirium:** A sudden loss of cognition
- Demographic:** Referring to characteristics of a certain population (e.g., race, age, income)
- Dendritic cell:** A cell with dendrites, or cellular projections; dendritic cells of the immune system produce antigens (or recognition sites) for T cells
- Dermatitis:** Inflammation of the skin
- Didactic:** Performing an educational function
- Differential diagnosis:** A systematic method of determining the cause of a patient's disease by exploring symptoms, referring to the patient's family, and examining the patient

- Diuretic:** A drug that increases urine production in the kidneys, causing an increase of water loss from the body
- DNA (deoxyribonucleic acid):** A double helix found in every organism for the purpose of storage, replication, and expression of cellular information; found in the nucleus of human cells
- Dye:** Used to stain, or color, specific parts of the cell either to make the cell more visible or to highlight particular parts
- Ecology:** The patterns of interaction of all various plants and animals within a specific environment
- Ectopic:** Displacement of a bodily organ, for example, the development of both kidneys on one side of the body
- Edema:** The swelling of an organ or tissue because of an excess of fluid outside the cells
- Electrolyte:** Ions (atoms with charges) found in the body used to maintain a charge across the membrane of the cell, particularly in nervous, cardiac, and muscular tissue
- Electron Microscope:** A microscope with a very high magnification that works by passing electrons through the sample to get a picture
- Electuary:** A drug made into a paste with sugar or honey to be administered orally
- Eliminate:** To remove all natural incidence of a disease from a given area
- Emergent disease:** A disease or variation of a disease that is increasing its presence in human populations for the first time, especially in an endemic or epidemic level
- Endemic:** Referring to a disease that is maintained in a population over a long period of time; from a certain area or population
- Enteric:** Referring to the intestines
- Enterotoxin:** A toxin produced from certain bacteria that affect the digestive system; food poisoning comes from the ingestion of these bacteria, whose toxins are poisonous
- Environment:** The external conditions in which an organism lives and with which it interacts
- Enzootic:** An “endemic” disease present in an animal rather than a human population
- Enzyme:** A protein that speeds up a reaction or process in a living organism
- Epiphenomenon (pl. epiphenomena):** A byproduct of another event
- Epithelial cells:** Those cells forming the issue that provides the lining of bodies (i.e. the skin, intestinal lining, respiratory lining, and mucus membranes)
- Epizootic:** An unusually widespread disease present in an animal population
- Eradicate:** To “uproot” or eliminate the natural occurrence of a disease completely from the earth; to date only smallpox has been eradicated
- Etiology:** The cause of a disease
- Ex voto:** A religious object dedicated to thanking a saint or deity, often for lifting an epidemic
- Exanthem (pl. exanthemata):** A widespread rash found on an individual; usually caused by a virus or bacterial infection or an allergic reaction to a drug
- Excreta:** An organism’s waste material
- Exotoxin:** A protein excreted by a microbe that is harmful to the host

- Express:** To show the characteristics of having a particular gene (e.g., expressing blonde hair as the result of having certain genes)
- False positive/false negative:** An inaccurate result of a test for the presence of a given disease
- Febrile:** Relating to a fever; an increase in body temperature
- Feudal:** Pertaining to the medieval European social and political hierarchy that was based upon the agricultural labor of peasant serfs and noblemen's oaths of homage
- Focus:** With reference to an epidemic disease, the geographic point of origin or a long-lasting reservoir
- Fomite:** Any inanimate object that may carry an infectious disease
- Genocide:** Deliberate destruction of, or attempt to destroy, an ethnic human population
- Genome:** The whole genetic sequence of an individual, including the coding and noncoding portions of DNA
- Genotype:** The genetic information stored for an individual, usually describing genes inherited for a particular trait; as compared to phenotype
- Genus (pl. genera):** The subgroup of organisms under the family; in the scientific name, the genus is the first, capitalized word
- Germ:** Generic term for a microorganism, usually pathogenic, such as a bacteria or fungus
- Gram-positive/Gram-negative:** The result of a Gram stain, which produces a purple (positive) or pink (negative) color depending on the composition of the bacteria's cell wall; the Gram stain is a method used to separate bacteria into two major groups
- Granuloma:** An area of dense inflammatory tissue, often associated with hypersensitivity toward a chronic infection
- Hematemesis:** Vomiting blood; caused by erosion of the stomach or esophagus as the result of an infection, ulcer, or other disease
- Hematuria:** Blood in the urine, observable in most conditions only by viewing red blood cells under a microscope
- Hemorrhage, -agic:** Bleeding, or relating to bleeding
- Herd immunity:** The theory that vaccinating the majority of the population for a disease will help prevent the rest of the population from acquiring it because of the lower number of carriers
- Heterozygote:** A person with two different versions of a particular gene
- Hominin:** A being that is a human or human ancestor, including chimpanzees
- Homozygote:** A person with two copies of the same version of a particular gene
- Horizontal gene transfer:** The transfer of genetic information between bacteria that is not from parent to offspring
- Host:** Any living organism that provides its machinery (reproductive, metabolic) for the use of a virus or parasite
- Humor:** Fluid in the body; comes from the ancient belief that a disease comes from the four fluids in the body (blood, yellow bile, black bile, and phlegm) being out of balance
- Hydronephrosis:** Stretching, or distension, of the kidney, as the result of a blockage of the uterine tube causing urine to build up in the kidney

- Hyperemia:** Increased blood flow to a particular part of the body
- Hypodermic:** Beneath the skin
- Hypotension:** Low blood pressure
- Hypothesis:** The premise that an experiment is designed to test
- Iatrochemical:** Relating to iatrochemistry, a branch of chemistry from the sixteenth and seventeenth centuries that attempted to find a cure for diseases with chemistry
- Immunity:** The ability of the body to fight off a disease easily because of previous exposure
- Immunogenic:** The ability to illicit an immune response
- Immuno-suppressed:** Having an immune system that is less active, either because of a disease or as the result of certain medical treatments (i.e., chemotherapy)
- In utero:** In the uterus
- In vitro:** Occurring in a controlled environment outside a living organism; literally, in glass
- In vivo:** In a live system
- Incidence:** The number of new cases of a disease (contraction, death) that develop over a particular period of time
- Incubation:** The process of disease development between the infection of a person and the first appearance of symptoms
- Indian Medical Service:** British colonial governmental organization (1886–1947) dedicated to the health care of British military and citizens, and by extension of the native peoples, in India
- Indigenous:** Native to a particular region or locale
- Infarction:** The loss of blood supply to part of an organ leading to death of tissue
- Infectious:** Referring to a disease caused by a microbial agent
- Infectious period:** Period of time during which an infected person can transmit a given disease to another
- Inflammation:** A response to an infection or irritant that results in swelling, redness, warmth, and pain
- Intracellular:** Inside the cell
- Laboratory assay:** An experiment performed in a laboratory that attempts to quantify a property of a substance
- Latent:** Present, but hidden; a disease that does not show symptoms for a period of time
- Lesion:** An abnormality in the tissue of an organ as a result of disease or injury
- Lethality:** The ability of a disease to cause death
- Leukocyte:** White blood cell
- Lipid:** A fat molecule, such as a fatty acid or steroid, that is insoluble in water
- Lymphocyte cell:** A kind of white blood cell that is involved in the immune response by producing antibodies, allowing for the specificity of the immune system
- Lyse:** To break open; usually referring to the breaking open of a cell by disruption of the cell membrane

- Macrophage:** A differentiated white blood cell that ingests dangerous foreign substances, such as bacteria or cancer cells
- Macroscopic:** Observable with the naked eye, not needing a microscope
- Malignant:** Referring to a disease that is progressively worsening; commonly referring to cancer that has spread to other parts of the body
- Memento mori:** A cultural symbol or reminder of human mortality and death
- Metabolic:** Referring to metabolism or the digestion of nutrients
- Miasma:** The historic theory that disease is spread through “bad air”
- Microbe:** A microorganism
- Microbiology, -ist:** The study of microorganisms, specifically those that are pathogenic, or cause disease; a person who studies microbiology
- Microorganism:** A microscopic living organism, such as a bacterium, fungus, or protozoan
- Mitosis:** The process by which cells divide in order to increase number of cells; particularly the dividing of the cell nucleus
- Monocyte:** A type of white blood cell found in the blood that is part of the immune system and fights bloodborne pathogens
- Morbidity:** The incidence or prevalence of total and/or new cases of a disease
- Mortality:** The number of deaths as the result of a disease
- Motile:** Able to move independently
- Mucus:** Secretion of the mucus membranes found in the nose, lips, throat, ears, and genitalia, used to collect foreign objects after they have entered the body or as a lubricant for movement such as food down the esophagus
- Murine:** Referring to rats or mice
- Mutate, mutation (genetic):** A change in information of DNA, resulting in different characteristics
- Neonatal:** Relating to a newborn infant, typically within four to six weeks after the child is born
- Neurasthenia:** A diagnosis made in the late 1800s for individuals expressing symptoms of fatigue, thought to be caused by an urbanized civilization; probably used to describe a wide variety of diseases
- Neurologic:** Referring to the nervous system; a disease that affects the central nervous system
- Neutrophil cell:** An immune cell that ingests foreign invaders (bacteria) through phagocytosis and digests them; they contain many sacs of digestive enzymes for this purpose
- Niche:** The ecological job of an organism in its environment, especially its role in the food chain
- Nonspecific:** Not specific, used to describe an infection caused by an unknown pathogen
- Nosological:** Referring to the classification of diseases
- Nucleus, -ei:** The membrane-bound organelle of the cell that contains genetic material (DNA), found in eukaryotic cells (not present in bacterial cells)
- OED:** Oxford English Dictionary; a standard source for English word etymology and history

- Opportunistic:** A disease that infects after another infection has weakened the immune system
- Organism:** A living being, existing as a single cell, such as a bacterium, or a multi-cellular organism, such as a human being
- Outpatient:** A patient who does not have to stay in a hospital for treatment; outpatient surgery allows the patient to return home the same day
- Papular:** Having papules, or raised bumps on the skin
- Parasite:** An organism that requires the resources of another organism (its host) to live and reproduce
- Parasitology, -ist:** The study of parasites and their relation to their hosts; one who studies parasites
- Paroxysm:** A sudden onset of symptoms, usually painful, from a disease
- Pathenosis:** The concept that in any given time and place a group of diseases exists together, but should one disappear, another will take its place
- Pathogen:** Any biological agent that causes disease (bacterium, virus, parasite)
- Pathogenic:** Capable of causing disease
- Pathological:** Referring to behaviors that are caused by mental illness or instability, and/or being abnormal or extreme
- Pathology, -ist:** The study of disease: its causes, development, treatment, and diagnosis
- Periodicity:** Occurring at discrete and regular intervals, usually time intervals
- Petri dish:** A shallow dish used to hold small biological samples for observation; may contain agar for bacterial growth
- Phage:** A virus that attacks a bacterial cell, also bacteriophage
- Phage Typing:** Using the mode of action of a virus to identify a particular bacterium that the phage specifically attacks; detection is done by staining the viruses prior to infection and identifying the stain following infection
- Phagocytosis:** The cellular process of ingesting large particles by means of folding the cellular membrane into a pocket that pinches off into the cell to form a vacuole
- Pharmacopoeia:** A book that contains a list of medicines in wide use as well as information about their preparation
- Phenotype:** The expressed genetic information for an individual that is visible to an observer; as compared to genotype
- Phlebotomy:** See “bloodletting”
- Physiology, -ist:** The study of the ways in which the human body functions; one who studies the body
- Placebo:** A pill or other medium with no medication given as a control in a study (to see if giving a remedy has an effect without the medication)
- Plague/pestilence:** Often used generically for epidemic disease outbreaks of various types, including insect infestations (e.g., a plague of locusts); specifically, plague refers to *Y pestis* infection
- Plasmid:** A circular extra piece of DNA typically found in bacterial cells; scientists alter plasmids, causing bacteria to make desired proteins

- Pneumonia:** An infection of the lungs in which the oxygen-containing sacs of the lungs become filled with fluid as an immune response to a foreign pathogen
- Polydactyly:** Having more fingers or toes than normal
- Polymorphism:** The existence of a variety of forms of gene, or alleles, present in a population
- Prevalence rate:** A calculated term used to describe how a disease has spread
- Prion:** a protein that acts as an infections agent causing such diseases as mad cow disease or Creutzfeldt-Jakob disease
- Prodromal:** period of time during which a disease is taking its course but not manifesting symptoms
- Progenitor:** An ancestor; a progenitor cell is an undifferentiated cell that can differentiate into specialized cells
- Prognosis:** A doctor's prediction of the development of a disease in a patient (how long the patient is expected to live)
- Prophylaxis, -actic:** An attempt to prevent an infection by protecting the body before an exposure to a pathogen; prophylactics are drugs, actions, or other means believed to protect a body or community against disease
- Proteinaceous:** Made of proteins, or the macromolecule composed of amino acids which act as enzymes, messengers, or antibodies, and also serve many other roles
- Proteomics:** The study all of the proteins of an organism
- Protist:** A member of the kingdom Protista, usually a single-celled, prokaryotic organism (a cell that does not have a membrane-bound nucleus)
- Pseudopod:** Literally, a false foot; an extension of the cellular membrane from an amoeboid cell used for locomotion or for sensing the environment
- Public health:** The study and practice of preventing and treating community-wide disease; community may be defined from local to global
- Pulmonary:** Referring to the lungs
- Purgative:** Causing cleaning or purging, particularly of the bowels; a medicine that does so
- Pus:** A yellow-white liquid produced as part of an inflammatory response to an infection that includes dead immune cells that have killed the pathogen
- Pustule:** A collection of pus directly under skin, a pimple made of pus
- Putrefaction:** (premodern) deterioration of the structure or life force of a person, organ, or other object as a result of the effects of corrupted air or other substance; (modern) the breakdown of tissues before or after death caused mostly by bacterial infections
- Quartan fever:** A fever that has lasted 72 hours (i.e., into a fourth, *quartus*, day) intermittently; this is indicative of a bacterial infection
- Quiescent:** Lacking activity, being at rest; a disease causing no symptoms
- Receptor (cell wall):** A protein found on a cell wall that responds to a specific protein or chemical signal to cause a change within the cell
- Reemergent disease:** A disease that once affected a particular area or population, was largely eliminated, and then reappeared in endemic or epidemic form

- Regimen:** A regulated course of action; for example, a schedule of daily antibiotics or a specific diet
- Replicate:** Making a copy; DNA replication is the method by which DNA duplicates to be passed to two daughter cells during cell division (mitosis)
- Reservoir:** A host for a pathogen in which the pathogen is often undetected for a long period of time
- Resistance:** Acquired or evolved ability of an organism to avoid being negatively affected by another organism or drug
- Respiratory:** Referring to the respiratory system; the organ system that deals with gas exchange in an organism
- Retrovirus:** A virus that contains RNA (instead of DNA) as its genetic material; these viruses contain proteins to allow the RNA to be copied as DNA and thus to be used by the host cell
- RNA (ribonucleic acid):** A form of genetic information storage that is mostly used for transmitting information from DNA to making proteins, copied from the DNA template
- Sarcoma:** A cancer of connective tissue (bone, blood, cartilage), as opposed to epithelial tissue of an organ
- Screening:** Studying a particular feature or physical trait through examining a large number of individuals
- Secondary infection:** An infection that occurs during or as a result of another infection
- Sepsis:** Also known as blood poisoning, an excessive immunological response to an infection, either caused by the infection or by a dysfunction in the immune system, which causes the circulatory system to malfunction and eventually to lead to organ failure
- Septicemia:** See sepsis
- Sequelae (pl. sequelae):** A continuing pathological condition caused by a previous infection or trauma
- Serogroup:** A group of microorganisms that have a common antigen
- Serological:** Pertaining to serology, or the characterization of immunological substances including antibodies and antigens
- Seropositive:** Having a particular antibody present in the blood; often used to test if an individual has been exposed to a particular infectious agent
- Serotype:** The testing of a microorganism for the presence of a specific antigen, or a microorganism that has a tested antigen
- Serum:** Plasma with clotting factors removed
- Simian:** relating to monkeys, apes, and other nonhuman primates
- Species:** The smallest classification of organisms in the scientific organization of all organisms, grouping organisms that are the closest related; for example, *Homo sapiens*, is the genus and species name of man
- Sporocyst:** A sack that encases spores, or the reproductive elements of asexual organisms; the larval form of parasitic worms
- Sputum:** Mucus or phlegm from the respiratory tract that comes up when coughing
- Stain:** The coloring of a specific biological element to distinguish it from others; for example, a bacterium can be stained to test if it is Gram-positive or Gram-negative (see definition),

or cells and tissues can be stained to visualize a particular component such as nuclei or DNA

Strain: A genetic type or variation of an organism, especially a human pathogen

Sylvatic: Referring to a wild as opposed to a domestic state of animals; pathogen that affects only wild (not domesticated) animals

Symbiotic: A relationship between two organisms of different species in which at least one of the organisms benefits and the other is not harmed

Symptom: A physical or psychological abnormality in a person that suggests the presence of one or more pathogens or disease states

Synchrony: Simultaneous or near simultaneous occurrence of two or more events

Syndrome: The combination of signs and symptoms of a patient's disease; the observable results of a disease that allow for detection

Systemic: Referring to a body system or the body in total

T cell: One type of cell of the immune system that helps to fight against infection by recognizing infection in other cells

Tertian fever: A fever that occurs every third (*tertius*) day (after 48 hours), usually referring to the fevers caused by malaria

Therapeutic: Ability to heal or to benefit the immune system

Therapy: The treatment of an illness or disease

Theriac: A premodern Western general remedy composed by apothecaries of many ingredients including snake flesh

Tissue: A collection of cells that perform a similar function, tissues combine to make organs

Toxin: A chemical that is harmful to an organism produced by living organisms

Transmission rate: Average number of people who catch a disease from an infected person over a given period of time

Unguent: An ointment used to soothe a wound on the surface of the body

Variolation: An outdated method to immunize an individual for smallpox by the controlled infection with the smallpox virus

Vector: An object or organism (often an animal) that does not cause a disease itself but that carries the pathogen from one organism to another

Vernacular: Language of the common people; often as opposed to Latin, Arabic, Sanskrit or other scholarly or literary languages with multicultural audiences

Virgin-soil epidemic: Initial outbreak of an infectious disease previously unknown to or absent from a specific geographical area for many generations

Virology, -ist: The study of viruses and diseases they cause; one who studies viruses and viral diseases

Virulence: A microorganism's level of ability to infect and cause disease

Zoonosis, -tic: A pathogen that is normally spread through animals

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About the Editor, Advisory Board Members, and Contributors

About the Editor

JOSEPH P. BYRNE (M.U.P., University of Washington, 1979; Ph.D. in History, Indiana University, 1989) is a cultural and social historian of medieval and early modern Europe and Professor of Honors Humanities at Belmont University in Nashville, Tennessee. He has written extensively for a wide variety of historical reference works and journals and has recently published *The Black Death* (2004) and *Daily Life during the Black Death* (2006) with Greenwood Press. Preparation of these present volumes has taken him to Harvard University, as well as London, Oxford, and Norwich in the UK. He is currently preparing a single-volume, interdisciplinary encyclopedia on plague in the medieval and early modern world.

About the Advisory Board

ANN G. CARMICHAEL possesses M.D. and Ph.D. degrees from Duke University and teaches the history of infectious diseases at Indiana University, Bloomington. One strand of her research publications focuses on plague, pestilence, and underlying health conditions in Renaissance Italian city-states, especially Florence and Milan. The most recent of these is “Universal and Particular: The Language of Plague, 1348–1500” in *Pestilential Complexities: Understanding Medieval Plague* (2008). Within the last decade she has also published several articles on the history of climate and infectious diseases.

KATHARINE DONAHUE heads a special collection focused on the history of medicine and biology with works dating from the fifteenth through twentieth centuries. Previous to her position with UCLA, she was the Museum Librarian of the Natural History Museum of Los Angeles County. She is interested in medical and natural history images and the techniques used to create them as well as the transmission and persistence of images through time.

JOHN PARASCANDOLA retired from the federal government in 2004 after 20 years of service as Chief of the History of Medicine Division of the National Library of Medicine and as Public Health Service Historian. His awards include the Surgeon General's Exemplary Service Award (1989 and 1996). His book *The Development of American Pharmacology: John J. Abel and the Shaping of a Discipline* was awarded the George Urdang Medal (1994) from the American Institute of the History of Pharmacology. His latest research project concerns the history of syphilis in America.

CHRISTOPHER RYLAND is Assistant Director for Special Collections at Vanderbilt University Medical Center's Eskind Library. He received his M.S.I.S. from the University of Tennessee.

WILLIAM C. SUMMERS is Professor of Molecular Biophysics and Biochemistry and of History of Science and Medicine at Yale University. His books include *Felix d'Herelle and the Origins of Molecular Biology*, and he edited the *Encyclopedia of Microbiology*, second edition. His current book manuscript focuses on the geopolitics of epidemic disease in Manchuria in the early twentieth century.

About the Contributors

AVA ALKON holds an M.P.H. and is a doctoral candidate in the Sociomedical Sciences Department at the Graduate School of Arts and Sciences and the Mailman School of Public Health at Columbia University. She studies history and public health, with a focus on vulnerable and institutionalized populations.

MARCELLA ALSAN holds an M.D. and an M.P.H. and is a Ph.D. candidate in Economics at Harvard University and a physician in the Howard Hiatt Global Health Equity Program at Brigham's and Women's Hospital, Boston. Her research is focused on the role of health interventions in poverty alleviation and human development.

ROBERT ARNOTT is Professor of the History and Archaeology of Medicine and Director of the Centre for the History of Medicine in the School of Medicine of the University of Birmingham (UK). He is an authority on the history of disease and medicine in the eastern Mediterranean in prehistory and his major work on *Malaria in the Aegean Bronze Age* will appear in 2008.

SUZANNE AUSTIN is Professor of History at the University of Delaware. Her books include *A Pest in the Land: New World Epidemics in a Global Perspective* and *Native Society and Disease in Colonial Ecuador*. She is currently working on a book, *Environment and Empire: European Colonialism and Environmental Change*.

ROBERT BAKER is William D. Williams Professor of Philosophy at Union College and Director of the Union Graduate College-Mount Sinai School of Medicine Bioethics Program. He has coauthored several books including *Ethics and Epidemics*, *The American Medical Ethics Revolution*, and *A History of Medical Ethics*. He is currently conducting research for a documentary history of American medical ethics and is researching the relationship between African American physicians and organized medicine.

RICHARD BARNETT completed his Ph.D. at the Wellcome Trust Centre for the History of Medicine at University College London. His current research focuses on British state medicine in the interwar period and the concept of degeneration in Victorian life science.

ANJA BECKER is a Postdoctoral Fellow at Vanderbilt University funded by the German Academic Exchange Service (DAAD). In her dissertation on Academic Networks of American Students at Leipzig University (1871–1914), she also discussed medical education in nineteenth-century Europe and America. Her current research is on higher education in the American South and West between the Civil War and World War II.

CHARLES V. BENDER earned his M.D. in 1974 from Ohio State University and currently is an Associate Professor of Obstetrics, Gynecology, and Reproductive Sciences at the University of Pittsburgh School of Medicine. He also serves both the Children's Hospital of Pittsburgh and Magee-Womens Hospital as a pediatrician and neonatal specialist.

THOMAS BENEDEK is Professor of Medicine, Emeritus, at the University of Pittsburgh School of Medicine. He is also past president of the American Association for the History of Medicine. His recent publications include "The History of Gold Therapy for Tuberculosis" (2004), "Gonorrhoea and the Beginnings of Clinical Research Ethics" (2005), and "The History of Bacteriologic Concepts of Rheumatic Fever and Rheumatoid Arthritis" (2006).

MARK A. BEST holds an M.D. and an M.B.A. from the University of Louisville and an M.P.H. from Case Western Reserve University. He is a former Fellow of the Veterans Administration National Quality Scholars Fellowship Program and is Associate Professor of Pathology. He coauthored *Benjamin Franklin: Verification & Validation of the Scientific Process in Healthcare* and has written numerous articles, book chapters, and book reviews on laboratory medicine, health-care systems, and health-care quality improvement.

SANJOY BHATTACHARYA is a Reader in History at the Wellcome Trust Centre for the History of Medicine at University College London. He specializes in the history of nineteenth- and twentieth-century South Asia, as well as the history of international and global health programs deployed on the subcontinent and beyond. Dr. Bhattacharya's current work examines the structures and workings of health programs sponsored and managed by United Nations' agencies like the World Health Organization; the development of public health and medical institutions at all levels of national and local administration; and the diversity of social and political responses to state- and non-governmental organization-run schemes of preventive and curative medicine. Dr. Bhattacharya is the author of several books and articles dealing with the history of medicine of South Asia and World Health Organization activity in the region.

KARL BIRKELBACH is a Ph.D. candidate in History at the University of Western Australia. His research interests include medieval and early modern plagues. His dissertation, *Plague Debate: A Turning Point in Historiography*, investigates shifting perceptions of plague and its history.

ANNE-EMANUELLE BIRN is Canada Research Chair in International Health at the University of Toronto. Her research explores the history of public health in Latin America

and the history and politics of international health. She is the author of *Marriage of Convenience: Rockefeller International Health and Revolutionary Mexico* (2006) and coauthor of the forthcoming *Textbook of International Health* (Oxford University Press). Her current project examines the early twentieth-century international circulation of child health ideologies and policies from the perspective of Uruguay.

DEVON BOAN is Professor of Honors and Director of the Honors Program at Belmont University in Nashville, Tennessee. He has a Ph.D. in Literature from the University of South Carolina and writes on cultural issues, religion, and the arts. His book *The Black "I": Author and Audience in African American Literature* is published by Peter Lang.

KRISTY WILSON BOWERS is Visiting Assistant Professor of History at Northern Illinois University. Her most recent article, "Balancing Individual and Communal Needs: Plague and Public Health in Early Modern Seville," appeared in the *Bulletin of the History of Medicine*. Her current projects include a book manuscript on the impact of plague in sixteenth-century Spain and an article examining debates on surgical methods in seventeenth-century Spain.

LINDSAY BROOCKMAN is a recent graduate of the Development Studies program at Brown University, with a thesis on water sustainability on the U.S.-Mexico border. She has led rural development projects in central Ecuador and Chiapas, Mexico. Currently she is a Manager at the AIDS Action Committee of Massachusetts and has significant experience with nonprofit program coordination and grassroots community organizing.

MARTIN CALLAGHAN, D.Phil., is a research scientist at the University of Oxford Department of Paediatrics where he works within the Oxford Vaccine Group. His current research interests focus on the development of novel vaccines against meningococcal meningitis, and his publications include articles on the molecular evolution of meningococcal adhesins, human genetic susceptibility to meningococcal disease, and the molecular evolution of bacterial restriction-modification systems.

DENNIS GREGORY CARAMENICO studied Italian history (largely that of Renaissance Florence), the history of biology and memory, and medieval Jewish-Islamic philosophy at Vanderbilt University. He received an MA in history from Vanderbilt (2006) with a thesis on Platonic *anamnesis* in Dante's *Paradiso*. He is currently studying the evolutionary psychology of memory.

K. CODELL CARTER is Professor of Philosophy at Brigham Young University. His books include *The Rise of Causal Concepts of Disease* and *Childbed Fever: A Scientific Biography of Ignaz Semmelweis*. He is currently conducting research on the philosophy of Immanuel Kant.

VINCENT J. CIRILLO, Ph.D., an independent scholar in the history of medicine, is past president of the Medical History Society of New Jersey. He is the author of *Bullets and Bacilli: The Spanish-American War and Military Medicine* (2004), published by Rutgers University Press.

ROGER COOTER is a Professorial Fellow at the Wellcome Trust Centre for the History of Medicine at University College London. The author of histories of phrenology, popular

science, and orthopedics, and the editor of volumes on child health, war, and medicine; alternative medicine; accidents; and, with John Pickstone, *The Companion to Medicine in the Twentieth Century*. He is currently engaged with Claudia Stein in a study of health posters and health exhibitions in Germany and Britain.

ROHAN DEB-ROY is an M.A. in History from the Presidency College Calcutta, India (2004) and holds a Diploma in Academic Research and Training from the Centre for Studies in Social Sciences Calcutta (2005). Currently he is a Doctoral Candidate at the Wellcome Trust Centre for the History of Medicine at University College London. He was awarded a three-year doctoral fellowship from the Centre (2005). His dissertation focuses on certain aspects of pharmaceutical botany, entomology, and knowledge of “malaria” in the nineteenth century. He has been awarded the Ashin Dasgupta Prize (Presidency College, 2004) and the Roy Porter Prize (University College London, 2005).

KLAUDIA DMITRIENKO is a doctoral candidate in the Department of Public Health Sciences at the University of Toronto with a background in health promotion and international relations. Her research interests focus on the political economy of global health; she is currently exploring the history of Canadian international health policy for her dissertation.

BART DREDGE is Associate Professor and Chair of Sociology at Austin College in Sherman, Texas. His research interests include labor in the American South, with special teaching attention to occupational disease and research on human subjects. His dissertation at the University of North Carolina at Chapel Hill was entitled “From Dust to Dust: Byssinosis and the Carolina Brown Lung Association, 1975–1990.”

JACALYN DUFFIN is Professor in the Hannah Chair of the History of Medicine at Queen’s University in Kingston, Canada. She is a physician, specializing in hematology, as well as a historian. Her books include *To See with a Better Eye: A Life of R. T. H Laennec*, *History of Medicine: A Scandalously Short Introduction*, and *Lovers and Livers: Disease Concepts in History*. Her current research is on medical miracles and medical saints.

ADRIANO DUQUE holds a Ph.D. from the University of North Carolina, Chapel Hill. He is at present Assistant Professor of Spanish at Rider University. Recent articles include “New Visions of the Mongols? Benedict the Pole and the Pian Carpine Mission of 1245” and “Imaginería religiosa in the Poema de Fernán González.”

MYRON ECHENBERG is Professor of History at McGill University. His books include *Plague Ports: The Global Urban Impact of Bubonic Plague between 1894 and 1901* (2007) and *Black Death, White Medicine: Bubonic Plague and the Politics of Public Health in Colonial Senegal, 1914–1945* (2001). He is currently writing a work of synthesis on cholera provisionally entitled “‘Snake in the Belly’: A Global History of Cholera, 1817–2006.”

RICHARD EIMAS, B.A., University of Colorado; M.A., University of Denver, is Curator Emeritus of the John Martin Book Room, Hardin Library for the Health Sciences at the University of Iowa. He was editor of *Heirs of Hippocrates: The Development of Medicine in a Catalogue of Historic Books in the Health Sciences Library* (1990), published by University of

Iowa Press, and author of numerous other publications and presentations at national and international meetings.

AMY FAIRCHILD is Associate Professor of Sociomedical Sciences at Columbia University's Mailman School of Public Health. Her book *Science at the Borders: Immigrant Medical Inspection and the Shaping of the Modern Industrial Labor Force, 1891 to 1930* was published by Johns Hopkins University Press in 2003. She is currently working on Hansen's Disease in America and patterns of societal reactions to it.

J. GORDON FRIERSON, M.D., recently retired from private practice in Oakland, California, and as Clinical Professor at the University of California San Francisco, where he was attending at the tropical disease clinic. He was awarded a Diploma in Clinical Medicine of the Tropics at the London School of Hygiene and Tropical Medicine, has worked in or studied tropical diseases in various areas of the world, and has contributed articles on parasitic diseases to three textbooks. He now devotes time to the history of medicine.

MATTHEW GANDY teaches geography at University College London and has published widely on urban, cultural, and environmental themes. He is author of *Concrete and Clay: Reworking Nature in New York City* and coeditor of *The Return of the White Plague: Global Poverty and the "New" Tuberculosis and Hydrophilis*.

ALEXANDRA GEUSAU holds a medical degree from the University of Vienna, Austria. She is Associate Professor of Medicine in the Division of Immunodermatology, Allergy, and Infectious Skin Diseases where she established the outpatient department for sexually transmitted diseases. She pursues research and clinical practice with both traditional STDs and with HIV/AIDS, and has published widely in both areas.

FREDERICK W. GIBBS is a Ph.D. candidate at the University of Wisconsin–Madison who studies the intersection of medieval medicine and natural philosophy with attention to how the body interacts with the world around it. His current project investigates the concept and contexts of poison in western medical literature from antiquity to the Renaissance.

PABLO F. GOMEZ is a Ph.D. Candidate in History at Vanderbilt University. Dr. Gomez holds an M.D. from the C.E.S. University in Colombia, holds a degree in orthopedic surgery from Pontificia Universidad Javeriana in Colombia, and has worked as a postdoctoral fellow in genetics and orthopedics oncology at the University of Iowa. His dissertation project *African Slaves' Health Practices in the Nuevo Reino de Granada* explores African influences in sanitary and cultural practices in Latin America.

DONATO GÓMEZ-DÍAZ holds a Doctorate in History from the University of Granada (1991) and served as professor of History and Economic Institutions at Granada; currently he teaches in the Department of Applied Economy at the University of Almería (Spain). He has published over 80 works within his area of specialization, which includes demography, primarily regarding the history of population and diseases (cholera and others), economic history, pedagogy, and new technologies.

CANDACE GREGORY-ABBOTT is an Assistant Professor of History at California State University, Sacramento, where she also teaches in the Humanities and Religious Studies department. Her research and teaching interests include the “other people of the Middle Ages,” medieval magic, alchemy, witchcraft, and heresy.

VICTORIA A. HARDEN retired in January 2006 as Director of the Office of NIH History and the Stetten Museum at the National Institutes of Health, an office she created during the 1986–1987 observance of the NIH centennial. She has written and edited several books, including *Rocky Mountain Spotted Fever: History of a Twentieth-Century Disease* and *AIDS and the Public Debate: Historical and Contemporary Perspectives*, and she oversaw an oral history project on the 1960s eradication of smallpox in West Africa.

LESLEY HENDERSON is Lecturer in Sociology and Communications at the Centre for Media and Communications Research, Department of Human Sciences, at Brunel University in London (U.K.), specializing in health and medical issues in mass media—especially television—and their impacts on society and culture. He has recently published “Sad Not Bad: Images of Social Care Professionals in Popular UK Television Drama” in the *Journal of Social Work* (2007).

JOHN HENRY of the University of Edinburgh, Scotland, has published widely on the history of science and medicine from the Renaissance to the nineteenth century. He is the editor, with John M. Forrester, of *Jean Fernel's On the Hidden Causes of Things: Forms, Souls, and Occult Diseases in Renaissance Medicine*.

JUSTO HERNÁNDEZ is Assistant Professor of History of Medicine at the Faculty of Medicine of the University of La Laguna, Tenerife, Canary Islands, Spain, and President of the Canary Society of History of Medicine. His main research deals with Renaissance medicine. His books include *Cristobal de Vega y su Liber de arte medendi (1564)*, *Ciencia y Medicina en la Biblioteca de la Universidad de La Laguna*, and *El enigma de la modorra*. Currently he is working on the development of humanist Galenism in sixteenth-century Spain.

GREGORY J. HIGBY is a third-generation pharmacist. He received his Ph.D. in the history of pharmacy from the University of Wisconsin–Madison in 1984. Since 1986 he has served as the executive director of the American Institute of the History of Pharmacy, located in Madison, Wisconsin. He is the editor of the quarterly journal *Pharmacy in History*.

JULIA F. IRWIN is a Ph.D. candidate in History, with a concentration in the History of Medicine and Science, at Yale University. Her research interests include the histories of public health and U.S. foreign relations. Her dissertation, “Humanitarian Occupations: Disasters, Diplomacy, and the American Red Cross,” examines U.S. international relief operations in the wake of war and natural disasters from 1900 to the early 1930s.

TINA JAKOB holds a Ph.D., and her research concentrates on health and disease patterns in archaeological skeletal populations using a bioarchaeological approach. She is currently a Teaching Fellow at the Department of Archaeology, Durham University, UK, and is

Course Director of the M.Sc. in Palaeopathology. Tina has worked on excavations in Germany, Turkey, Britain, Jordan, and the Sudan.

ERIC JARVIS teaches history at King's University College, London, Ontario. He has the article "A Plague in Paradise: Public Health and Public Relations during the 1962 Encephalitis Epidemic in St. Petersburg, Florida" forthcoming in the *Florida Historical Quarterly*.

SUSAN D. JONES is Associate Professor in the Program for the History of Science, Technology and Medicine and the Department of Ecology, Evolution and Behavior at the University of Minnesota. She is the author of *Valuing Animals: Veterinarians and Their Patients in Modern America* and several articles on the history of animal disease.

EZEKIEL KALIPENI is a population, medical, and environmental geographer interested in demographic, health, environmental, and resource issues in Sub-Saharan Africa. He has carried out extensive research on the population dynamics of Malawi and Africa, in general concentrating on fertility, mortality, migration, and health-care issues. He is currently working on HIV/AIDS in Africa and population and environmental issues in Malawi.

TOM KOCH, Ph.D., is Adjunct Professor of Medical Geography at the University of British Columbia and of Gerontology at Simon Fraser University. His books include *Cartographies of Disease: Maps, Mapping, and Medicine*, a survey of the history of medical mapping. He is currently preparing a volume on mapping as a medium for the construction of medical science: *Mapping Medicine, Making Science: Searching for Disease*.

LARA J. KUNSCHNER, M.D., is an Assistant Professor of Neurology at Drexel University College of Medicine and an attending Neurologist and Neurooncologist at Allegheny General Hospital in Pittsburgh, Pennsylvania. Research interests including neurovirology and neurooncology have led to numerous peer-reviewed articles in the medical literature.

WILLIAM LONDON is Assistant Professor of European History at Northern Kentucky University. Currently, he is writing a monograph titled "Patronage and Plague in High Renaissance Florence: Lorenzo di Filippo Strozzi and Niccolò Machiavelli," which includes the first English translation and Italian critical edition of an important, though neglected, plague tract. His first monograph, *Politics, Patriotism and Language*, which focused on Machiavelli, was published in 2005.

LAUREL LENZ is an Assistant Professor in the Department of Immunology at the University of Colorado and the National Jewish Medical and Research Center. His research and teaching focus on understanding basic mechanisms of bacterial pathogenesis and host immunity to microbial pathogens. His publication record includes numerous highly cited publications in microbiological and immunological journals and books.

TERESA LESLIE is a visiting associate professor of history at the University of West Georgia. She earned her doctorate in medieval history at Emory University. Her current research focuses on prayer rituals associated with death in medieval monastic communities.

JEFFREY LEWIS received his Ph.D. in European history from Ohio State University in 2002. His research has focused largely on the history of molecular biology in Germany, but he is also very interested in the importance of science and technology for national security. He has published several articles and book chapters on the history of biology as well as on technology and security issues.

LIEW KAI KHIUN is currently a postdoctoral fellow at the Asia Research Institute, National University of Singapore. His academic research has included the historical involvement of non-government health organizations, infectious diseases such as SARS and influenza, as well as cultural studies. His current project explores the representation of medicine in East Asian films and television dramas.

THOMAS LAWRENCE LONG is professor of English at Thomas Nelson Community College, Hampton, Virginia. He is the author of *AIDS and American Apocalypticism: The Cultural Semiotics of an Epidemic* and of numerous articles on religious discourses in culture.

LOUISE MARSHALL is Senior Lecturer in the Department of Art History and Film Studies at the University of Sydney, where she teaches late medieval and Renaissance art. She is an authority on Renaissance plague images, on which she is preparing a book. Other research interests include Renaissance devotional imagery, the cult of the saints, and representations of purgatory.

ANGELA MATYSIAK is an independent scholar with a Ph.D. in history from George Washington University. Her dissertation, *Albert B. Sabin: The Development of an Oral Vaccine Against Poliomyelitis*, examines the relationship between the science and the scientist in the development of that vaccine. She is expanding it into a full scientific biography of the life and work of Albert Sabin.

ANTHONY McMICHAEL, medical graduate and environmental epidemiologist, was previously Professor of Epidemiology, London School of Hygiene and Tropical Medicine, UK. He has worked with the World Health Organization and IPCC on health risks of climate change, including infectious diseases. His books include: *Human Frontiers, Environments and Disease* (2001), published by Cambridge University Press, and *Climate Change and Human Health: Risks and Responses* (2003), published by WHO.

HENRY MEIER is a final-year doctoral candidate in the history of medicine at the University of Oxford, UK. His thesis examines the history of smallpox in seventeenth-century London, focusing on the epidemiology and various social and economic repercussions of the disease.

LUCY MKANDAWIRE-VALHMU is an Assistant Professor in the College of Nursing at University of Wisconsin–Milwaukee. She received her Ph.D. in nursing from the University of Wisconsin–Madison. Her areas of interest are violence against women in Southern Africa and the intersection of violence and HIV in the lives of women in Southern Africa.

DAVID M. MORENS, M.D., joined U.S. Centers for Disease Control and Prevention (CDC) staff, serving as a medical virologist studying enteroviruses and enteric gastroenteritis viruses, as Chief of CDC's Respiratory & Special Pathogens Branch, and for two years studied Lassa fever in Sierra Leone, West Africa. From 1982 to 1998 he was Professor of Tropical Medicine at the University of Hawaii, and from 1987 to 1998 Professor and Chairman, Epidemiology Department, School of Public Health. Dr. Morens has studied the epidemiology of viral hemorrhagic fevers, viral pathogenesis, and the integration and role of epidemiology in biomedical science and research. His career interest for over 25 years has been in emerging infectious diseases and in diseases of unknown etiology. In the past decade he has published and spoken on numerous aspects of the history of epidemiology and infectious diseases. Currently Dr. Morens is on University leave, working in the Office of the Director, National Institute of Allergy & Infectious Diseases, National Institutes of Health.

HILARY S. MORRIS is a medical historian and Senior Lecturer in the School of Education at the University of Brighton and the Brighton and Sussex Medical School (U.K.). She is also past Deputy President of the Worshipful Society of Apothecaries. Her most recent book is *History of Medicine with Commentaries* (2005), co-authored with Robert Richardson.

SANDRA W. MOSS is a retired internist and clinical professor of medicine with a master's degree in the history of technology, the environment, and medicine. Her publications include many historical papers with a focus on nineteenth-century American medicine. She recently contributed a chapter to *Clio in the Clinic* and regularly presents papers at local, state, and national history meetings.

STEVE MURPHREE is Professor of Biology at Belmont University in Nashville, Tennessee. He is a medical entomologist with broad interests in entomology, ecology, and science education. Dr. Murphree is a native of Tennessee and holds a Ph.D. in Entomology from Auburn University and B.S. and M.S. degrees, both in biology, from Middle Tennessee State University.

ERIC D. NELSON is Assistant Professor of Classics at Pacific Lutheran University. His work includes academic publications on medical history, popular books on Greece and Rome in *The Complete Idiot's Guide* series, and contributions to programs for the History and Discovery channels. He is currently conducting research on the role that facial expressions have played in popular and medical diagnosis of mental states.

QUENTIN OUTRAM is Senior Lecturer in Economics at Leeds University Business School, UK. His interest in the Thirty Years' War arose from studies of warfare and famine in modern Liberia, West Africa.

DANIEL PALAZUELOS holds an M.D. from Brown University and is currently completing his Global Health Equity/Internal Medicine Residency at Brigham and Women's Hospital, Harvard Medical School. He works with the Boston based NGO, Partners in Health, on a project training Community Health Promoters in Chiapas, Mexico.

MELISSA PALMER is an internationally renowned hepatologist and the author of the best-selling book *Dr. Melissa Palmer's Guide to Hepatitis and Liver Disease*. She maintains perhaps the largest private medical practice devoted to liver disease in the United States. Dr. Palmer graduated from Columbia University and was trained in liver disease at the Mount Sinai School of Medicine in New York City.

JOHN PARASCANDOLA retired from the federal government in 2004 after 20 years of service as Chief of the History of Medicine Division of the National Library of Medicine and as Public Health Service Historian. His book *The Development of American Pharmacology: John J. Abel and the Shaping of a Discipline* was awarded the George Urdang Medal. His latest research project concerns the history of syphilis in America.

MARK PARASCANDOLA is an epidemiologist at the U.S. National Cancer Institute. He holds a Ph.D. in philosophy of science from Cambridge University and an M.P.H. in epidemiology from Johns Hopkins University. Dr. Parascandola has published numerous articles on the history of epidemiology and the use of epidemiologic methods in public policy.

KIM PELIS received her Ph.D. in the history of medicine at the Johns Hopkins University. In addition to several articles on the history of bacteriology and of transfusion medicine, she is the author of *Charles Nicolle, Pasteur's Imperial Missionary: Typhus and Tunisia*. Dr. Pelis is currently head speechwriter to the director of the National Institutes of Health in Bethesda, MD.

THOMAS QUINN, D.O., graduated from the Philadelphia College of Osteopathic Medicine and is Board-Certified in Family Practice and Occupational Medicine. He completed his 24-year military career as State Surgeon of the Pennsylvania National Guard. Currently, he is Clinical Associate Professor at Lake Erie College of Osteopathic Medicine-Bradenton and completing *The Feminine Touch: History of Women in Osteopathic Medicine*.

NICK RAGSDALE completed his Ph.D. in Physiology at the University of Tennessee, Memphis. He spent two years investigating antibiotic resistant *Streptococcus pneumoniae* at the St. Jude Children's Research Hospital in Memphis, Tennessee. Currently, he serves as Associate Professor of Biology and Pre-Health Advisor for Belmont University. His current research focuses on environmentally induced Parkinson's Disease.

MRIDULA RAMANNA teaches at the University of Mumbai and researches the history of medicine in India. Her publications include *Western Medicine and Public Health in Colonial Bombay, 1845–1895* (2002), chapters contributed to edited volumes published in the United Kingdom and India, and several articles in refereed research journals. She is currently working on a monograph entitled *Health Care in Bombay, 1896–1930*.

KAREN MEIER REEDS is a Princeton Research Forum, Visiting Scholar, History and Sociology of Science, University of Pennsylvania, formerly Science/Medicine Editor, Rutgers University Press, and independent scholar. Her recent books include *A State of Health: New Jersey's Medical Heritage* and *Visualizing Medieval Medicine and Natural History, 1200–1550* (coeditor). Recent exhibition projects include "Come into a New World: Linnaeus and America" and "Smallpox and the Revolutionary War."

CAROLE REEVES is the Outreach Historian at The Wellcome Trust Centre for the History of Medicine, University College London. She was picture editor and biographer for *The Dictionary of Medical Biography* and is currently researching the history of malaria in eighteenth-century England. Her illustrated articles on medical history, including "Plagues, Pestilence and Public Health," may be read at www.historyworld.net.

JONATHAN REINARZ is a Wellcome Research Lecturer at the Centre for the History of Medicine, University of Birmingham, UK. Between 2000 and 2003 he was the primary research fellow on the University Hospital Birmingham, NHS Trust-funded project, "Healthcare and the Second City: a history of the Birmingham teaching hospitals, 1779–1939." He has published on aspects of medical, labor, brewing, and local history. He is currently writing a Wellcome Trust-funded history of medical education in provincial England, 1800–1948.

HEIDI M. RIMKE is Assistant Professor of Sociology at the University of Winnipeg in Manitoba, Canada. Her doctoral thesis, *Ungovernable Subjects*, documents and analyzes the social history of the doctrine of moral insanity. Currently she is conducting research into the historical relationship between religion, law, and science in nineteenth-century Western medical discourses on dangerousness and immorality.

LISA ROSNER is Professor of History at the Richard Stockton College of New Jersey. She is the author of books and scholarly articles on the history of medical education, including *Medical Education in the Age of Improvement* and *The Most Beautiful Man in Existence*. Currently she is conducting research into the relationship between universities and academies of science during the Enlightenment.

ROBERT SALLARES holds a Ph.D. from the University of Cambridge and is Research Fellow at the University of Manchester Institute of Science and Technology. He is the author of *Malaria and Rome: a History of Malaria in Ancient Italy* (2002), *The Ecology of the Ancient Greek World* (1991), and numerous articles in medical history, ancient history, and biomolecular archeology.

JAMES SCHALLER, M.D. and M.A.R., is the author of 25 books and 25 peer-reviewed journal publications. He is a self-funded full-time researcher and part-time clinician with books and articles in ten areas of medicine, with many focusing on stealth or commonly missed infections. His specialty is patients who fail routine treatments.

JOLE SHACKELFORD is Adjunct Assistant Professor at the University of Minnesota. His books include *A Philosophical Path for Paracelsian Medicine: The Ideas, Intellectual Context, and Influence of Petrus Severinus (1540/2–1602)*. Currently he is researching the history of Paracelsian uroscopy.

DAVID F. SMITH is Senior Lecturer in the History of Medicine in the Schools of Medicine, Divinity, History, and Philosophy, at the University of Aberdeen, Scotland. He is editor of *Nutrition in Britain*, coeditor of *Food, Science, Policy and Regulation in the Twentieth Century*, and principal author of *Food Poisoning, Policy and Politics: Corned Beef and Typhoid in Britain in the 1960s*.

MELISSA SMITH is a postdoctoral fellow at George Washington University. She has published articles on plague and early modern drama and was assistant editor for *Reading Early Modern Women*. She is currently working on a book-length study about the impact of plague and syphilis on early modern drama, as well as a new project about contagious emotions.

DIONYSIOS STATHAKOPOULOS is a Research Fellow at the Department of Byzantine and Modern Greek Studies at King's College London. His book *Famine and Pestilence in the Late Roman and Early Byzantine Empire* was published in 2004. Currently he is conducting research on late Byzantine charity.

JACOB STEERE-WILLIAMS is a Ph.D. student in the History of Medicine and Biological Sciences at the University of Minnesota. His research interests include the history of disease, public health, and epidemiology in nineteenth-century Britain. His dissertation is focused on changes in waterborne disease epidemiology after the investigations of John Snow.

MARTHA STONE is Coordinator for Reference Services, Treadwell Library, Massachusetts General Hospital, Boston, and is a member of the Academy of Health Information Professionals. Her essay on French midwife Marie Boivin (1773–1847) was published in *Notable Women in the Life Sciences*. Her book reviews appear in a wide variety of publications.

MARY SUTPHEN is a Research Scholar at The Carnegie Foundation, working on a study on nursing education. She has also conducted historical research on diversity in U.S. medical schools and the history of public health in Britain's Empire. Sutphen received her B.A. from Brown University, her M.A. from Duke University, and her Ph.D. in history of medicine from Yale University.

VICTORIA SWEET is Associate Clinical Professor of Medicine at the University of California, San Francisco, with an M.D., as well as a Ph.D., in the history of medicine. She is a practicing physician and an active writer and historian. Her books include *Rooted in the Earth, Rooted in the Sky: Hildegard of Bingen and Premodern Medicine* and *God's Hotel: The Last Almshouse in America*, in manuscript.

JOHN M. THEILMANN is Professor of History and Politics at Converse College. He is the author or coauthor of a book and more than 30 articles and book chapters including "A Plague of Plagues: The Problem of Plague Diagnosis in Medieval England," in *Journal of Interdisciplinary History*, and "The Regulation of Public Health in Late Medieval England," in *The Age of Richard II*.

SELMA TIBI-HARB is a community pharmacist, practicing in Oxford, England, where, for the past year, she has run her own pharmacy. Having a strong interest in medieval Islamic medicine, she completed a doctoral thesis on the subject at Oxford University in 2003. This was published by Brill Academic Publishers as *The Medicinal Use of Opium in Ninth-Century Baghdad*.

REBECCA TOTARO is Associate Professor of English at Florida Gulf Coast University and author of *Suffering in Paradise: The Bubonic Plague in English Literature from More to Milton* (2005). A 2006–2007 participant in the Folger Shakespeare Library Year-Long Colloquium

on vernacular health and healing and recipient of a short-term fellowship at the Folger for 2007–2008, she is editing an interdisciplinary anthology of early modern responses to plague and completing a monograph on early modern meteorology and physiology.

ALAIN TOUWAIDE is a Historian of Sciences in the Botany Department of the National Museum of Natural History at the Smithsonian Institution. He obtained a Ph.D. in Classics (Belgium) and specialized in the history of medicine and pharmacy in the ancient Mediterranean, working on manuscripts in Greek, Latin and Arabic, as well as on early printed books (fifteenth and sixteenth century). He is an internationally recognized expert in the history of therapeutic uses of plants in Mediterranean cultures. The recipient of many honors and grants, he has extensively published on these topics and lectured worldwide. He is the current president of the International Association for the History of Nephrology; the President-Elect of the Washington Academy of Sciences, and the Secretary of the International Society for the History of Medicine.

TANFER EMIN TUNC is an Assistant Professor of American Culture and Literature at Hacettepe University, Ankara, Turkey. She received her Ph.D. in History from SUNY Stony Brook in 2005, where she specialized in the history of science, medicine, and technology. Her research focuses on the history of women's health; gender, sexuality, and reproduction; and feminist theory. She is currently preparing her manuscript *Technologies of Choice: A History of Abortion Techniques in the United States, 1850–1980* for publication.

NICK TURSE is a recent Ph.D., with a Masters of Public Health, working in the Social Psychiatry Research Unit of the Department of Epidemiology at the Center for the History and Ethics of Public Health in the Mailman School of Public Health at Columbia University.

FRED R. VAN HARTESVELDT is Professor of History and Interim Department Head at Fort Valley State University, Georgia. Among his six books is the edited anthology *The 1918–19 Pandemic of Influenza: The Urban Impact in the Western World*. He is currently researching the role of the Royal Army Medical Corps on the Western Front in World War I.

NÜKHET VARLIK is a Ph.D. candidate in Near Eastern Languages and Civilizations at the University of Chicago. She is interested in the history of diseases and public health in the early modern Mediterranean world. Her dissertation, *Disease and Empire: A Study of Plague Epidemics in the Ottoman World (1453–1600)*, is a study of the relationship between state formation and plague epidemics.

JEFFERSON VAUGHN is currently an Associate Professor of Biology at the University of North Dakota. He began studying arboviruses as a junior researcher at the U.S. Army laboratory at Fort Detrick, MD, and since 2002 has chronicled the spread of West Nile virus into the birds and mosquitoes of eastern North Dakota.

MARK WADDELL is a Visiting Assistant Professor in the Lyman Briggs School of Science at Michigan State University. He has published articles in *Centaurus* and *The Canadian Journal of History* and is currently at work on a book manuscript which explores the links

between the meditative and spiritual traditions of the Jesuits on the one hand and, on the other, their attempts to deal with invisible natural phenomena in the seventeenth century.

BARBRA MANN WALL is Associate Professor of Nursing and Associate Director of the Barbara Bates Center for the Study of the History of Nursing at the University of Pennsylvania. She has written numerous articles on nursing history. Her most recent book is *Unlikely Entrepreneurs: Catholic Sisters and the Hospital Marketplace, 1865–1925*. Currently she is conducting research on a second book that extends her analysis of Catholic hospitals into the later twentieth century.

JOHN WALLER is an Assistant Professor in the history of medicine at Michigan State University. His research is focused on ideas of heredity in Western history, and he has also published books on British social history, the advent of the germ theory of disease, and the making of scientific reputations. He is currently completing a book on the dancing mania of Strasbourg in 1518 and a detailed study of Western hereditarian thought since the collapse of the Roman Empire.

ADAM WARREN is an Assistant Professor of history at the University of Washington, Seattle, where he is currently finishing a book project on colonial medical reforms and the politics of disease prevention in eighteenth- and nineteenth-century Lima, Peru. Although his primary training is in Latin American history, most of his research and publications have addressed questions of colonial medical practices.

MARK WHEELIS is Senior Lecturer in Microbiology at the University of California, Davis. For the past 20 years, his research has focused on the history and control of chemical and biological weapons. He is coeditor of *Deadly Cultures: Biological Weapons since 1945*.

STEFAN WÖHRL is Associate Professor for Dermatology and Venerology and Senior Physician for the Division of Immunology, Allergy and Infectious Diseases at the Medical University of Vienna, Austria. He received his medical degree from the University in 1999 and has since presented 45 papers, many internationally, and published 34 coauthored articles, including “A Clinical Update: Syphilis in Adults” with A. Geusau in *Lancet* (2007).

JACQUELINE H. WOLF is Associate Professor of History of Medicine in the Department of Social Medicine at Ohio University where she specializes in the history of women’s health, children’s health, and public health. She is the author of numerous articles and a book—*Don’t Kill Your Baby: Public Health and the Decline of Breastfeeding in the 19th and 20th Centuries* (2001)—on the history of breastfeeding practices in the United States and the effect of those practices on children’s health and public health.

WILLIAM H. YORK is Assistant Professor of Interdisciplinary Studies (Humanities) at Portland State University. His dissertation *Experience and Theory in Medical Practice During the Later Middle Ages: Valesco de Tarenta (fl. 1382–1426) at the Court of Foix*, examines the ways in which physicians applied knowledge, garnered from theoretical manuals about disease, in their medical practice. His current research continues to examine these problems.

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Index

Note: page numbers in **bold font** refer to main articles about the specified topic.

- Abraha (Prince), 759
- Account . . . of Inoculating the Small-Pox, An* (Mather), 403
- Account of the Bilious Remitting Yellow Fever, as It Appeared in the City of Philadelphia, in the Year 1793, An* (Rush), 605
- acetylsalicylic acid, 473
- Ackerknecht, Erwin, 423
- Acquired Immune Deficiency Syndrome. *See* Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS)
- ACT UP. *See* AIDS Coalition to Unleash Power (ACT UP)
- acute hemorrhagic conjunctivitis, 127
- Adams, John, 652
- Adonais* (Shelley), 706
- Aedes aegypti*
- dengue, 700
 - discovery of, 590
 - yellow fever, 130, 234
- Aedes aegypti* mosquito
- dengue, transmission, 321, 700
 - ideal habitat, damp climate, 795
 - yellow fever, as vector of, 590, 745, 781, 785
- Aedes albopictus*, 697. *See also* Asian tiger mosquito
- Africa Malaria Report 2003, The* (WHO), 388
- African AIDS Epidemic, The* (Iliffe), 3
- African germ theory, 403
- “The Age of Degenerative and Human-Made Diseases,” 263
- Agramonte, Aristides, 321
- AIDS. *See* Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
- AIDS, literature, and the arts in the United States, 13–17
- arts of stage and screen, 15–16
 - as “epidemic of signification,” 13
 - literature, 14–15
 - social stigma and, 14
 - visual arts, 16–17
- AIDS Coalition to Unleash Power (ACT UP), 15
- “AIDS guidelines,” 2
- AIDS in Africa, 1–6
- causes and consequences, 4
 - efforts to combat the HIV/AIDS, international organizations, 5

- AIDS in Africa (*continued*)
 geographic spread, 3–4
 initial response to the epidemic, 1–3
 prevention and treatment, 4–6
- AIDS in United States, 7–13
 diagnostic tests for HIV, 8
 doubters and quackery, 10–11
 gay-related, 7
 in new millennium, 11–13
 public education programs, 10
 recognition as new disease, 7–8
 social, religious, and political reactions, 8–10
- AIDS Memorial Quilt, The, 17
- air and epidemic diseases, 18–19
- Alchemists, 472
- Alexandria, and third plague pandemic, 489
- Ali, Muhammad, 487
- Alighieri, Dante, 26
- Alison, William Pulteney, 727
- alkaloids, invention of, 473
- al-Khatib, Ibn, 517
- Al-Maqrizi, 48
- al-Maqrizi, 517
- Al Qaeda, 55
- al-Qanun fi al-tibb (*The Canon of Medicine*; Avicenna), 33
- Al-Walid, 48
- American Civil War. *See* United States Civil War
- American cordons sanitaires, 138, 140
- American Family Association, 17
- American Federation for Sex and Hygiene, 747, 748
- American Medical Association, 423
- American Pharmaceutical Association, 28
- American Psychiatric Association (APA), 681
- American Society for Sanitary and Moral Prophylaxis, 747
- American Vigilance Association, 748
- Anabrus simplex*. *See* Mormon cricket
- And the Band Played On* (Shilts), 369
- “And Thou art Dead, as Young and Fair” (Byron), 707
- Angel of Bethesda, The* (Mather), 403
- Angels in America: A Gay Fantasia on National Themes* (Kushner), 15
- animal diseases (zoonoses) and epidemic disease, 19–22
 ecology of bubonic plague and, 20
 evolution of influenza and, 21
 origin of, 21
 transmission of zoonoses, 20
- Yersinia pestis*, 20
- zoonotic diseases and, 20
- Animal Liberation* (Singer), 24
- animals and research, 23–24
 pharmaceuticals, testing and standardization of, 23
 of transmission and contagion, 132
- typhoid fever, 721
- vaccination and inoculation, 745
- Animal Welfare Act (1966), 24
- Anopheles gambiae*, 698
- anthrax bacteria, 458
- anthrax letters, 53
- antibiotics, 24–26, 157, 159
 for bartonella diseases, 43
 development of new, 26
 fluoroquinolones, 25
 penicillin, 24, 460
 problem of use, 25
 streptomycin, 25
 tetracycline, 25
 for tuberculosis, 703
 for bubonic plague, 74
 for conjunctivitis, bacterial, 128
- anti-rabies treatment, 458
- anti-vaccination campaigns, 466
- anti-vivisection movement, 23
- Antonine Plague, 152, 221. *See also* Plague of Justinian; plagues of the Roman Empire
 discovery of, 536
 of mid-second century, 761
- APA. *See* American Psychiatric Association (APA)
- Apollo, Greek God, 525
- “Apollo disease,” 127
- apothecaries, 472
- “apothecary,” 27
- apothecary/pharmacist, 26–30
 Anglo-American differences, 27–30
 changing roles of, 28, 30
 defined, 27
 education, 28
 guilds and pharmacopeias, 27
 manufacturing and the, 28
 modern Europe, 27
United States Pharmacopoeia, 28
- Appleby, A. B., 485
- Araki, Gregg, 15

- Archive for Pathological Anatomy and for Clinical Medicine* (Virchow), 750
- Arenaviridae, 243–244
- Aristotle, 295
- Armed Forces
 - epidemic disease and, 755–786
 - German, 127
 - Institute of Pathology, 316
 - Japanese, 760
 - malarial in, 381
 - United States, 384, 755–786
 - war, and venereal diseases, 760
- Armstrong, Richard, 30–31. *See also* Measles Epidemic in Fiji
- Arning, Eduard, 294
- Arnold, Benedict, 651–652
- Arnold, David, 122–123, 125
- arsenic
 - as rat poison, 485
 - sleeping sickness, prevention of, 426
 - water-related disease, cause of, 765
- Artemisia plant, 38
- arthropods. *See* insects, other arthropods, and epidemic disease
- Articella*, 417
- Asahara, Shoko, 54
- Asian lady beetle, 319
- Asian tiger mosquito, 319
- Aspirin. *See* acetylsalicylic acid
- astrology and medicine, 31–33
 - celestial influence and, 32
 - individual diagnosis, 32
 - judicial, 31
 - prognosticative, 31
 - zodiac signs, 32
- Atlantis* (Doty), 15
- At Risk* (Hoffman), 14
- Aum Shinrikyo Attacks (1990–1995), 54–55
- Aurelius, Marcus (Emperor), 221
- Australia*, 511
- autumn fever, 393
 - malaria prevention and, 394
 - modern Latin America, 394
- Avian influenza virus, 307–308
 - emergence of, 741
 - NGOs, role in prevention of, 446
- Avicenna (Abu Ali Al-Husayn Ibn Abdullah Ibn Sina), 33–34, 417, 477
- ayurveda, 507. *See also* ayurvedic disease theory and medicine
- ayurvedic disease theory and medicine, 34–35, 213
 - and Buddhism, 35
 - Caraka's Compendium*, 35
 - janapada-uddhvamsa*, 35
 - tridosā*, 35
- azidothymidine (AZT), 7, 11, 288
- AZT. *See* Azidothymidine (AZT)
- Babes, Victor, 37
- babesia
 - Artemisia preparations to kill, 38
 - other conditions caused by, 37
 - as pathogen, 42
 - signs and symptoms of, 37, 38
 - treatment of, 38
- Babesia canis*, 37
- Babesia microti*, 37
- babesiosis, 37–38. *See also* babesia
- Bacchae, The* (Euripides) 370
- Bacille Calmette-Guerin (BCG), 355, 705
- bacillus, 240
- Bacillus anthracis*, 53, 55
- Bacillus typhosus*, 721
- bacterial infections, 42
- bacterium/bacteria, 39–42. *See also* antibiotics
 - Behring's concept to destroy, 44
 - definition of, 39
 - genetic code of, 41
 - Leeuwenhoek's research on bacteria, 39
 - lipid compositions of, 40
 - relationship between disease and, 40
 - reproduction by binary fission, 42
 - sharing basic metabolic pathways, 40
 - spore forms of, 41
- Baillou, Guillaume de, 773
- Balmis, Francisco Xavier, 124
- Balmis Expedition, 124
- Barratt, Thomas, 462
- Barres, Carlos Finlay, 797
- Barrie, Dennis, 15
- Barton, Alberto L., 43
- Bartonella
 - agents to infection, 42
 - discovery of, 43
 - signs and symptoms, 43
 - treatment of, 43
- Bartonella bacilliformis*, 43
- Bartonella diseases, 42–43
- Bartonella rochalimae*, 43
- Baumé, Antoine, 27, 473

- bazaar fly, 318
- Bazalgette, Joseph, 617
- BCG. *See* Bacille Calmette-Guerin (BCG)
- Behring, Emil von, **44–45**, 160
 - administering injection of antitoxin, 45
 - concept to destroy bacteria, 44
 - received first Nobel Prize in Physiology (1901), 45
 - studying Diphtheria, 45
- Beijing, China, and SARS disease, 215, 741
- Bela Schick, 161
- Ben cao gang mu*, 89
- Benedict, Carol, 495
- Bennett, Michael, 15
- Bernouli, Daniel, 146
- Betrothed, The* (Manzoni), 368
- Better Health through Cleanliness*, 464
- Bhatvadekar, Bhalchandra Krishna, 508
- biblical plagues, **45–47**
 - Deuteronomy, 45
 - in Egypt during Israel's bondage, 45
 - Hebrew, recounted in First Book of Samuel, 46
 - new infections, in biblical lands, 47
 - vicissitudes of pestilence, 47
- Biggs, Hermann, 715
- "Bills of Mortality," 146
- bimaristan/maristan, **48–49**
 - caregivers in, 49
 - definition of, 48
 - managing epidemics, role play, 48
 - treatment given in, 48–49 (*see also* astrology and medicine)
- binary fission, 42
- biological war, 763
- biological warfare, **49–52**. *See also* biological weapons; Hussein, Saddam
 - ban on biological weapons, 52 (*see also* bioterrorism)
 - Biological Weapons Convention (BWC), 51
 - bioterrorism, 19
 - Cold War era, 51
 - Contemporary world, 52
 - and disease, 49
 - disease as weapon used by European settlers, 50
 - smallpox as weapon during American Revolution, 50
 - before twentieth century, 49
 - World War I and II, 50–51
- biological weapons
 - Japanese military, 764
 - plague as, 500
 - Saddam Hussein and, 763
- Biological Weapons Convention (BWC), 51
- bioterrorism, **53–56**
 - definition of, 53
 - envelopes containing anthrax spores, 53
 - U.S. Anthrax Letter Attacks (2001), 53
- bioweapons, 763–764
- bioweapons program., 51
- bird flu. *See* Avian influenza virus
- Black, Jeff, 14
- Black Death, **56–63**
 - accounts and descriptions of, 57
 - casualties caused by, 67
 - Christian versus Muslim reactions to, 60
 - cultural changes and, 62–63
 - definition of, 56
 - description of plague, 57
 - economic and demographic effects of (*see* black death, economic and demographic effects of)
 - economic impact of, 60–62
 - historical effects, 60
 - historical record of, 56
 - identified as, bubonic plague, 73
 - initial outbreak in Europe, 134
 - intellectual impact of, 62
 - and Late Medieval Christianity, 63–65
 - medical response to, 59–60
 - miasmatic concept of disease, 59
 - modern medical debate on, 73
 - nature of the disease, 57
 - persecution of Jews triggered by, 69
 - personal liberties and epidemic disease, 465
 - prompting consilia authors, 70
 - reactions to plague, 60
 - religious responses to, 58
 - ships in spreading, role of, 58
 - significant result of, 60
 - social response, 58–59
 - symptoms of, 57
 - urbanization and epidemic disease during era of, 739
- Black Death, economic and demographic effects of, **65–67**
- Black Death, flagellants, and Jews, **67–69**
- Black Death: literature and art, **69–72**
- Black Death: modern medical debate, **72–73**
- Black Death and late medieval christianity, **63–65**

- black rat. *See* *Rattus rattus*
- Black Americans, AIDS and, 466
- Blindness, 370–371
- Blood of the Lamb* (Vries), 369
- Blue, Rupert, 512, 513
- Blumenbach, J. F., 589
- Board of Health, first, 84
- Boccaccio, Giovanni, 56, 58, 214, 368, 524
- body fluid tests, 148
- Boerhaave, Hermann, 419
- “Bolivarian Alternative for the Americas,” 226–227
- Bombay, plague outbreak during British rule, 506–507
- Bombay Bacteriological Laboratory, 509
- Bombay Medical Union, 508
- Bonaparte, Napoleon, 760
- Booklet on Mentulagra, Otherwise Known as the French Disease* (Grunpeck), 692
- Booklet on the Epidemic that Is Commonly Called the French Disease* (Leonico), 692
- Boorde, Andrew, 230
- Bordetella pertussis*, 773
- Borrelia*, 374. *See also* Lyme disease
- Botulinum toxin, 54
- Boucheron, Robert, 14
- bovine spongiform encephalopathy (BSE), 142, 300–301
- Boyle, Robert, 145–146
- Bram, Christopher, 14
- “Brazen Jack.” *See* yellow fever
- Bretonneau, Pierre, 720
- Brill, Nathan, 724
- Brill-Zinsser disease, 724
- British Emergency Public Health Laboratory Service, 722
- British Medical Association, 603
- British Medical Journal*, 464
- Bronte, Charlotte, 370
- Bronze Age, 738
- Brother to Brother: New Writings by Black Gay Men* (Hemphill), 14
- Brown, Helen Gurley, 634
- brown rat. *See* *Rattus norvegicus*
- BSE (bovine spongiform encephalopathy), 142, 300–301
- bubonic plague, 50, 56, 74–76, 321
- in the eighteenth century, 469
 - in Hawaii, 511
 - identification of Black Death as, 73
 - origin and spread of, 487–488
 - origins and spread of, 57
 - proponents of, 72–73
 - social responses to, 75
 - three forms of, 57
 - treatment of, 74
 - in United States, 77–79
- Bubonic Plague in Nineteenth Century China* (Benedict), 495
- bubonic plague in United States, 77–79
- Buchan, William, 462
- Buchanan, George, 767
- Budd, William, 721
- Bunyaviridae, 244
- Burgdorfer, Willy, 374
- “burger bug,” 155
- Burgundy, John of, 523
- Burnet, Sir Frank MacFarlane, 154
- BWC (Biological Weapons Convention), 51
- Byron, Lord, 707
- Cabot, Richard C., 274
- CAHCIM. *See* Consortium of Academic Health Centers for Integrative Medicine (CAHCIM)
- Cairo, Egypt, plague epidemics in, 518
- Caius, John, 686
- Calmette, Albert, 715, 798
- Camus, Albert, 368
- Canadian Tuberculosis Association, 715
- Canon, The*, 33
- Canon* (Avicenna), 477
- Canon of Medicine* (Avicenna), 417
- Canterbury Tales* (Chaucer), 70
- Cantlie, James, 402
- Capac, Huayna, 414, 758
- Cape Town, and bubonic plague, 489–490
- capitalism, 81–83
- development and access to treatments, 82–83
 - and epidemic disease, 81
 - financial investments in developing new drug, 82
 - medical care and, 82
 - stewardship of resources, 82
 - laissez-faire*, 565, 615–616
- Caraka's Compendium*, 35
- Carrier theory, 722
- Carroll, James, 321
- Carson, Rachel, 470
- Carter, Henry Rose, 783
- case fatality rates (CFRs), 105, 115
- catarrhal conjunctivitis, 127
- Catchmay, Lady Frances, 216

- Caventou, Joseph Bienaimé, 27
- CCHF. *See* Crimean Congo hemorrhagic fever (CCHF)
- CDC. *See* Centers for Disease Control and Prevention (CDC)
- CDR (crude death rates), 762
- “cell,” 433
- Cellular Pathology* (Virchow), 750
- Celsus, 396, 477
- Centers for Disease Control and Prevention (CDC), 7, 54, 76, 141, 159, 274
- Cephalosporin, 232
- CFRs (case fatality rates), 105, 115
- Chadwick, Edwin, 84–85, 300
 - formation of first Board of Health, 84
 - presiding Sanitary Institute and the Association of Sanitary Inspectors, 85
 - report on sanitary condition of laboring population of Great Britain, 146
- Chagas’s disease, 83
- Chain, Ernst, 460
- Charles II (king), 462
- Charles Mallory*, 30
- Charleston, South Carolina, yellow fever in, 792–793
- Chaucer, Geoffrey, 70, 480
- chemistry tests, 148
- Chicago Society for Social Hygiene, 748
- children and childhood epidemic diseases, 85–88
 - and communal health, 85
 - diarrhea, 86–87
 - infant death syndrome, 88
 - measles in, 86
 - other diseases triggering in, 88
 - poliomyelitis, 86
 - respiratory ailments, 87
 - ricketts, 88
 - sexually transmitted infections, 88
- Chinese disease theory and flight, 213
- Chinese disease theory and medicine, 89–91, 133
 - distinction between internal and external aspects of body and illness, 89
 - important texts in, 89
 - scholarly work and popularized works on exoticism, 89–90
 - Western influences in, 496
- Chinese government
 - plague epidemic, control of, 496–497, 499
 - Manchurian Plague Prevention Service, 501
- Chinese medicine, 476
- Chlamydial infection
 - chlamydial conjunctivitis, 128
 - Chlamydia trachomatis*, 232
 - epidemiology of, 232–233
- Chlamydia trachomatis*, 128, 232
- cholera, 91–95
 - Africa’s continuing struggle with, 115–116
 - campaigns of personal hygiene, 104
 - caused by *Vibrio cholerae*, 92
 - cause of, 105
 - concern in nineteenth century, 123
 - division between O1 group and non-O1 group, 92
 - Elements controlling, 112
 - El Tor role in, 114
 - endemic disease in colonial India, 112
 - entering in body through transmission, 93, 94
 - in Europe, expansion of, 96
 - factors spreading, 101–102
 - historical effects of first through third pandemics, 102–104
 - historical effects of fourth through sixth pandemics, 110–112
 - Latin American and African reactions to the seventh pandemic of, 116
 - leading factors predisposing, 94
 - mass vaccination in twentieth century, 111
 - McNeill, William, contribution in treatment of, 97
 - in Mecca, 114–115
 - microorganism of, 471
 - mortality in, 98
 - nature of disease involved, 97
 - origin of, 92, 95–96
 - origins and spread in fifth pandemic of, 107–109
 - origins and spread in first pandemic, 98–99
 - origins and spread in fourth pandemic of, 105–107
 - origins and spread in second pandemic, 99–100
 - origins and spread in seventh pandemic through present of, 114–117
 - origins and spread in sixth pandemic of, 109–110
 - origins and spread in third pandemic, 100–101
 - before pandemics (*see* cholera before pandemics)

- pilgrimage and, 481
 reactions of first through three pandemics, 102
 reactions of fourth through sixth pandemics, 110
 treatment of, 93
V. cholerae O1 (*see V. cholerae* O1)
 Venezuelan experience, 116
 in Western countries, 94
 cholera before the pandemics, 95–96
 cholera: first through third pandemics (1816–1861), 98–104
 cholera: fourth through sixth pandemics (1862–1947), 105–112
 cholera: seventh pandemic (1961–present), 114–117
 cholera in Europe, 110
 inoculations and, 111–112
 multinational control programs, 112–113
 cholera in Italy, 110
 cholera in Japan, 109
 cholera in Philippines, 109
 “cholera morbus”97
 cholera origins and spread
 in fifth pandemic of, 107–109
 in first pandemic, 98–99
 in fourth pandemic of, 105–107
 in second pandemic, 99–100
 in seventh pandemic through present of, 114–117
 in sixth pandemic of, 109–110
 in third pandemic, 100–101
 Christian teaching, and flight from plague, 214
 Christopher, Duncan, 73
 Cicero, 396
 cinema and epidemic disease, 117–120, 557
 diseases and epidemic outbreaks in, 118
 portrayal of epidemic disease, 120
 Cipolla, Carlo, 503
 ciprofloxacin (cipro). *See* fluoroquinolones
 circulatory system, 277
 Citizens’ Health Commission, 513
 Civil War, United States. *See* United States Civil War
Claviceps purpurea, 207–208
 Cleanliness Institute, New York, 464
Cleanliness Journal, The, 464
 clinical trials, using penicillin, 460
 Clua, Jaime Ferran y, 239
 Coleridge, Samuel Taylor, 706
Ceremonies (Hemphill), 15
 colonial cordons sanitaires, 137–138
 colonialism and epidemic disease, 121–126
 Columbus, Christopher, 345, 356, 397
 Comfort, Alex, 634
 Commodus, 221
Compendium Medicinæ (Gilbert), 674
 Condorcet, Marquis de, 399
 Confucianism, 476
 Confucius, 356, 476
 conjunctivitis, 126–129
 adenoviral, 127
 bacteria causing, 128
 bacterial, 128
 epidemic keratoconjunctivitis, 127
 of newborn (*see* ophthalmia neonatorum)
 parasitic, 129
 pharyngoconjunctival fever, 127
 viral, 127
 viruses, 128
 Conseil, Ernest, 729
 consilia, 70
 Consortium of Academic Health Centers for Integrative Medicine (CAHCIM), 216
 contagion
 major epidemic of syphilis, 134
 theory of disease, premodern, 133
 and transmission, 131–132
 contagion and transmission, 129–132
 concepts and usages, 132
 concepts of, 130, 132
Contagion (Cook), 368
 contagion theory of disease, 468
 Contagion Theory of Disease, Premodern, 133–135
 contagious diseases, 130
 convulsive ergotism, 208
 cordon sanitaire, 136–140
 Corigliano, John, 15
 Cornaro, Marco, 378
 Cornwallis, Charles, 652
 corpses and epidemic disease, 141–143
 Cortés, Hernán, 392, 758
 Cortés, Hernando, 740
Corynebacterium diphtheria, 158
 cowpox. *See Variolae vaccinae*
 Crimean Congo hemorrhagic fever (CCHF), 686–687
 Crimean War
 cholera, arrival of, 100, 101
 nursing and, 448
 typhus and, 734, 761

- Crosby, Alfred, 22
 crude death rates (CDR), 762
 Cruz, Oswaldo, 789, 790
Culex mosquito, 603, 699
 Cullen, William, 389, 720
 “cunning women,” 216
curanderismo, 215
Curiosa Americana (Mather), 402
 Curzon, Daniel, 14
 Cyprian, 597
- Danse Macabre*, *The*, 62
 Daonan, Shi, 495
 Darwin, Charles, 400
David Copperfield (Dickens), 707
 Davis, Bernard, 172
 Davis, Brad, 15
 DDT (dichloro-diphenyl-trichloroethane), 726
Death of Ivan Ilych, *The* (Tolstoy), 369
 “Death of Rats” (Daonan), 495
 Decameron, 70
Decameron, 214
Decameron, *The* (Boccaccio), 367–368, 524
 Defoe, Daniel, 468, 494, 524, 525
De humani corporis fabrica (Vesalius), 419
 Dekker, Thomas, 422
 Delany, Samuel R., 14
 Delicado, Francisco, 692
 Democratic Republic of Congo (DRC), 246
 demographic data collection and analysis, history of, **145–151**
 dengue fever. *See* hemorrhagic fevers; hemorrhagic fevers in modern Africa
 Desert locust, 317–318
Deuteronomy, 597
 Diacinto Gramigna, 419
 diagnosis and diagnostic tools. *See also* diagnosis of historical diseases
 clinical history, 147–148
 laboratory tests, 148–151
 physical exam, 148
 sensitivity and specificity, 147
 diagnosis of historical diseases, **151–154**
 discoveries in nineteenth-century, 152
 epidemiology and, 154
 theoretical approaches to, 154
Diagnostic and Statistical Manual IV (DSM IV), 681–682
Diagnostic Pitfalls Identified during a Study of Three Thousand Autopsies (Cabot), 274
 diagnostic tools. *See* diagnosis and diagnostic tools
- diarrhea, 86–87
 Díaz de Isla, Rodrigo Ruiz, 692
 dichloro-diphenyl-trichloroethane (DDT), 726
 Dickens, Charles, 707
Dictionary of Epidemiology, *The*, 197
Die Infusionstierchen als vollkommene Organismen (Ehrenberg), 39
 diet and nutrition
 food-transmitted disease, 155
 and susceptibility to epidemic disease, 156–158
 rise of populations, cause of, 261
 diet, nutrition and epidemic disease, **154–158**
 digestive system, 278–79
 Dioscorides, 237
 diphtheria, 23, **44**, **158–161**
 clinical picture and treatment of, 159
 definition of, 158
 history of, 159–160
 immunization of, 161
 laboratory confirmation of, 159
 research and control of, 160–161
 spread of, 159
 diphtheria, pertussis, and tetanus (DPT), 775
 diphtheria antitoxin
 discovery of, 341
 production of, 161, 473
 contaminated with tetanus spores, 648
 Directly Observed Therapy (DOTS), 704, 717
 disease, social construction of, **166–169**
 Disease and Military Opportunism, 758
 disease, in pre-Columbian Americas, **162–166**
 Aztec and Inca understandings of, 164–166
 present before contact, 162–163
 variation across populations, 163–164
 disinfection and fumigation, 170
 DNA and genetic testing, 149
 doctor. *See* empiric; physician; quack; surgeon
 Doctor of Pharmacy (Pharm. D.), 28
 Domagk, Gerhard, 474
Domesday Book (William), 145
Domestic Medicine (Buchan), 462
 Domestos, household bleach, 463
 Donaldson, Sir Liam, 712
 Donghua Hospital, Hong Kong, 499
 DOs (Doctors of Osteopathy), 478
 Dostoevsky, Fyodor, 370
 DOTS (Directly Observed Therapy), 704, 717
 Doty, Mark, 15
 Dou, Gérard, 583
 Douglass, William, 402
 Downer, Carol, 636

- DPT (diphtheria, pertussis, and tetanus), 775
- Drake, Daniel, 393
- Drake, David, 15
- Drake, Francis, 414
- drug resistance in microorganisms, 171–173
 “adaptation versus mutation,” 172
 Davis’s review on bacteria, 172
 Ehrlich describing drug action on microbes, 171–172
 resistance transfer factors (RTFs), 172–173
 work in microbial genetics by Luria, 172
- drug-resistant TB (XDR-TB), 718
- DSMIV. *See Diagnostic and Statistical Manual IV (DSM IV)*
- Duesberg, Peter, 10
- Dumas, Alexandre, 707
- Dworkin, Andrea, 635
- dysentery, 173–176
 biological causes of, 174–175
 causes of, 175–176
 definition of, 173–174
 epidemiology of, 175–176
 known as “bloody diarrhea”, 279
- Early Frost, An* (Lipman and Cowen), 16
- early humans, infectious diseases in, 177–180. *See also* diagnosis of historical diseases
 from animal sources, 178
 animal-to-human passage of zoonotic infectious disease, 179
 category of heirloom infections, 177
 human-adapted infections, rise of, 178
 multicentered agrarian transition, 179
- Ebers, Georg, 476
- Eberthella typhosa*, 721
- ebola. *See* hemorrhagic fevers
- ecology. *See* environment, ecology, and epidemic disease
- ectoparasites, 180–182. *See also* animal diseases (zoonoses) and epidemic disease
 definition of, 180
 fleas, 181
 lice, 181
 mites, 180–181
 ticks, 181–182
- Egypt
 leprosy in ancient, 357
 malaria in, 396
 plague epidemic (1360–1500), 517–518
 smallpox in ancient era, 677–678
- Ehrlich, Paul, 44, 118, 182–183
 description of drug action on microbes, 171–172
 and Salvarsan, 683
- electrocardiogram, 150
- electroencephalogram, 150
- electromyogram, 150
- Eliot, Charles W., 748
- Eliot, T.S., 368
- ELISA. *See* enzyme-linked, immunosorbant assay (ELISA)
- Elizabeth I (Queen)
 plague in Britain, 491–494
 public health during the rule of, 484
- Ellis, Havelock, 708
- El Tor biotype, 92–93, 94, 114
- empiric, 183–184
- Encephalitis, 184–187. *See also* encephalitis;
 epidemic outbreaks in twentieth century
 anti-encephalitis campaign, 186–187
 defined, 281
 “encephalitis lethargica,” 185
 environmentally driven, 186
 in Paris, 185
 triggered by nonepidemic reactions, 184
 virus transmission, 185–186
- encephalitis, epidemic outbreaks in twentieth century, 187–188
 “encephalitis lethargica,” 185
- Enders, John Franklin, 189, 403
- endocrine system, 278
- endoscopy, bronchoscopy, otolaryngoscopy, laparoscopy, and cystoscopy, 151
- Endymion* (Keats), 706
- Enemy of the People, An* (Ibsen), 368
- England, plague and developments in public health, 483–484
- English legislation, public health control, 484
 “English Sweat,” 686
- Entamoeba histolytica*, 175
- enteric fevers, 190–193
 cause of, 155
 definition of, 190
 distinction of, 191
- environment, ecology, and epidemic disease, 193–197
 altered environment and habitat with population sizes of species, 194–195
 biodiversity change and habitat fragmentation, 195
 conclusion of, 197

- environment, ecology, and epidemic disease
(*continued*)
ecosystem changes, loss of predators, and
host-species, 195
global climate change, 196–197
history of, 193–194
land use and environmental change, 194
niche invasion, 195–196
- Environmental Protection Agency (EPA),
470, 571
- enzyme-linked, immunosorbant assay
(ELISA), 8
- EPI (Expanded Program on Immunization),
408, 544
- epidemic and pandemic, 197–200
definition of, 197–198
history of, 198–199
modern concepts of, 199–200
- epidemic disease. *See also* cholera
and capitalism, 81
children and childhood, 85–86
cholera, 91–92
and cinema, 117–118
cinematic portrayals of, 120
and colonialism, 121
consequences of, 83
corpses and, 141, 143
diet, nutrition, and susceptibility to,
156–158
diet, nutrition and, 154
etiology of, 136
external pernicious influences, result of, 89
foods as vehicles for disease, 155
foreign policy and, 226–227
geopolitics and, 227
globalization, effects of (*see* globalization)
history of, 222–223
international disease campaign, 223
in later colonial societies, 122
in Latin America, 121–122
mechanisms of transmission, 130
in Neolithic Period (*see* Neolithic Period)
news media and (*see* news media and epi-
demic disease)
NGOs (*see* non-governmental
organizations (NGOs) and epidemic
disease)
preventing measures of, 124–126
scapegoats and (*see* scapegoats and
epidemic disease)
Scientific Revolution and (*see* Scientific
Revolution and epidemic disease)
- sexuality and gender and (*see* sexuality,
gender, and epidemic disease)
slavery and (*see* slavery and epidemic dis-
ease)
in Spanish colonies, 122
theatrical films dealing with, 119
understanding and explaining, 123
Western secular medicine, 125
- Epidemic Disease and Foreign Policy, 226–227
- Epidemic Diseases Act (1897), 507
- “epidemic highway”, 766
- epidemic keratoconjunctivitis, 127
- “epidemic of signification,” AIDS as, 13
- epidemiology, 154, 202–204. *See also* histori-
cal epidemiology
of Chlamydial infection, 232–233
definition of, 200–201
of dysentery, 175–176
history of, 201–202, 204–207
modern, 202–204
- epidemiology, historical. *See* historical
epidemiology
- epidemiology, history of, 204–207
- Epitaphs for the Plague Dead* (Boucheron), 14
- ergotism, 207–209
convulsive, 208
definition of, 207
gangrenous, 208
posing potential health hazard, 209
- Escherichia coli*, 40
- Essay on the Principle of Population, An*
(Malthus), 399
- ethnicity. *See* race, ethnicity, and epidemic
disease
- “eugenics era,” 411
- Euripides, 370
- European cordon sanitaire, 136–137
- European plague laws, 466
- European plague literature, 214
- European public bathing, 462
- Eusebius, 597
- exoticism, 89–90, 582
- Expanded Program on Immunization (EPI),
408, 544
- extrinsic incubation*, defined, 781
- Facing It: A Novel of A.I.D.S.* (Reed), 14
- Falsettos*, 15
- Farben, I. G., 683
- Farr, William, 211–212, 767
- FDA. *See* Food and Drug Administration
(FDA)

- Felix, Arthur, 722
Female Eunuch, The (Greer), 634
 Fernández deOviedo, Gonzalo, 692
 Fernel, Jean, 212–213
 Ferrán, Jaime, 745
 Ficino, Marsilio, 524
 Fierstein, Harvey, 15
 Fifth International Sanitary Conference, 790
 Filatov, Nil, 404
 film. *See* cinema and epidemic disease
 Filoviridae, 244–245
 “filthy habits,” 489
 Finlay, Carlos, 590, 783
 Finn, William, 15
 Finsen, Niels Ryberg, 711
 first domestic rodent with plague, 78
 First General International Sanitary Convention of the American Republics, 790
 First Gulf War, 758. *See also* Hussein, Saddam
 first plague pandemic. *See* Plague of Justinian
 flagella, 67
 flagellant movement, 58
 flagellants, 63, 67. *See also* Black Death, Flagellants, and Jews
 flagellation, 67
 flaviviridae, 245
flaviviridae virus, 779
 fleas, 181
 Fleming, Alexander, 460
 Flexner, Abraham, 420
 Flick, Lawrence, 714
 flight, 213–215. *See also* Black Death
 bubonic plague, 75
 cause of epidemic spread, 215, 215
 economies and civil administration, effect on, 441, 493
 as effective form of prevention, 524
Flight from Nevèrjón (Delany), 14
 Florence, Italy, plague in, 502, 503
 Florey, Howard, 460
 flu, 215
 fluoroquinolones, 25
 folk medicine, 215–217
 African American method, 216
 European, 216
 inoculation for smallpox, 216
 traditional, 215
 types of, 216
 Food and Drug Administration (FDA), U.S.
 AIDS prevention regulations, 8
 AZT approval as HIV/AIDS drug therapy, 7
 Food and the Principles of Dietetics (Hutchison), 156
 Ford, Gerald (President), 307
 Foucault, Michel, 494
 Four Horsemen of the Apocalypse, defined, 47
 Fracastoro, Girolamo, 217–218, 295, 422, 626, 627, 691, 692
 Fraenkel, Karl, 776
 France
 biological weapons program, 51
 demographic data collection and analysis (*see* *méthode numerique*)
 French Revolution, 270, 574
 mortality of cholera, 98
 pharmaceutical industry, 473
 public health, 565, 574
 second pandemic, cholera, 99
 Frankland, Edward, 767
 Franklin, Benjamin, 462
 Frederick II (King of Sicily), 26
 French cleansing rituals, 462
 French, W., 583
 French disease. *See* syphilis
 Froriep, Robert, 749
 Frost, Wade Hampton, 218–219
 Fry, R. M., 431
 Fry, Stephen, 42
 fumigation, 48, 521. *See also* disinfection and fumigation
 Gage, Henry, 512
 Galas, Diamanda, 15
 Galen, 221–222, 237, 295, 396, 476–477, 581
 Galenus, Claudius. *See* Galen
 Gangrenous ergotism, 208
Gardy and Erin (Black), 14
 Gatta, Bartolomeo della, 526
 gay-related immune deficiency (GRID), 7
Genius: Some Revaluations (Jacobson), 708
Genocide: The Anthology (Barrus), 14
 geopolitics, international relations, and
 epidemic disease, 222–227
 epidemic disease and foreign policy, 226–227
 epidemic disease and globalization, 223–226
 first international disease campaigns, 223
 first international health meetings/treaties/and organizations, 223
 LNHO, 223
 Gerhard, William, 724
 German pharmaceutical industry, 474

- germ theories of disease, 40, 458
- germ theory, 44, 498, 767. *See also* germ theory of disease
- African, 403
 - by Koch, 472
 - by Lister, 229
- germ theory of disease, 135, 228–230
- developing, 228–230
 - early explanation of disease, 228
- germ warfare. *See* biological war
- GFATM. *See* Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM)
- Giardia* virus, 701
- Gilman, Charlotte Perkins, 370
- Girolamo Fracastoro, 19
- Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), 388
- globalization
- concept of, 223–224
 - and epidemic disease, 224–225
 - problems of, 225–226
- Global Malaria Eradication Campaign, 223
- gonococcal infection symptoms, 231–232
- gonococcus, 230–231
- gonorrhea
- Boorde's explanation of, 230
 - Chlamydia trachomatis*, 232
 - definition of, 230
 - epidemiology of (*see* Chlamydial infection)
 - gonococcus, 230–231
 - persistence of symptoms, 233
 - symptoms of, 231–232
 - treatment of, 232
- gonorrhea and chlamydia, 230–233
- Goodenough Report, 267
- Gorgas, William Crawford, 233–235, 382, 763, 782, 784, 789
- Grant College Medical Society, 508
- granuloma, 283
- Grassi, Giovanni Batista, 604
- Graunt, John, 146
- “Great Conjunction,” 32
- “Great Depression,” 324, 360
- “Great Extinction,” 517
- Great Plague of London. *See* London, Great Plague of
- Great Pox. *See* syphilis
- Greco-Roman medical theory and practice, 133, 213, 235–237, 521
- Greek humoral theory. *See* Greco-Roman medical theory and practice
- Greer, Germaine, 634
- Gregg, Charles, 515
- GRID (gay-related immune deficiency), 7
- Grünpeck, Joseph, 691, 692
- Guérin, Camille, 715
- Gulf War. *See* First Gulf War
- Gunn, Thom, 15
- Guo, Zhan, 395
- gypsy moth, 319
- Haffkine, Waldemar Mordechai, 239–240, 508
- Haffkine Institute, 240
- Haffkine's vaccine, 239
- Halley, Edmund, 146
- Hamlet* (Shakespeare), 370
- Hand, Wayland D., 216
- Hansen, Gerhard Armauer, 240–241, 352
- Hansen's disease, 240. *See also* leprosy
- Hantavirus. *See* Hemorrhagic Fevers
- Harbin, China, 496
- Hare, Charles B., 78
- Haring, Keith, 17
- Harmonia axyridi*. *See* Asian lady beetle
- HART. *See* highly active antiretroviral treatment (HAART)
- HAV, hepatitis A virus (HAV)
- Haynes, Todd, 15
- HBV. *See* hepatitis B virus (HBV)
- HCV. *See* hepatitis C virus (HCV)
- HDV. *See* hepatitis delta virus (HDV)
- “healers,” 216
- Hebrew First Book of Samuel, 46
- Hebrew scriptures
- leprosy and, 363–364
 - Old Testament of the Christian Bible, 45
 - plague as divine punishment, 632
- Hedgehog Saint (St. Sebastian), 526–527
- Hefner, Hugh, 634
- Helmont, Jan Baptista van, 625
- hematological tests, 149
- hematologic and immunologic systems, 278
- hemorrhagic fevers, 141, 241–245
- in Africa (*see* hemorrhagic fevers in modern Africa)
 - of animal origin (zoonotic), 242
 - as biological weapons, 243
 - definition of, 241
 - families of, 243–245 (*see also* hemorrhagic fever viruses, families of)
 - source of spreading, 242
 - transmission of, 242

- treatment of, 243
- hemorrhagic fevers in modern Africa, 246–251
- caused by viruses, 246
 - Challenges faced, 248–250
 - Ebola outbreak in Zaire, 247
 - epidemics of Dengue, 247
 - measures in the detection and treatment of, 250–251
 - occurrence of Ebola and Marburg, 246
 - prognosis of a patient suffering from, 247
- hemorrhagic fever viruses (HFVs), 242–253
- animal origin of, 242
 - Arenaviridae family, 243–244
 - as biological weapons, 243
 - Bunyaviridae family, 244
 - Filoviridae family, 244–245
 - Flaviviridae family, 245
 - future research on, 245
 - in modern Africa, 246–251
 - transmission, 242
 - treatment, 243
- Hemphill, Essex, 14, 15
- Henderson, Donald Ainslie, 251–252
- Henry VII (King), 686
- Henry VIII (King), 484
- hepatitis, 252–255
- categories of, 253
 - definition of, 252–253
 - diagnosing, 255
 - history of viral, 253
 - incidence and prevalence of, 254
 - symptoms and physical signs of, 254
 - transmission of, 254
 - treatment and prevention for, 255
 - viruses of, 253
- hepatitis A virus (HAV), 253
- hepatitis B virus (HBV), 253
- hepatitis C virus (HCV), 253
- hepatitis delta virus (HDV), 253
- hepatitis E virus (HEV), 253
- hepatitis G virus (HGV), 253
- “herd immunity,” 466
- heredity and epidemic disease, 255–257. *See also* human subjects research
- HEV. *See* hepatitis E virus (HEV)
- HGV. *See* hepatitis G virus (HGV)
- highly active antiretroviral treatment (HAART), 11, 83
- Hippocrates, 257–260, 396, 476, 584
- Hippocratic corpus, 235. *See also* Hippocrates
- Hippocratic theory, epidemic disease, 766
- Hirsch, August, 727
- histology and cytology (pathologic examination of body tissues), 149
- historical disease, diagnosis of, 57
- historical epidemiology, 260–263
- Black Death, 57
 - demographic transition, 261–262
 - epidemiological transition, 262–263
 - origins of discipline of, 260
 - relationship between demographic changes and patterns of disease, 263
 - vital role in public health, 261
- Hitler, Adolf, 760
- HIV/AIDS. *See* Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS)
- HLA. *See* human leukocyte antigen (HLA)
- HMS *Dido*, 410
- “H5N1” influenza, 22
- “H1N1” virus, 22
- hoaxes, 55–56
- Hoffman, Albert, 208
- Hoffman, Alice, 14
- Holland, Walter, 15
- Home, Francis, 405
- homemade soaps, use of, 462
- Hong Kong plague, 495–496
- Hooke, Robert, 432
- hospitals
- cleanliness, 463
 - in developing countries, 275
 - and epidemic disease, 273–274
 - origins of, 48
 - quality of, 274
 - since 1900, 272–273
- hospitals and medical education in Britain and the United States, 264–269
- hospitals in the West to 1900, 269–271. *See also* hospitals since 1900
- hospitals since 1900, 272–276
- How to Use the Wood of the West Indies: A Healthful Remedy for Every Injury and Incurable Illness* (Delicado), 692
- HPV. *See* human papilloma virus (HPV)
- HTLV-I. *See* human T-cell lymphotropic virus, I (HTLV-I)
- HTLV-II. I. *See* human T-cell lymphotropic virus II (HTLV-II)
- Huang di nei jing, 89
- Hudson, Rock, 9, 15
- Hughes, Griffith, 792
- Hugo, Victor, 707

- human body, 276–281
 circulatory system, 277
 digestive system, 278–79
 endocrine system, 278
 hematologic and immunologic systems, 278
 integumentary system, 276
 lymphatic system, 277–278
 muscular and skeletal system, 280–81
 nervous system, 281
 reproductive system, 279–280
 respiratory system, 276–277
 urinary system, 281
- human immunity and resistance to disease, 282–284
 barriers to infection, 282
 detection of invading microbes, 283
 impact on host resistance, 283–284
- human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), 284–289
 American homosexuals in mid-2000s, 466–467
 current situation of, 289
 definition of, 284
 history of research and control of, 287–289
 sociocultural construction of, 287
 transmission of, 286–287
 effect on the human body, 285
- human insulin (humalin), 475
- human leukocyte antigen (HLA), 256
- human papilloma virus and cervical cancer, 290–292
- human papilloma virus (HPV)
 and cervical cancer, 290–292
 discovery of, 292
- Human Sexual Response* (Masters and Johnson), 634
- human subjects research, 293–294
- human T-cell lymphotropic virus, I (HTLV-I), 287–288
- human T-cell lymphotropic virus II (HTLV-II), 287–288
- humoral theory, 48, 295–296. *See also* Greco-Roman medical theory and practice
 Fernel, Jean, view of, 212
 medical education in the West 1100–1500, 418
- Hunter, John, 335, 745
- Hunter, William, 684
- Hussein, Saddam, 52, 758, 763. *See also* biological weapons
- Hutchison, Robert, 156
- Hutten, Ulrich von, 692
- Huygens, Christian, 146
- hygiene, meaning of, 461
- hyperacute bacterial conjunctivitis, 128
- I promessi sposi* (Manzoni), 469
- ibn al-Wardi, Abu Hafs Umar, 70
- IBSA (India–Brazil–South Africa), 227
- Ibsen, Henrik, 368
- Idiot, The* (Dostovsky), 370
- IHC. *See* International Health Commission (IHC)
- IHR. *See* International Health Regulations (IHR)
- Iliad*, 597
- IMF. *See* International Monetary Fund (IMF)
- immunity. *See* human immunity and resistance to disease
- immunization. *See* vaccination and inoculation
- immunodiagnostic tests, 149
- immunology, 297–299
- India–Brazil–South Africa (IBSA), 227
- industrialization and epidemic disease, 299–302
 concomitants of, 301–302
 food production and processing, 300–301
 “mad cow disease,” 300
 miasmas, germs, and people, 300
- industrial medicine, 303–304
- Industrial Revolution, 302–304. *See also* industrialization and epidemic disease
 industrial medicine and, 303–304
 tuberculosis and the, 710
 waves of, 302–303
- infant death syndrome, 88
- infantile paralysis. *See* poliomyelitis
- infectious diseases
- infectious diseases, prehistory of, 177
- influenza, 304–308. *See also* influenza epidemic (1889–1890); influenza pandemic (1918–1919)
 avian, 307–308
 in birds, 305
 evolution of, 21
 future research, 308
 history, 306–307
 influenza, study of origin, 21
 mutability and variation, 306
 potentially lethal respiratory illness, 304
 secondary bacterial infections, encouraging, 305

- structure, 305
 treatment of, 307
 influenza epidemic (1889–1890), 19, 309–313
 influenza pandemic (1918–1919), 20, 22, 313–317, 478, 756
 infusoria, 39
In Memory of Angel Clare (Bram), 14
 inoculation. *See* vaccination and inoculation
 insecticide. *See* pesticides
 insect infestations, 317–319
 Asian lady beetle, 319
 Asian tiger mosquito, 319
 bazaar fly, 318
 gypsy moth, 319
 Japanese beetle, 319
 Lovebug, 318–319
 Mormon cricket, 318
 periodical cicadas, 318
 trade and travel, 319
 insects, other arthropods, and epidemic disease, 320–322
 bubonic plague, 321
 dengue, 321
 elephantiasis and, 320
 germ theory of disease causation, 320 (*see also* germ theory of disease)
 malaria, 321
 Manson's research on, 320
 Onchocerciasis, 321
 sleeping sickness, 321
 “Texas cattle fever,” 321
 typhus, 321–322
 Institute for Healthcare Improvement (IHI), 274
 Institute for Study of Infectious Diseases, Tokyo, 496
 Institutional review board (IRB), 294
 integumentary system, 276
 interferon gamma (IFN), 282
 international health agencies and conventions, 322–326, 323
 Conseil Supérieur de Santé de Constantinople, 323
 Eight International Sanitary Conference, The, 324
 Eleventh International sanitary Conference, 323–324
 First Sanitary Conference, 323
 importance of, 322–323
 International Office of Public Hygiene (OHIP), 324
 International Statistical Congresses, the, 323
 LNHO, failures and success of, 324–325
 Office International d'Hygiène Publique, 324
 Pan American Sanitary Bureau, 324, 325
 Roemer's eight principles, 326
 Seventh International Sanitary Conference, 323
 WHO, 325–326
 World War I, aftereffects of, 324
 International Health Commission (IHC), 790
 International Health Division, The, 790
 International Health Regulations (IHR), 227
International Journal of Leprosy and Other Mycobacterial Diseases, 366
 International Monetary Fund (IMF), 223–224
 International Office of Public Hygiene (IOPH), 112
 International Office of Public Hygiene (OHIP), 324
 International Plague Conference, China, 497
 International Red Cross Society, 118
 International Sanitary Congresses, 698
 International Sanitary Convention, 488
 Internet, 442
 Irish potato famine and epidemic disease (1845–1850), 327–331
 blight in potatoes, 328
 British government's report, 329–320
 dangers of monoculture, 327
 diseases during, 330
 emigration and disease transfer, 330–331
 high mortality, 328, 329
 life of poverty, 327
 Peel's role, 328
 relief work, 328
 Irish potato famine migration, 591
 Ishii, Shiro, 763
 Islamic culture in Baghdad, 26
 Islamic disease theory and medicine, 48, 133–134, 331–333
 Islamic disease theory and medicine (Galen), 222
 Islamic medical theory, 517
 Islamic teaching, and flight, 214
 Ismaili Khojas, 508
 Italy
 developments in public health, 482
 plague epidemics in, 503–504
 Jacobson, Arthur, 708
 James II (King), 760
 James I of England, and plague in Britain, 491–494
janapada-uddhvamsa, 35

- Jane Eyre* (Bronte)
 Japanese beetle, 319
 Jarisch-Herxheimer Reaction, 593
 Jenner, Edward, 298, 335–336, 458, 648, 745
 cowpox vaccine, clinical trials, 293–294
 experiments with inoculation, 336
 discovery of vaccination for smallpox, 420, 666
 Jenner, William, 721
 Jewish community, 69
 JEWS. *See* Biblical Plagues; Black Death, Flagellants, and Jews
 JMP. *See* Joint Monitoring Program (JMP)
 Johnson, Toby, 14
 Joint Commission on the Accreditation of Healthcare Organizations (JCAHO), 274
 Joint Monitoring Program (JMP), 768
Journal of A Plague Year (Defoe), 524, 525
Journal of Ethnology (Virchow), 750
Journal of the American Medical Association, 291, 708
Journal of the Plague Year, 468
Journal of the Plague Year (Defoe), 422, 494
Journal of the Plague Years (Holland), 15
Joy of Sex, The (Comfort), 634
 Judd, Gerritt, 30
 Justinian, 584

kahuna, 30
 Kalaupapa, 360, 362–363
 Kalipeni, Ezekiel, 3
 Kamehameha III (King), 30
 K'ang (Chinese emperor), 743
 Keats, John, 706
 Kenya, and HIV/AIDS, 2
Kesari, 508
 Kesey, Ken, 370
 Khan, Aga, 508
kholera/kholeria, 110
 Kilborne, Fred Lucius, 321
King Death, 71
King Lear (Shakespeare), 370
 “King’s Evil,” 709
 King, Wong Chut, 512
 Kinsey, Alfred, 634
 Kinyoun, Joseph, 512
 Kircher, Athanasius, 627
Kitab al-Hawi fi al-tibb (The Comprehensive Book of Medicine; Rhazes), 600
 Kitasato, Shibasaburo, 44, 161, 229–230, 239, 339–340, 496, 498
 Klaproth, Martin, 27

 Klebs, Edwin, 160
 Klein, Michael, 14
 Koch, Robert, 40, 44, 340–342, 498
 germ theory and, 229, 420
 Pettenkofer’s opposition to theories of, 472
 tuberculosis, 703
 Konkola, Kari, 485
 Koop, C. Everett, 9
 Koplik, Henry, 404
 Kramer, Larry, 15
Kremers and Urdang’s History of Pharmacy, 28
 Kushner, Tony, 15

 “La Belle Dame Sans Merci” (Keats), 707
La Bohème (Puccini), 707
Lady of the Camellias, The (Dumas), 707
 Laennec, Rene, 713
laissez-faire capitalism, 565, 615–616. *See also* capitalism
Lancet, 211
 lassa fever. *See* hemorrhagic fevers
 Latin America, colonial: demographic effects
 of imported diseases, 343–347
 background of, 343
 historical record of, 343–344
 nature of diseases, 344–345
 origin and spreads of, 345–347
La Traviata (Verdi), 707
 Laveran, Alphonse, 234, 378, 763
 Laveran, Charles Louis Alphonse, 347–348
 lazaretto. *See* leprosarium; pest houses and lazarettos
Lazaretto Nuovo (New), 469
Lazaretto Vecchio (Old), 469
 Lazear, Camp, 784
 Lazear, Jesse, 321
 League of Nations Health Organization (LNHO), 223
 Leeuwenhoek, Antony van, 349, 432
 LeFebvre, Nicaise, 27
Legionella pneumophila. *See* Legionnaires’ disease
 Legionnaires’ disease, 350–351
 Lemery, Nicolas, 27
 Lennon, John, 635
 Leonicensi, Niccolò, 691–692
 leprosaria. *See* leprosy
 leprosarium, 351–352
 leprosy, 47, 352–355
 decrease in cases of, 354, 355
 endemic nature of, 353–354
 history of origin, 355

- incubation period of, 353
infection of, 353
lepromatous leprosy, 353
Mycobacterium leprae and, 352
pilgrimage and, 481
in premodern world (see leprosy in premodern world)
society's reactions toward (see leprosy, societal reaction to)
in United States (see leprosy in the United States)
treatment of, 354–355
tuberculoid leprosy, 353
- Leprosy: An Imperial Danger* (Wright), 635
- leprosy, societal reaction to, **363–366**
in Africa and Asia, 365–366
Chinese society, 364
Europe's attitude, 365–366
Hebrew scriptures, 363–364
during late 1980s, 366
medieval Christianity, 364–365
Quran and Muhammad's doctrine, 364
from 2000s, 366
- leprosy in premodern world, **356–358**
ancient Greece and Rome, 357–358
ancient Near East and Egypt, 357
China, India, and the Western Pacific, 356–357
medieval Europe, 358
- leprosy in the United States, **358–363**
Kalaupapa, treatment, 360, 362–363
Louisiana Leper Home, 359–360, 361
low rate of incidence, 359
Penikese Hospital of Massachusetts, 359
- Les Misérables* (Hugo), 707
- Lever, William, 462
- Lever Brothers, 463
- Liberace, 15
- lice, 181
- Lifebuooy “disinfectant” soap, 463
- Life* (St. Sebastian), 526
- Lind, James, 420
- Lister, Sir Joseph, 420, 463, 685
germ theory and, 229
instituting use of carbolic acid sprays, 44
- Listerine, 463
- literature, disease in modern, **367–371**
AIDS and, 369 (see also AIDS)
Black Death, 367–368
blindness, 370–371
bubonic plague, 368
ebola and small pox, 368
epidemic, 368
epilepsy, 370
limited use in, 367
mental illness in, 370
red death in, 371
tuberculosis in, 368–369 (see also tuberculosis)
- Little Ice Age, 485
- little leprosy (lepra), 413
- Living End, The* (Araki), 16
- Livy, 397
- LNHO. See League of Nations Health Organization (LNHO)
- London, nineteenth century public baths and washhouses, 462
- London, Great Plague of, 137, 141, **371–373**, 485
- Longtime Companion*, 15
- López de Villalobos, Francisco, 692
- Louisiana Leper Home, 359–360, 361
- Love Alone: 18 Elegies for Rog* (Monette), 14–15
- Lovebug (*Plecia nearctica*), 318–319
- Love! Valour! Compassion!* (McNally), 15
- Lucas, Craig, 15
- lungwort. See *Pulmonaria officinalis*
- Luria, Salvador, 172
- Lymantria dispar*. See gypsy moth
- Lyme disease, 37, **374–376**
carriers of, 374
caused by, 374
diagnosis of, 374–376
treatment of, 376
- lymphatic system, 277–278
- macabre imagery and themes, 523
- MacArthur, Douglas, 382
- Madagascar, 490
- “mad cow disease,” 300
- Magellan, Ferdinand, 670
- magic and healing, 377–378
astrology, 378
Black Death, 378
magical beliefs, 377
religion, 377
- Magiccada spp.* See periodical cicadas
- Maitland, Charles, 743
- malaria, 321, **378–381**
biological agent and its effects, 378–379
epidemiology and transmission, 379–380
pilgrimage and, 481
public health impact and control of, 380

- malaria and modern military history, **381–385**
 in World War I, 381
 in World War II, 382–383
 in Vietnam War, 384
- malaria in Africa, **385–389**
 agricultural development and, 387
 colonial political economy and, 386–387
 dealing with, 385–386
 as protozoan disease, 386
 WHO's contribution to prevention,
 387–388
- malaria in medieval and early modern Europe,
389–391
 found in, 389–390
 impact of, 390–391
- malaria in the Americas, **391–395**
 Caribbean Islands, 391
 colonial Americas and African slaves, 393
 colonial North America, 392
 debate on, 391
 South America, 392–393
 United States, 393
- malaria in the ancient world, **395–398**
 Africa, South of the Sahara, 397
 China, 395
 Egypt and Mesopotamia, 396
 Greece and Italy, 396
 Pacific and the Indian Oceans, 395
- Malkowal, Punjab, 508
- Mallon, Mary, **398**, 721
- Malthus, Thomas Robert, 399
- malthusianism, **399–400**
- Manchuria, plague epidemic in, 500–501
- Manchurian Plague Prevention Service, 501
- mandatory vaccination, 466
- Manny, Sir Walter, 141
- Manson, Patrick, 320–321, 386, **400**, 603
- Man with Night Sweats, The* (Gunn), 15
- Manzoni, Alessandro, 368, 469
- Maratha* (newspaper), 508
- marburg virus. *See* hemorrhagic fevers; hemorrhagic fevers in modern Africa
- Marseilles, France, 504
- Masque of the Red Death, The* (Poe), 371
- Mather, Cotton, **402**
- Mather, Increase, **402**
- Mather, Richard, 402
- Maxcy, Kenneth, 725
- May Act (1941), U.S., 761
- McKeown, Thomas, 261–262
- McNally, Terrence, 15
- McNeill, William, 495
- MDGs. *See* Millennium Development Goals (MDGs)
- MDR-TB. *See* multidrug-resistant strains of tuberculosis (MDR-TB)
- Mead, Richard, 422
- measles, 86, **403–406**
 disease, 404
 history, 404–406
 interaction of agent, host, and environment, 407
 vaccines, 406
 viruses, 403–404
- measles, efforts to eradicate, **408–409**
- Measles, Mumps, Rubella (MMR), 408
- measles epidemic in Fiji and eugenics, **410–412**
- measles in the colonial Americas, **412–417**
- Medela Medicinæ: A Plea for the free Profession, and a Renovation of the Art of Physic Tending to the Rescue of Mankind from the Tyranny of Diseases* (Fracastoro), 627
- media. *See* news media and epidemic disease; popular media and epidemic disease: recent trends
- Medical Education in the United States and Canada* (Flexner), 420
- medical education in the West 1100–1500, **417–419**
 astrology and, 418
 Greco-Roman, 417
 humoral theory, 418
- medical education in the West 1500–1900, **419–421**
 1900–present (*see* hospitals and medical education in Britain and the United States)
- medical ethics and epidemic disease, **422–428**
 contagion theory and, 422
 of experimentation, 425
 physician's duty, 423
 public health, 422, 424
 sleeping sickness, 426
 of vaccination, 425
- Medical Observations and Inquiries* (Rush), 406
- Medicina* (Fernel), 212
- Meiss, Millard, 70
- Meister, Joseph, 458
- Melville, Herman, 370
- meningitis, 281, **429**
 biological agents, 429
 epidemiology, 430
 research to control, 430
 symptoms, morbidity, and mortality, 429

- Mesny, Girard, 496
 Metchnikoff, Elie, 44, 239, 472
méthode numerique, 146
Method of Healing (Galen), 222
 Mexican-American War, and yellow fever, 788
 “miasmas.” *See* industrialization and epidemic disease
 miasma theory. *See* air and epidemic diseases
 microbial coinfection, 131–132
 microbiologic tests, 149–150
Micrographia (Hooke), 432, 433
 microscope, 432
 military. *See* war, the military, and epidemic disease
 military research, infectious disease, 763
 milkborne Bournemouth outbreak, 722
 Millennium Development Goals (MDGs), 227
 mites, 180–181
 mitochondria, 40
 MMR. *See* Measles, Mumps, Rubella (MMR)
Moby Dick (Melville), 370
 Moghul Empire, plague epidemics and, 520
 Mohr, Carl Freidrich, 27
 Moi, Daniel arap, 2
 Monette, Paul, 14
 Montagu, Lady Mary Wortley, 216, 743
 Montgomery, Richard, 651
 Mooser, Herman, 725
Morbidity and Mortality Weekly Reports, 7
 More, Thomas, 492
 Mormon cricket, 318
 Morrow, Prince, 747
 Morrow, William, 512
 Morse, Edward, 462
 Morton, Richard, 709
 Moscow, Russia, 504
 Muhammad, Prophet, 214, 517, 759
 Müller, Otto Friedrich, 39
 multidrug-resistant strains of tuberculosis (MDR-TB), 717, 718
 Murger, Henri, 707
 “murine typhus,” defined, 725
 Murray, Polly, 374
 Mursilis II, 595
 muscular and skeletal system, 280–81
 Mussolini, Benito, 380, 759
Mycobacterium bovis, 179
Mycobacterium leprae. *See* leprosy
Mycobacterium tuberculosis, 702
Nanyo Maru, 78
 Napoleonic Wars, 435–437. *See also* Bonaparte, Napoleon
 National Academy of Sciences, U.S., 10
 National Association for the Prevention of Tuberculosis, The, 710
 National Health Service (NHS), 267–268
 National Quarantine Service, China, 497
Natural History of Barbados (Hughes), 792
 Nedham, Marchamont, 627
 Neisser, Albert, 240
 Neisser, Albert L., 230–231
Neisseria meningitides, 699
 Neolithic Period
 diseases during, 438–440
 economic and social development in, 438
 evidence of disease, 440
 Paleolithic period, 438
 Neolithic Revolution and epidemic disease, 438–440. *See also* Neolithic Period
 nervous system, 281
New England Journal of Medicine, 16
 New Haven, Connecticut, and yellow fever, 793
 Newman, Sir George, 85
 New Orleans, yellow fever in, 795–796
 news media and epidemic disease, 440–443
 broadcast journalism, 442
 emerging diseases, coverage of, 442
 freedom of press, 440
 germ theory, coverage of, 441–442
 government’s role, 441
 influenza pandemic of 1918–1919, coverage of, 442
 media’s role, 443 (*see also* cinema and epidemic disease; popular media and epidemic disease)
 newspapers, arrival of, 441
 printing press, arrival of, 440–441
 SARS coverage, 443
 satellite and Internet, 442
 shaping public responses, 441
 yellow fever and plague, coverage of, 441
 New York City
 children death due to diphtheria in, 160
 first pest house, 469
 plague epidemic scare in, 77
 yellow fever in, 793–794
 Nichols, Mike, 15
 Nicolle, Charles Jules Henri, 444–445, 725, 729
 Nikon, 221

- Nightingale, Florence, 270, 685, 734
Night Larry Kramer Kissed Me, The (Drake), 15
Nippon Maru, 77
 Nixon, Richard, 51
 Nocard, Edmond, 431
 non-governmental organizations (NGOs) and epidemic disease, **445–447**
Normal Heart, The (Kramer), 15
 North Manchurian Plague Prevention Service, 497
Notes from Underground (Dostoevsky), 370
 Nureyev, Rudolf, 15
 nurses and nursing, **447–449**, 479
- “Ode on a Grecian Urn” (Keats), 707
 “Ode to a Nightingale” (Keats), 707
 O1 group antigen, 92
 OHIP. *See* International Office of Public Hygiene (OHIP)
 Old World diseases, 588
 Onchocerciasis, 321
On Contagion and Contagious Diseases and Their Cure (Girolamo), 217
On Contagion and Contagious Diseases (Fracastoro), 422
On Contagion (Girolamo), 217
One Flew over the Cuckoo’s Nest (Kesey), 370
On Medicine (De re medica; Celsus), 477
 Ono, Yoko, 635
On the Hidden Causes of Things (Fernel), 212
On the Medicine Guaiacum and the French Disease, Book One (Hutten), 692
 ophthalmia neonatorum, 129
 oral rehydration therapy (ORT), 279, 769
 Oroya fever, 43
 ORT. *See* oral rehydration therapy (ORT)
 Orta, García da, 95
Orthopoxvirus genus, 677
 Osler, William, 264
 Ottoman Empire
 plague epidemics, effects of, 519
 plague literature of sixteenth-century, 214
 plague treatment in, 522
Outbreak (Cook), 368
Oxford Textbook of Medicine, 718
 Oxford University, and penicillin use, 460
 “Ozymandias” (Shelley), 707
- Pacini, Florentine, 103
 Page Law, 748
 PAHO. *See* Pan American Health Organization (PAHO)
- Palliative treatments, 216
 Pan American Health Organization (PAHO), 791
 Pan American Sanitary Bureau, 324, 325
 Panum, Peter, 404
 parasitic conjunctivitis, 129
 Pardee, George, 512
 Parets, Miquel, 504
 Paris Peace Settlement, 315
 Parker, Matthew, 493
Parting Glances, 15
 Pasteur, Louis, 40, 386, 745, **457–460**
 anti-rabies treatment, 458
 developing germ theory, 44
 germ theory and, 229
 Pasteur Institute, 457, 459–460, 789
 “patent medicines,” 473
Pathologia, 212
 PCP. *See* pneumocystis carinii pneumonia (PCP)
 PCR. *See* polymerase chain reaction (PCR)
 Pears, Andrew, 462
 Pears’ soap, 462
 Pelletier, Pierre Joseph, 27
 penicillin, 232, **460–461**. *See also* antibiotics;
 pharmaceutical industry
 Penikese Hospital of Massachusetts, 359
Pennsylvania Packet, The (newspaper), 462
 Pennsylvania Society for the Prevention of Tuberculosis, 714
People in Trouble (Schulman), 14
 periodical cicadas, 318
 personal hygiene and epidemic disease, **461**
 classical tradition, 461–462
 cleanliness, 462–464
 and public health in Islamic society, 486, 576
 personal liberties and epidemic disease, **464–467**
 pertussis. *See* whooping cough
 pest houses and lazarettos, **468–469**
 pesticides, **470–471**. *See also* insects, other
 arthropods, and epidemic disease
 carbamates, 470
 in controlling epidemic and epizootic diseases, 470–471
 DDT dust, 470
 inorganic pesticides, 470
 natural pyrethrum, 470
 organic pesticides, 470
 organochlorine pesticides, 470
 organophosphates, 470

- pyrethroid pesticides, 470
silicon dioxide, powders, 470
- Peter, the Great of Russia (Czar), 759
- Petrarch, Francesco, 70
- Pettenkofer, Max Josef von, 471–472
- Pettenkofer's theory, 471
- Petty, William, 146
- Pfeiffer, Richard, 431
- phage typing, 722
- Pharm. D. *See* Doctor of Pharmacy (Pharm. D.)
- “pharmaceutical care,” 28
- pharmaceutical industry, 472–475
drug discovery and development, 472–473
economic globalization and, 475
German, 474
patent medicines, 473
penicillin, 461
regulation of drugs by FDA, 474
United States, 474
- pharmacist. *See* apothecary/pharmacist
- pharyngoconjunctival fever, 127
- Philadelphia*, 16
- Philadelphia, yellow fever in, 793
- Philadelphia College of Pharmacy, 28
- Philosophical Transactions*, 743
- Phthisiologia: or, a Treatise of Consumptions* (Morton), 709
- phthisis. *See* tuberculosis
- physician, 475
ancient Egyptian, 476
Asian traditions, 476
Greek era, 476
medieval and early modern West era, 477
Muslim, 477
in nineteenth and twentieth centuries, 478
prehistoric, 476
Roman era, 476–477
twenty-first-century, 479
- Physiologia*, 212
- Pieter Brueghel the Elder, 70
- pilgrimage and epidemic disease, 480–481
- pilgrimages, 466
water-borne diseases caused by, 766
source of population mixing and smallpox contagion, 672
and epidemic disease, 480–481
- pilgrims. *See* pilgrimage
- pink eye. *See* conjunctivitis
- Pizarro, Francisco, 392, 758
- Plague: A Novel about Healing* (Johnson), 14
- plague: end of the second pandemic, 484–487
cordon sanitaire and pest houses, 486
in Egypt, 487
in European countries, 484–486
in Islam, prevention of, 486–487
quarantine, 486
- Plague, The* (Camus), 368
- plague and developments in public health, 482–484
- plague images
changing God's mind, 525–526
multiplicity of heavenly protectors, 525
protestant, 529
Roch and plague buboes, 527–529
Sebastian, 526–527
- plague in Africa: third pandemic, 487
origins and spread, 488–490
bubonic plague, 487–488
- plague in Britain 1500–1666, 491
English monarchs and their advisory councils, role of, 492–493
London's Great Plague, 491
playhouse, role of, 494
printing press and medical writing, 493
- plague in Britain 1500–1666, 491–494
- plague in China, 495–497
connecting rat deaths and, 495
histories of, 495
in Hong Kong (1894), 495–496
in 1920–1911, 496–497
Wu Lien Teh's work and, 496–497, 776–777
- plague in East Asia: third pandemic, 497–501
China, 498–499 (*see also* plague in China)
Japan, 500
Java, 499–500
Manchuria, 500
Mongolia, 500
Taiwan, 499
Vietnam, 499
- plague in Europe, 1500–1770s, 502–506
- plague in India and Oceania: third pandemic, 506–509
- plague in medieval Europe 1360–1500, 510–511
- plague in recent times, 76
- plague in San Francisco, 511–513
- plague in the contemporary world, 514–516
in 20 countries, 516
United States, 515–516
during Vietnam War, 515
- plague in the Islamic world 1360–1500, 516–518

- plague in the Islamic world 1500–1850, 519–522
- plague in the United States, cases of, 79
- plague literature and art, early modern European, 522
- macabre imagery and themes, 523
- plague images, 525
- plague tracts, 523–524
- shock tactics, 524–525
- plague of Athens, 524, 738, 760
- plague of Justinian, 20, 75, 516, 739, 758
- plague prayers of King Mursilis, 595
- Plague Research Commission, 509
- Plague Research Laboratory (PRL), 508, 509
- Plagues and Peoples* (McNeill), 97, 495
- plagues of the Roman Empire, 536–538
- plague tracts, 70, 523–524
- Plecia nearctica*. See Lovebug
- pneumococcal disease, treatment of, 131
- Pneumocystis carinii pneumonia* (PCP), 7
- pneumonic and septicemic plague, 540–542
- pneumonic plague epidemic, 487
- pneumonic plague in Surat, Gujarat, India (1994), 215, 542–543
- Poe, Edgar Allan, 371
- Poets for Life: Seventy-Six Poets Respond to AIDS* (Klein), 14
- Poison* (Haynes) 15
- poison libel, 69
- poliomyelitis, 86
- polio vaccine, 474
- “political arithmetic,” 146
- polymerase chain reaction (PCR), 705
- Pope Clement VI, 69
- Popillia japonica*. See Japanese beetle
- popular media and epidemic disease: recent trends, 556–558
- poverty, caused by epidemics, 462
- Pre-Raphaelite painters, 707–708
- Prevention of Malaria, The* (Ross), 603
- primary transmission, 242
- “Principle of Population,” 399
- PRL. See Plague Research Laboratory (PRL)
- Prontosil. See sulfa drugs
- Protestant plague imagery, 529
- public health reform
- Chadwick’s report on disease and sanitation, 84
- for childhood epidemics, 86
- first board of health, 84
- influence of Chadwick on, 85
- Puccini, Giacomo, 707
- Pulex irritans* (flea) and bubonic plague, 72
- Pulmonaria officinalis*, 710
- “purity of blood” (limpieza de sangre), 588
- Qiuming, Zuo, 395
- quack, 581
- quacks, charlatans, and their remedies, 581–584
- alchemists, 582
- apothecaries, 582
- empirics, 582
- epidemic, 582
- London plague, 582
- medical pretenders, 581
- mountebank, 582
- paracelsians, 582
- scientific revolution, 582
- quaranta giorni*, 585
- quarantine, 584–586
- AIDS, Ebola, and SARS, 586
- animal diseases, 586
- Black Death, 585
- cholera and smallpox, 585
- hospitals, 584
- leprosaria, 584
- pest houses, 584
- sanatoria, 584
- Quran and Muhammad’s doctrine regarding leprosy, 364
- race, ethnicity, and epidemic disease, 587–590
- epidemic disease, 587
- Old World diseases, 588
- slavery, 588
- Radcliffe, John Netten, 767
- radiology, 150
- Rajneesh Attacks (1984), 53–54
- Ramazzini, Bernardino, 303
- Rand, W. C., 508
- Rape of Lucrece, The* (Shakespeare), 494
- Rat Bohemia* (Schulman), 14
- Rattus norvegicus*, 485
- Rattus rattus*, 485
- Ray, Randy, 9
- Ray, Ricky, 9
- Ray, Robert, 9
- Reagan, Ronald (U.S. President), 2
- Red Crescent. See non-governmental organizations (NGOs) and epidemic disease

- Red Cross. *See* non-governmental organizations (NGOs) and epidemic disease
- Reed, Paul, 14
- Reed, Walter, 234, 425, **590–591**, 756, 780, 783, 789, 797
- Reed Commission. *See* Yellow Fever Commission
- Rees, David, 4
- Reform of Medicine* (Mediscinische Reform; Virchow), 750
- relapsing fever, **591–593**
 antibiotics, 592
Borrelia bacterium, 591
 personal hygiene, 591
 prevention of, 593
 transmission, 592
- religion and epidemic disease, **593–600**
 ayurvedic, 594
 divine agency and divine cure, 594–95
 heavenly bookkeeping, 596
 heavenly helpers, 599
 hostile demons, 598
 pilgrimages, 599
 plague of Justinian, 597
 religion as help and hindrance, 599
 spirits of the dead, 597
 supernatural forces, 594
 understanding causes, 594
 what makes the gods angry?, 596
- Report on the Mortality of Cholera in England 1848–1849*, A (Farr), 211
- Report on the Pestilence* (Boccaccio), 70
- Report on the Sanitary Conditions of the Labouring Population of Great Britain*, 300
- reproductive system, 279–280
- resistance transfer factors (RTFs), 172–173
- respiratory system, 276–277
- Result of Observations* (Rush), 604
- Revolutionary War, 473
- Reynolds, Bronson, 748
- Rhazes, 404
- Rhazes (Abu Bakr Muhammad Ibn Akriyya Al-Razi), **600**
- ricketts, 88
- Ricketts, Howard Taylor, 723
- Rickettsia prowazekii*, 723
- Rickettsia typhi*, 723
- rifampicin, 718
- Roch, images of plague, 527
- Rockefeller, John, Jr, 748
- Rockefeller Foundation, 118, 790. *See also* non-governmental organizations (NGOs) and epidemic disease
 autumn fever, prevention of, 394
 17D vaccine, production of, 696
- Roemer, Milton, 326
- Rogers, Sir Leonard, 112
- “Roll Back Malaria,” 387
- romanticism. *See* tuberculosis and romanticism
- Romantic Movement, and tuberculosis, 705–706
- Romulus, 396
- Roosevelt, Franklin D., 768
- Roosevelt, Theodore (President), 234, 746
 “root wives”
- Ross, Campbell Claye Grant, 602
- Ross, Ronald, 234, 382, **602–604**, 763, 776
- Rothman, Lorraine, 636
- Rousseau, Jean-Jacques, 399
- Roux, Emile, 798
- ruminants, 40
- Rush, Benjamin, 423, **604–605**
- Russia
 Biological Warfare, 51
 breeding ground for MDR-TB, 224
 cholera pandemic, 99, 110
 plague epidemic control, 503–505
 plague epidemic in, 504–505
- Russian Black Sea fortress, and bubonic plague, 757
- S. dysenteria* (Sd1), 176
- Sabin, Albert, 298, **607–608**
- Safavid Empire, plague epidemics, effects of, 520
- Safe Drinking Water Act (1974), U.S., 768
- Safe Sex* (Fierstein), 15
- Saint Christopher, 525
- Saint Roche, 63
- salicylic acid, invention of, 473
- Salk, Jonas, 298
- Salk, Jonas E., **609–611**
- Salmonellae*, 155
- Salmonella typhi*, 721
- Salmonella typhi* antigen, 722
- Sanatorium
 closing down of, 614
 definition of, 611
 flourish in 1890s, 612–613
 Sanitation Movement, 613 (*see also* sanitation movement of the nineteenth century)

- Sanatorium (*continued*)
 slowdown in 1920s, 613–614
 tuberculosis and, 611–612
 sanatorium, **611–614**
- San Gregorio Lazaretto, Milan, 469
 “sanitary Bolshevism,” 382
- Sanitary Conditions of the Labouring Population of Great Britain, The* (Chadwick), 84
- Sanitary Institute and the Association of Sanitary Inspectors, 85
- sanitation movement of the nineteenth century, **615–618**, 740
 Chadwick’s report, 616–617
 in Europe and the United States, 617
 industrialization and urban poverty, 615–616
 interpretation of, 617–618
 personal liberty versus collective health, 615
 sanitation and social reforms, 616
- Saramago, José, 370–371
- SARS. *See* Severe Acute Respiratory Syndrome (SARS)
- satellite, 442
- Savannah, yellow fever in, 796
sayādilah, 26
- scapegoats and epidemic disease, **618–620**
- Scenes of the Bohemian Life* (Murger), 707
- Schaudinn, Fritz Richard, **620–621**
- Scheele, Carl Wilhelm, 27
- Schilling, Klaus, 383
- Schistocerca gregaria*. *See* Desert locust
- Schistosomiasis
 causative agents of, 621
 diagnosis and treatment, 623
 epidemiology and control of, 623–625
 history of, 621–622
 human pathology and disease, 622–623
 life cycle of, 622
- schistosomiasis, **621–625**
- Schulman, Sarah, 14
- Scientific Revolution, 23, 270, 503. *See also* Scientific Revolution and epidemic disease
- Scientific Revolution and epidemic disease, **625–627**
 atomism, mechanism, and fermentation, 626
 new technologies, 626–627
 organization, communication, and the state, 627
- Scott, Susan, 73
- Scrofula. *See* Tuberculosis
- second plague pandemic. *See* plague: end of the second pandemic; plague in Britain 1500–1666; plague in China; plague in Europe, 1500–1770s
- Semmeweis, Ignaz, 420, **628–629**
- Senegal
 HIV/AIDS prevention in, 5
 plague pandemic in, 490
- Sentiments on the Small Pox Inoculated* (Mather), 403
- septicemic plague. *See* pneumonic and septicemic plague
- Sertuerner, Friedrich Wilhelm Adam, 27, 473
 “17D” virus, 696
- severe acute respiratory syndrome (SARS), 224, 225, **629–631**, 741
 epidemic in Beijing, 215
 factors behind, 629–630
 impacts of, 630–631
 origin of, 629
 symptoms of, 629
 trade and travel, 700
 treatment for, 630
 urbanization and, 741
- Sex and the Single Girl* (Brown), 634
- Sexual Behavior in the Human Female* (Kinsey), 634
- Sexual Behavior in the Human Male* (Kinsey), 634
- sexuality, gender, and epidemic disease, **631–633**
 AIDS, as postmodern plague, 633
 in ancient world, 632
 in medieval and early modern worlds, 632–633
 modern medicine, primitive metaphors of, 633
 “plague” and “pestilence,” coinage of terms, 631–632
- sexually transmitted diseases (STDs), 279, 466
- sexually transmitted infections, 88. *See also* sexually transmitted diseases (STDs)
- sexual revolution, **634–637**
 brief history of, 634–635
 impact on epidemic disease, 636–637
- Shakespeare, William, 494
 “The Shaman,” 476
- Sherwood, Bill, 15
- Shibasaburo Kitasato, 44
- Shigella*, 175
- Shilts, Randy, 369
- shock tactics, 524

- Short Discourse Concerning Pestilential Contagion, and the Methods to Be Used to Prevent It*, A (Mead), 422
- Shrewsbury, J. F. D., 72
- “*shui qi*”, 395
- Silent Spring* (Carson), 470
- Simon, John, 767
- Simond, Paul Louis, 511, **637–638**
- Simpson, William John Ritchie, 240, 402, **638–639**
- Singer, Peter, 24
- slavery and epidemic disease, **639–643**
- African slavery to the New World, impact of, 640
 - in ancient world, 640
 - cholera, spread of, 642
 - malaria, spread of, 641
 - sailors and captains, experiences of, 641
 - small pox, 641–642
 - typhus, spread of, 642
 - yellow fever, spread of, 640–641
- slaves. *See* slavery and epidemic disease
- sleeping sickness, 321, **643–646**, 763
- causative organisms of, 643
 - diagnosis and treatment of, 646
 - epidemiology and control of, 646 (*see also* smallpox eradication)
 - history of, 643–644
 - organisms and vector, 644
 - pathology and clinical disease, 644–646
 - prevention with arsenic, 426
- smallpox, **647–650**
- history of, 647–650 (*see also* small pox and the American Revolution)
 - incubation period of, 647
 - mortality rate of, 647
 - pilgrimage and, 481
 - prevention (*see* smallpox eradication)
 - symptoms, 647
- small pox and the American Revolution, **650–652**
- smallpox eradication, **652–654**
- smallpox in ancient world, **677–679**
- ancient Greek and Roman worlds, 678–679
 - ancient Near East and Egypt, 677–678
 - camel domestication in the Bronze Age, 677
 - China, 678
 - India and Japan, 678
 - late antiquity, 679
 - Orthopoxvirus* genus, 677
 - smallpox in Canada and the United States since 1783, **655–658**
 - Jenner’s treatment method, 655
 - new strain of, 657
 - twentieth century, condition in, 657–658
 - urban epidemics of nineteenth century, 655–657
 - vaccination, 655
- small pox in colonial Latin America, **659–662**
- and “great leprosy,” 659
 - historical effects, 662
 - historical record, 659–660
 - individual and societal reactions, 661–662
 - origin and spread of, 660–661
- smallpox in colonial North America, **663–666**
- during Columbus period, 663
 - during eighteenth century, 664–665
 - during fifteenth century, 663
 - during seventeenth century, 663–664
 - during sixteenth century, 663
 - treatment and prevention, 665–666
- smallpox in European Non-American colonies, **667–672**
- Africa, 670–671 (*see also* slavery and epidemic disease)
 - Australia and the Pacific, 669–670
 - disease import, 667
 - Europe, 667–668
 - India and Indian Ocean region, 668–669
- smallpox in premodern Europe, **673–677**
- determinants, 673
 - early modern Europe, 674–675
 - factors for spreading, 673
 - historical evidence of, 673–674
 - inoculation of, 676–677
 - medieval Europe, 674
 - reactions and responses, 675–676
- Smith, Edwin, 476
- Smith, Theobald, 321
- Snow, John, 103, **680**, 698, 767
- and disputes over cholera control, 102–104
 - study of an 1854 cholera outbreak, 147
- Snow, William Freeman, 748
- Snows of Kilimanjaro, The* (Hemingway), 369
- social construction of disease. *See* disease, social construction of
- Social Disease and Marriage* (Morrow), 747
- social psychological epidemics, **681–682**
- Society of Apothecaries of London, 473
- Socrates, 524

- Sophocles, 596
- South Africa, third plague pandemic in, 490
- Spanish America
 epidemic disease in, 122
 measles in, 412–413
 smallpox in, 659
- Spanish-American War
 epidemic disease and, 756
 leprosy in American servicemen during, 354
 nurses, role of, 448
 smallpox, vaccination for, 657
 yellow fever in American troops, 784, 787
- Spanish influenza. *See* influenza
- “Spanish” influenza, 756
- Spanish influenza pandemic, 274
- Spores forms of bacteria, 41
- sporulation, 41
- St. Domingue, 786
- St. Gregory, the Great (Pope), 597
- St. John, 47
- St. Sebastian
 life and association with plague, 58, 526–527
 plague images, 526
- St. Vitus’ Dance, **608–609**
- Stanley, Thomas, 137
- STDs. *See* sexually transmitted diseases (STDs)
- Sterling Products, 474
- Sternberg, George, 431
- Streptomyces*, 25
- streptomycin, 614, 712, 716. *See also* antibiotics
- Study of British Genius*, A (Ellis), 708
- sulfa drugs, 232, **683–684**
- sulfonamide, discovery of, 474
- Summa on Medicine, with a Treatise on the “Bubas” Pestilence*, A (Villalobos), 692
- Summary of the Natural History of the Indies* (Oviedo), 692
- “Summer of Love”, 635
- Sunlight soap, 462
- surgeon, **684–686**
- Susruta Samhita*, 395
- sweating sickness, **686–687**
- “swine flu,” 307
- Sydenham, Thomas, **687–688**
- syphilis, 279, **688–689**
 biological agent of, 688–689
 control of, 690
 current state of, 690–691
 epidemiology, 690
 transmission of, 689–690
 treatment for, 688
Treponema pallidum, 688
 WHO’s treatment programs, 690
- Syphilis, or the French Disease* (Fracastoro), 217, 692
- syphilis in sixteenth-century Europe, **691–693**
 American origin theory, 692–693
 arguments on origin of, 692–693
 books on effects of, 692
 Fracastoro’s poem, 692
 Grünpeck’s treatise, 691
 hospitals for, early, 693
 Leonicensis’s views on disease’s nature, 691–692
 López de Villalobos’s views, 692
 symptoms, 693
 Torrella’s views, 692
 treatments of, 693
- Systematic Treatise, Historical, Etiological, and Practical, on the Principal Diseases of the Interior Valley of North America*, A (Drake), 393
- TAC. *See* Treatment AIDS Campaign (TAC)
- Tacuinum Sanitatis*, 462
- Taghribirdi, Ibn, 517, 518
- TASO. *See* Treatment AIDS Campaign (TAC)
- TB. *See* tuberculosis
- Television, and HIV/AIDS, 15
- Testevuide, Germain-Leger, 366
- tetracyclines, 25, 74. *See also* antibiotics
- “Texas cattle fever,” 321
- Thackrah, Charles Turner, 303
- The AIDS Support Organization (TASO), 5
- Theiler, Max, **695–696**
- Theiler, Sir Arnold, 695
- Therapeutice*, 212
- Theriac to Piso* (Galen), 222
- third pandemic of the nineteenth century, 73
- third plague pandemic. *See* bubonic plague in the United States; plague in Africa: third pandemic; plague in China; plague in East Asia: third pandemic; plague in India and Oceania: third pandemic
- Thirty Years’ War, **696–697**
- Thomas, John, 652
- Thompson, Ashburton J., 509
- Thucydides, 524, 584, 738

- ticks, 181–182
- Tilak, Bal Gangadhar, 508
- Tim, Barrus, 14
- Timonis, Emmanuel, 743
- toilet paper, use of, 463
- Tolstoy, Leo, 369
- Torrella, Gaspar, 692
- Torrey, Fuller, 19
- trade, travel, and epidemic disease, **697–701**
- cholera, 698
 - dengue fever, 700–701
 - hepatitis A, 699
 - HIV/AIDS, 699
 - malaria, African, 698
 - plague, 697
 - SARS, 700
 - syphilis, 688–689
- Trade Related Intellectual Property Rights (TRIPS), 225–226
- tragedy at Hamburg, 110
- transfusion-transmitted virus (TTV), 253
- transmission of disease. *See* contagion and transmission
- travel. *See* trade, travel, and epidemic disease
- Treatise on the Flowing Pestilence, or the French Disease* (Grünpeck), 691
- Treatise on the “serpentine” diseases* (Isla), 692
- Treatise with Advice Against “Pudendagram” or the French Disease* (Torrella), 692
- Treatment AIDS Campaign (TAC), 5
- Treaty of Paris, 473
- Trelawney, Edward John, 706
- trench fever, 181
- Treponema pallidum*
- syphilis, 688
 - transmission of, 689–690
- Treponema pallidum*, 688, 689
- trido.sa*, 35
- TRIPS. *See* Trade Related Intellectual Property Rights (TRIPS)
- Triumph of Death, The* (Brueghel), 70
- Trommsdorff, J. B., 473
- Tropical Diseases: A Manual of the Diseases of Warm Climates* (Mansoon), 402
- Trudeau, Edward L., 715
- trypanosomiasis. *See* sleeping sickness
- tuberculosis, **702–705**
- agent and effects, 702
 - BCG for, 704
 - DOTS for, 704
 - future research, 704–705
 - Mycobacterium tuberculosis*, 702
 - research and treatment, 703–704
 - and society, 703
 - transmission, 703
 - urbanization and, 740
 - vaccination, 704–705
- tuberculosis and romanticism, **705–709**
- tuberculosis in England since 1500, **709–712**
- tuberculosis in North America since 1800, **713–717**
- 1882–1943, 714–716
 - before 1882, 713–714
 - clinical diagnosis, 713
 - 1943–present, 716–717
 - prevention, 714
- tuberculosis in the contemporary world, **717–720**
- Tuscan town of Montelupo, 503
- Twigg, Graham, 72
- Tyabji, Badruddin, 508
- typhoid fever in the West since 1800, **720–723**
- Typhoid Mary. *See* Mallon, Mary
- typhus, 321–322, **723–726**
- biological agent and its effects on the human body, 723–724
 - current state of the disease, 726
 - epidemiology, 724
 - history, 724–725
 - research, prevention, and therapeutic efforts, 726
 - transmission, 724
 - waterborne outbreak in Croydon (1937), 722
- typhus and poverty in the modern world, **727–730**
- nineteenth-century patterns, 727–728
 - origins, 727
 - treatment with vaccines and antibiotics, 730
 - twentieth century mysteries, 728–730
- typhus and war, **731–735**
- Crimean War, 734
 - early appearances, 731–732
 - early modern trends, 732
 - English Civil War, 732
 - louse-borne, 731
 - modern era, 733–735
 - Napoleonic Wars, 733
 - symptoms, 731
 - United States Civil War, 733
 - War of Spanish Succession, 733
 - World War I and II, 734

- UN. *See* United Nations (UN)
- “Undesirable immigrants,” 586
- UNICEF (United Nations Children’s Fund), 38
- United Kingdom. *See* England
- United Nations Children’s Fund (UNICEF), 38
- United Nations (UN), 227. *See also* international health agencies and conventions
- United Service Organization (USO), 761
- United States
- Anthrax Letter Attacks (2001), 53
 - Army Commission on Yellow Fever in Havana, 797
 - Mexican immigrants, infectious diseases and, 465
 - Office of Scientific Research and Development, 474
 - penicillin, production of, 461
 - personal hygiene, public health campaigns, 463–464
 - pest houses, 469
 - pesticides, use of, 470
 - pharmaceutical industry, 473, 474
 - plague epidemic in, 515–516
 - Typhoid Board, 756
- United States Army Commission, 321
- United States Civil War
- cholera, death rates, 107
 - epidemic disease and, 759
 - nurses, role of, 448
 - sanitation movement, 617
 - smallpox, 655
 - typhus, cases of, 733
 - Red Cross, role of, 448
- United States Pharmacopoeia*, 28
- Upper Silesia, 727
- urbanization and epidemic disease, 737–741
- beginning of, 737–739
 - Black Death, era of, 739
 - during Bronze Age, 738–739
 - European expansions and early modern cities, 739–740
 - HIV/AIDS, 741
 - SARS, 741
 - TB, 740
- urinary system, 281
- USO. *See* United Service Organization (USO)
- Utopia, The (More)*, 492
- V. cholerae*, 93
- vaccination, 458
- defined, 745, 752
 - early history of, 743, 745
 - Ferrán, Jaime, and, 745
 - and inoculation, 743–746
 - Jenner, Edward, and, 745
 - Montague, Lady Mary Wortley, and, 743–744
 - opposition to, 746
 - Pasteur, Louis, and, 745
 - smallpox and development of, 743
- vaccination and inoculation, 743–746
- variant-Creutzfeldt-Jakob Disease (vCJD), 155, 301
- Variolae vaccinae*, 745
- Varrier-Jones, Pendrill, 711
- Vaughan, Megan, 122
- venereal disease and social reform in progressive-era America, 746–749
- Venetian Adriatic colony of Ragusa (Dubrovnik), 468
- Venice Conference of 1897, 488
- Venus and Adonis* (Shakespeare), 494
- Verdi, Giuseppe, 707
- Vesalius, Andreas, 419
- Vibrio*, cholera, 698
- Vibrionia, 39
- Vietnam War
- malaria during, 384
 - plague epidemic during, 515
 - venereal diseases during, 760
- Villemin, Jean-Antoine, 714
- viral conjunctivitis, 127
- Virchow, Rudolf, 727, 749–750
- Virchow’s Archiv* (Virchow), 750
- Virgin Mary, 58, 525
- “virgin-soil epidemic,” 411
- “virulence” antigen, 722
- virus, 246, 750–753
- chicken pox, 752
 - definition, 750
 - effects on the host, 752
 - HIV, 752
 - immunological responses in host, 751–752
 - initial entry and multiplication, 751
 - molluscum contagiosum*, 752
 - release and viremic phase, 751
 - virulence and transmission, 752–753
- Visconti, Gian Galeazzo (Duke), 468
- visual arts, and HIV/AIDS, 16–17

- “vivisection,” defined, 23
vomito prieto, 785
 von Ehrenberg, Carl Gustave, 39
 Vries, Peter De, 369–370
- Waksman, Selman, 25, 716
 Walpole, Horace, 378
 war, the military, and epidemic disease, **755–764**
 armed forces, 760–761
 biological agents, use of, 763–764
 bubonic plague, 757
 on campaign, 759–760
 camp conditions and life, 756–758
 cholera, 757
 crude death rates (CDR), 762
 First Gulf War, 758
 and military opportunism, 758–759
 military research on disease and treatment, 763
 postwar conditions, 762
 reemergent epidemic disease, 762–763
 returning troops and refugees, 761–762
 siege, 760
 U.S. Armed Forces, 755–756
 war and reemergent epidemic disease, 762
 warfare, 49
 Washington, George, 651
Waste Land, The (Eliot), 368
 water and epidemic diseases, **765–769**
 current problems of, 768–769
 drinking and sanitation, 766
 link between, 767–768
 Waterhouse, Benjamin, 336
 Webster, Noah, 793
 Weichselbaum, Anton, 431
 Weigl, Pole Rudolf, 734
 Welch, William Henry, 424
 West Nile fever, 699–700, 757, **770–772**
 biological agent and its effects, 770
 epidemiology, 771
 history of major outbreaks, 771–772
 prevention, 772
 transmission, 770–771
 West Nile virus (WNV), 700
 White, Ryan, 9
 “white man’s grave,” 385
 white plague. *See* tuberculosis
 WHO. *See* World Health Organization (WHO)
 whooping cough, **772–775**
 Bordetella pertussis virus, 773
 diagnosis of, 774
 treatment and prevention, 774–775
 Widal, Fernand, 721
Widening Circle, The (Murray), 374
 Wildmon, Donald, 17
 Willis, Thomas, 626, 773
 WNV (West Nile Virus), 700
 Wolsey, Thomas Cardinal, 492
 Woodcock, Herbert de Carle, 710
 Woodhead, German Sims, 776
 World Bank (WB), 223–224
World Can Break Your Heart, The (Curzon), 14
 World Health Organization (WHO), 22, 38, 76s, 275, 325–326, 791. *See also*
 International Health Agencies and Conventions
 Africa Malaria Report 2003, The (World Health Organization), 387–388
 DOTS, 704
 IHR, 227
 international health regulations, implementation of, 215
 malaria eradication program, 768
 malaria in Africa, contribution to, 387–388
 plague as “reemerging” disease, 490
 reports, death due to plague, 516
 smallpox eradication programs, 466 and UNICEF (*see* Joint Monitoring Program (JMP))
 World Medical Association, 428
 World Trade Organization (WTO), 223–224, 225–226
 World War I
 biological weapons, use of, 50–51, 470, 619
 death mortality rate in America due to malaria, 394
 encephalitis during, 185
 influenza, evolution of, 21
 international health agencies, role of, 324
 malaria during, 381–382
 Paris Peace Settlement, 315
 pharmaceutical industry and, 474
 prevention of typhus, 726
 Public Health Service in U.S., role of, 568
 relapsing fever outbreak in Africa, 591
 sexually transmitted diseases in Australian soldiers, 761
 typhus during, 273, 734
 United States’ entry into, 790
 yellow fever, 779

- World War II
biological weapons, use of, 50–51, 513
war crimes, 383
dengue epidemic, 321
eugenics activities, 411
international health agencies, role of, 324
malaria in, 382–383
nursing and, 448
pharmaceutical industry, 474
plague as bioterrorism threat, 76, 500
Public Health Services in U.S., role of, 569
relapsing fever during, 591
schistosomiasis during, 624
scrub typhus during, 180
syphilis during, 690
trench fever in Eastern Europe, 181
typhus epidemic, 273
venereal diseases, 760
WHO's malaria eradication campaign, 223
- Wright, H. P., 365
- Wrong Apple, The* (Rees), 14
- WTO. *See* World Trade Organization (WTO)
- Wu Lien Teh (Wu Liende Or Wu Liande), 496, 500, **776–777**
- Wyman, Walter, 512
- XDR-TB. *See* drug-resistant TB (XDR-TB)
- Xenopsylla cheopis*, 75
- Xenopsylla cheopis*, 485, 488, 724
- yeast
discovery of, 457
inflammatory disease and, 285
- yellow fever, 695, 759, **779–782**
defined, 779
epidemiology, 781
etiology, 779–780
extrinsic incubation, 781
prevention, 782
public health, 782
social impact, 781–782
Theiler's work on, 695
transmission, 780–781
virus (*flaviviridae*), 779
- Yellow Fever Commission, U.S., **783–784**, 789
- yellow fever in colonial Latin America and the Caribbean, **785–787**
- yellow fever in Latin America and the Caribbean (1830–1940), **787–791**
Brazil, Panama, and Cuba, spread of, 788–789
Hemispheric Health Organization and, 790–791
Mexican-American War, 788
Rio and Panama, spread and elimination, 789–790
- yellow fever in North America to 1810, **791–794**
- yellow fever in the American South (1810–1905), **794–797**
- Yersin, Alexandre, 229–230, 239, **798**
- Yersin, Alexandre E. J., 460, 498
- Yersinia pestis*, 57, 72, 74, 488, 514
discovery of, 798
named by Dr. Yersin, 498
plague caused by, 77
research into, 77
- Yolken, Robert, 19
- Yuan Shih-kai, 776
- Yunnan Province, China, 495
- Zinsser, Hans, 724, 729
- zoonosis. *See* animal diseases (zoonoses) and epidemic disease
- zoonotic diseases. *See* animal diseases (zoonoses) and epidemic disease
- Zulu, Leo, 3