Hospital Infection

From Miasmas to MRSA

Graham A. J. Ayliffe
and Mary P. English

CAMBRIDGE
UNIVERSITY PRESS

PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE
The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS
The Edinburgh Building, Cambridge CB2 2RU, UK
40 West 20th Street, New York, NY 10011-4211, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
Ruiz de Alarcón 13, 28014 Madrid, Spain
Dock House, The Waterfront, Cape Town 8001, South Africa

http://www.cambridge.org

First published 2003

Printed in the United Kingdom at the University Press, Cambridge

Typefaces Minion 10.5/14 pt and Formata *System* LaTeX 2_ε [TB]

A catalogue record for this book is available from the British Library

ISBN 0 521 81935 0 hardback
ISBN 0 521 53178 0 paperback

Contents

1

Theories of infection: from magic to miasmas

The management of patients with infectious diseases, the control of epidemics and the planning of hospitals have always been dependent on the contemporary theories of infection. For this reason, it may be useful to devote some space to a brief history of the development of infection theory over the centuries.

In ancient times, belief in black magic and the malevolence of witches and evil spirits was universal and, despite the rise of Christianity, had an immensely firm grip on people and their rulers right through to the Tudor period and beyond. The help of practitioners of the occult was called upon regularly in times of sickness, and even today raw beef features in a magical cure for warts. During the Great Plague in London (1664–5), some recommended the wearing of a tassel of tarred rope to ward off the disease, and a doctor who felt the symptoms coming on after he had dissected a plague victim placed a dried toad on his chest to draw off the poison. Pepys used a hare's foot to keep away the colic, but when the charm failed a friend pointed out that it did not include the joint; after it had been replaced by a complete specimen, Pepys was never troubled by colic again.[1] Perhaps the most generally accepted belief was the cure of the King's Evil (scrofula, or tuberculosis of the glands) by means of the royal touch. This piece of pagan magic was christianized by Henry VII, who invented a church ritual during which the ceremony was performed, a ceremony that was only removed from the Book of Common Prayer by George I.[2]

With the advent of Christianity, these pagan beliefs were very slowly superseded by the idea that sickness was a punishment from God for the sins of the victim or the community, and that consequently the only sure remedy was prayer and penance until His forgiveness was granted. As late as the sixteenth century, the Elizabethan Prayer Book required clergymen visiting sick parishioners to remind them of this, and it was held that the ministrations of physicians and surgeons would be successful only if they had prayed beforehand. From an early date, in times of plague, masses and prayers were addressed to holy relics, but by degrees, bitter experience and the deaths of hundreds of priests and monks showed such faith to be ineffectual; indeed, it has been suggested that one factor reducing opposition to

the Reformation was disillusion with the healing power of relics.[2] Throughout the history of human thought, magic, religion and science have fought for supremacy in the explanation of disease, and it was only in medieval times that science began to get the upper hand.

At the end of the fifteenth century, the ancient Greek doctrine of the humours was still the basis of disease theory. Patients were believed to belong to one of four groups or 'complections' – choleric, melancholic, phlegmatic or sanguine – each associated with an appropriate 'humour' – yellow or green bile, black bile, phlegm and blood, respectively. Badly balanced humours predisposed to specific types of disease, but it was admitted that some diseases, mostly those known to be infectious, were exceptions.[3]

The oldest of the more 'scientific' theories of the spread of epidemic disease was that of the corruption of the air, an idea that began at least in the sixth century, and was to persist into the nineteenth century. Corruption could be induced by any extremes of weather, such as excessive dryness, heat or rain,[4] or more locally by the putrid miasmas arising from decaying organic matter, corpses, cesspools, marshes and the like. Limited public health measures were aimed at cleaning up such places; for instance, in 1488 Henry VII issued a statute regulating slaughterhouses in towns, and in 1495 he decreed that marshes near towns must be drained before they were built over. It was believed that when inhaled, miasmas (which some held to consist of poisonous particles) were absorbed in some way by the body, and then attacked the humours to cause disease. Some suggested that epidemics occurred when the process was made more virulent by a malign conjunction of the stars. There was also supposed to be a factor of individual predisposition, a concept that was combined with a stress on the importance of personal cleanliness,[5] an unexpected concept considering the general disregard for such matters at the time. As yet, no distinction was made between different infectious diseases, so that any miasma could cause any disease.

For the whole medieval period, including the terrible years of the Black Death, the main prophylactic measure against infectious diseases was fumigation by the burning of incense, herbs and aromatic essences.[6]

The belief that disease is spread by corrupted air, distinguishable from pure air by its noxious smell, is, as already discussed, a very ancient one, and over the centuries means have been sought to contain epidemics by removing evil odours. It was not until the eighteenth century that a distinction was clearly made between merely concealing the stench with aromatic scents and actually destroying it. At that time, fumigation became widely recommended as one of the measures for preventing the spread of typhus.

Fumigation usually refers to the production of smoke or a vapour, often odorous such as incense, to remove infection, pests, evil spirits or unpleasant smells. An

early account of fumigation was given by Homer in the *Odyssey* in about 800 BC, in which Odysseus used sulphur dioxide to fumigate his house on his return after he had killed his wife's suitors. In early Indian writing (Sushruta 800–600 BC), the fumigation of an operating room with fumes of mustard, butter and salt might be considered an early form of 'antisepsis'[7] of the air, although it was also used to get rid of evil spirits. Sulphur fumigation was commonly used to prevent the spread of plague in the Middle Ages. In the seventeenth century, the possible connection between fermentation and disease was recognized by Robert Boyle. Francis Bacon (1663) also related gangrene to putrefaction and listed substances that would prevent putrefaction, including sulphuric acid, salts and sugars.

Despite the universal acknowledgement of the divine wrath and putrid air as the generators of disease, practical observation had forced on man since the earliest times the idea that in the case of leprosy contagion was a factor in its spread, but it was not until the Middle Ages that a turning point was reached and the ravages of the epidemic leprosy of the time, together with the plague, forced a full recognition of infection as a cause of some diseases.[8] No explanation of the phenomenon would, however, be put forward until the sixteenth century, with the result that, although stringent precautions were taken against the spread of both leprosy and plague, no attempt was made to segregate other fever patients in hospitals. For instance, in 1148 all sick people, regardless of whether they were suffering from diseases now known to be infections, were being admitted to St Bartholomew's Hospital, London.[9] By about 1300, however, Bernard Gordon of Montpellier had listed eight diseases that he recognized as infectious – bubonic plague, phthisis, epilepsy, scabies, erysipelas, anthrax, trachoma and leprosy.[8] With regard to erysipelas, Walshe records that a special order of monks was created to work in hospitals dedicated to patients suffering from St Anthony's fire, which he takes to be synonymous with erysipelas, considering that this is an early recognition of the contagiousness of the disease. But 'St Anthony's fire' was a term used indiscriminately at the time for erysipelas and the gangrene and subsequent withering of limbs that resulted from ergot poisoning, a mysterious and terrifying, though non-infectious, disease that could well have precipitated the setting up of a dedicated nursing order.

The Black Death, or bubonic plague, was probably brought to Europe by a ship trading from the Near East, which docked at Messina in Sicily in 1347. From there, the disease spread throughout the continent with devastating speed. It is estimated that one-quarter to one-half of the entire population of Europe was wiped out between 1348 and 1359, and at least half the population of Britain succumbed.[6]

The causal bacterium, *Yersinia*, formerly *Pasteurella, pestis* (see Chapter 9), was carried by its vectors, the black rat and its flea *Pulex irritans*. The black rat, the common species of the age, lives and breeds in houses, unlike the brown rat that

has now replaced it and prefers outhouses and sewers to domestic premises. The association of rats with the disease was unrecognized for several centuries after the Middle Ages, although there are two intriguing biblical references to mice in conjunction with epidemics, which are now considered to have been plague – the 'emerods' with which Ashod smote the Hebrews (1 Samuel: v), and the plague visited by the Lord on the army of Sennacherib (2 Kings: xix, 36).[6]

Monasteries were decimated by the plague early, the first casualties being those of the Dominicans and Friars Minor of Messina, who were left behind to attend to the first European victims after the rest of the population of the city had fled. In England, the communities of St Albans, Glastonbury and Bath abbeys were halved.[10] Lepers were particularly vulnerable, both because of their concentration in lazar houses and because of their lack of immunity due to their underlying disease.[9]

The obvious infectivity of the Black Death not only reinforced the idea of the segregation of victims to protect the rest of the community, but also the panic it created resulted in the introduction for the first time in history of two further forms of prophylaxis. The possibility of spread through patients' clothing, bedding, etc. led to the disinfection or burning of fomites, and the use of quarantine began as a means of safeguarding whole communities. Municipal authorities placed the homes of plague victims under a ban; they and all their contacts were also banned, and their food was provided for them. The dead were passed out of houses and removed in carts for burial outside the city, and their houses were fumigated (although only with the usual incense and aromatic herbs), and their effects burned. Occasionally, a group of people, knowing they harboured plague cases, made the heroic decision to immolate themselves so as to prevent the disease from spreading further. Perhaps the most famous case, in 1666, is the village of Eyam in the Derbyshire Peak District, the inhabitants of which, after a few wealthy families had fled, drew a cordon sanitaire about half a mile around the village. Food was brought to the boundary, but no person crossed it, neither entering nor leaving the village. The inhabitants were decimated, 259 of them dying before the end of the outbreak.[3]

In Europe, Venice was the chief port for trade with the Orient, and it was here that quarantine was practised for the first time. In 1348, a committee of three prominent citizens was set up with powers to isolate suspected ships, goods and people, a practice that spread throughout Europe. Then in 1377, the municipal Council of Ragusa (Dubrovnik) ordered that ships be held in isolation for a period of 30 days (later extended to 40 days, this being the origin of the word 'quarantine'). In 1383, citizens of Marseilles erected the first quarantine station, where all incoming vessels and their contents were rigorously inspected and exposed to air and sunshine, and their crews isolated in special lazar houses.[5] Such isolation hospitals might also be built outside towns at the beginning of an outbreak in the hope of controlling it.

Although by the Middle Ages contagion had been recognized as a factor in the spread of disease, its cure was still the preserve of the Church and even residual pagan beliefs. Doctors could offer little more in the way of treatment than bloodletting and purification of the air. The intercession of the saints was therefore of extreme importance, and one saint in particular was associated with the Black Death. St Roche was born in Montpellier in the south of France in about 1350, and spent his life going on pilgrimages and working among the sick. While on a pilgrimage to Rome, he fell victim to the plague and fled to a neighbouring forest to die, but he was brought a daily supply of bread by the dog of a local landowner, recovered, and was eventually pronounced cured by an angel. This is why he is accompanied by a dog, an angel or both in the statues that grace his many shrines in France and Italy. After his recovery, the saint set out on his last pilgrimage to Angera, but was accused of being a spy and thrown into prison, where he died, leaving a scribbled message on the wall of his cell saying, 'He who is seized of the plague and seeks refuge in Roche will gain relief in the disease.' From that time on, plague victims sought St Roche's intercession, and many hospitals in Europe were dedicated to him. His cult reached England, where his statue used to stand in a number of churches. In Exeter, in the early sixteenth century, there were a chapel and hospital dedicated to the saint, which were commemorated until very recent times by a small roadway called Rock Lane, but even this has now disappeared. It is perhaps of interest that statues of St Roche usually show him pointing to a lump a little above one of his knees, clearly a bubo. In fact, the bubo would have been situated in his groin, but this was an awkward site to display in a statue!

In the first half of the sixteenth century, Girolamo Fracastoro (1483–1553), working in Venice, gradually reasoned his way to an astonishingly modern theory of infection. His initial interest was syphilis, recently introduced into Europe and by then reaching epidemic proportions, but his work gradually extended to include all epidemic diseases. In the 1530s, he considered, like others, that corrupted air was the cause of epidemics, but he suggested that the source of the corruption was astrological, different conjunctions of the planets causing different diseases in different hosts. Here we have the first mention of the specific nature of diseases and their causes, an idea which, with remarkable prescience, he particularly emphasized.

But it was his essay on contagion, published in 1546, that anticipated the science of bacteriology by 300 years. First, he was clear that infection was the cause, of which epidemics were the consequence; second, he suggested that contagion was caused by infective 'seeds' – he called them 'seminaria' – which were too small to be visible to the naked eye; third, he stated that these seeds were specific for specific diseases; and finally, he suggested that the seeds were self-propagating and acted on the humours and vital spirits of the body, although careful reading of the text makes it clear that there is no suggestion that 'seeds' are living organisms.[8] He also recognized

that infection could take place in three ways: by direct contact between people, by fomites (a term he introduced), and at a distance through the air. However, he continued to believe implicitly in astrology and the power of the conjunction of the stars as the source of the phenomena that he described. For a while, his ideas were widely accepted, but gradually they were forgotten and supplanted once again by the old, erroneous miasmatic theory,[11] together with a continued belief in witchcraft, sorcery and alchemy.

No further advances were made until the seventeenth century, but by then the repeated outbreaks of plague were crying out for an explanation. In 1658, Athenasius Kircher (1602–88), a Jesuit priest, published a tract on plague entitled 'Scrutinium Pestis'. Although he did not cite Fracastoro, he did in fact follow him in believing that both God and the stars had a hand in the occurrence of epidemics, but that 'natural causes were also important, and that these included self-propagating seminaria specific to each disease'. But Kircher had the advantage over Fracastoro in that he possessed a 'very delicate' microscope. Though he could not possibly have seen bacteria with this instrument, he could see small moving objects, and when he made observations – 'experiments' he called them – on rotting meat, decaying wood, soil and such materials, he could describe the living 'worms' and 'creeping things' that he saw, some of which turned into winged forms. He concluded from his observations that the bodies of those who died from plague generated corpuscles, which might be living or non-living, and which could infect bread, wood and other porous substances as well as the air, and so spread the disease by finger contact or inhalation. Among the 12 different ways in which contagion might take place, he lists the physician attending plague cases since the 'virulent corpuscles which have been breathed out or transferred by manual contact will adhere to the innermost recesses of the pores so that contagion may readily be communicated to those not already infected with the disease'.[8] Perhaps this is the first mention of iatrogenic disease. Kircher emphasizes throughout that the 'seeds' specific to plague are the essential cause of the disease and are always present, and that the living seeds reproduce themselves in vast numbers in the victim's body, to be given off eventually through all body openings to infect new hosts and fomites.[8]

Despite Kircher's continuing belief in the deity and the stars as additional causes of epidemics, his 'Scrutinium Pestis' was the first effective recognition that living, multiplying organisms specific to a disease are the primary cause of that disease, a recognition that he backed up with 'experiments', however inadequate to modern eyes, to prove it. His theory immediately attracted attention throughout Europe, including England, but here, one otherwise extremely advanced and influential clinician, Thomas Sydenham (1624–89), continued to insist that it was the 'epidemic constitution' of the atmosphere that was responsible for epidemics.[8] At the end of his life, however, Sydenham broadened his theory somewhat. The outbreak of

'fever' in 1658–60 did not appear to be related in the usual way to the weather or the season, so he suggested that there must have been 'some secret and remarkable change in the bowels of the earth', rather than in the air, to account for it, an idea that was expanded by his friend Robert Boyle. Sydenham believed that the poisonous effluvia were mineral particles that originated in the earth's crust, where they could, in some undefined way, spread or multiply, and from which they were liberated by eruptions or slower movements of the crust.[12]

Meanwhile, from Italy emerged yet another brilliant scientist, Francesco Redi (1620–98), a medical man, philosopher and naturalist.[13] As a doctor, he advocated observation as opposed to theory, and hygiene rather than therapy. As a naturalist, he was particularly interested in insects, and it was this interest that led to his major contribution to science, the first experimental refutation of the theory of spontaneous generation, at least so far as it applied to insects and larger organisms. He did this by exposing pieces of meat in jars to the warm summer air, some with the jars uncovered and some with their mouths covered by pieces of gauze. While the meat putrefied under both conditions, maggots were generated only from the unprotected pieces, those covered with gauze remaining maggot free, although blowflies were attracted to the jars and maggots hatched from the eggs they laid on the gauze. Redi's conclusion – that in all cases where living things had apparently been produced by dead matter, the 'seeds' of the life form had in fact been introduced from outside – was readily accepted by others. But this brilliant deduction could not, of course, be applied to the as yet undiscovered micro-organisms. Another discovery by Bonomo in 1687 was that of the scabies mite, which some considered a turning point in medicine in that it made doctors think of exogenous pathogenic agents rather than disturbed humans. Nevertheless, it was not until the nineteenth century that the theory of spontaneous generation was finally laid to rest for both putrefaction and disease.

The century's advances were completed by a Dutchman, Anthony van Leeuwenhoek (1632–1723), whose brilliant observations with the simple microscopes of his day first disclosed to man the protozoa and the bacteria.[14] He described cocci, rods and filaments in rainwater and saliva, and although he did not relate these to disease he was the first to describe them. He even noted that his 'animalcules' died in the presence of pepper and wine vinegar and was probably the first to describe the effects of chemicals on actual micro-organisms.[7] We can see now that by then science was sufficiently advanced to have made it possible to have put together a theory of infectious disease approaching that of modern times, but then the medical world failed to marshal the new facts into a cohesive whole and draw the necessary conclusions.

During the period under review, the theories held by the medical profession on the manifestations and relationships of the fevers were changing in line with

those on infection. At the beginning of the period, fevers were thought to be a continuum: they were considered to be a single disease with different malignancies, taking different courses. Thus different types of rash were regarded as indications of the relative severity of the fevers rather than distinguishing one fever from another. But by the later seventeenth century, this view was changing as a number of new theories were put forward.[15] The humoral theory of disease was gradually replaced by a more mechanistic approach emphasizing malfunctions of the body fluids and the vessels through which they flowed. For instance, it was suggested that normal blood contained particles natural to it, but in a disease it became clogged by foreign particles emanating from the disease process; for recovery, these foreign particles had to be removed by the body itself or, failing that, with the intervention of the doctor. Another suggestion was that the fever process was a fermentation. These theories, even if untenable in the light of modern knowledge, represented a totally new outlook on fevers, the symptoms could be assigned to specific material causes, and the whole approach to them and their management, not only clinical but social, was open to change.[16] For instance, Thomas Sydenham, in the first edition of his book on fever therapy, written in 1666, clearly regarded all fevers as a unity, but by the third edition (1676) careful observation had caused him to acknowledge some clear distinctions, especially in the cases of smallpox and plague.[17] Other authors at this time increasingly began to write about smallpox and measles, in particular, as distinct from other fevers.[15]

Except for a widespread outbreak in 1603, little is heard about bubonic plague in Britain between the time of the Black Death and London's Great Plague in 1665, but in fact there were limited but lethal outbreaks, all over the country and especially in London, and throughout Europe too, between the two major outbreaks. As in earlier years, outbreaks were at first attributed to the divine wrath, but this theory became less and less tenable as it dawned on the populace that priests and monks were as likely to succumb as the most disreputable layman. The miasmatic theory as expounded by the medical profession then began to come into its own. Various sources for the corruption of the air were suggested, including stagnant water, carrion, overcrowding and, as ever, the conjunction of the stars.[2,6] In Italy, the hypothesis was put forward that the corruption consisted of venomous atoms generated from any of the above sources as well as from infected people. Not only were the atoms poisonous but they were also exceptionally sticky, so that they adhered to any solid body, and if they were inhaled or absorbed through the pores of the skin, they would poison the body causing the death of the infected person: hence followed the practice of some doctors of washing the face, neck and hands in vinegar before seeing patients, in order to close the pores.[18] The atoms could also be passed from person to person, and from an animal or an inanimate object to a person, a theory that led naturally to the use of isolation procedures and

quarantine to control the spread of the disease. The waxed cotton robes worn by doctors as personal protection against the plague were based on the theory that the slipperiness prevented the venomous particles from sticking to them, an example of a successful preventive measure based on a hopelessly incorrect theory; for of course, the waxy surface did prevent the fleas with which the patients were infected from transferring themselves to the doctor. In fact, in 1657, Father Antero Maria de San Bonaventura, the administrator of the pest house at Genoa, unaware of the prescience of his words, remarked: 'The waxed robe in a pest house is good *only* [our italics] to protect one from the fleas, which cannot nest in it.' Father Antero was driven to this remark by his experiences in the lazaretto:

> I have to change my clothes frequently if I do not want to be devoured by fleas, armies of which nest in my gown, nor have I force enough to resist them, and I need great strength of mind to keep still at the altar. If I want to rest for an hour in bed, I have to use a sheet, otherwise the lice would feed on my flesh; they vie with the fleas – the latter suck, the former bite.[19]