

EFFECTS OF UNTREATED SYPHILIS IN THE NEGRO MALE, 1932 TO 1972: A CLOSURE COMES TO THE TUSKEGEE STUDY, 2004

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They said it was a study that would do you good.

(Ernest Hendon, 1908 to 2004,¹ last survivor of Tuskegee Study of Untreated Syphilis)

I am sorry.

(President Clinton, May 16, 1997,² apologizing for United States' role in study)

When Ernest Hendon died in January 2004 at the age of 96, a closure finally came to the Tuskegee Study of Untreated Syphilis (TSUS) of 1932 to 1972. Mr. Hendon, who was the last survivor of the TSUS, made the above remark shortly before his death, describing why he participated in a research project that nowadays—just a few decades later—is not even conceivable. Mr. Hendon's recent death occasions a retelling of this most infamous chapter in the history of American medicine. Awareness of TSUS is important because the "Tuskegee effect" still impedes African-American participation in medical research (Video clip 1).

CONCEPTION OF THE TSUS: 1929

The study was officially titled "The Effects of Untreated Syphilis in the Negro Male." It was sponsored by the U.S. Public Health Service (USPHS) and is believed to be the longest observational study ever conducted. The TSUS originated in 1929 when the USPHS began to review the high incidence of syphilis in the rural South and to explore the possibilities of mass treatment.^{3,4} During

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the 1920s, 36% of the 27,000 residents of Tuskegee, Macon County, Alabama were infected with syphilis, giving this place a syphilis prevalence among the greatest in the United States.^{3,4} In addition, 82% of the Tuskegee residents were of African-American descent.⁵ To Dr. Taliaferro Clark, a distinguished venereologist and chief of the USPHS Venereal Disease Division, Tuskegee thus had ideal properties⁴:

As long as syphilis was so prevalent in Macon and most of the blacks went untreated throughout life, it seemed only natural that it would be valuable to observe the consequences . . . it was a "ready-made situation" and an unusual opportunity for a classic study in nature that probably could not be duplicated anywhere else in the world.

Syphilitic complications were widely considered to be influenced by race (ie, neurosyphilis more common in whites, cardiovascular disease more common in blacks, and overall complications more common in whites than in blacks). Some studies of the day suggested that syphilis did not always need to be treated—that it could often remain quiescent, especially in blacks.⁶ Moreover, treatments for syphilis during the 1920s—arsphenamine, bismuth, iodide—were of uncertain efficacy and were often painful, even deadly.⁷ Thus emerged various rationales for TSUS; a written protocol never existed. Ironically, an observational study of syphilis in whites living in Oslo, Norway—perhaps the stimulus for Dr. Clark's study—was halted in 1910 when arsenic therapy was discovered.⁶

Enrollment began in October 1932.³ Organizations collaborating for decades in the study included the USPHS, Alabama Board of Health, Tuskegee Veteran's Affairs Hospital, Andrew Hospital, and Tuskegee Institute. The two hospitals and the Tuskegee Institute were African-American institutions. The role of African-American leaders, including physicians, in this study has been underemphasized. Many young African-American nurses and doctors participated in the project, ap-



A



B

FIGURE 1. Photographs of Nurse Eunice Rivers, probably circa early 1950s, shown (A) in cotton fields of Macon County, Alabama with a study subject, and (B) with officials of U.S.P.H.S., identified as Mr. David Albritton (left) and Dr. Walter Edmondson (right).¹¹ Photographs courtesy of U.S. National Archives.

parently bolstering their professional resumes by doing so.^{8,9}

STUDY ORGANIZATION: 1932 TO 1933

To facilitate recruitment of African-American men, a 33-year-old African-American nurse, Eunice Rivers, R.N., was employed and assigned as a scientific assistant to the Venereal Disease Program of the Macon County Health Department³ (Fig. 1). Nurse Rivers traveled within the community, visiting job sites, churches, barber shops, and social gatherings to solidify participation. For poor men in Macon County, an element of social prestige was conferred on them by their participation in the project and their association with Nurse Rivers. The TSUS was so closely identified with her that it became known locally as “Miss Rivers’ Study.”¹⁰ The central role of Nurse Rivers in recruiting and retaining men for the study was the subject of the award-winning motion picture “Miss Evers Boys”

(HBO, 1997), acknowledged by the producers as “fiction based on fact.”

Men with positive serology were contacted, told they had “bad blood,” and persuaded to participate by incentives such as free lunches, transportation, and medical care.³ Those running the study clearly capitalized on the low educational and socioeconomic levels of the African-American men and their willingness to participate, without questioning, in a study that “might help them.” Wrote one of the study physicians, “We must remember we are dealing with a group of people who are illiterate, have no conception of time, and whose personal history is always indefinite.”⁴ The concept of informed consent had not yet evolved, and no written permission was ever given by any of the participants.

More than 4000 men were screened for tertiary syphilis to enroll 399 men.¹¹ Men in the study received medical follow-up (eg, physical examinations, blood tests, and lumbar punctures), but no specific treatment. The USPHS investigators informed the men that vitamins, tonics, and aspirins would help cure their “bad blood” and that these treatments would be provided free in the study.¹² In the first years of the project, a few men received sporadic treatment with arsenicals and bismuth. The main purpose of the project was to evaluate the extent of medical deterioration over time among a group of men with untreated syphilis.³ The original timeframe of 6 to 8 months was found to be too brief to allow such an evaluation, and, subsequently, a decision was made to follow up each participant until his eventual death and post-mortem examination. Thus was autopsy added as a final endpoint, and thus did the TSUS continue for 40 years, becoming the longest observational study in medical history.

CONDUCT OF THE STUDY: 1933 TO 1964

The study was modified in two important ways. Autopsies were added as an “endpoint” and a control group of 201 nonsyphilitic men (including Mr. Hendon) was added.¹⁰ Additionally, \$50 burial stipends were given as incentives to recruit additional patients. Cash payments of \$25 were given to the men for each year they participated in the trial.

Researchers went to extreme measures to keep participants enrolled. In 1941, with the entry of the United States into World War II, the military draft threatened to undermine the study by dispersing the men. Emphasizing the scientific importance of the experiment, the USPHS was able to convince the Macon County draft board to decline conscription of men who were enrolled in the TSUS.¹³

After World War II, penicillin became widely available for civilian use.¹³ At this time, the USPHS

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER
The Associated Press

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they

have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men,

story, the Department of Health, Education, and Welfare formed an advisory panel to investigate.¹⁸ The panel focused on two main issues, penicillin therapy and informed consent, and concluded the TSUS was ethically unjustified.⁴ The Department halted the TSUS in March 1973 by authorizing treatment.

During the 40 years of the study, more than 100 participants died directly of syphilis or its complications, according to one source.¹ How many wives and girlfriends contracted syphilis from these men and how many of their children were born with congenital syphilis is not known.^{1,19} Ultimately, 13 peer-reviewed publications were derived from the study.²⁰ Nurse Rivers was co-author of several of these publications, thus becoming the first African American to co-author a paper in the *Journal of the American Medical Association*. The U.S. Senate Subcommittee on Health, chaired by Senator Ted Kennedy, D-Mass, held hearings on the TSUS in 1973. In "Miss Evers Boys," Nurse Rivers (played by Alfre Woodard) is portrayed as a prominent witness (Video clip 2).

On July 23, 1973, Fred Gray, a civil rights activist and lawyer, filed a 1.8-billion dollar class-action suit in the U.S. District Court for the Middle District of Alabama.¹³ The lawsuit alleged the study had violated rights guaranteed to the men under the "Fifth, Ninth, Thirteenth, and Fourteenth Amendments to the Constitution of the U.S. and the Alabama Constitution of 1901."¹³ The suit never went to trial, and in December 1974, the U.S. government agreed to a settlement of \$10 million dollars.¹³ No participant received more than \$40,000. Most got less than \$20,000. For his services, Mr. Gray was paid more than \$1 million.¹³

OFFICIAL APOLOGY: 1997

On May 16, 1997, President William J. Clinton called the TSUS survivors and descendants to the White House for a formal apology for the United States' role in the study (Video clip 3). Ernest Hendon, who was to become the last survivor, was watching from his home in Tuskegee, as President Clinton said² (Video clip 4):

The United States government did something that was wrong—deeply, profoundly, morally wrong. It was an outrage to our commitment to integrity and equality for all our citizens . . . and I am sorry.

AFTERMATH

The National Research Act, the first U.S. measure to codify the protection of human subjects in medical research, was passed by Congress in 1974 as a direct result of the Kennedy hearings.²¹ The Commission created under this act met from 1974 to

FIGURE 2. Article by Jean Heller, front page, *New York Times*, July 26, 1972. Investigative journalism first brought the story to public attention. (News story reprinted with permission of Associated Press via Valeo Intellectual Property, Inc.)

began to administer penicillin to patients with syphilis nationwide, including those in Macon County, but penicillin was intentionally withheld from the men involved in the TSUS, so that additional information regarding the natural history of the disease could be obtained.^{10,14} The investigators believed that a similar group of untreated individuals would not be found again, and the rationalization was offered that penicillin might even be harmful to men with a long history of syphilis (ie, the Herxheimer reaction).^{10,15,16} Even the widely adopted Declaration of Helsinki, issued in 1964 by the World Health Organization to protect human rights in medical research, failed to halt the project.

INVESTIGATIVE JOURNALISM ENDS THE TSUS: 1966 TO 1972

Beginning in 1966, Peter Buxton, a venereal disease investigator for the USPHS, expressed concerns about TSUS by way of letters to the Centers for Disease Control. In November 1968, Buxton wrote "I have grave moral doubts as to the propriety of this study."¹⁷ In 1972, when the Centers for Disease Control had failed to respond, Buxton contacted Jean Heller, an Associated Press reporter. Heller's story was published on the front page of the *New York Times* on July 26, 1972 (Fig. 2). In response to the public outcry generated by the

1978, and its conclusions are known as The Belmont Report, which served as the basis in 1981 for Title 45, Part 46 of the Code of Federal Regulations (“Protection of Human Subjects”).

Although an element of closure to the TSUS came with the death of the last participant, a lingering distrust of medical research has continued in some segments of the African-American community (Video clip 5). A survey in 1998 showed that 51% of African Americans who were aware of the TSUS would be unwilling to participate in any form of medical research.²² In urology, this attitude often translates into a critical underrepresentation of African-American men in studies of prostate cancer, a population in which the disease is especially severe.^{23,24} Increasing participation of African Americans (and other minority people) in clinical trials has become a priority issue for many national organizations, including the National Medical Association by way of Project IMPACT.²⁵ As a result of efforts such as Project IMPACT and because of the social changes seen in the United States during the past four decades, progress has recently become apparent.²⁶ Although some progress has been made, enrollment in clinical trials of various racial and ethnic groups continues to lag.²⁷ In the words of President Clinton, “We have put the curse behind us, now we must bring the benefits (of medical research) to all Americans” (Video clip 5).

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