

● *Clinical Investigation*

THE STUDY OF UNTREATED SYPHILIS IN THE NEGRO MALE

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Purpose: The participation of minorities in clinical studies is the subject of much discussion and has even become the subject of Federal law. The project known as the Tuskegee Syphilis Study and officially titled “The Tuskegee Study of Untreated Syphilis in the Negro Male,” is one of the great debacles of American medicine and a national shame. Despite the fact that its existence is well known, many do not know the historical facts of the study nor the context of the study. My purpose here is to recount the facts of the study and its historical context.

Methods: The history recounted here is taken from documents gathered during a U.S. Senate investigation of the study, original papers located in National Library of Medicine, and books about the trial.

Results: The trial began in 1931 as a survey of the natural history of untreated tertiary syphilis in Black men. This study enrolled 399 men with syphilis and 201 uninfected men to serve as controls. All were at least 25 years old at enrollment. The men were told they were in a study, but never educated about the implications. Later, men were not informed that there was a treatment for effective treatment for their disease—a treatment that was being withheld from them. This trial continued till 1972.

Conclusion: Many of the issues that led to the study and caused it to continue for 40 years still exist. The lessons of the Public Health Study of Untreated Syphilis in the Untreated Negro include the dangers of paternalism, arrogance, blind loyalty, and misuse of science. “*Those who do not appreciate history are condemned to repeat it*” (Alfred North Whitehead). © 1998 Elsevier Science Inc.

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INTRODUCTION

When we think of the Tuskegee Institute, the first thing we should think of is its rich history—Booker T. Washington, George Washington Carver, and the Tuskegee Airmen. The first thing we think of should not be the Tuskegee Syphilis Study. Indeed, the study, officially titled “The Tuskegee Study of Untreated Syphilis in the Negro Male,” should really be referred to as the “U.S. Public Health Service Study of Untreated Syphilis in the Negro Male.”

My purpose here is to recount the facts of the study and its historical context. Unfortunately, the facts of what truly happened from 1931 to 1972 are widely misunderstood. Rumor and prejudice have replaced fact, a situation that has been made worse by the recent Home Box Office film entitled “Miss Ever’s Boys.” This television movie, which was billed as “fiction based on a factual event,” certainly deviated from the truth. Despite this deviation, it is largely viewed as fact and not the fiction that it is. Finally, incomplete and inaccurate news coverage has obscured what really happened.

The history recounted here is taken from a review of documents gathered during the U.S. Senate hearings and investigation in 1972, original papers located in the National Library of Medicine, and the book *Bad Blood* by

James Jones (1). This history is conveyed through the eyes of an African-American physician who has designed and conducted clinical trials. As I recount the history, I will attempt to discern established fact from interpretation.

It is my belief that the lessons of the PHS syphilis study are numerous. These lessons apply, not only to those of us who conduct clinical trials, but to literally everyone involved in any aspect of medicine. These lessons apply to the counseling of and the informing of the lay public by medical professionals and lay advocates. Many of the individuals who supported or helped conduct this tragic study likely deceived themselves into believing that they were doing the right thing. The first lesson involves the obligation of those of us who take a leadership role in the delivery of health care to learn and understand medicine ourselves. The second lesson involves the obligation of health care providers and advocates to go beyond merely informing to teaching. Patients must understand the ramifications of a decision and freely choose to participate in a study or accept health care.

THE AMERICAN SOUTH IN THE 1920s

The context of the times is important to the history of the study. In the late 1920s, a number of survey studies sug-

gested that over 35% of Black men in the rural south were infected with syphilis. These surveys suffered from selection biases that likely magnified the estimates. The conclusions of these studies were widely publicized by concerned parties and organizations in an effort to force public health officials to do something. The limits of and potential selection biases of the studies were not widely disclosed.

At this time "Race Medicine" was still widely accepted in the United States. Central to "Race Medicine" was the belief that Blacks were different from whites and that a disease could have differing effects on Blacks vs. whites. There was considerable belief that syphilis was a more indolent disease in Blacks than in whites. It was noted that many Blacks had syphilis and few were dying of it. This argument and the fiscal limitations of the depression made it even easier for federal, state, and local public health officials to ignore the problem of syphilis in Blacks.

The common therapies for syphilis at that time were difficult to administer, expensive, painful, and dangerous. The efficacy of these therapies (arsphenamine, bismuth, and mercurial compounds) were, and still are, debated within the medical community. Importantly, these were the accepted treatments of the time. Few American Blacks were treated for syphilis because medical care was expensive. Indeed, most southern Negroes, being poor, had never seen a physician for any reason.

In the 1920s and 1930s, the discipline called "public health" was relatively new. The Division of Venereal Diseases of the U.S. Public Health Service was comprised of a group of committed young public health physicians. The PHS teamed with representatives of several charitable foundations, and began treating Blacks for syphilis in several sites in the Southern U.S.A. These activities were to demonstrate that both logistically and medically difficult anti-syphilis treatments could be administered to rural Blacks.

One of the demonstration projects was in Macon County, AL, home of the Tuskegee Institute. Macon county was rural and more than 80% Black. The poor living conditions of Macon County were startling to the PHS officers; chronic malnutrition and other diet-related illnesses, such as pellagra, were common. One PHS officer, Thomas Parran, who later would become U.S. Surgeon General, wrote about the poverty of Macon County in his book *Shadow on the Land* (2). The demonstration project started in 1930 and was terminated in just over a year due to insufficient funds, with many people having received an incomplete course of therapy.

The initial study

In 1933, the PHS returned to Macon County. There was such a high incidence of unusual syphilitic pathology that it was felt that a study of persons with a long history of syphilis could be done. PHS physician, Dr. Taliaferro Clark devised a study that would provide data on how syphilis differed in the "Negro vs. the White." The initial plan was to identify people who had syphilis for a long time, examine them, and record physical and laboratory findings. The original project, as planned, would last less than a year and

would treat those diagnosed with syphilis. There was some concern that the persons involved would not get the standard 18 months of treatment, but it was felt that some treatment would be better than no treatment. Some speculated that, at least, these people would be rendered uninfected to others.

The PHS officers went to the all-Black Andrew Hospital at the Tuskegee Institute to enlist support. The Principal of the Institute and the director of the hospital (both Black men) enthusiastically agreed to support the project. Tuskegee and Andrew Hospital would be paid to provide clinical space, as well as laboratory and radiological support to the study. This would also be a beneficial learning experience for the young Black medical interns at Andrew Hospital. Tuskegee would provide hospitalization, when necessary, and be the site of autopsies. Tuskegee agreed to hire one of its nurse graduates interested in public health, Eunice Rivers, R.N., to serve as data manager for the study.

This was to be a study of tertiary syphilis. Late in the design phase, the study was changed to a survey of men because women, having internal genitalia, frequently did not know when they were infected. This study enrolled 399 men with syphilis and 201 uninfected men to serve as controls. All men enrolled were at least 25 years old at enrollment.

The second study

The initial survey was completed, as planned, in about a year. It was at this point that all therapy was terminated. Some men received as little as a month of antisiphilitic therapy, and others received therapy for several months. It was decided that the pathology seen was so impressive that PHS physicians would return annually to follow the course of these patients, and they did so for 3 decades to assess men at so called "round-ups." Rivers, whose employment was eventually transferred to the U.S. Public Health Service, was entrusted to keep track of the study subjects to assure that as few as possible were "lost to follow-up."

The men in this trial participated voluntarily and most continued coming to "round-ups" believing there was value in the annual physical examinations; however, there is no evidence that any diagnosed illnesses were treated. Vitamins, tonic, and aspirin may have been given to some men who complained of minor pains and ailments.

Some men submitted to lumbar punctures, believing that the procedure was a therapeutic "spinal shot;" however, it was purely for research purposes. The morbidity associated with these spinal shots should not be under-emphasized; indeed, it was a most terrible experience. Men who received these shots experienced severe back pain, headache, and even temporary paralysis. Some men suffered from the results of these "spinal shots" for years.

In the late 1930s, several men died and were not autopsied. The Milbank fund was convinced to provide funds to the Tuskegee Institute for \$50 burial stipends. This was a successful effort to encourage families to notify Nurse Rivers immediately upon death of a study subject, so that an

autopsy could be arranged. Participation of the Tuskegee Institute and its hospital decreased significantly after 1945, although the burial stipends, some laboratory tests, X-rays, and autopsies continued to be performed by Andrew Hospital physicians into the 1960s. The Tuskegee Veterans Administration Hospital, another predominantly Black institution, also provided some support of the trial into the late 1960s.

Many of the strategies we discuss today as necessary for overcoming barriers to clinical trials recruitment were pioneered in this study. Nurse Rivers would recruit patients to the trial by going to their places of work, going to barber shops, going to churches, and providing transportation. She was the educated and respected friend who guided these men through the study. Other things done to preserve the trial were quite unusual and extreme. In 1941, more than 250 of the men were less than 45 years old and draftable. The PHS, however, was able to convince the local draft board not to conscript any of these men, therefore preventing the men from being moved out of the area, diagnosed, and treated.

Several beliefs about this study, commonly held by the public, are clearly false. Many think that men in the study were infected by those running the study. The trial actually enrolled men who could identify a syphilitic skin lesion more than 5 years before entry. Controls who developed infection were continued in the study and, clearly, some men in the study infected others during the trial. Today, many erroneously believe that these men were unaware that they were in a study. Many men bragged that they were taking part in "Nurse River's Study." Indeed, in Macon County, it was a social honor to be in her study. Although they were informed, it is obvious that those who had syphilis did not understand that they had a sexually-transmittable disease, and many in the control group did not know or believe they were healthy. However, the men were aware that they had "bad blood," but did not know what that meant.

In 1943, penicillin was introduced in the PHS national antisiphilic campaign. Unlike previous therapies, it was clearly effective, inexpensive, and easy to administer. It is unknown who made the decision to continue the study and not treat these men. The PHS did convince the local draft board to support the study by excluding participants from the draft. If drafted, a participant would be diagnosed and treated. Penicillin was used in Macon county by the PHS, but care was taken *not* to treat the men in the Study. Local physicians, some of them Black, supported the study by agreeing not to treat men on the trial. There is no evidence that these men were informed that a cure for syphilis existed and that decision had been made not to cure them. There is some evidence that, in the mid 1940s, some PHS officers discussed treatment and felt that penicillin might be harmful to men with a long history of syphilis.

It is unclear why the study continued for 3 decades after the development and widespread availability of penicillin. Some involved with the trial actually claimed that it was a

unique opportunity to learn the natural history of syphilis and that the trial was more important than ever, given that there was an effective treatment. Even if the physicians really believed this, they were forgetting that many men in the trial had been partially treated prior to the advent of penicillin. It is obvious that they felt no obligation to the men in the trial, and did not learn from the Nuremberg trials of the late 1940s that led to the Nuremberg Code of Principles of Human Experimentation or the many changes in how clinical research was conducted.

Contrary to common belief, the study was not a secret. From 1933 to 1965, more than a dozen peer-reviewed papers with results from the study were published in respected journals such as *Public Health Reports*, *Archives of Internal Medicine* and the *Journal of Chronic Diseases*. These articles explained that the data came from a study in which a large number of Black men with syphilis were being observed and not treated. The title of one paper was "Untreated syphilis in the male Negro: A prospective study of the effect on life expectancy" (3). Ironically, some of these papers have become classics and are still cited in the literature today. Nurse Rivers was the first Black to be coauthor in several prestigious medical journals.

Few in the American medical community really questioned the study until the middle 1960s. In 1965, one physician did write to the PHS and ask how this study could be performed, but his letter was not answered. In 1968, the PHS even convinced a group of predominantly Black physicians in Macon County to endorse the study and agree not to treat participants. It was not until a PHS officer named Peter Buxton, who read a paper about the trial, raised questions about the trial, that questions led to the trial's end.

THE END OF THE TRIAL

After several years of questioning by Mr. Buxton, several news articles were published, leading to a Senate investigation headed by Senator Edward Kennedy. The investigation forced the trial's closure in 1972. The reaction to the trial would lead to enactment of legislation establishing the Office for Protection from Research Risks within what is now the Department of Health and Human Services, and the requirement for Institutional Review Boards. Institutional Review Boards are designed to assure that trials are ethical and participants in clinical studies give informed consent.

A lawsuit was filed by the famed civil rights attorney Fred Gray against the Centers for Disease Control, of which the PHS Division of Venereal Disease had become part in the 1940s. A suit of the Federal government was complicated, and it was finally settled out of court for \$10,000,000. Syphilitic men or their estates (in the case of men who had died) received up to \$37,500 apiece. Controls received up to \$16,000. Survivors of the trial and some wives and children affected by syphilis also received free medical care for the remainder of their lives. Mr. Gray received a \$1,000,000 fee for his legal work. No individual associated with the trial was ever sued, prosecuted, or even formally reprimanded. In

May 1997, the President of the United States formally apologized to the trial participants and their families. It was the Federal Government's first official admission of responsibility, and that inappropriate things occurred in the conduct of the study. Seven survivors of the trial were alive at the time of the apology.

LESSONS TO LEARN

Alfred North Whitehead once said that "those who do not understand history are doomed to repeat it." The lessons of the U.S. Public Health Study of Untreated Syphilis in the Negro male include the dangers of paternalism, arrogance, blind loyalty, and misuse of science.

Many have judged the PHS officers who ran the trial as evil racists. Those who initially started the trial actually had reputations as committed public health physicians with commitment and concern regarding the health of Negroes. They argued in scientific papers that the high prevalence rates of syphilis among blacks were not due to inherent racial susceptibility, but to their poor social and economic status. They also helped many of the Black Andrew Hospital interns receive postgraduate training at elite traditionally all-white institutions. Indeed, several were critics of the poverty and circumstance of Blacks in the South. It is conceivable that these physicians somehow fooled themselves into believing they were doing a service to Blacks as a whole by running this study.

The concept of "Race Medicine" remains with us. Unfortunately, it can still lead us to scientific tragedies and social injustice. It is interesting that some current literature (medical and lay) and legislation assume the old "race medicine" premise that Blacks are biologically different from whites, who are biologically different from Asians, etc. In fact, scientists frequently publish rates by race or ethnicity, encouraging many to quickly conclude that if a disease occurs more frequently in or appears to be more deadly in a particular race or ethnic group, it *must* be because of inherent biological or genetic differences. Furthermore, outcomes are often attributed to race when modifiable factors, such as culture or socioeconomic status, might be the major underlying cause.

The tragedy of the study can be attributed in large part to the arrogance and paternalism of the people running the study. Arrogance prevented complete peer review, which might have prevented the study from being started, and even intermittent peer review by persons concerned with the safety of the men in the trial certainly would have stopped it with the advent of penicillin.

Furthermore, there were a number of Black physicians and laboratory technicians assisting in the conduct of this trial, especially in the early years, but even into the 1960s. Some may even have been guilty of believing that they were better than the uneducated poor Blacks entering this trial. Classism among Blacks did and, unfortunately, still does exist. Some Blacks and some whites were likely guilty of failing to understand and learn all about the trial on which they were working.

Much has been made of Rivers' participation. She retired from the study in 1965, but came back as a consultant every year until its termination. From interviews and depositions given by Rivers after the trial was stopped, it appears that she was a sincere woman who cared about the men and the study and just did not understand.

PHS officials in the 1950s and 1960s were guilty of not rigorously assessing the value of the trial and, clearly, did not consider its ethics. They allowed the trial to become entrenched in the PHS bureaucracy and felt no sense of personal responsibility. Furthermore, government personnel may not have questioned the trial because it was historically associated with several distinguished PHS officers. Thomas Parran, who had gone on to become Surgeon General and John R. Heller, who became head of what would become the National Cancer Institute.

One person with a profound respect for the truth could have, and eventually did, stop this tragedy. Additionally, going beyond merely informing participants to instructing participants about the study and receiving truly informed consent might also have prevented this tragedy. This lesson is still valid today for those of us involved in routine clinical practice and trials. It is our obligation, not just to inform our participants, but to go beyond and assure that our patients fully understand the study. There is also the obligation that we ourselves must fully comprehend any subject matter before we teach or advocate it.

As more sophisticated screening, diagnostic, and treatment technologies are developed, it must be realized that the errors of this study can and do occur today. Those of us who counsel patients, whether lay health advocates, nurses, or physicians, have a personal responsibility to be fully informed and an obligation to fully inform. We must have a commitment to tell our patients the truth. The urge to oversimplify a complicated concept and deny individuals information that will allow them to make informed decisions affecting their lives is still frequent.

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