Unraveling the Tuskegee Study of Untreated Syphilis

TODAY WE repeatedly hear about the Tuskegee Study of Untreated Syphilis (TSUS) in the media. The TSUS was the 1932 through 1972 US Public Health Service (USPHS) study involving approximately 400 African American men with syphilis who were found untreated in rural Alabama and were observed to autopsy. As a control, there was also a comparable group of 200 African American men without syphilis who were observed to autopsy.1

The TSUS is a topic in the domain of which includes not only medicine and research but also the social and political sciences. In the popular press and medical literature, it is linked to discussions about maternal-infant transmission of human immunodeficiency virus (HIV) trials in developing countries,2 the cold-virus trials,3 and alleged CIA distribution of cocaine in Los Angeles, Calif.4,5 The myths include many scenarios, ie, that the 400 men in the study were infected with syphilis by the government, that no African Americans knew about the study until the study was exposed in 1972, and that none of the men received penicillin.5,6 Sir William Osler has called syphilis, in its late stage, “the great imitator” because it could simulate or complicate practically every condition known to internal medicine.7 And so has the TSUS, at this late stage, become “the great imitator.” It has been used to exemplify and validate government mistrust and conspiracies, primarily those against African Americans.

Absent from current discussions are the historical policies, programs, and procedures surrounding syphilis and public health in relation to and/or concurrent with the TSUS. This includes activities by the government and nongovernment entities. If Americans do not understand the historical context and the successes and failures of past public health policy and medical practices, we may repeat similar errors.

A historically correct, empirically based analysis of the TSUS is presented in this article. This is important given the impact that previous interpretations (ie, racism, genocide, and conspiracy) of the TSUS have had on present-day research, medical practice, and race relations. Four areas that begin to provide clarity and specificity in understanding the TSUS are the focus of this article: (1) the public health context, (2) the age of the 400 male syphilitic participants, (3) the publication of articles about the TSUS by the American Medical Association (AMA), and (4) the public relations context as interpreted by media and historiographers. These discussions will emphasize the historical perspective with respect to the standards of medical practice and public health at the beginning and during the first 20 years of the study.

A PUBLIC HEALTH PROBLEM

Former Surgeon General Thomas Parran (1936-1948) provided the following definition of a public health problem:

whenever a disease is so widespread in a population, so serious in its effects, so costly in its treatment, that the individual unaided cannot cope with it himself.5

With this definition in mind, the immediate prior research events that contributed to the genesis of the TSUS will be briefly described.

In the early 1930s, the Rosenwald Memorial Fund, a Chicago-based philanthropic foundation, undertook what had not been performed before in America—a study of the prevalence of syphilis among African Americans. The study was performed with the cooperation of the USPHS. The purpose of the study was to determine the practicability and effectiveness of measures for mass control of syphilis. Macon County, Alabama, was one of 6 rural counties chosen for study; the other counties were Albermarle County, Virginia; Pitt County, North Carolina; Bolivar County, Mississippi; Tipton County, Tennessee; and Glynn County, Georgia. Macon County was included because of its proximity to the Tuskegee Institute and its hospital, the John A. Andrew Hospital, and the Tuskegee Veterans Administration Hospital—both African American–run institutions. The county and state health departments were also cooperative.9

The Rosenwald Study was the first successful attempt to control venereal disease in rural areas. The techniques developed from this historic project were adopted by the USPHS as a model for venereal disease control nationwide. Although the treatment given was not extensive enough to cure all patients, the USPHS physicians were able to render most of the cases noninfectious.10,11 Because of the different socioeconomic conditions in the 6 counties, the USPHS also, with regard to syphilis, learned that factors such as social and economic conditions had a more important im-
impact on disease prevalence than race. Dr Taliaferro Clark, consultant to the Rosenwald Memorial Fund and one of the USPHS officers who initiated the TSUS, stated that “syphilis is not peculiarly a racial disease, but is also influenced in large measure by environment and social standards.”

Macon County, the poorest of the 6 counties, had the highest syphilis prevalence rate—approximately 40%. Clark surmised that the high prevalence rate was a result of the low rate of previous antisyphilitic treatment (33 treated out of 1200 seropositives [3%]), ie, treatment while the patient was infectious. Evidence from Albermarle and Pitt counties, which had the lowest prevalence rates (10% and 13%, respectively), supported this view. Although the treatment that was received by the residents in Albermarle and Pitt counties seemed inadequate, Maxcy and Brumfield, medical faculty members at the University of Virginia, believed it may have been sufficient to render early cases noninfectious, thereby halting the spread of syphilis. The differences between residents in Albermarle and Pitt counties and Macon County were a function of access to social, economic, and educational opportunities. Parr’s definition of a public health problem fit syphilis in the population of poor black sharecroppers in Macon County in the early 1930s. Clearly, according to Clark, “the extensive prevalence of syphilis” in Macon County constituted “a public health problem of prime importance.”

The findings from the Rosenwald Study and the decision to treat patients to render them noninfectious were presented and recorded at a constituent meeting of the 1932 Annual Convention of the National Medical Association (NMA) at Howard University, Washington, DC. This information was provided to African American physicians by Clark of the USPHS about a month and a half prior to his initiation of the TSUS. There were no objections to Clark’s presentation recorded in the minutes. Critics of the TSUS do not condemn the provision of curative treatment in the Rosenwald Study—a study whose objectives were seemingly positive. In the Rosenwald Study, treatment consisted of 8 or 9 doses of an arsenical, which was less than the adequate treatment of 20 doses and far short of the definitively curative treatment of 70 doses.

Dr Charles Johnson, a rural sociologist from Fisk University, Nashville, Tenn, wrote a classic book about the people of Macon County who the Rosenwald Memorial Fund surveyed. In his book Shadow of the Plantation, Johnson commented that the physicians noted the large number of positive Wassermann test results (ie, seropositive for syphilis) among elderly men and women. On examination of these people, the physicians expected to find more than a positive blood test result (eg, evidence of syphilitic destruction). They further noted that the peak positive Wassermann test result was in the group aged 25 to 29 years for men and 20 to 24 years for women. Subsequent to these peaks, there was a decrease in the percentage of positive serological results with advancing age that was more abrupt and marked than anticipated. Data from the other 5 rural counties supported this pattern of the “disease” becoming asymptomatic and demonstrating serologically negative test results later in the life of an untreated patient—characteristics previously described in the Oslo Study, a retrospective study of untreated primary and secondary syphilis. The physicians ruled out a treatment effect, death, and incapacitation by neurologic or cardiovascular syphilis as causes for the decreasing percentage of positive serological results with age.

Public health officials were concerned about whether clinical and serological evaluations could serve as a surrogate for the frequency of syphilitic infection in latent syphilitic disease. Primary, secondary, tertiary (neurologic and cardiovascular), and pregnancy-related syphilis have easily evaluable study end points, such as infectious lesions, skin lesions, visceral lesions, and pregnancy outcome, respectively. Latent syphilis, however, with a positive blood test result in the presence or absence of clinical findings, was more difficult to evaluate and required considerable time (ie, 10-20 years) to determine the outcome. Specifically, the question arose whether clinical and serological evaluations were as accurate as autopsy examinations in determining the presence or absence of disease. In fact, Dr Felix Underwood, a Mississippi public health official, after listening to the presentation of an article on the Rosenwald Study, contemplated whether syphilis was a major public health problem in African Americans. He questioned whether syphilis caused damage that resulted in loss of time from work and decreased work efficacy as well as neurological and cardiovascular disease. It appeared to Underwood that since there was such a low percentage of African Americans receiving treatment, “either syphilis is not causing the negro of the South much discomfort, or the medical practitioners of the respective states are not diagnosing 95 per cent of the syphilis” in these states. However, the USPHS officers believed that the TSUS “should forever dispel the rather general belief that syphilis is a disease of small consequence to the Negro.”

The results of the Rosenwald Study and the debate over the results and about whether syphilis caused damage in African Americans may have contributed to the scientific thought that led to the TSUS. The specific precursors seemingly were to observe patients with untreated latent syphilis to autopsy and verify the presence or absence of syphilitic destructive lesions. No other prospective study of this type had ever been performed. Based on the prior experimental data available from the Rosenwald Study, the risk to the men did not appear to exceed the importance of the information that could be derived.

AGE OF THE MALE PARTICIPANTS

In 1973, William J. Curran reviewed the report of the ad hoc advisory panel to the Department of Health, Education, and Welfare (DHEW) that investigated the TSUS. He reported that he had hoped a more thorough historical review of the study would have con-
duction by the panel. He also wrote that more information would have been helpful regarding the characteristics of the African American male participants—namely, their ages. Age appeared to have an influence on treatment at the inception of the TSUS and for 20 years into the study. For example, the USPHS reported that primarily younger men (approximately 178) in the TSUS received some treatment (ie, 1-15 doses of an arsenical).25,26 Given that the 9-member panel voted (with its chairman abstaining) that the TSUS was unethical at inception in 1932, I will consider syphilis and age in historical context.

SYPHILITIC PATIENTS OLDER THAN 50 YEARS

In 1935, Dr Charles Gordon Haig, President of the American Medical Association (AMA), introduced a 9-reel film series of educational lectures by nationally reputable syphilologists. Dr Paul O’Leary of the University of Minnesota discussed latent syphilis and its treatment.27 O’Leary described a 62-year-old white man who had syphilis for 40 years. The farmer received “pills” when the secondary signs were recognized; he received no other therapy; he had no symptoms; and his blood test result was strongly positive for syphilis. O’Leary's recommendation was that no treatment was indicated. His rationale was as follows: (1) the farmer had controlled his disease for 40 years, (2) the man was noninfectious, and (3) nothing could be gained with treatment. Thus, according to O’Leary, the syphilis and the positive blood test result for syphilis could be ignored. The only action necessary for the farmer was a reexamination once a year.

Many of the contemporary reviews of the TSUS do not cite the work of Dr William A. Hinton of Harvard Medical School.5,17,18,28 Hinton was well known by the NMA, the National Association for the Advancement of Colored People (NAACP), and the syphilology community for his work in syphilis.28 Of note was his development of a sensitive syphilis serological test named after him—the Hinton test. He was also credited with being the first African American physician to write a medical textbook, *Syphilis and Its Treatment*, which was published in 1936. In his book, he devoted 40 pages to describing primary and secondary syphilis and 4 paragraphs to latent or asymptomatic tertiary syphilis.29

In an article in the *New England Journal of Medicine*,30 Hinton discussed the disposition of a patient with only seropositive syphilis and the difficulties in determining the indication for treatment. He maintained that if he were the patient (ie, >50 years), as an informed man with seropositive syphilis and no clinical findings who was presumably infected 25 years earlier, he would not want treatment. He believed that 15 to 20 years after the primary infection it was unlikely for an untreated individual to have serious (ie, cardiovascular or neurologic) injury from syphilis.20 In the discussion that followed, other syphilologists agreed with Hinton relative to the treatment disposition of the noninfectious, seropositive man—an individual similar to approximately 30% of “the male Negroes” in the study of “untreated syphilis.”26

At about that same time, physicians at the Stanford University School of Medicine31 felt that (1) latent syphilis was overtreated; (2) evidence of the efficacy of antisyphilic therapy for late-latent syphilis was lacking; (3) patients with late-latent syphilis suffered no discomfort or disability from their infections; and (4) if these patients suffered, it was from anxiety and social disruption caused by the stigma attached to syphilis. As a result of these beliefs, it was the policy of the Stanford Clinic to withhold treatment intentionally from patients with late-latent syphilis (presumed duration of infection >4 years) who were older than 50 years.

Dr Charles Barnett and colleagues31 at Stanford studied 1900 whites (300 of these were “Oriental, Filipino, and American Indian”) and 666 Negroes; 1472 were men and 1094 were women. Of the 2566 patients, 628 patients were observed for 5 years (ie, minimum of 4 years to latency plus 5 years), and 316 patients were observed for 9 or more years (ie, minimum of 4 years to latency plus 9 or more years). “About 800” of these patients were “intentionally untreated.” The untreated patients served as controls for comparison with those patients receiving arsenic and heavy-metal treatment. In general, entry criteria into the study included the following: (1) no symptoms or physical signs of syphilis infection (ie, neurosyphilis, cardiovascular syphilis, or benign tertiary syphilis); (2) presumed duration of infection greater than 4 years; (3) serologic evidence of syphilis; (4) negative cerebrospinal fluid test results if the patient allowed cerebrospinal fluid to be taken; and (5) negative findings on fluoroscopic examination of the chest for aortitis. No further details of the study procedures were provided in the article.

Regional studies of syphilis had names. The study of untreated syphilis (ie, primary and secondary cases) at the University of Oslo was entitled the “Oslo Study of Untreated Syphilis,” and the study of untreated syphilis (ie, patients with latent syphilis who were 25 years or older) at the Tuskegee Institute was entitled the “Tuskegee Study of Untreated Syphilis.”22,32 The study of untreated syphilis (ie, patients with late-latent syphilis who were 50 years or older) at Stanford University could perhaps be entitled the “Stanford Study of Untreated Syphilis.”

SYPHILITIC PATIENTS YOUNGER THAN 50 YEARS

Two intertwined controversies regarding treatment and survival confronted the management of syphilitic patients younger than 50 years. In 1943, the Alabama legislature passed a unique law that mandated blood tests for syphilis for all its civilians between the ages of 14 and 50 years. Family members younger than 14 or older than 50 years underwent blood testing only if another family member in the same household tested positive. Early in the program treatment included 8-, 16-, or 30-week heavy-metal therapy for early syphilis and a 40-week alternating course of heavy-metal therapy for late-latent syphilis.34

Two years later, in the Birmingham and Jefferson County arm of the
Restricting penicillin to patients with early syphilis was not limited to Alabama. This may have been national research policy. In 1945, the USPHS and 11 treatment centers across the nation began a study among syphilitic patients called the Blue Star Study. The objectives of the Blue Star Study were to determine the efficacy of various penicillin treatment schedules with or without other agents in curing primary, secondary, and latent syphilis and to prevent infectious relapse or serological relapse and the late development of crippling complications. Intensive posttreatment follow-up was required, mandating rigorous patient screening. Initially, the inclusion criteria permitted the enrollment of syphilitic patients with untreated early syphilis; however, no recommendation for late-latent syphilis was made.

In 1948, enrollment in the study was limited to patients with untreated early syphilis. The Blue Star Study accrued 1,588 patients (543 whites and 1,045 blacks). Among the syphilitic patients enrolled, there were 26 with latently infected syphilis (4 whites and 22 blacks) and 968 with early syphilis (255 whites and 713 blacks). Although the authors implied that information on the efficacy of treatment for patients with late-latent syphilis would be provided, no data on the outcome for these patients appeared in the publications. Penicillin was recommended to treat early syphilis; however, no recommendation for late-latent syphilis was made.

Regarding the relationship of age to survival, Heller and Bruyere described mortality data after the first 12 years of the TSUS. In comparison with the nonsyphilitic group, life expectancy of the untreated syphilitic group between the ages of 25 and 50 years was reduced by 20%. After age 50 years, the differences between the untreated and control groups decreased with age. They also noted a distinct peak in the mortality rate curve for their untreated black syphilitic patients at approximately age 50 years. Usilton and Miner described a similar peak in black men and attributed it to deaths from cardiovascular syphilis at this age. In contrast to the men in the TSUS, these men had been under treatment for at least 6 months. There was no similar peak for white men.

Interestingly, the article that followed the Heller and Bruyere article examined, retrospectively, the effect of treated syphilis on life expectancy. The data were derived from the University of Virginia Hospital clinical records. The hospital drew patients from 11 counties and the city of Charlottesville. From 1920 to 1941, the period studied, 2,908 people with acquired syphilis were admitted to the hospital (whites, 540 men, 405 women; blacks, 979 men, 984 women). Based on the number of syphilitic patients admitted to the hospital, crude prevalence rates of syphilis in the area can be estimated at 7% for black men, 1.6% for white men, 7% for black women, and 1.3% for white women. In that service area, the Rosenwald Study reported similar prevalence rates for blacks. Both clinic and private patients were included in the record review. The authors claimed that this group of patients received more treatment than a comparative group elsewhere. However, life expectancy of syphilitic patients was reduced with treatment in comparison with nonsyphilitic patients.

If the data of Smith and Bruyere are examined in the same way that Heller and Bruyere analyzed their data (ie, calculation of differences and percentage life expectancy reductions for 5-year age groups between 25 and 50 years), additional findings become apparent. White syphilitic patients who received treatment had their life expectancy reduced more than blacks. Specifically, white women who received treatment had their life expectancy reduced more than black women (18% vs 3%); white men who received treatment had their life expectancy reduced more than blacks. Black female controls had approximately a 2-year disadvantage in life expectancy compared with white female controls. This was reversed in the syphilis groups that received treatment (ie, black women who received treatment experienced a 2-year advantage in life expectancy compared with white women who received treatment). Also, in the Smith and Bruyere data set, white men and women had a distinct peak in their mortality rate curves between ages 45 and 50 years; mortality curves of the black patients did not have the distinct peak. It is un-
Is the reduction in life expectancy a result of lack of treatment (Heller and Bruyere) or treatment (Smith and Bruyere)? There were at least 2 prevailing views to explain these data, depending on the focus on the men's race. First, the journal editors who published both articles commented and provided a USPHS perspective (Dr John Heller, editor) on the 2 articles with seemingly conflicting data (ie, no treatment reduced the survival rate and treatment reduced the survival rate with syphilis infection). The editors focused on the black men who received treatment in the Smith and Bruyere article, who had a reduction of life expectancy of 8% to 15% in the age groups of 25 to 50 years. The editors stated that no information was provided in the article on the amount of treatment given. Therefore, inferences could not be made regarding the amount of treatment required to counter the influence of syphilis on life expectancy. The editors wrote that the 2 articles indicated that treatment prolonged life.

The second perspective was from Dr Paul Rosahn of Yale University School of Medicine. Rosahn had a major interest in the biological, clinical, and pathological aspects of syphilis. In his article on the adverse effect of syphilis on longevity in humans and mice, he demonstrated a clear understanding of the implications of the first 3 TSUS articles that had been published. He wrote that “the morbidity in the untreated male syphilitic Negroes far exceeded that in a comparable presumably nonsyphilitic group,” “the untreated Negro men of age 25 to 50 years with syphilis had their life expectancy reduced on an average of about 20%,” and “an untreated syphilitic population exhibits a greater frequency of morbid states than an unaffected population of similar characteristics and environment.” When Rosahn reviewed the Smith and Bruyere data, he was most impressed with the 20% reduction in life expectancy in the white male age group of 25 to 29 years. He found that this reduction in life expectancy in the syphilitic white men who received treatment was “identical” to the finding in the untreated black men in the TSUS.

Rosahn’s basic science work demonstrated that mice infected with syphilis had reduced survival compared with uninfected mice. When infected with syphilis, the mice did not show any lesions from the syphilis. Based on these data and other, similar data described in his article, he had strong convictions that evidence is not available by which it can be determined whether the reduced longevity of untreated syphilitic patients was the result of absence of therapy, or whether the reduced longevity of treated patients was related to exposure to treatment itself.

According to Rosahn, patients infected with syphilis had not only the risk of syphilitic lesions but also the risk of mortality from nonsyphilitic disease. The latter risk was a risk that may not respond to antisyphilitic treatment. Rosahn’s article received first prize in the annual essay contest of the American Dermatological Association in 1952.

THE AMERICAN MEDICAL ASSOCIATION

There were 14 known articles (2 articles were published twice) about the TSUS published under 9 different journal titles. Three of the articles that document the existence and continuance of the TSUS were published by journals of the AMA. The last 2 of these 3 articles were published after the AMA House of Delegates adopted a document entitled Principles of Ethics Concerning Experimentation With Human Beings in 1946. These were the first written principles of research drafted in the United States and included provisions for consent of the human subject, scientific rationale, and scientifically competent investigators; they were written in response to the Nuremberg doctors’ trial.

Apparantly, the medical establishment and the peer-review process failed to recognize and act appropriately toward a study that has come to symbolize racism in medicine.

THE FIRST TSUS ARTICLE

The first article on the TSUS was read before the Section on Dermatology and Syphilology at an AMA session in Kansas City, Mo. It was in the first article that the USPHS officers acknowledged the cooperation and assistance of Tuskegee Institute’s hospital, the John A. Andrew Memorial Hospital, and the Tuskegee Veterans Administration Hospital, both African American–run facilities. This article documented that the morbidity in African American men with untreated syphilis far exceeded that in the nonsyphilitic control group. Sixty-one percent of the controls had no morbid findings, and 16% of the patients with untreated syphilis had no morbid findings. In the group younger than 40 years, 77% of the controls had no morbid findings and 25% of the patients with untreated syphilis had no morbid findings. In the group older than 40 years, 49% of the controls had no morbid findings and 8% of the patients with untreated syphilis had no morbid findings. The cardiovascular system was most commonly found to have morbid findings. Twenty-four percent of the controls had cardiovascular findings (eg, x-ray or clinical evidence of aortitis), and 47% of the patients with untreated syphilis had cardiovascular findings. In the group younger than 40 years, 6% of the controls had cardiovascular findings and 25% of the patients with untreated syphilis had cardiovascular findings. In the group older than 40 years, 38% of the controls had cardiovascular findings and 63% of the patients with untreated syphilis had cardiovascular findings.

The first article was the only TSUS report to have a treated comparator arm. This third arm of 275 African American men with syphilis was derived from the syphilis clinics of 5 major universities (the Clinical Cooperative Group). The men had received treatment within 2 years of their primary infection. Adequate treatment in early syphilis...
was stated to be important to prevent infectious relapse and early complications of syphilis. Adequate treatment was defined as 20 doses of arsenicals and heavy-metal therapy within the first 2 years of infection; inadequate treatment was less than 20 doses of arsenicals. Only 68 (25%) of the 275 African American men received adequate treatment. However, adequate treatment in the early phase of infection prevented all 68 patients from returning within 15 years of follow-up with evidence of destructive lesions of syphilis.

The first article was published twice—in JAMA and in Venereal Disease Information. The text of the 2 publications was identical. The only difference was that an abstract of the discussion that followed the oral presentation was also published in JAMA.

The discussion included information about racial differences with regard to central nervous system syphilis, common administration of inadequate therapy for syphilis in actual community practice, comparative prevalence rates of syphilis, symptom and clinical evaluation correlations of cardiovascular syphilis by sex, and the problem of history taking in the men of the TSUS.

Was the information from this first article about the TSUS readily available to African American physicians? Historical data suggest that this was the case and document an ongoing relationship between the USPHS and representatives of African American organized medicine. In 1912, the John A. Andrew Clinics were founded at the John A. Andrew Hospital in Tuskegee. Six years later the John A. Andrew Clinical Society was founded. These continuing medical education activities were founded by and for African Americans. Their work filled a void in the growth and development of African American medical professionals in a segregated society. African American physicians traveled to Tuskegee to the John A. Andrew Clinics and the John A. Andrew Clinical Society every spring, where they provided service to the needy sick, professional training for African American physicians, interregional interaction, and interracial interaction. One of these interracial interactions took place in 1938 when Dr Raymond Vonderlehr of the USPHS presented data from the first AMA publication on the TSUS at the John A. Andrew Clinical Society. Over 100 African American physicians may have attended his presentation and possibly many more received a copy of his article when the Annual Bulletin was distributed to the entire membership. Vonderlehr was invited to speak again the following year at the Annual Convention of the NMA in New York and 2 years later at the Public Health Meeting of the John A. Andrew Clinical Society. Apparently, he had an ongoing relationship with African American physicians and the leadership of their organizations.

This ongoing relationship was generalized to the USPHS and its leadership. A letter from the president of the NMA criticized the USPHS for providing public health fellowships to aliens but denying the same opportunity to African American citizens. Dr Roscoe Giles remarked that African Americans found the USPHS fair, that Surgeon General Cummings had extended himself for African American causes, and that the current surgeon general (Parran) was considered a friend by the NMA. It was during Cummings’ and Parran’s terms as surgeon general that the TSUS was initiated and continued.

THE SECOND TSUS ARTICLE PUBLISHED BY THE AMA

The second AMA article was published after 22 years had elapsed. That issue of AMA Archives of Dermatology was dedicated to August von Wassermann. The success of penicillin in the treatment of early syphilis had resulted in the “and Syphilology” being dropped from the title of the journal. At the time of publication, the prevalence of infectious syphilis had declined by about 90%. Two articles preceding “Untreated syphilis in the male Negro” in the AMA Archives of Dermatology reported on the use of penicillin in the treatment of syphilis: one was an overview by J. F. Mahoney, and the other, by Niedelman, reported the results of the use of penicillin in the treatment of late-latent syphilis.

The latter article claimed that late-latent syphilis (ie, positive serologic result, asymptomatic, and duration >4 years) was relegated to the background with regard to treatment compared with early infectious syphilis. The reasons for the lack of interest in this stage of the disease included varying opinions as to the value of therapy in the treatment of late-latent syphilis, the feeling of patients that a positive serologic test result for syphilis placed a stigma on them, and the fact that these patients had no symptoms or signs and were not incapacitated. Niedelman claimed that people older than 60 years with late-latent syphilis were often exempted from any therapy. He thought that other natural causes would end their lives before syphilitic progression. In 1957, a panel of prominent syphilologists from the University of Pennsylvania and the World Health Organization writing for the Archives of Internal Medicine reviewed the data from this 1956 article on penicillin in the treatment of late-latent syphilis. The panel dismissed its relevancy because the follow-up of the patients was less than 3 years.

In the second AMA article, Olansky et al reported that among the male Negroes with untreated late-latent syphilis only 38 of 299 who had serological follow-up received no treatment prior to the first follow-up examination in the late 1930s. The other 261 subjects were treated as follows: 137 subjects received less than 3 doses of arsenicals or heavy metal (eg, mercury), 116 subjects received 3 to 11 doses of arsenicals, and 8 subjects received more than 12 doses of arsenicals. In the article by Schuman et al, the Sing Sing criteria for adequate therapy for syphilis were defined—no treatment: no treatment or less than 12 doses of arsenicals and/or bismuth injections; inadequate treatment: 12 doses of arsenicals and/or bismuth but less than adequate or less than 2.4 × 10^9 U of penicillin; and adequate treatment: 20 doses each of arsenicals and bismuth or 30 injections within 2 years or a rapid treatment schedule of
2.4 \times 10^6 \text{ U} \text{ or more of penicillin. According to the Sing Sing criteria for treatment, only 8 of the 299 subjects would have been considered to be adequately treated.}

Based on the serologic reversal data in this article, the USPHS officers revised the definition of \textit{untreated} to patients who received fewer than 3 arsenical doses. They considered 124 of the 299 subjects as “treated.” The best serological reversal occurred in the treated subjects aged 25 to 39 years with a duration of infection of less than 15 years. The worst serological reversal occurred in the untreated subjects aged 25 to 39 years with a duration of infection of less than 15 years. Intermediate serological reversal occurred in both the treated and untreated subjects aged 40 to 54 years with a duration of infection of 15 to 29 years. Untreated subjects aged 55 to 69 years with a duration of infection of 30 to 44 years had a serological reversal comparable with the aforementioned best group (ie, treated, younger subjects with a shorter duration of infection).

Interestingly, the same panel that reviewed the article by Niedelman reviewed the second AMA article. Both reviews of these 2 articles were in the section entitled “Penicillin in Late Latent Syphilis.” Although the panel of experts offered an opinion on the penicillin article (ie, that the follow-up period was “much too brief”), they only reported the conclusions of the second AMA article. No other opinions were offered.

\textbf{THE THIRD TSUS ARTICLE PUBLISHED BY THE AMA}

The third AMA article was published after the TSUS had existed for 30 years. It was read before the Annual Symposium on Recent Advances in the Study of Venereal Diseases in Houston, Tex. The authors commented that after the age of 55 years, the process of aging had become evident and significant in both the syphilitic subjects and controls. Eleven (12\%) of the 90 syphilitic subjects had evidence of late syphilis at their 1963 examinations. Most of these 11 subjects had evidence of late syphilis at their 1948-1949 examinations; only 2 new cases of late syphilis were detected at the 1963 examinations.33

This article identified patients who had received penicillin and had syphilitic abnormalities. Seven patients received penicillin in the 1950s. Three of these patients had tertiary syphilitic abnormalities and appeared to receive penicillin accidentally, incidentally, and unintentionally for the treatment of syphilis (ie, a 2- to 4-year interval between the detection of an abnormality and the initiation of penicillin). Eight other patients had tertiary abnormalities and received no penicillin.33

In an earlier article, Schuman and collaborators claimed that some of the men in the TSUS were “inadvertently rounded up and sent to rapid treatment centers” and treated with penicillin. The 32 men who were identified as having received inadequate penicillin therapy (ie, <2.4 \times 10^6 \text{ U}) may have been those men. Twelve other men were described as having received adequate penicillin therapy for pneumonia and as a premarital precaution. Four of these men received penicillin in the late 1940s. Between the 2 reports, 26 men in the TSUS had received adequate penicillin therapy.

The third AMA article, published in the \textit{Archives of Internal Medicine}, prompted a response from one of its readers. Dr Irwin Schatz of Detroit, Mich, wrote to the USPHS authors about his objections. Schatz objected to the denial of effective therapy for a potentially fatal disease. According to Schatz, even if the benefits of the results outweighed the risks, the investigators required re-evaluation of their moral judgment. This was the first complaint of its kind received by the USPHS about the TSUS.60

After 40 years, numerous publications in the medical literature, and presentations of the data at national and international medical meetings, an Associated Press exposé evoked public outcry and led to the cessation of the TSUS.41 What may have been a scientifically valid endeavor at inception was now cast as government-sanctioned malpractice on poor and uneducated guinea pigs. This reconceptualization seemed to fuel outrage of laypeople and the media.

Initially white and black physicians approached the issues surrounding the TSUS with more reason than outrage. Shortly after the media's exposé, however, Dr Rudolph Kampmeier, editor-in-chief, wrote an article in the \textit{Southern Medical Journal} outlining the medical and scientific grounds for his disagreement with the unethical overtones placed on the TSUS.65 He based his opinion on his review of the TSUS published reports, the 1972 recommendations of the National Commission on Venereal Disease, and other publications concurrent with the TSUS. His points included doubt that treatment was purposefully withheld from subjects if desired, doubt that arsenic or penicillin was efficacious in the treatment of late-latent syphilis, and a belief that few indigent rural Southern people would have received full treatment. Kampmeier's background was in syphillology, a specialty whose specific journals had ceased to exist 2 decades earlier in the United States, and, in general, the importance of syphillology as a field was in sharp decline.66 He was also well respected in organized medicine.

In the \textit{Journal of the National Medical Association}, Dr Montague Cobb, editor-in-chief, wrote an article outlining the development of the study and the issues that needed to be addressed.67 He based his opinion on his review of the TSUS published reports, other publications concurrent with the TSUS, and the report of the ad hoc advisory panel to the DHEW. Cobb made several points: (1) A valid question existed in 1932 whether syphilitic subjects did better if left untreated. (2) Syphilitic subjects who were classified as “cured through treatment” in the 1930s had a mortality rate that was 10% to 20% higher than that of those who were untreated or inadequately treated. (3) The effect of penicillin on the public health control of venereal diseases in the 1950s had not been all salutary. (4) There was a national rise in the prevalence of venereal disease while penicillin was readily available in 1973. (5) The report of the ad hoc advisory panel to
the DHEW was not a comprehensive objective report. (6) Evidence did not appear to have been brought forward in proof that anyone was subjected to the avoidable risk of death or physical harm. (7) There was no way to know if any beneficial findings were derived from the TSUS. Finally, according to Cobb, a study like the TSUS should not be done again. Cobb was well respected and his background was in the history of medicine, African American organized medicine, and civil rights.

Here were 2 men of medicine, white and black, respectively, discussing the scientific and medical issues surrounding the TSUS. Kampmeier represented a medical organization with a history of racially restrictive membership.66 Cobb represented a medical organization dedicated to dissolving racially restrictive memberships.66 Although their organizations had differences, they appeared to express more reason than outrage about the TSUS.

Then historiographers entered the debate. They reviewed not only the published reports and other concurrent publications but correspondences and meeting minutes of the USPHS and other organizations. Dr Allan Brandt, as a graduate student at Columbia University, New York, NY, was one of the first historians to conduct such an analysis.38 His review of information that was presumably not easily available to the public, editors of journals, or peer reviewers, resulted in a number of historical and ethical conclusions.

Brandt’s historical conclusions included the following: (1) The medical profession supported the turn-of-the-century prediction that the newly emancipated African American populace would become extinct in the 20th century as a result of crime, vice, and disease—particularly venereal disease. (2) Physicians discounted the socioeconomic explanations for the condition of African Americans. (3) Better medical care would not alter the evolutionary outcome of the extinction of African Americans. (4) The USPHS officers who initiated and continued the TSUS accepted these mainstream assumptions about African Americans and syphilis. (5) In the 1950s, penicillin was the preferred treatment for syphilis.

Brandt’s ethical conclusions included the following: (1) The USPHS regarded the men in the TSUS as less than human and believed that the experimental circumstances occurred naturally because the men would not be treated anyway. (2) The USPHS did not tell the men they were in an experiment. (3) Since only the offer of treatment would maintain the interest of the men in the study, the men participated under the guise of treatment. To accomplish this end, the USPHS deceived the men into believing they were receiving treatment. (4) The USPHS prevented the men from receiving treatment. (5) Bringing the men to autopsy required deceptions and inducements. (6) The entire health of the community was at risk by leaving a communicable disease untreated. (7) The USPHS lied to the men.

Raising some of the same issues, Dr James Jones, professor of history at the University of Houston, wrote a lay-oriented book, Bad Blood.60 Bad Blood is considered the major authoritative book on the TSUS. However, this was achieved at the expense of physicians. Jones’ book constitutes a major negative commentary on the medical profession, the editors of its journals, the peer-review process, and the clinicians who read the journals. According to Jones, “For many blacks, the Tuskegee Study became a symbol of their mistreatment by the medical establishment, a metaphor for deceit, conspiracy, malpractice, and neglect, if not outright genocide.”

Bad Blood, however, may not be reliable historiography because Jones handled information on whites and blacks differently, suggesting bias. For example, the author used full-face photographs of the white physicians involved with the TSUS in a separate section of the book, while clear photographs of black physicians were noticeably absent. Moreover, there were 2 photographs of a black physician involved with the TSUS shown with his face partially covered; in the spinal tap photograph, his name was not preceded by “Dr.” as it was for the names of the other physicians in the photographs in that section of the book. In addition, the photograph in which Dr Stanley Schuman appears was mislabeled; the person in the goggles with him performing floroscopy was not Mr Bouie but Dr Jesse Jerome Peters.50 In a group photograph, the affiliation of Dr G. C. Branche was incorrectly given as the USPHS; Branche was the clinical director of the Tuskegee Veterans Administration Hospital. In another example, Jones provided the educational backgrounds (eg, medical school attended and training) of the white physicians (eg, Drs Vonderlehr, Clark, Wenger, Heller, and Parran) who were involved with the TSUS. However, he did not provide similar information about the black physicians who were involved (eg, Drs Eugene Dibble, Peters, Branche, and J. Ward). Moreover, 4 of the 5 names and titles of the all-white 1969 ad hoc committee members were printed in the text of the book, whereas 7 of the 9 names and titles of the ad hoc advisory panel of the DHEW, the most of whom were black, appeared only in a footnote in the back of the book.

Second, Jones presented dissenting views in a biased manner. White professionals were cited prominently in the text, while black professionals were cited in footnotes or in the back of the book. For example, there was a solo dissenter during the 1969 ad hoc meeting to discuss continuance of the TSUS; information about the dissension of Dr Eugene Stollermer was in the text of the book. There was a solo abstainer for the first question charged to the ad hoc advisory panel of the DHEW (ie, whether the study was justified in 1932 and whether it should have been continued when penicillin became generally available), but information about the abstention of Dr Broadus Butler, chairman of the panel, was in a footnote in the back of the book. Additionally, commentary on Kampmeier’s article65 dissenting on the charges against the TSUS was in the text of the book, while commentary on the article by Dr Charles McDonald,1 which described the contribution of the TSUS to medical knowledge, was in the “A Note on Sources” section in the back of the book.
Third, Jones documented racism in medicine in the early 1900s solely from mainstream medical and historical sources. African American historical references and history relating to activities of the NMA, NAACP, Tuskegee Civic Association, and Urban League in and around Tuskegee prior to and concurrent with the TSUS were absent from the book. These were organizations dedicated to eradicating the unhealthy environment of African Americans as it was depicted in the mainstream medical literature.

In another example, Jones described Ms Eunice Rivers, the African American public health nurse and her role in the TSUS in detail. Although Rivers coauthored 2 of the TSUS manuscripts,64,66 6 other women’s names (Geraldine A. Gleeson, Dorothy S. Rambo, Anne Roof Yobs, Martha C. Bruyere, Lida Usilton, and Eleanor V. Price) appeared on 10 of the TSUS articles under 7 different journal titles.26,59,68,71-73 Five of these women were statisticians; Dr Yobs was a physician and chief of medical research of the Venerable Disease Research Laboratory, Communicable Disease Center, PHS, DHEW.

Finally, Jones presented oral history from white physicians who were involved with the TSUS. The book did not present oral history from any black physician. Jones’ Bad Blood treated African Americans and their issues in a biased and unbalanced manner. Perhaps, like the USPHS, Jones’s initial intent was benevolent, but the end product was malevolent. Other comprehensive articles in peer-reviewed journals by Drs Cave, Brandt, and Reverby seem to demonstrate some of the same biases.79-10

Bad Blood seems to be viewed as the definitive analysis of the TSUS,5,71-73 and no negative review of the author’s methods and conclusions appears in scientific or medical journals. However, a review of an unrelated book by Jones, a biography of Alfred Kinsey, presented no critical in-depth analysis, selective deletion of critical characters, and careless use of sources.74 Similar biases and lack of balance were evident in Bad Blood.

COMMENT

The approach in the current article is to view the TSUS and activities preceding and surrounding it with the eyes of the medical experts who were taking care of syphilitic patients and creating and executing public health policy at the time the study was undertaken. An alternative view of what may have happened becomes apparent when we focus on the public health problem, the age of the 400 male syphilitic participants, the publications on the TSUS by the AMA, and the public relations dilemma. Although more questions may be raised than answered, this alternative perspective warrants attention and consideration. It provides possible reasons why there were no public complaints about the TSUS in the medical community for so long. It also begins to unravel issues and allegations of exploitation, differential treatment of blacks compared with whites, and denial of state-of-the-art treatment in the TSUS.

The magnitude of syphilis in Macon County in the early 1930s fit Parran’s definition of a public health problem. The prevalence rate was extremely high. Treatment was costly, was of long duration, and required expertise. Syphilis had serious implications for the community and complications for the afflicted if not treated in its early, infectious stage. Conditions in Macon County demonstrated that the problem would not resolve on its own without help. Government agencies, philanthropic organizations, and local leadership combined to address the problem. Dr Thomas Benedek corroborated the need to study syphilis in Macon County in a critique of the TSUS.75 He wrote that the clinical ramifications of a disease could be studied most efficiently in the environment in which it is most prevalent.75 Since data from a prior study (the Rosenwald Study) indicated that socioeconomic conditions had an impact on syphilis, conditions in Macon County appeared optimal.

There were other reasons why African Americans appeared to receive an excessive degree of attention regarding their health. First, it was not popular to spend money on the health of African Americans at the time the TSUS began. African Americans could not finance their own health care. Many hospitals and clinics refused to treat African American patients, and it was only with great difficulty that tax-supported medical facilities were made available for African Americans, especially in the South. The attitude was: “Having no place to send the Negro for medical care it is easily assumed that there is small need to carry on an active and continuous health educational campaign.”76 The USPHS and the Rosenwald Memorial Fund responded to this gross disparity in the allocation of health care dollars. As an example of their intended action, in 1929, Dr Oliver Wenger, one of the future USPHS investigators of the TSUS, informed Michael Davis of the Rosenwald Memorial Fund that he would take the data from his recent survey of syphilis in Mississippi to the Mississippi legislature. According to Wenger, since the public health problems of the African American population had been ignored, this action was necessary.77 The health of African Americans in Alabama was also ignored. Perhaps, in parallel fashion, in the early to mid-1940s, the morbidity data from the first AMA publication of the TSUS were used to convince Alabama lawmakers to include African Americans in the mandatory blood testing program for syphilis for its citizens between the ages of 14 and 50 years.20

Second, the appearance of exploitation of African Americans in syphilis studies was an issue that was contemplated by the USPHS. In 1930, Michael Davis of the Rosenwald Memorial Fund had concerns about the reaction of blacks in the North to the syphilis studies in the South (ie, the celebrated Rosenwald 6-county studies). Clark of the USPHS wrote that it was the active cooperation of blacks in the South that determined the use of blacks in these studies. Clark believed it was an unfortunate handicap in the ef-
fort for venereal disease control among the white population that they (the USPHS) could not secure such cooperation. The choice of blacks for the studies, according to Clark, was a matter of cooperation, not discrimination.78

These privately written words expressed attitudes that public health officials also stated publicly. A year later, at the Section on Public Health at the Southern Medical Association Annual Meeting, Clark commented on the large number of black patients who came forward in the Macon County survey and the high proportion of syphilitic subjects who received successful treatment. He further stated that these numbers were large compared with the small number of whites willing to come forward for treatment.33 Also, according to the state health officers (Rosenwald investigators) in Tennessee, the history of primary syphilitic lesions was more accurate for blacks than whites in the 1930s—information that was shared at a Joint Session of the Health Officers and Epidemiology Sections of the annual meeting of the American Public Health Association. The timing of a primary syphilitic lesion was an important factor for determining the approximate duration of infection—a criterion for inclusion in the TSUS.

Age, duration of infection, and stage of disease were the determinants for the application of state-of-the-art treatment for syphilis. Approximately 30% of the men who participated in the TSUS were above the age of 50 years and had late-latent syphilis; this is an estimate because many of the men in the study were uncertain of their age. In addition, about 52% of the men who participated in the TSUS had syphilis infections for 15 years or longer (41% for ≥20 years).32 Many major academic centers did not treat all patients with late-latent syphilis; this is an estimate since many of the men in the study were uncertain of their age. In addition, about 52% of the men who participated in the TSUS had syphilis infections for 15 years or longer (41% for ≥20 years).32 Many major academic centers did not treat all patients with late-latent syphilis older than 50 years in the 1930s and 1940s because a 15- to 20-year duration of syphilis from the time of primary lesions was assumed. Based on this information, if any of the men who participated in the TSUS and were older than 50 years had sought second opinions at the Mayo Clinic,27 Harvard,30 or Stanford,31 the syphilologists may have recommended no treatment.

There are practical examples illustrating that the treatment of patients with late syphilis younger than 50 years was not much different in the prepenicillin and early penicillin eras. In the initial blood screen for syphilis for residents of Alabama in the mid-1940s, civilians older than 50 years were excluded by law. Men in the TSUS (ie, those younger than 50 years) who tested positive for syphilis by mandatory blood testing may have been sent to the rapid treatment center in Birmingham. Like other blacks and whites with late-latent syphilis, they may have been denied penicillin treatment and sent home.35 As late as 1948, although penicillin appeared to have great promise for the treatment of latent syphilis, penicillin’s use was discouraged because of a shortage of the antibiotic and because it was believed that a large long-term study was needed to demonstrate its efficacy.31 Ironically, had the men in the TSUS been treated in Birmingham in the 1940s, the USPHS would still have considered them to have been inadequately treated. This is because they would have received half the amount of penicillin that was considered adequate for treatment in the 1950s.26

In another example, a national perspective illustrates how patients with late-latent syphilis were excluded from treatment programs. Although the Blue Star Study was initially set up to evaluate the efficacy of penicillin schedules in all stages of syphilis (including the late-latent stage), patients with late-latent syphilis were excluded from the study about 3 years into the program. Patients with readily evaluable untreated dark-field–positive secondary syphilis were prime candidates for this 1700-patient study that was offered in treatment centers across the country. Had any of the men in the TSUS younger than 50 years with late-latent syphilis sought entry into the Blue Star Study at treatment centers in Birmingham, New York City, Chicago, or San Francisco–Oakland, they may have been denied access.37-39

Without challenging the credibility of some of the survivors of the TSUS who lived to be 90 years or older, it appears that the non­treatment of patients with late-latent syphilis was the policy for blacks and whites in Alabama and elsewhere in the mid-to late 1940s. Two survivors of the TSUS claim that when they were sent to the rapid treatment center in Birmingham, they were sent home without treatment.50,80 What the survivors described (ie, not obtaining treatment) may not have had anything to do with the TSUS. The outcome was the same. Some of these men were not treated with penicillin in Birmingham. However, the reasons treatment was not given in Birmingham may have been historically different than those given in the story as it was later revised—revised to fit, presumably, a victim model.

The standard of care in local white communities was not always practiced as described in textbooks,18,71 and this may be illustrated by 3 examples. First, after the presentation of the first AMA article on the TSUS, a discussion ensued.31 Dr Harry M. Robinson from Baltimore, Md, stated that many of his former students were not recommending a full course of antisyphilitic therapy to their patients (ie, state-of-the-art treatment; weekly arsenotherapy or a heavy metal for 70 weeks).86 Because of practice competition in their communities, they were prescribing 7 to 10 injections of arsenotherapy or bismuth compounds as a complete treatment for syphilis.

Second, 3 years later, Dr Paul Dudley White in Boston, Mass, provided data that gave credence to Robinson’s claim. White and colleagues studied patients for evidence of cardiovascular disease whose primary syphilis dated back 15 to 25 years.81 Seventy-one percent of the patients (172 of 241) (all whites except 1 “ negro”) had received 0 to 12 doses of arsenotherapy within the first 5 years after infection. Seventy percent of these patients (121 of 172) were again inadequately treated with 0 to 12 doses of arsenotherapy within 5 to 15 years after infection. This latter period was a second treatment opportunity for these patients, but they, like the “male Negroes in the study of untreated syphilis,” received inad-
equate treatment. There was no indication in the report that the patients would receive additional antisyphilitic therapy. Perhaps additional treatment was not offered because White and colleagues, as they wrote in their article, believed that treatment 15 years after infection would not prevent cardiovascular syphilis.61

Third, syphilologists and public health officials recognized that only 15% to 25% of people with infectious syphilis completed a full course of arsenic and heavy-metal therapy. A combination of social (eg, embarrassment), economic (eg, cost), and medical (eg, remission of symptoms) reasons contributed to these widespread lapses of therapy.7,82,83 It appears that this behavior (the failure to complete curative therapy) was tolerated and accepted by public health officials. Although not curative by the standard of the time, the small amount of treatment received by these people rendered them noninfectious. With regard to early syphilis, this accomplished a basic public health goal: to halt the spread of syphilis.56 The men in the TSUS had endured the primary and secondary stages of syphilis without treatment and were noninfectious when they entered the study.

What was an experiment in Tuskegee (ie, nontreatment of syphilitic patients who were older than 50 years and/or had late-latent syphilis) may have been public health policy and standard medical practice nationwide in the 1930s and 1940s. In fact, there was a similar “untreated syphilis” study conducted at Stanford University. It was run by well-respected syphilologists and examined a sizable white population who had treatment purposefully and intentionally withheld.31 Certainly, this could alter and possibly diminish the racist charge of the TSUS, since it is claimed in the literature that what happened in Tuskegee would never occur in a white population.6,80 In Macon County in 1932, there was no treatment program for patients with early and late-latent syphilis; the USPHS found these poor sharecroppers untreated, some for as long as 20 years.14,26,33,52,84 In contrast, at the Stanford Clinic, there was a treatment program in place, and in 1935 these physicians willfully and intentionally denied treatment to patients with late-latent syphilis older than 50 years. Moreover, this newly uncovered information illustrates more than just the prevalent medical opinion at the Stanford Clinic during the period when the first half of the TSUS was conducted. It reveals how patients similar to those in the TSUS—whites and blacks—were treated by a major medical institution.

This may help to explain why, despite sufficient information in the articles and information available elsewhere, there was a failure to recognize and act on a study whose racist and unethical nature today appears so obvious.18,19,71 A peer-reviewed article or editorial in a medical journal decrying the TSUS was not published before a newspaper article exposed it.69 The scientific and medical information contained in the TSUS-related articles published by the AMA did not disturb the editors, peer reviewers, and readership, perhaps because many of those involved participated in the prevalent public health activities and medical practices of their communities at the time.

Nonetheless, the charge that medical officials lied to and deceived patients was not identifiable in the published reports but was uncovered years later in documents in the National Archives.18,80 Unfortunately, evidence of such alleged ethical misconduct was not readily available to the editors of journals, peer reviewers, and clinicians who read journals.85,86

Finally, penicillin therapy was available in the later stages of the TSUS. By 1952, 28% of the syphilitic patients examined in the TSUS had received penicillin therapy. Ironically, only 33% of the controls received it.26 Why would the USPHS withhold penicillin therapy from controls? Although the TSUS was a nonintervention trial, critics tend to hold the USPHS responsible for penicillin therapy being withheld from the men with syphilis who participated. Perhaps the decisions regarding treatment and nontreatment with penicillin were not based solely on medical and research factors, but de facto social and economic realities (eg, lack of access to health care and poverty)80 were also major contributing factors. Alternatively, at the time, a number of syphilologists may have attributed the approximate 30% rate of penicillin administration in the TSUS to “happenstance penicillin.” From 1947 to 1954, penicillin was widely used to treat many minor nonsyphilitic illnesses. This practice may have been responsible for the 90% reduction in infectious syphilis between 1947 and 1954. Subsequently, because of the fear of anaphylactic reactions to penicillin, physicians withheld penicillin from general usage. In the subsequent 5-year period, the incidence of infectious syphilis tripled in the United States.87,88 Although the USPHS may have deprived the men participating in the TSUS of penicillin therapy, it was unsuccessful in stopping the administration of “happenstance penicillin.”

Nevertheless, the critics of the TSUS have presumed that there was clear scientific evidence for penicillin treatment of late-latent syphilis while the TSUS was being conducted.18,60,73 There was not. In fact, there was a prevailing belief that the late use of penicillin to treat syphilis of long duration might be useless and/or harmful and that the optimal time for therapy was during early syphilis.81,89,90 The mechanism of harm from treatment in the case of aortic disease (a potential problem in the TSUS) was thought to occur through therapeutic resolution of inflammation with subsequent scar formation and the development of progressive aortic regurgitation. The paradoxical worsening of uncomplicated syphilitic aortitis in patients receiving high-dose penicillin compared with patients who were not treated is an example of harm that may result from treatment in the late stages of syphilis.81 Since cardiovascular syphilis was a major potential risk in the TSUS, this problem was a real concern.

To address these and other issues, the DHEW convened a national commission of private medicine and public health in 1971 to review venereal disease and its treatment. The 17-member commission
had representation from the AMA (Dr C. A. Hoffman, president-elect), American College of Physicians (Dr Rudolf Kampmeier), American Public Health Association (Dr John C. Hume), and NMA (Dr John A. Kenney, Jr), as well as other experts from government, academic, and private organizations. The report of the commission stated that the evidence supporting penicillin treatment for primary and secondary syphilis was clear and irrefutable. However, the report also stated that it was unclear what role currently available penicillin preparations had in the treatment of late-latent syphilis, that many patients were allergic to penicillin, and that there were reports of spiral organisms resembling Treponema pallidum in the cerebrospinal fluid and aqueous humor of patients who had received adequate penicillin therapy for latent syphilis. The commission recommended additional research to determine the role of penicillin in the treatment of late-latent syphilis. Ironically, this report was issued in 1972—5 months before the TSUS was exposed by the press.

Twenty years later, the status of penicillin research for the treatment of late-latent syphilis remained unchanged. Hook and Marra made the same claim about the persistence of viable treponemes in latently infected people after receiving curative doses of penicillin to treat early disease. They further stated that “there has been no large systematic study of therapy of late-latent syphilis with penicillin G benzathine.” Although penicillin may have been recommended to treat late-latent syphilis because of its ease of administration, minimal toxic effects, and low cost, the evidence supporting its efficacy was lacking.

Again, this may explain how the TSUS continued beyond the discovery, investigation, and celebration of penicillin (ie, the lack of evidence of its efficacy in the treatment of late-latent syphilis). Scholarly journals, such as the New England Journal of Medicine and the Archives of Internal Medicine, published voluminous literature reviews on syphilis in the 1940s, 1950s, and 1960s, including reviews of the TSUS publications. The TSUS literature was intermingled with discussions about the virtues of penicillin. One assumes that these expert authors from Johns Hopkins University, University of Pennsylvania, Harvard University, University of North Carolina, and the World Health Organization were not all racially biased. They had the expertise to detect the paradox of the efficacy of penicillin in the treatment of latent syphilis and the continuation of the TSUS. With all the information at their disposal, they had the opportunity, the medium, and the power to at least comment about the ambiguity of the efficacy of penicillin therapy and the continuation of the TSUS.

CONCLUSIONS

The medical profession should be more cognizant of the issues surrounding the TSUS for several reasons.

First, current representations of the TSUS have contributed to negative perceptions in the African American community, with the following results: Many African Americans are reluctant to participate in clinical trials. Few African Americans participate as organ donors. The health outcomes of African Americans are worse because of their mistrust of the health care system.

Second, President William Jefferson Clinton recently apologized for the TSUS on behalf of the government. The President’s apology included the following statements about the TSUS: The study was clearly racist. The men were used without their knowledge and consent. The men were denied help. The men were lied to and betrayed by the government. The physicians in Tuskegee were wrongfully associated with the study. His apology was intended to respond to the lack of trust African Americans have in the health care system.

The apology, however, represented clear contradictions with the historical and scientific context of the TSUS. On the one hand, the TSUS supposedly was a racist medical experiment initiated and sustained by the federal government, a study whose unethical nature was obvious, a study in which treatment was indicated at inception and denied, and a study that continued through the penicillin era. On the other hand, information from readily available, peer-reviewed literature suggests that the high prevalence of syphilis in Macon County constituted a major public health problem; that a valid scientific, medical, and public health rationale was the basis for the initial design of the study; that at the study’s initiation and at least for the following 16 years at many major academic centers, it was public health policy and standard practice to permit nontreatment of patients with latent syphilis older than 50 years; that although there was a clear indication for treatment of early, infectious syphilis (ie, an issue of public health), the treatment of late-latent syphilis—the condition of the men who participated in the TSUS—was a lower priority; that the TSUS results were presented at medical meetings and published in mainstream peer-reviewed medical journals; that a few patients in the TSUS were known to have received penicillin; and that black medical professionals were experts on syphilis and seemingly valuable collaborators with white physicians in the TSUS.

The presidential apology is now past. What is the value of an apology from the government for its role in the TSUS? What role can medical professionals play now in health care and health research, especially for the benefit of African Americans? With the information contained in this article, medical professionals and researchers have alternative information to discuss with their patients and their patients’ families about some of the issues surrounding the TSUS. As a result of these dialogues, perhaps many African Americans will actively maintain their health, not delay treatment, participate in clinical research trials, and volunteer as organ donors. If so, the future may hold promise for narrowing health outcome disparities between blacks and whites. Let us hope the apology does not backfire by generating desperation and fear. Unfortunately, there is evidence that when real or perceived racist events occur in America or internationally, the TSUS is still thought of as an example of racism,
Let us hope deception, exploitation, and/or active denial of effective therapy in medical research.101,105,106 Let us hope that the heated rhetoric associated with discussions about the TSUS does not continue to replace reason with outrage.

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