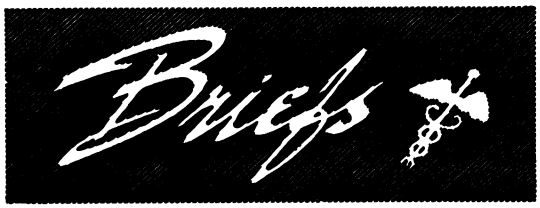
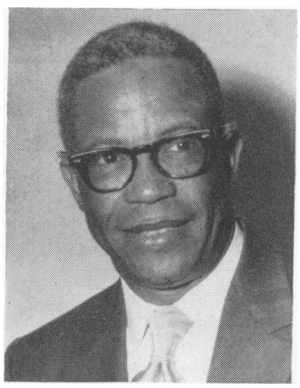


THE TUSKEGEE SYPHILIS STUDY

Despite a voluminous literature and over four centuries of scientific investigation, the natural history of syphilis remains unsatisfactorily known and understood. The traditional remedies of mercury and the iodides and later bismuth and the arsenicals often had adverse effects upon the patient. Moreover, as late as the 20s, many experienced physicians questioned the value of this treatment after the secondary stage and some held the view that left alone, the disease would "wear itself out."



DR. BROADUS N. BUTLER

This opinion was first expressed by William Ferguson, Inspector General of Hospitals of the Portuguese Army, in 1812. He reported that Portuguese soldiers who contracted syphilis and received no treatment fared better than British troops who were treated with mercury, often showing toxicity from the metal itself.

The classic controlled study of this matter was undertaken by C.P.M. Boeck of Oslo, Norway, in 1891 and continued to 1910, with follow-up observations by Bruusgard in 1929 and Gjestland in 1955. These were reviewed by Clark in 1964. Boeck deliberately withheld treatment from 1,978 patients with primary and secondary syphilis during the twenty-year period, 1891-1910, hospitalizing them until they were no longer infectious. Significant information was obtained on about 80 per cent of this group, which showed that about 65 per cent went through life with a minimum of inconvenience. The therapeutic value of mercurials is thus unsubstantiated, although their toxic potential is undisputed. After arsenicals began to supplant mercurials in 1911, it became quickly apparent that they were just as toxic as mercurials.

In 1932 when the Tuskegee Study was initiated, three years after the appearance of the Bruusgard Norwegian report in 1929, a valid question thus existed as to whether syphilitics were better left untreated than subjected to the therapeutic modalities then in vogue. Moore in 1933 compared mortality rates for treated and untreated syphilitic patients and Usilton in 1937, the rates for syphilitics and the general population. All syphilitics showed an excess of mortality compared with non-syphilitics to the extent of 140%. However, the syphilitics classified as "Cured through treatment" had a mortality 10 to 20% higher than those untreated or inadequately treated. This led Goldwater of Duke University to state in March 1973 that, "as was true of mercury, treatment of syphilis with arsenic may have done more harm than good."

Following the introduction of penicillin therapy for syphilis in 1943, the subject was exhaustively studied under the auspices of the Penicillin Panel of the National Research Council, the Syphilis Study Section and the Venereal Disease Rapid Treatment Centers of the U.S. Public Health Service, the Army and the Navy and many university hospitals and clinics.

By 1947 the value of this epochal advance was fairly clear. It was also recognized that many questions remained to be answered. Goodman and Gilman wrote in 1958 that, "the effects of penicillin therapy on the public health control of venereal diseases have not all been salutary and measures must be devised to meet this new situation." Since in 1973 there has been a widely publicized national rise in venereal disease, particularly in our great cities like New York, with penicillin abundantly available, it is obvious that the penicillin matter with respect to the Tuskegee Study should be most objectively analyzed.

The Ad Hoc Advisory Panel's report (*vide infra*) states that, "the Tuskegee Study was one of several investigations that were taking place in the 1930's with the ultimate objective of venereal disease control in the United States. Beginning in 1926, the United States Public Health Service, with the cooperation of other organizations, actively engaged in venereal disease control work. In 1929, the United States Public Health Service entered into a cooperative demonstration study with the Julius Rosenwald Fund and state and local

departments of health in the control of venereal disease in six southern states; Mississippi (Bolivar County); Tennessee (Tipton County); Georgia (Glynn County); Alabama (Macon County); North Carolina (Pitt County); and Virginia (Albemarle County). These syphilis control demonstrations took place from 1930-1932 and disclosed a high prevalence of syphilis (35%) in the Macon County survey. Macon County was 82.4% Negro. The cultural status of this Negro population was low and the illiteracy rate was high.

"During the years 1928-1942 the Cooperative Clinical Studies in the Treatment of Syphilis were taking place in the syphilis clinics of Western Reserve University, Johns Hopkins University, Mayo Clinic, University of Pennsylvania, and the University of Michigan. The Division of Venereal Disease, USPHS provided statistical support, and financial support was provided by the USPHS and a grant from the Milbank Memorial Fund. These studies included a focus on effects of treatment in latent syphilis which had not been clinically documented before 1932. A report issued in 1932 indicated a satisfactory clinical outcome in 34% of untreated latent syphilitics."

A background paper on the Tuskegee Study prepared by the Venereal Disease Branch, State and Community Services Division, Center for Disease Control at Atlanta, Georgia, under date of July 27, 1972, stated that in the late 20s and early 30s, surveys in rural areas of the south revealed a high incidence of syphilis among blacks and it was determined that many of those infected remained untreated. Because of the lack of knowledge of the pathogenesis of syphilis a long term study of untreated syphilis was considered desirable in establishing a more knowledgeable syphilis control program.

"A prospective study was begun late in 1932 in Macon County, Alabama, a rural area with a static population and a high rate of untreated syphilis. An untreated population such as this offered an unusual opportunity to follow and study the disease over a long period of time. In 1932, a total of 26% of the male population tested, who were 25 years of age or older, were serologically reactive for syphilis by at least two tests, usually on two occasion. The original study group was composed of 399 of these men who had received no therapy and who gave historical and laboratory evidence of syphilis which had progressed beyond the infectious stages. A total of 201 men comparable in age and environment and judged by serology, history, and physical examination to be free of syphilis were selected to be the control group."

"In 1943, Dr. John Mahoney reported the first cures of primary and secondary syphilis with penicillin. When this drug first became widely available (1946-47), the questions naturally arose concerning the advisability of treating all of those in the syphilitic group. A decision was made at that time not to recommend treatment because 1) no data were available on the efficiency of penicillin treatment in late syphilis and 2) the short and long term toxic effects of this drug had not as yet been well documented. The judgment was made that the possible risks to the patients from treatment outweighed their risks from the disease. Reassessments of the advisability of treating all the Tuskeegee Study syphilitics have been made periodically since 1946 (the last being made in 1969), and the conclusions have remained the same: the benefits of non-treatment have been judged to outweigh the benefits conferred by such treatment."

"Although it will not be possible to recreate the milieu of social and scientific opinion in which the decisions not to treat the syphilitic persons in the group have been taken, it is appropriate to undertake a review of the case records to reconstruct the risks and benefits from treatment both in the light of current knowledge and in the light of knowledge presumed to be available to the various decision makers of each juncture in the study, including the present. (It should be noted that of the 76 syphilitic patients now known to be living, 75 have at some juncture in the past received antibiotic therapy, and in approximately 30 per cent such therapy is thought to have been adequate for the cure of syphilis)."

The background study concludes, "Although this study has been widely publicized in professional circles since its inception, and although persons in the study group were informed they had syphilis, were informed that they could request and receive syphilis treatment at any time, and were treated appropriately for other medical conditions as they arose, it has been necessary throughout the course of the study to make judgments whether to recommend to all the syphilitic patients that they receive treatment. At no time in the course of the study has treatment been without risk, and the judgment has been consistently made that this risk has outweighed the benefits anticipated from treatment."

The premises of the Tuskegee Study are thus set forth. A glaring omission appears at once, however, in the fact that for really valid conclusions, there should have been a subdivision of the syphilitics into those who received no treatment and those who did accept treatment, since according to the reports some did. Moreover, in view of the difficulties in communication between the patients and the clinicians, the affirmation given the persons in the study group as to their condition and privileges would require some documentation.

The public interest in the Study was aroused by stories appearing first in a medical news periodical and later carried by the national press, to the effect that the U.S. Public Health Service had withheld from the patients in the study a positive cure for syphilis in the form of penicillin, which should have been given them once it became available. The sense of outrage thus created in the public mind led to the appointment of a *Tuskegee Syphilis Study Ad Hoc Advisory Panel* to the Assistant Secretary for Health and Scientific Affairs, DHEW.

The Panel was charged with advising the Assistant Secretary for Health on the following specific aspects of the Tuskegee Syphilis Study:

1. "Determine whether the study was justified in 1932 and whether it should have been continued when

penicillin became generally available.

2. "Recommend whether the study should be continued at this point in time, and if not, how it should be terminated in a way consistent with the rights and health needs of its remaining participants.

3. "Determine whether existing policies to protect the rights of patients participating in health research conducted or supported by the Department of Health, Education, and Welfare are adequate and effective and to recommend improvements in these policies, if needed."

This Ad Hoc Panel was appointed on August 28, 1972, and terminated on April 30, 1973. The nine members of the Panel were:

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The panel held 12 meetings, including six subcommittee meetings, between September 22, 1972, and March 28, 1973. Its report was transmitted to the Assistant Secretary, Dr. Charles C. Edwards, on April 30, 1973, by Dr. Broadus N. Butler, president of Dillard University, the chairman.

It is apparent from the broad spectrum composition of the panel that a comprehensive objective report was hoped for which would both clarify the allegations made with reference to the Tuskeegee Study and contribute to future formulations for experimental studies involving human beings. An examination of the report does not indicate that this result was achieved.

In respect to the first charge, the panel concluded that the Study was ethically unjustified in 1932 when it was begun. However, its statement, "One fundamental ethical rule is that a person should not be subjected to avoidable risk of death or physical harm unless he freely and intelligently consents," is moot. Evidence does not appear to have been brought forward in proof that anyone was subjected to avoidable risk of death or physical harm.

It is clear that no protocol has been found to exist which documents the original intent of the Study. It is almost unbelievable that the Public Health Service would have allowed a study to be initiated or to continue for which no guidelines or statement of purpose could be found. What became of the protocol?

With respect to its second charge, the Panel recommended that the Study be terminated immediately and that a Select Specialist Group, composed of competent doctors and other appropriate persons, with experience in the problems arising from this study, be promptly appointed to make medical judgments with regard to the treatment or referral of all the surviving participants and others within and without Macon County who may be identified in cooperation with the appropriate medical societies and health departments.

The bulk of the report is concerned with charge three to the Panel. It deals with an evaluation of current DHEW policies for the protection of human research subjects and deals with all the moral and legal concepts involved. It recommended that the Congress establish a National Human Investigation Board which apparently would in its authority and responsibility, "cover the waterfront" in respect to research involving human subjects. Perhaps the Panel's comprehensive approach to the matter of human experimentation was justified and can be useful, perhaps not. The subject is much broader than was the province of the panel.

It is interesting that the chairman of the Panel, Dr. Broadus N. Butler, distinguished president of Dillard University, abstained from signing the recommendations relative to charges one and three. The Panel was unanimous in its recommendations with respect to charge two.

What seems to remain is that the Study has been concluded; that there is no way of knowing what if any beneficial findings were made because there are no intention or funds to make an exhaustive study of the results; and that an enterprise of this kind should not be embarked upon again.

W. MONTAGUE COBB, M.D.

STATEMENT OF DR. VERNAL G. CAVE before the U.S. SENATE SUBCOMMITTEE ON HEALTH HON. EDWARD M. KENNEDY, CHAIRMAN April 30, 1973

Mr. Chairman, Distinguished Members of the Senate Health Subcommittee, my name is Dr. Vernal G. Cave. I am one of nine persons appointed by the former Assistant Secretary for Health and Scientific Affairs, Dr. Merlin K. Duval, to the Ad Hoc Tuskegee Syphilis Study Advisory Panel on August 28, 1972. First let me extend my sincere thanks and appreciation to the Subcommittee for its gracious invitation to me to appear today. The Panel as you know was originally scheduled to terminate on December 31, 1972. On request of the Panel it was extended to March 31, 1972, and we were instructed to submit our final report by April 30, 1973. Today is April 30, 1973. It is my understanding that the report will be submitted to the Assistant Secretary for Health, Dr. Charles C. Edwards on this day. It is my further understanding that this report is concurred in by mail or phone by the vast majority of the members of the Panel although some of the members of the Panel may be submitting individual reservations, explanations or amplifications.

I am the Chairman of the Board of Trustees of the National Medical Association and Chairman of its special committee investigating the Tuskegee Study. This committee will make its report to the annual convention of the Association in New York City in August.

I am not authorized to speak for any individual or any group, so it should be clear from the outset that the remarks and observations that follow are my responsibility alone.

What, if anything, did the study add to the body of medical knowledge? While some information was added to medical knowledge, as indeed information from experimental animals might add to medical knowledge, it was chiefly confirmatory information—information that could be and was acquired by far more humane means.

First and foremost, I would say that the information provided by this study confirmed what had been known for ages and had been previously reconfirmed by the Oslo study—that syphilis had a deleterious effect on the health and welfare of its victims. The study illustrated what was already known—that some persons whose syphilis untreated will end up as disabled or insane or crippled human beings and that some will die. It was apparent from this study that the illnesses of individuals with untreated syphilis included significantly higher incidences of sometimes fatal diseases not thought to be related directly to syphilis. Thus, the presence of untreated syphilitic infection apparently predisposed its victims to other illnesses. The study also confirmed that some victims of untreated syphilis live on without developing any of the late manifestations of this disease. However, since we don't possess the Divine wisdom that would let us know which syphilitics are chosen to escape its late manifestations, the fact that some cases escape late disease cannot be used to justify withholding the administration of a known cure, any more than, for example, the knowledge that the body's defenses may overcome a pneumonia infection would justify withholding a known cure from a person suffering from pneumonia.

I have used the term "untreated syphilis." But at this point I must state that fortunately the information shows that most of the participants in this study received antibiotic treatment at some point in their lives either for syphilis by some doctor who was not aware of the study or for some some other illness. This was a source of dismay to some of the administrators of this study. Incidentally, the fact that a majority of the patients were given antibiotic treatment, albeit inadequate therapy, at some point in their lives compromised the objective of this study to follow the course of truly untreated syphilis. One must bear this fact in mind evaluating. There are other considerations from a strictly scientific point of view that brand this study as not very productive of scientific information that I will mention shortly.

The first report on the study to appear in the medical literature in 1936, four years after the study commenced, made it quite clear that the results of no treatment would be disastrous to a significant portion of the group. Cardiovascular, central nervous system and bone and joint system abnormalities were found to be about four times greater in the syphilitic group under age forty, when compared to the control group. The study revealed that only in one-fourth of the untreated syphilitics were no additional abnormalities found. At this point a comparison was made between 86 inadequately