UNTREATED SYPHILIS IN THE MALE NEGRO

A PROSPECTIVE STUDY OF THE EFFECT ON LIFE EXPECTANCY[1]

J. K. SHAFER, M.D.,[2] LIDA J. USILTON, SC.D.,[3] AND GERALDINE A. GLEESON, A.B.[4]

DETERMINATION of the quantitative effect of a disease on the life expectancy has posed numerous difficulties, both statistical and medical. This is more apparent in chronic disease than in acute disease where determination of death or survival is, relatively speaking, revealed without delay.

In discussion of chronic disease, with limited funds available for public health activities, the determination of which diseases shall be made the target of concerted effort often is based on the economic effects of disease, that is, the economic effects as they relate to the need for hospitalization or care of the individual out of public monies. Certainly more concern should be given to the fact that life has value, happiness, and dignity which are greater in health than in disease.

The problems inherent in answering quantitative questions relating to the lethal effects of chronic disease have been reviewed repeatedly (1–3). They will not be discussed here other than to state that one of the chief obstacles in such determinations is that data have to be secured on the basis of *retrospective* rather than *prospective* bases.

THE SYPHILIS PROBLEM

Syphilis is a disease with an acute span of about two years

[1] From the Venereal Disease Program, Division of Special Health Services, United States Public Health Service, Washington 25, D. C.

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[2] Medical Director, Assistant Chief, Division of Personnel, United States Public Health Service; formerly, Chief, Venereal Disease Program.

[3] Public Health Administrator, Venereal Disease Program.

[4] Statistician, Venereal Disease Program.

and with chronicity which may persist throughout the life span. Most of its lethal and crippling manifestations occur during the first fifteen to twenty years of the chronic period. It has been the subject of extensive study; not only as a disease, but also in relation to the social, educational, and economic aspects of the lives of those infected with it and of the community in which it is found. The development of the structure of the present day national venereal disease control program reflects the results of this study, in spite of important areas of ignorance which still remain.

Realization of the widespread prevalence of syphilis and the related venereal diseases was responsible for the first nation-wide program in public health control of venereal diseases. These diseases accounted for one of the chief causes of draft rejection in the first World War, and this fact gave impetus to establishment of the control program. The program collapsed soon after the end of the war, but over the next fifteen years the ground was prepared for epidemiologic, morbidity, and mortality studies, and for determination of effective methods of diagnosis and cure. These studies were needed to provide the stimulation and justification for another attempt to control the spread of syphilis and the other venereal diseases. This program was initiated in 1938 and still is being successfully carried on.

A recent study on syphilis mortality (4) during the period of the Fifth Revision of the International Lists of the Causes of Death, 1939 through 1948, shows that the reduction in total syphilis mortality during the ten years following the initiation of the control program in 1938 proceeded at a faster rate than the reduction in deaths from all causes. The number of syphilis deaths was reduced approximately 41 per cent between 1939 and 1948, and the syphilis death rate was reduced about 47 per cent in the same period. The progress made in reducing syphilis mortality during this ten-year period has been equivalent to the progress made against death from all causes in the forty-nine-year period from 1900 through 1948.

In spite of the vast volume of studies on syphilis found in the medical literature of both this continent and Europe relative to all aspects of the disease, there were, in 1930, no accurate data relative to the effect of syphilis in shortening of life. Of course, the facts relative to the occurrence of central nervous system syphilis, cardiovascular syphilis, and congenital syphilis were well known from the point of view of diagnosis and pathologic findings once the disease had become manifest. However, there was no accurate idea about the natural history of the disease leading up to these complications. This information was necessary in order to evaluate the effectiveness of programs of public health control with a reasonable degree of understanding of the natural history of the disease.

The Bruusgaard Study

The findings of Bruusgaard of Norway on the results of untreated syphilis became available in 1929 (5). Boeck, chief of the Dermatology and Syphilology Clinic at the University of Oslo, treated 2,181 patients with early syphilis by hospitalization and simple, symptomatic remedies. He kept them under hospital care until all of the signs and symptoms of the acute, infectious stage had passed. He did not use arsenicals when they became available, nor did he use even mercury, so that his patients were allowed to run the normal course of syphilis essentially uninfluenced by therapy. By virtue of the size of the country, the centralization of records, and the workings of Norway's venereal disease control system it was possible to secure follow-up data upon a large portion of this group of patients.

Bruusgaard's analysis showed outcome of the disease in a group of 473 patients at three to forty years after infection. For the first time, data were available to suggest the probability of spontaneous cure, continued latency, or serious or fatal outcome. Of the 473 patients included in Bruusgaard's study, 309 were living and examined, and 164 were dead. Among the 473 patients, 27.7 per cent were clinically free from symptoms with the Wassermann negative, 14.8 per cent had no clinical

symptoms with the Wasserman reaction positive. On the basis of diagnoses made at examination or at autopsy, 14.0 per cent had cardiovascular disease, 2.8 per cent were found to have paresis, and 1.3 per cent were diagnosed as having tabes dorsalis.

Bruusgaard's findings met with immediate objections, many of which were based on the validity of the basic data. Some of the questions regarding the analysis included; how accurate was the original diagnosis in many cases; how many of the cases were diagnosed and treated prior to the discovery of the dark-field microscope; was there any assurance that the course of disease in those followed was the same as in those lost from observation? (It should be noted that the Bruusgaard material recently has been subjected to an intensive review with clinical examination of most of the known survivors, and subsequent findings will be published (6).

The shortcomings of Bruusgaard's work and of other retrospective studies, the most complete of which is that of Rosahn (7), have pointed up the need for other long-term studies. These should be planned to overcome the objections to the earlier studies and to provide answers related to the area and population groups in which the problem is concentrated.

Life Table Technique Applied to Syphilis

One of the first studies in which the life table technique was used to measure the effect of syphilis in shortening of life was published in 1937 (8). The mortality experience of the population included in the Cooperative Clinical Studies was used as a basis for this study. It was found that the life expectancy of males with acquired syphilis is shortened from that in the general population from ages 30 to 60 by 17 per cent in the white males and 30 per cent in the Negro males. Any comparison of the reduced life expectancy in this study with the findings in the present study is precluded, because of disproportionate changes in the life expectancy of population groups during the fifteen-year interim, 1937–1952.

Background of Tuskegee Study

In the late 1920's various of the Foundations (Rockefeller, Rosenwald (9) etc.) began their studies of health conditions in the South which were to eventuate in the development of local health units. One of the most striking findings in the early surveys of disease prevalence was the high rate of syphilis among the majority of the Negro groups studied. In one of the study areas (Macon County, Ala., home of the Tuskegee Institute) initial efforts at control of syphilis were followed by further moves on the part of the United States Public Health Service to bring diagnosis and treatment to the population. With the finding of high prevalence of syphilis in the survey and with certain other factors apparent in the community it became evident that it might be possible to institute in this region a prospective—in contrast to a retrospective—study of the results of untreated syphilis in the Negro male. Such a study was needed to assist in the planning and execution of the national venereal disease control program which was then being planned for a later time.

While details of the program are available elsewhere (10–12), the plan may be summarized by stating that it was decided to confine the study group to males so that there would be no problem of the transmission of congenital syphilis. The study group patients were selected as having syphilis on the basis of the best serologic and clinical knowledge available at the time. A competent syphilologist spent almost a year in residence to set up the study group. The control patients were selected to provide a valid matching group from the same socioeconomic and age groups. Documentation of the validity of the control group from the socioeconomic standpoint is offered in another report (13).

In order to assure careful observation of the group, a Negro nurse, resident of the community and just out of training, was employed to take local responsibility for follow-up of all patients, both syphilitic and nonsyphilitic, under the direction of the local health officer (14).

Finally, in order to provide maximum validity to the findings, arrangements were made to secure autopsies on all deceased patients.[5] On completion of each of the gross examinations, specimens were sent to the Pathology Division of the National Institutes of Health for microscopic study. The first report on the findings of the postmortem examinations is being prepared (15).

A few patients, both syphilitic and control, have migrated from the area, particularly to the North, but even so, a sizable portion of those patients have been followed for examination and a few, even for autopsy. The characteristics of the group, though, have been such that most have remained where they were originally examined; both control and syphilitic groups have continued to enjoy essentially the same kind of life (13) and the same types of medical and public health care. The same nurse and pathologist-radiologist have been working with and observing the two groups since they originally were selected for study.

It is evident, then, that these patients provide an unusual group: the original selection, the physical and serologic examinations through the years, and the postmortem studies were based upon knowledge of the desideratum to supply valid information concerning certain aspects of the chronology of a chronic disease. It has been possible to carry out the study in accordance with the original experimental design. Now, the results of the twenty-year physical examination of the group and certain other aspects of the study are available to add to the interim observations (16, 17).

The amount of specific antisyphilitic treatment given (18) has been insufficient to modify significantly the course of the disease, so that comparison of the life expectancy of the two groups is a valid procedure. Furthermore, serologic study at this last examination included performance of *Treponema pallidum* immobilization (TPI) test, a laboratory procedure

[5] Fees for autopsies and other expenses which official agencies were not able to assume were paid for by the Milbank Memorial Fund.

which indicates with a high degree of accuracy the fact of existence of syphilis in the latent stage at some time in the patient's life without regard to whether or not specific therapy has been given (19). Results of this test indicated a high degree of accuracy in the original diagnoses. Thus, the comparison of life expectancy can be considered to be one between two comparable groups, differing only in the presence or absence of syphilis at the time when the study was initiated.

Statistical Method and Analysis

The present study group consists of 408 untreated syphilitic and 192 nonsyphilitic patients, all of whom were entered in the study during 1932–1933 and who maintained their original status relative to the presence or absence of syphilitic infection. Of the syphilitic patients 165 (40.4 per cent) have died and of the nonsyphilitic patients 51 (26.6 per cent) have died since the beginning of the study through 1952. Approximately 60 per cent of these 216 patients have been examined postmortem.

In Table 1, the life expectancy of the nonsyphilitic individuals included in this study is shown in comparison to the expectancy for all nonwhite males as presented in life tables prepared by the National Office of Vital Statistics. These tables

Table 1. Life expectancy for the nonsyphilitic individuals in the Macon County study group, and for all nonwhite males in the United States, 1950, by age-group.

Age-Group 1932–1933 (in Years)	Life Expectancy in Years	
	Nonsyphilitic Individuals in Macon County Study Group	All Nonwhite Males in United States, 1950
25–29	41.6	39.7
30–34	38.2	35.5
35–39	34.1	31.5
40–44	29.7	27.5
45–49	25.2	23.8
50–54	20.7	20.5
55–59	16.4	17.6
60–64	12.3	15.2
65–69	8.4	13.3
70–74	4.5	11.1

were based on the 1950 mortality experience for the entire country (20). The similarity of the figures within each age-interval group indicates that the experience of the nonsyphilitic group in this study is sufficiently stable to serve as a measure of normal life expectancy.

The basic data used in the computation of the life expectancies of the two groups consists of (a) the number of deaths occurring in each group during the twenty years, 1933 through 1952, the deaths being tabulated by age-interval of occurrence, and (b) the total number of patient years of observation contributed by the individuals in each age-group during the period under study (Table 2). Age-specific mortality rates were obtained by relating the number of deaths occurring within a particular interval to the number of patient years of observation within the interval. Due to the relatively small numbers involved, it was necessary to combine the single years into five-year age groups for ages 25 through 74 years and to exclude the data for ages 75 years and older. From Table 2 (column 3) it is evident that the mortality rate for the untreated syphilitic group is higher than that for the nonsyphilitic group in each of the five-year age intervals.

It will be noted that the rates for both the syphilitic and the nonsyphilitic groups display a general upward trend with age, as would be expected, but show the lack of stability characteristic of rates computed from small numerical values. To overcome this instability and to provide for the interpolation of rates for single years of age, necessary for the construction of the life tables, the rates for the five-year age groups were fitted to cubic parabolas ($a + bx + cx^2 + dx^3$). The resulting values are shown in column 4 of Table 2. These adjusted rates were applied successively (by single years of mortality experience) to a theoretical population of 100,000 persons alive at age 25. As the mortality rates were applied, the number of survivors at each age-year, 25 through 74, was obtained by subtracting the number who would have died in the theoretical population had they been exposed to the mortality rates computed from the

Age Interval in Years	Untreated Syphilitic Patients					
	Mortality Experience			Application to Theoretical Life Table Population		
	Patient Years of Observation (1)	Number of Deaths Occurring (2)	Number of Deaths per 1,000 Years of Observation (3)	Average Number Dying during Interval, of 1,000 Alive at Beginning of Interval (4)	Number Surviving at Beginning of Age-Period of 100,000 Alive at Age 25 (5)	Life Expectancy Through Age 74 of Those Individuals Surviving to Age-Period (6)
25–29	305.2	3	9.8	12.2	100,000	34.73
30–34	565.0	9	15.9	10.4	94,036	31.78
35–39	724.5	6	8.3	10.2	89,203	28.37
40–44	884.5	7	7.9	11.7	84,713	24.75
45–49	832.3	14	16.8	15.1	79,846	21.10
50–54	838.2	23	27.4	20.6	73,975	17.57
55–59	763.8	15	19.6	28.4	67,203	14.07
60–64	666.0	24	36.0	38.7	58,166	10.86
65–69	442.0	27	61.1	51.7	47,727	7.68
70–74	219.8	14	63.7	67.6	36,578	4.25

Table 2. Abridged life tables based on mortality experience of untreated syphilitic and presumably nonsyphilitic patients, Negro males 25 through 74 years of age, Macon County study group, 1933-1952.

study groups. The number of survivors was cumulated to represent the patient years of life at each single-year interval. At this point, the patient-years were combined into five-year intervals to serve as base figures in the computation of the life expectancy of each five-year age group. The figures in column 5 of Table 2 represent the number of individuals surviving to the beginning of each five-year age interval rather than the total number of individuals to which the rates were applied during the five-year interval. The average number of years of life through age 74 remaining to individuals reaching a given age is shown in column 6, and is presented graphically in Figure 1.

The last two columns in Table 2 represent the number of years and percentage of reduction in the life expectancy among individuals in the syphilitic group. It will be noted from the table that the difference in the average number of years of expected life for nonsyphilitic and syphilitic patients decreases gradually from the youngest age-interval, 25 through 29 years, to the oldest, 70 through 74 years. This is to be expected since

Presumably Nonsyphilitic Patients						Average Reduction in Life Expectancy of Those in Syphilitic Group	
Mortality Experience			Application to Theoretical Life Table Population				
Patient Years of Observation (1)	Number of Deaths Occurring (2)	Number of Deaths per 1,000 Years of Observation (3)	Average Number Dying During Interval, of 1,000 Alive at Beginning of Interval (4)	Number Surviving at Beginning of Age-Period, of 100,000 Alive at Age 25 (5)	Life Expectancy Through Age 74 of Those Individuals Surviving to Age-Period (6)	Number of Years	Per Cent
143.5	1	7.0	7.7	100,000	41.60	6.87	16.5
269.5	2	7.4	5.3	96,184	38.16	6.38	16.7
354.0	1	2.8	3.7	93,628	34.13	5.76	16.9
447.0	1	2.2	3.3	91,879	29.74	4.99	16.8
424.5	2	4.7	4.4	90,363	25.19	4.09	16.2
434.5	3	6.9	7.4	88,373	20.70	3.13	15.1
415.5	4	9.6	12.9	85,089	16.40	2.33	14.2
355.0	12	33.8	21.1	79,699	12.32	1.46	11.9
250.0	5	20.0	32.5	71,588	8.42	.74	8.8
136.5	7	51.3	47.4	60,643	4.47	.22	4.9

the effect of the natural aging processes reflected in both study groups tend to overshadow any difference due to the syphilitic process in the older age-groups. Percentagewise, however, the difference in the two groups, syphilitic and nonsyphilitic, remains fairly constant during the first five age-intervals, indicating that the life expectancy of a Negro male between the ages of 25 and 50 years, infected with syphilis and receiving no appreciable treatment for his infection, is reduced by about 17 per cent. The twelve years (1933 through 1944) of patient observation on which the original life study (18) of the patients was based yielded information that the life expectancy in the syphilitic group is reduced by 20 per cent among persons in the twenty-five to fifty year age group. It is interesting to note that the additional eight years of mortality experience available for the present study reduced the difference in life expectancy between the study groups from 20 per cent to 17 per cent.

Summary

1. The rationale for and establishment of the controlled prospective study of the effect of untreated syphilis in the male Negro are discussed.

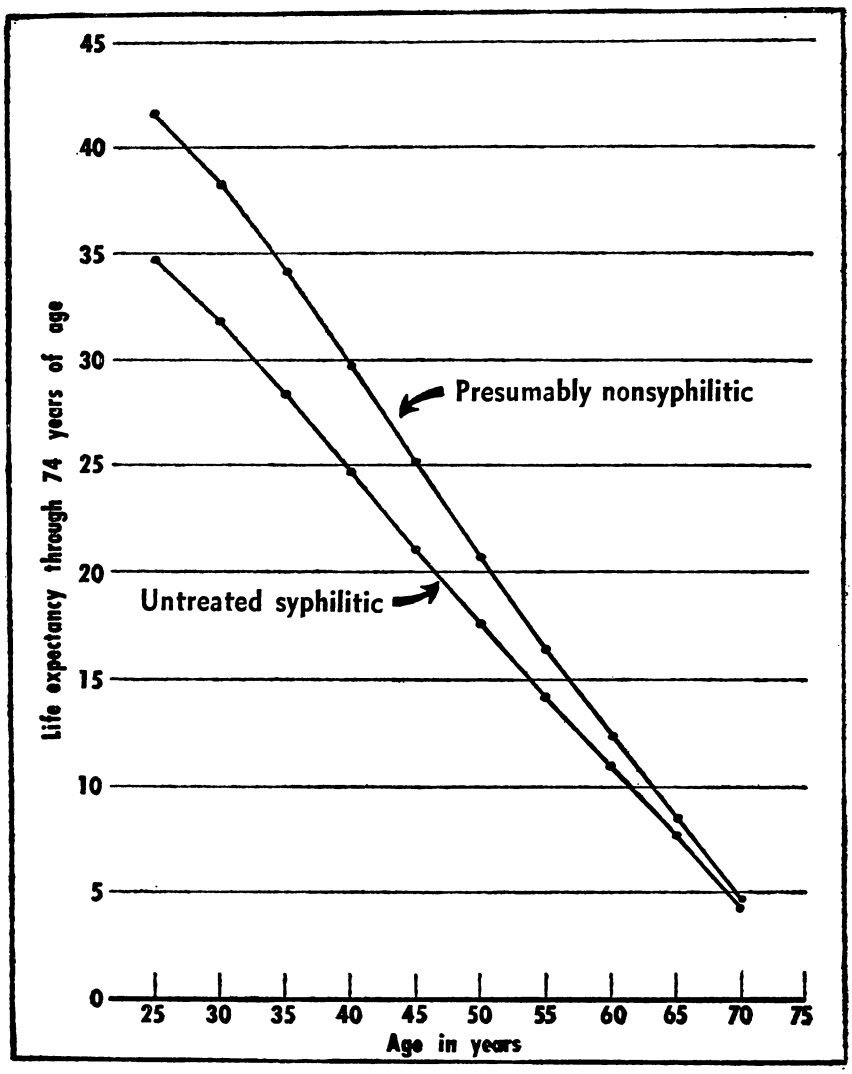

Fig. 1. Comparison of life expectancy through age 74 in untreated syphilitic and presumably nonsyphilitic patients surviving to specific age intervals, Macon County study group.

2. The prolonged nature of a chronic disease or a disease with a chronic stage, such as syphilis, necessitates long-term study of the natural history (or pathogenesis) of the disease before the effectiveness of programs for the control of the disease can be evaluated properly.

3. Based on the mortality experience among 408 untreated

syphilitic and 192 presumably nonsyphilitic patients, the general trend of mortality is higher among the syphilitic individuals between the ages of 25 and 74 years.

4. The life expectancy of an individual 25 to 50 years of age with syphilis, for which he has received no appreciable amount of therapy, is approximately 17 per cent less on the average than that of an individual in the same age interval of a nonsyphilitic population.

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