STUDIES IN SYPHILIS EPIDEMIOLOGY*

BY

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The venereal disease control programme in the United States has as one of its objectives the eradication of syphilis from the country by 1972, by continuous reduction of the reservoir of infection through case-finding and early treatment.

Studies are now in progress to construct quantitative models of the relationship between the effort expended in control and eradication measures and the effects produced. The models being constructed are deterministic, that is, only a single sequence of events will ensue with the given set of initial conditions. Perhaps probability models, where chance plays a part, may be indicated, because a variety of factors during each disease generation may intervene to alter the spread of syphilis to potential victims of the next disease generation.

To develop these quantitative models, it was necessary to specify certain conditions regarding the incubation period and the early stages of syphilis. These conditions were:

- (1) From the date of infection, the disease would remain in an incubation period for 3 weeks;
- (2) This 3-week incubation period would be followed by a 5-week period of primary syphilis;
- (3) This 5-week period of primary syphilis would be followed by a 6-week period of secondary syphilis;
- (4) The syphilitic infection would then progress into the latent stage.

In summary, the course of untreated syphilis is categorized into a 3-week period of incubation, a 5-week period of primary syphilis, a 6-week period of secondary syphilis, and a final period of latency. The process from infection to latency occupies 14 weeks and 11 of the 14 would be considered the infectious period.

A nation-wide epidemiological study of primary and secondary syphilis was conducted in 1963. The results of this study indicated that 1,000 primary

cases of syphilis were treated, on the average, 2 weeks after the onset of the signs and symptoms of primary syphilis and that they had infected 340 other persons during this 2-week period. Projecting this estimate of the parameter linearly, we would expect 850 other persons to be infected if 1,000 primary syphilis cases went untreated for the full 5-week primary period. Similarly, 1,000 secondary cases, who were treated 4 weeks after the onset of secondary manifestations, had infected 200 other persons during the 4-week secondary period. Thus, we would expect 300 other persons to be infected during the period of secondary syphilis if 1,000 secondary syphilis cases went untreated for the full 6-week secondary period. Therefore, according to the conditions specified, 1,000 untreated patients with primary and secondary syphilis would be expected to infect 1,150 other persons if they progressed through the total infectious period. This is a spread rate of 1.15.

I should like to discuss two models to contrast how effective control measures might control and eradicate syphilis.

In the first situation where 1,000 cases progress untreated through the total infectious period in the first cycle, we would expect 1,150 other persons to be infected in the second cycle. Compare these results to the results we might expect in the second situation where all control measures are utilized including an educational programme; all 1,000 cases would recognize their primary signs and symptoms and seek medical attention within 1 week after the onset of the primary lesion. Since these 1,000 cases had their signs and symptoms of primary syphilis for 1 week or less, all spread contacts must still be in the incubation period. Rapid examination of these contacts within 1 or 2 days would bring all potential spread cases to medical examination before they developed clinical syphilis. Adequate preventive treatment would abort any incubating syphilis in

* Received for publication September 9, 1965.

these contacts. The 1,000 cases would spread no further in the next disease generation, resulting in the effective eradication of syphilis. In other words, under these conditions, our spread rate is zero.

Considering the second model, we may postulate that continuous prompt diagnosis of a certain percentage of infectious cases, rapid examination of the contacts exposed, and the use of preventive treatment may result in the control and eradication of syphilis from the United States. The degree to which these factors are implemented will determine when syphilis will be eradicated.

I should like to comment at this point that we are not satisfied with some of the assumptions we had to make in the above study, and that our statisticians are continuing to test them out with new epidemiological information, thus refining the model.

It is apparent that finding and treating new cases of syphilis in the primary stage is the key to our control and eradication programme in the United States.

Most of our epidemiological studies in the United States are geared to our control and eradication programme. Some background information is presented so that the studies to be discussed will be more meaningful to the reader.

60 per cent. of the 22,000 cases of primary and secondary syphilis reported in 1964 were brought to treatment through case-finding efforts. Because of signs or symptoms, 40 per cent. sought medical attention of their own volition either at a private physician's consulting room or at a public clinic.

In a nation-wide study conducted in 1963, 49 per cent. of the patients placed under treatment as a result of public health case-finding efforts were aware of lesions or rashes but did not seek medical attention. One of the major objectives of our control and eradication programme is to find these persons and bring them rapidly to diagnosis and treatment to prevent further spread.

About two-thirds of all reported cases of primary and secondary syphilis brought to treatment through case-finding are found through the epidemiological follow-up of contacts and suspects of infectious cases. Hence, epidemiology is the most important arm of our control and eradication programme in searching for unknown infectious cases.

The interview of the infectious patient for contacts and suspects is the first step. This interview must be performed so effectively that the information obtained will result in finding all contacts exposed within the period of infectivity and in finding any additional persons of the same socio-sexual groups that may have been exposed to an infectious person. To conduct this interview, a worker must have a

thorough knowledge of the medical and aetiological aspects of syphilis as well as training in methods of interviewing and finding people with minimal information.

Interviewing is simple in theory, but complex in practice. Its complexities result from the patient's attitude toward the interview. The degree of epidemiological success rests with how well the interview removes barriers and produces the necessary information to find the contacts or suspects.

Briefly, I should like to discuss several recent studies concerning the productivity of the epidemiological interview process.

About 75 per cent. of the infectious syphilis patients name more than one contact and 50 per cent. name one or more suspects. About 80 per cent. of all contacts and suspects are located and brought to examination.

We are frequently asked which contact is the most productive—the first, second, or the last one named by the patient.

In 1961, a study was conducted on the epidemiological value of contacts on the basis of the order in which the patient named the contacts (Swank, 1964). The study indicated that the first and second contacts named accounted for 53 per cent. of the contacts brought to treatment with syphilis, the third and fourth contacts for 17 per cent., and the fifth and subsequent contacts for 30 per cent.

If over 50 per cent. of the contacts brought to treatment are the first or second contact named, it would appear that the original interview is the most important. However, many patients name the third, fourth, or fifth contact at a second or third re-interview. If 30 per cent. of all contacts placed under treatment are the fifth or subsequent contacts named by the patient, the importance of the interviewer's tenacity in successfully transforming the patient's barriers to earnest responses cannot be over-emphasized.

In a similar study conducted in 1963, we investigated the frequency of exposure between the patient and his contacts during the period of infectivity in relation to contracting the disease (Swank and Axnick, 1963). We classified the contacts into three groups: marital contacts, multiple-exposure contacts during the interview period of possible infectivity, and single exposure contacts during this period. The results indicated that 57 per cent. of the marital partners, 39 per cent. of the contacts with whom the infectious patient admitted multiple exposure within the period of infectivity, and 30 per cent. of the single exposures were infected.

The study also indicated that the last group is very important epidemiologically because one of every

In the same study, we also investigated the case-finding technique known as the cluster procedure or social group epidemiology. This technique is designed to motivate patients to name persons other than their sex contacts whom they feel would profit by an examination for syphilis. In addition, when named contacts are investigated, they are also asked to indicate persons in their social group whom they feel would likewise benefit from an examination. On the basis of our experience in the United States, we have found that socially related groups have an abundance of knowledge about the sexual behaviour of their friends and associates, and are often well informed about their physical condition, including syphilitic signs and symptoms. The eliciting of this type of information has been epidemiologically productive in bringing persons with syphilis to treatment.

- (1) Persons named by the diagnosed patient, which we called “suspects”.
- (2) Persons named by the sex contacts of the diagnosed patient, which we called “associates”.

The first group of "suspects" consisted of persons that the patient thought had clinical signs or symptoms similar to his own. About one in eleven of such persons named as suspects will be brought to treatment for syphilis. The yield from this type of suspect roughly equals the yield from contacts to primary and secondary syphilis cases.

The last group of "suspects" consisted of members of the patient's household or family not designated as sex contacts by the patient. One of every 33 of these suspects will be brought to treatment with syphilis.

In the study, when contacts were persuaded to talk about other members of their social group who had clinical signs or symptoms suggestive of syphilis, one of every thirty named by the contacts required treatment. Many of the contacts interviewed suggested persons who were having sexual relations with other known cases in their group. One of every 35 of these persons required treatment for syphilis.

In summary, the study showed that an untreated case of syphilis was brought to treatment as a sex contact in one of every two cases interviewed and an untreated case was also brought to treatment as a community suspect or associate in one of every seven primary or secondary syphilis cases interviewed.

In 1962, a nation-wide study was conducted in the United States to determine the geographical mobility of infectious syphilitic patients and their sex contacts (Donohue, 1964). One per cent. of the contacts named during the study period lived in other countries (Fig. 1), and contacts were named in seventeen foreign countries, mostly in the Americas and Europe.

FIG. 1.—Countries of residence of sex contacts named by patients in United States in March, 1962.

This study suggested that problems posed by mobility in the control and eradication of syphilis may increase as the speed and volume of international travel increase. As control and eradication progress throughout the world in the future, the international reporting of cases of syphilis and exchange of contact information may be of paramount importance in alerting a country as to the presence of syphilis and the opportunity to control and eradicate it.

In 1963-64, several epidemics were investigated retrospectively to determine how to control and prevent epidemics (Ball, 1965; Buchanan, Tiedeman, Creagh, Poole, and De Foor, 1964). The investigations were primarily concerned with the effectiveness of rapid examination of contacts and the use of preventative treatment of contacts with no clinical or serological evidence of syphilis.

The rapid examination of sex contacts to primary or secondary syphilis appears to be effective in reducing the spread of syphilis (Fig. 2). In one epidemic, rapid location and examination of the male contacts controlled the spread by diagnosing 25 of 29 male cases in the primary stage, with penile

lesions with a duration of 1 to 7 days (Ball, 1965). On the other hand, ten of the sixteen female cases were diagnosed in the secondary stage, with secondary manifestations for 1 to 2 months. In this epidemic, all contacts found to be negative on the initial examination (and who had been exposed during the previous 60 days) were treated epidemiologically with 2.4 million units of benzathine penicillin.

In several other studies with similar rapid examination of contacts, all negative contacts on initial examination were followed serologically monthly for 3 months. In these epidemics, 5 to 20 per cent. of the negative contacts serologically followed subsequently developed syphilis. Females exposed to males developed syphilis twice as often as males exposed to females in the 3-month serological follow-up. Similar results have been obtained in recent chemotherapeutic studies in the placebo group.

The technique of preventive treatment mentioned above, sometimes called "epidemiological treatment", proposes to assure the treatment of infections before any possible spread by treating clinically and

FIG. 2.—Infectious syphilis epidemiological chain of infection in South Carolina, January to June, 1964.

serologically negative sexual contacts of infectious cases as if they had demonstrable syphilis. This technique, which is recommended by the Public Health Service and which has been considered favourably by the American Medical Association, is gaining acceptance, and the most definitive study of the application of this procedure has recently been completed (Moore, Price, Knox, and Elgin, 1963).

Five large venereal disease clinics participated in this study of over 1,600 contacts. For this study, contacts are defined as individuals who, within 90 days before their initial examination, had had sexual relations with persons later found to have primary or secondary syphilis. Since this definition was established on the basis of the maximum incubation period of syphilis, it is obvious that actual exposure to infectious syphilis was likely, though by no means certain.

Only contacts who were serologically and clinically negative at the time of initial examination were included in the study. In other words, the contacts included in the study are those who would be diagnosed under normal circumstances as "not infected".

Eight schedules of treatment were evaluated. These included penicillin in dosages ranging from 600,000 to 2,400,000 units, tetracycline, and chloramphenicol. After treatment, contacts were to be observed for a period of 90 days, with physical inspection bi-weekly and serological examination monthly. Of the 1,635 contacts studied, 77 per cent. were observed for more than 60 days.

The following are the most significant findings:

(1) *The 2,400,000 unit penicillin schedule was the only one totally effective in aborting incubating syphilis.*—The rate of infection was 0.6 per cent. following 1,200,000 units and 2.8 per cent. following 600,000 units. The comparable rate for a placebo (untreated) group was 10.9 per cent.

The 2,400,000 unit schedule evaluated employed benzathine penicillin G. However, there was no difference between benzathine and procaine penicillin G in oil when only 1,200,000 units were administered. The delayed absorption preparations, for single injection therapy, did appear superior to aqueous procaine penicillin G.

In the dosages employed (one and two g.) neither tetracycline nor chloramphenicol were effective in aborting incubating syphilis. The rates of infection were 9.6 and 5.5 per cent, respectively.

(2) *The probability of infection is greatest in contacts most recently exposed to primary syphilis* (Fig. 3).—One out of every five contacts, clinically and serologically negative on initial examination, who had been exposed to primary syphilis within the previous 30 days, developed syphilis if untreated. The chance of being infected dropped to approximately one in eight if the last exposure has been 30 to 60 days before examination. In contacts of secondary syphilis, the chance of developing syphilis was about the same whether exposure was within 30 days or 30 to 60 days before examination. Less than 3 per cent. of the contacts of primary or secondary syphilis developed syphilis if the last exposure had been as long as 60 to 90 days before examination.

FIG. 3.—Untreated contacts of primary and secondary syphilis.

(3) *The highest rate of infection occurred in females exposed to primary syphilis within 30 days preceding examination* (Fig. 4).—If untreated, 26 per cent. of the females developed syphilis within the succeeding 90 days; the rate dropped to 13 per cent. after treatment with antibiotics other than penicillin, to 9 per cent. after 600,000 units of penicillin, and to 2 per cent. after 1,200,000 units. As stated previously, no infections developed in those

FIG. 4.—Females exposed to primary syphilis within 30 days before treatment or administration of placebo.

treated with 2,400,000 units of penicillin. In the untreated group, only 9 per cent. of the males as opposed to 26 per cent. of the females developed syphilis if exposed to primary syphilis within the preceeding 30 days.

Although females could be anatomically more susceptible to infection than males, the sex differential more likely results from the greater ease in diagnosing sero-negative primary syphilis in males and hence a disproportionate exclusion of this group from the study.

(4) *Most contacts who developed syphilis had ample opportunity to transmit their disease before it was diagnosed.*—Only nine of the 64 patients developing syphilis were diagnosed in the sero-negative primary stage. In fact, seventeen had already developed secondary syphilis before the infection was diagnosed. This finding draws attention to the fact that, even with careful follow-up examinations, contacts may develop syphilis and while undetected spread the infection further. This observation stresses the advantage of epidemiological treatment over serological follow-up.

We have recently launched some studies related to epidemiology under the broad definition of the word. For example, we are studying what educational techniques and media are most effective in motivating persons to recognize or suspect signs of syphilis, thus causing them to "volunteer" for examination and treatment. We are also conducting a physician attitude study to determine factors involved in the lack of complete case reporting by private physicians.

Finally, I would like to mention some surveillance studies that contribute to an eradication programme.

Great emphasis has been placed on the follow-up by the health department of reactive serological tests for syphilis as an aid in controlling syphilis.

Over one million reactive serological tests are detected by public, private, and hospital laboratories each year. The majority of these tests are a result of testing persons admitted to hospitals. In a national

survey conducted in 1962, 6,424 hospitals reported giving 17 million serological tests for syphilis, largely to adult in-patients (Brown and Mahoney, 1963). Another 15 million serological tests are performed in public and private laboratories as a result of specific examinations for syphilis in public clinics and private physicians' consulting rooms, general physical examinations, premarital, and prenatal examinations. Some 700,000 of these latter tests are reactive.

The thousands of previously untreated cases of latent syphilis brought to treatment through the follow-up of reactive serological tests reported to health departments by laboratories contribute significantly to the reduction of syphilis prevalence in the United States. Furthermore, 20 per cent. of the total primary and secondary syphilis cases reported each year are discovered through this follow-up programme.

In summary, we have a diversified group of epidemiological studies in the United States, but they all have one common objective—the eradication of syphilis.

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