SYPHILIS—WHEN IS IT CURED?

By IRVING R. BANCROFT *

WHEN the spirochaeta pallida was discovered in 1905, and especially when it was cultured on artificial media and also inoculated successfully in rabbits and monkeys, it seemed as though we would soon know all about syphilis, but if one studies the vast literature of syphilis he will find it like the Bible—any thesis may be proved which fits the fancy of the individual. For instance, using the work of Warthin as a basis one might conclude that the present-day treatment did no more than to drive the spirochaetae into inaccessible parts of the body like the walls of the blood vessels, especially of the aorta and the heart. He found evidence of syphilis in practically every necropsy of a person who ever had syphilis and in 40 per cent of 750 general autopsies. His studies are all in stained tissue and are made with great thoroughness. For instance, one of his assistants spent a whole year in the study of eight cases, and six weeks were spent on one heart before spirochaetae were found. His conclusions are that the blood vessels and other organs are affected more or less in every person with syphilis. Graves, working along more neurological lines, stated that a syphilitic ought never to marry, as our cures were symptomatic only. Elberson, working from the animal experimental side, showed that syphilis, when outwardly inactive and latent as far as we could discover, still may be associated with spirochaetae which are located in the glands and semen and which may be successfully inoculated into other animals.

If we approach the problem from a therapeutic point of view we come to the researches of Naguchi in testing the action of drugs on the growing spirochaetae. He measured the amount of various drugs which were necessary to kill the spirochaetae as they were growing in a certain amount of culture medium. Neoarsphenamine was a spirochaeticide in a proportion of 1 to 2500, and after reculturing for several generations six times the original amount of the drug was necessary to kill the organisms. Arsphenamine was three times stronger than neoarsphenamine. Mercury was an efficient spirochaeticide (1 to 100,000), but by reinoculation for several generations a strain of spirochaetae was developed which required thirty-five times the original dose to kill. He also found that after a rest for a generation or two without the addition of any drug that the original sensitiveness to the drug returned. This would seem to indicate that rest periods and a change of remedies are a logical procedure. If we estimate that one-thirteenth of the body weight is blood and .6 gram is the dose of neoarsphenamine used, we would have to use approximately fourteen times the dose we do to get the spirochaeticidal effect, if human blood was used as a culture medium. In the course of syphilis a certain degree of natural immunity seems to be developed as time goes on. At first the blood contains spirochaetae, but after a time none can be demonstrated. Certain workers have used the blood from donors who were known to have had syphilis some time previously for transfusion without infecting the recipients. Juregui and Lacelotti have infected llamas and kept them infected for nine years, and have used the serum from these animals in the treatment of fifty cases of syphilis with results well comparable with specific drug treatment. However, it is fair to say that these results have been questioned. The basis of the specific protein and malarial treatment is also probably that of increasing the natural immunity, and possibly the so-called spirochaeticides do the same thing. At any rate it seems probable that the reaction of the human organism to a syphilitic infection is to develop a definite immunity.

In addition to the natural immunity which all evidence seems to indicate is a factor in the elimination of a syphilitic infection from the body we have the so-called syphilitic specifics. The experiments of Chesney and Kemp give much information and encouragement on this subject. Their experiments were performed on rabbits which were inoculated with spirochaetae and then treated with arsphenamine. They found that after a course of treatment that inoculations of extracts from the glands and organs of the rabbits were not infectious to healthy rabbits, but the untreated controls were capable of causing syphilis in another group of healthy rabbits and cures took place equally well in both old and recent cases. The doses given corresponded to .6 gram for a 132-pound man. He did other experiments in which a strain of organisms were used which had proved refractory to treatment in the human patient, and yet by inoculation experiments and treatments was proved to have been entirely cured in the rabbit. This would indicate that the rabbit has more immunity to syphilis than man.

Let us then cling to the belief that syphilis can be definitely cured, although we know that there are persons in whom the organism lies dormant or harmlessly latent for years and then may awaken to activity. All individuals who have ever had syphilis should have occasional health surveys to see if there is any evidence of renewed activity. If a definite criterion of cure is wanted the army standard is possibly the best. This requires one year of observation after all treatment has been stopped. During that year there must be no positive Wassermanns, and at the end of the year a negative spinal test and a provocative Wassermann, but in one hundred such cured patients again observed at the end of the second year, 14 per cent had relapsed and nine were doubtful. Most authorities permit marriage in an individual who has had no symptoms for two years following the cessation of two or three years' treatment and irrespective of the Wassermann. This differs little from the standard of the older Founier, and I cannot see why the presence of either a positive or a negative Wassermann has much to do with the matter.

The Wassermann reaction if positive probably means an active response of the body tissue to syphilitic infection and as such is of value from a diagnostic point of view. It is probable that a positive reaction may also exist when there is a cured or

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latent syphilitic. Chesney and Kemp showed that a rabbit which had been treated for an old infection and still had positive reaction was not infectious when its glands and organs were inoculated into a healthy rabbit. Walserlin and Carroll, on the other hand, while using rabbits showed that in recent cases the positive Wassermann existed when there were active lesions and became negative when the active lesions subsided. The positive Wassermann then indicates that syphilis is present and in old and treated cases may mean that spirochaetae are hibernating in inaccessible parts of the body and that the individual may live his normal expectancy unless something happens to disturb the balance. We all know that there are patients in whom the infection is old, who have a positive Wassermann and in whom no treatment or combination of treatment can make negative. In a series of this character who were treated at the New York Hospital for an average period of forty months only 56 per cent were made negative, so don't get discouraged if some of your old patients still have a positive Wassermann. *Above all do not hasten a fatal issue by too intensive treatment.*

Most syphilitic patients are led to believe that their great cross is a plus Wassermann. They think themselves cheated if after a few doses of salvarsan it still remains positive. They even become syphilophobiac simply because of the 4 plus Wassermann. As soon as it becomes negative they say, "At last I am cured." Some physicians even encourage or support this view, but if they would stop to think they would realize that a negative Wassermann does not mean a cure. If the Wassermann reaction is not a reliable index of cure, what are we to rely upon? Physical examination surely will not definitely determine whether or not a cure has been effected. Warthin cites five cases where the Wassermann of both parents was negative and syphilitic babies were born, so therefore it seems fair to conclude that there is no definite criterion as to the cure of syphilis.

The important conclusion to be drawn, then, is not when a syphilitic patient is cured, for that is sometimes a question of academic interest and no one can tell definitely. The real question is when and in what amounts and for how long treatment should be given. Most early lesions can be made harmless, latent or cured, but the period during which treatment should be given should be longer than is usually advised and an occasional survey should be made of the individual for many years afterward. Patients with early lesions require, as a rule, from one to three years' treatment, and most of those with late lesions should have nearly as long a course of treatment, but the doses should be smaller. Nerve syphilis may require some form of intraspinal or malarial treatment, but that is another story. Late heart and organic types should have an entirely different procedure. Arsenic is often injurious to them and should be preceded by iodide and mercury and then small doses of arsenic preparations given carefully. The treatment of all patients should be modified by their conditions and an annual examination should be made for many years to see if any signs of syphilitic degeneration can be detected.

Special Article

HYPOPHYSIS VERSUS HYPOTHALAMUS

By H. Lisser *

THE writer prefaced a chapter on the pituitary body with the following quotation:

"Thus do interpretations throng and clash, and neatly equal the commentators in number. Yet possibly each one of these unriddlings, with no doubt a host of others, is conceivable, so that wisdom will dwell upon none of them very seriously" (from Jurgen, by Cabell).

This quaint bit of irony, to some extent at least, reflects the present status of pituitary problems.

Several years ago (about 1920) Camus and Roussy declared war on the then prevalent conceptions of pituitary function. They seized upon a relatively unexplained region, the hypothalamus, not far from the hypophysis, and established their base of operations in the tuber cinereum. They contented themselves, modestly at first, by stealing the diabetes insipidus syndrome from pituitary ownership, which they produced experimentally in dogs by injuring the tuber cinereum (the hypophysis remaining intact). Before long they made another invasion and laid claim to proprietary rights over Frölich's adiposogenital dystrophy which had been in possession of the pituitary since Frölich's first description in 1901. They had reproduced this clinical complex in dogs by traumatizing the hypothalamus (again, supposedly, without harm to the hypophysis).

Meanwhile the pituitary body was torn asunder. Originally separated into two parts, a front and a behind, further investigation produced further divisions: a pars intermedia, and a pars tuberalis (surrounding the infundibular stalk and extending up into the floor of the third ventricle). The respective guardians of these several lobes claimed certain characteristics, powers and functions for their pet portions which conflicted or trespassed one upon the other. In the confusion such matters as skeletal growth, genital disturbances, obesity, emaciation, polyuria and polydipsea, and interrelations with other ductless glands (especially the thyroid, suprarenals, and gonads) became involved and disputed. Laborious classifications of the several functions of the several lobes, whether clinical, pathological or physiological, did not serve to clarify the confusion. Laudable efforts they were, but their orderliness did not rest on sufficiently secure foundations.

The attacks of Camus and Roussy, aided and abetted by Bailey and Bremer, Houssay, Leschke, Curtis and others, caused dismay in the ranks of the

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