last point: when removing an appendix from a tubercular patient we should be careful to remove any enlarged glands in the immediate vicinity, otherwise a sinus is apt to follow. I have noted one instance in my own practice and one, each, in the practice of two other surgeons. Those of us who conduct Sanatoria should do, or have done, all needful surgery in our cases of pulmonary tuberculosis. As I have pointed out upon another occasion these people require a good deal of nose and throat work in order to afford them (some of them) the best chance of recovery from their lung disease.*

NOTES ON SYPHILIS OF THE CENTRAL NERVOUS SYSTEM.*

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It seems evident, even to the most critical, that syphilis, as we know it, is the result of invasion of the body by the treponema pallida. This organism has been isolated from the primary lesion and from the tissues of the body in the secondary and tertiary periods. It has been secured in pure culture and re-inoculated into susceptible animals has reproduced the disease in the characteristic forms peculiar to the animals experimented upon. That the organism has not been found in the affected tissues in certain of the later appearing lesions is no reason for believing that these structural changes require the intevention of any special condition for their development. They can all be explained as end results of the primary tissue reaction.

It has been shown also that the disease may be propagated without the occurrence of the primary lesion, namely, by inoculation directly into the heart, testicle or blood stream of susceptible animals. Syphilis has been transmitted in man during the operation of transfusion of blood and by accidental wounds received at operation without a chancre appearing at the point of inoculation. This evidence and the not infrequent appearance of syphilis in individuals who have no remembrance of ever having had chancre has led some authorities to believe that, under certain conditions, it may be possible for the spirochete to gain access to the body through an apparently unbroken skin. Certain factors not understood at present render inoculation by other than the usual manner, i. e., into surfaces covered by flat epithelium and well supplied with lymphatics, a rather difficult matter.

The evidence justifying the belief in extraordinary methods of inoculation is sufficient, however, to cause one to assume the possibility of syphilis being present in any case presenting symptoms which may be explained by the presence of this disease even though the history of the patient is undeniably negative.

If one may base an opinion, in this matter, on the known behavior of the treponema pallida during its later residence in the body it would seem probable that, in an otherwise healthy individual with normal resisting power, the organism must first be able to secure a suitable resting place in the lymphatic tissues before its habitancy of the body becomes tenable. Beginning with the initial lesion the reaction produced in the tissues by the presence of the spirochete is substantially the same throughout. Whether the effect noted be in the skin, parenchymatous glands or in the central nervous system or its enveloping membranes the presence of the organism in the peri-vascular lymph spaces seems necessary before the characteristic reaction begins. It would thus seem reasonable to believe that syphilis is primarily a lymphatic disease. The early involvement of the lymphatic tissues, the length of time necessary for the disease to become disseminated throughout the body and its apparent progression and persistence in the lymph glands, peri-vascular lymph spaces and lymph cisterns of the central nervous system furnishes evidence in support of this idea.

The later manifestations of the disease are not caused by the organism per se but are determined by the encroachment of new formed tissue accretions upon important functioning structures. Thus partial or complete obliteration of blood vessels with consequent changes due to a lack of sufficient blood supply; the presence of gummatous infiltration causing pressure upon vessels otherwise healthy or upon other structures disturbing their normal physiological function determines the clinical symptoms which occur throughout the course of the disease.

Positive evidence in support of the belief that the central nervous system is involved very early in syphilis is accumlating rapidly. The idea is not a new one for as long ago as 1880 Lang[1] stated that the headache, lassitude and lethargy present in the second stage of this disease were due to meningeal and nervous system involvement. It has been left to improved methods of investigation, however, to show how often and to what extent this involvement occurs.

Routine examination of the cerebro-spinal fluid and more careful and complete investigation of the nervous system, especially those portions of it connected with the organs of sight and hearing, have furnished that positive evidence which was denied to earlier observers. Thus Ravaut,[1] in 118 cases of acute syphilis, noted changes in the spinal fluid in 71; Eicke,[2] in 136 cases in the primary and secondary stages found alterations in the spinal fluid in 60. Wile and Stokes,[1] Altman and Dreyfus,[1] Fahr[1] and others have noted similar changes. In many of these cases only a single examination was made and the figures, consequently, do not exactly represent the number in which changes might have been found had a number of examinations been undertaken.

Wile and Stokes[3] have recently shown that careful examination of the second and eighth nerves together with an examination of the general nervous system will add to the number having a positive spinal fluid. These observers examined twenty-six cases in this manner, and state: "From the point of view of all the methods used by us to ar-

* Abstract of remarks before the Riverside County Medical Society, May 8, 1916.

* Read before the San Francisco County Medical Society, September 14 1915.

rive at the condition of the nervous system, only one of the twenty-six cases in the series was frankly negative, and in this case the eighth nerve was not investigated. Two other patients presented, respectively, exaggerated patellar and Achilles tendon reflexes and slight decrease in bone conduction with normal hearing. The remaining twenty-three cases were positive in two or more particulars of the examination. Changes in the fundus oculi, as indicated by a neuro-retinitis, were noted in twelve of twenty-one cases examined. Eighth nerve involvement, as evidenced by decreased bone conduction and changes in high and low limits of sound perception, was present in eleven of sixteen cases examined. In twenty-two cases subjected to a complete neurologic examination nine were positive in some particular other than the second and eighth nerve involvement."

The figures just quoted represent the demonstrable nervous system involvement as it occurred in the usual run of cases applying for treatment at a dermatologic clinic and does not include those early fulminating types in which the nervous system suffers to such an extent as to place the patient, at once, in the hands of the neurologist.

It seems not unlikely that between the receipt of the primary infection and the end of the second stage there is a generalized syphilosis and that the lymphatics in and about the central nervous system receive their proportion of the infecting organism in all cases. That this cannot be demonstrated, clinically or biologically, in every case is not sufficient evidence in proof of the contention that the nervous system frequently escapes.

Whether or not this early infection of the central nervous sytem is responsible for the later manifestations of the disease such as paresis, tabes and cerebro-spinal syphilis is not positively known. Thus Collins,[1] quoting McIntosh and Fildes, states that "The reason for the slight reaction with a large number of spirochetes in acute syphilis and an extensive reaction with a small number of spirochetes in chronic syphilis is due to the fact that the tissues become sensitized, i. e., become altered in their susceptibility to the action of the virus. This corresponds to the alterations in the reactions produced by certain viruses, the so-called allergie of von Pirquet. The type of hypersusceptibility present in tertiary syphilis is developed as an immunity response of an intoxication of the tissues occurring in the acute stage of syphilis. The actual occurrence of the lesion is due to an exacerbation of activity of spirochetes which have been dormant. When the interstitial tissue of the central nervous system is the sensitized part exposed to the delayed or persistent action of the spirochetes, the result is a gumma. When the parenchyma is the tissue affected, the disease that results is paresis or tabes or both."

Is it not likely that just the opposite of this takes place? That is, that during the progress of the disease an active immunity is produced throughout the body, an immunity which acts upon the syphilitic organisms causing their destruction, or at least inhibiting their activities, in proportion as the immunizing bodies are brought in contact with them; that the tissues of the body also become immune in proportion as they come under the influence of the immunizing substance; that there exist foci of exudate into which this immunizing substance imperfectly penetrates leaving in the interior an area in which the organisms may remain undisturbed until, as the state of immunity in the surrounding tissues decreases, they again set up their customary local reaction and, finding their way into the lymph or blood stream, reinfect other structures in the body where the state of immunity has ceased to exist. This would be in accord with the so-called "Non-sterilizing immunity" of Ehrlich. Syphilis is a disease which is characterized by numerous remissions, the symptoms disappearing from time to time either spontaneously or as the result of treatment.

The presence of numerous lymph spaces about the central nervous system and the passive state in which these structures exist offers a favorable resting place for the spirochete and may have some influence in determining recurrences in this region. It seems that where these lymph spaces are largest tissue reactions are most common as at the base of the brain and along the posterior surface of the spinal cord.

To state the matter briefly, syphilis evidences itself in the central nervous system first upon the blood vessels and this primary change consists in an infiltration of lymphocytes and plasma cells in and about the arteries and veins with subsequent thickening of the intima and adventitia, a lessening in diameter of the vessel lumen, a coalescence of the perivascular infiltrated areas and the production of a more or less extensive thickening which in the meninges may involve large areas. This is the so-called gummatous infiltration or meningitis syphilitica. A more localized accumulation of the same elements produces the tumor-like masses known as gummata.

To circulatory disturbances in the thickened blood vessels, to encroachment upon the unprotected roots of the cranial and spinal nerves and to pressure upon the brain and cord by the thickened meninges is ascribed the varied picture which we know as cerebro-spinal syphilis.

The secondary changes such as paresis, tabes, myelitis and the like can be explained as end results of the primary changes mentioned above although there are writers who believe that paresis and tabes especially require the intervention of other factors for their production. It is not unlikely that in every case of syphilis a number of influences are always at work in determining the extent of the effect which the invading organism will have upon the tissues. It is only necessary to mention the variation in the virulence of the spirochete, the resistance, or lack of resistance, of the individual, his mode of life and habits, of which, perhaps, the most important are his food, his drink and his work.

That the present day treatment of syphilis of the central nervous system is unsatisfactory is evidenced by the constantly appearing descriptions of new methods of administering the well known specifics mercury and arsenic, to say nothing of the contradictory statements for and against each method.

When the disease has progressed to the extent that conducting tracts are degenerated as in posterior columns in tabes, nuclear degeneration as in cerebro-spinal syphilis or softening of cortical cells and disappearance of fibres as in paresis we may as well admit at once that treatment of any kind will forever prove futile in so far as absolute cure is concerned. But it is often impossible to state that these changes have taken place for extensive gummatous infiltration of the meninges about the frontal lobes may simulate some of the phases of paresis just as a like infiltration in the membranes enclosing the posterior roots may produce a clinical picture not easily distinguished from that seen in some types of tabes. Indeed I believe that one would not be far wrong in expressing the opinion that most of the good results recorded as obtaining in the treatment of paresis and tabes are to a large extent due to the cure of a co-existing meningitis and arteritis.

Treatment, however, must be administered in any case and should be checked up, where possible, by examination of both blood and spinal fluid in order that improvement or the reverse may be noted and treatment governed thereby. Whether the drug selected be mercury or salvarsan, or both, they must be pushed to the limits of the patient's endurance. Nothing defeats the end which treatment is expected to bring about like half-hearted treatment. The spirochete becomes immune to salvarsan and perhaps to mercury also, when administered in quantities insufficient to kill it. One should also remember that the benefits following a dose of salvarsan reach their maximum, in the majority of cases, in forty-eight hours after the dose is administered and after three to five days none of the drug remains in the body. It was because of this rapid elimination that Prof. Wechselmann [4] recommended the injection of neo-salvarsan epi-fascially shortly after the administration of the salvarsan, in order that, by reason of its slower absorption, the action of the arsenic might be continuous. The pain caused by the administration of the drug in this manner may be lessened, if not entirely prevented, by first injecting a small amount of a 2% sol. of novocaine in the trial injection used to determine that the needle is in contact with the deep fascia.

Another result of the occasional dose of salvarsan other than that affecting the spirochete may be explained in this manner: Given a mass of exudate into which the drug penetrates with difficulty or not at all, the effect of a single dose is expended on the periphery, the resulting solution of the cellular elements reached by the drug permits the remaining intercellular substance to contract about the mass and its peripheral portion, increasing in density in this manner, forms an additional barrier to the ingress of future medication.

It must also be borne in mind that relief of presenting symptoms affords no assurance that the patient is freed of his infection nor have we any available sure means of telling when he is cured. The Wassermann reaction may become negative, the spinal fluid appear normal, clinical examination of the nervous system disclose no disturbance of function yet in a year or two the patient returns with a cranial nerve palsy, a syphilitic paraplegia or evidences of an active meningitis. The only positive evidence of cure is shown in the ability of the individual to accept a new infection and this means of proof is, at present, out of the question.

There is a time in the history of every syphilitic patient when a complete cure may be brought about. Clinical experience and experimental evidence show that in salvarsan we have an agent which is capable of destroying the treponema pallida, in vivo, if the drug can be brought into contact with the parasite. This effect is to be expected only before the tissue reaction has produced those conditions, mechanical or biological, which seem to protect the organism from the effect of the drug. The ideal to be sought for in syphilis therapy is to prevent the disease from entering upon the second stage. The responsibility, in many cases, rests with the physician who sees the case first.

Too, syphilis is just as much a matter for public control as are smallpox and scarlet fever and it should be a part of the function of public health boards to disseminate literature instructing the laity in the necessity for early treatment, warn them that any genital sore may be syphilitic, provide means for securing adequate treatment for those unable to pay for it and to secure legislation prohibiting treatment of the primary sore by persons not qualified to do so.

A proper appreciation of the syphilis question by both medical men and laity and education as to the greater relative value of early treatment over that administered late in the disease will do much toward abolishing the evil effects of the often incurable tertiaries.

There is much evidence in support of the theory that leptomeningitis is the forerunner of the later and more fixed types of central nervous system syphilis such as paresis and tabes but for our purpose it is not necessary to know by what means these later effects of the syphilitic infection are determined. To know whether by a sensitization of the nerve structures this end is accomplished or whether the spirochete, finding a congenial nidus for hibernation and propagation in the lymph spaces of the central nervous system, secretes itself here until conditions favorable for its active existence present themselves, would be interesting from a scientific standpoint but that with this information the indications for treatment would be any clearer than they are now is doubtful. What must be borne in mind is that all of those conditions which were once known as the para-syphilides are due to infection of the body by the organism which causes syphilis and that, other things being equal, the longer the period of time allowed to elapse after the primary infection before adequate treatment is instituted the greater will be the difficulty of obtaining a cure.

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