would indicate that grave metabolic disturbances were brought about by the inability of the lymphatic circulation to carry on its function. At the last meeting of the Society, Dr. Moore demonstrated the presence of the *Treponema pallidum* in the brain and showed that this organism lay at a considerable distance from the blood vessels and the lymphatic channels. The problem of therapy, therefore, is not only that of the inaccessible spirochæte, but also of the blocked lymph-spaces. This latter fact is possibly largely responsible for the diffuse and uniform parenchymatous degeneration which is so manifest in paresis, in contrast with the vascular localized disturbances of other types of cerebrospinal syphilis.

THE DIRECT TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

By Homer Swift, M.D., and A. Ellis, M.D.

Syphilis of the central nervous system is one of the most important manifestations of a chronic infectious disease. The discovery of the *Treponema pallidum* in general paralysis by Noguchi and Moore has enabled us to properly classify this condition, so that parasymphilis today must be regarded as active syphilis of the central nervous system. If, in any disease, we have an etiologic agent present and still active, and if we have specific therapeutic agents to use against the microörganism, it seems rational to apply the drugs until all evidence of activity of the virus is removed.

Syphilis of the central nervous system is one of the most resistant forms of the disease to treatment. The symptoms are often mechanical, and improve or disappear when treatment is applied, but the entire eradication of the disease is most difficult. These difficulties are increased by the anatomical peculiarities of the central nervous system. The perineuronal lymph spaces and the perivascular lymphatics are the sites of the most intense round-cell infiltration. These spaces are directly connected with the subarachnoid space. Drugs and antibodies are but little eliminated into the cerebrospinal fluid, so that treatment intravenously only reaches the disease on the side of the blood stream. Attempts to introduce salvarsan by means of lumbar puncture have resulted in intense irritation of the meninges in monkeys. Serum is practically the only substance known which it is safe to repeatedly introduce into the subarachnoid space.

It has been shown that the serum of patients who have been treated with salvarsan has definite effect upon spirochætal diseases: (a) clinically on congenital and secondary syphilis, (b) by inhibiting the growth of *Treponema pallidum* in cultures, (c) by inhibiting the growth of spirochæte of relapsing fever in mice, and (d) clinically in central nervous syphilis by introducing serum directly into the subarachnoid space.

The technique that we have employed is to treat the patient intravenously with salvarsan or neosalvarsan, one hour later withdraw 40 to 50 c.c. of blood into a sterile centrifuge tube, centrifugize the blood, and separate the serum from the clot. 12 c.c. of the serum is diluted with 18 c.c. of normal serum and heated to 56° C. for one half hour. A lumbar puncture is made and spinal fluid withdrawn until the pressure is reduced to 30 mm. of cerebrospinal fluid. The forty per cent. serum is then injected by gravity through the lumbar puncture needle.

The following lantern slides were shown: First, reduction in the cell count, globulin and Wassermann reaction in the spinal fluid in patients who had received intravenous treatment. These patients were then treated with combined intravenous and intraspinal treatment and the cerebrospinal fluid brought to normal. Three slides were then shown of patients who had received intraspinal treatment alone and whose cerebrospinal fluids were brought to normal. Several slides were shown of patients with combined intravenous and intraspinal treatment, where the therapeutic effect was most marked. It was emphasized that the intraspinal treatment was not introduced as a substitute for other forms of treatment, but as an additional form of treatment to apply in those cases of cerebrospinal syphilis, tabes, and perhaps general paralysis, where the intravenous treatment alone was not sufficient or where a rapid therapeutic effect was desired.

Professor K. Heilbronner, of the University of Utrecht, who was invited by the President to open the discussion on the paper of Drs. Swift and Ellis, said he could only thank the Society for the privilege of being present, and of having had the opportunity of listening to this very interesting presentation of the subject of treating cerebrospinal syphilis by a new and direct method.

Dr. John A. Fordyce (by invitation) said that while he felt a certain amount of hesitation in discussing the treatment of syphilis of the nervous system before neurologists yet his experience with these manifestations of the disease from the standpoint of a syphilographer might prove of some value. He wished to say at the outset that he had had no experience with the intraspinal method of treatment as described in the paper by Dr. Swift and Dr. Ellis but he had had during the past two and one half years considerable experience with salvarsan given intravenously in syphilis of the cerebrospinal system. Although many of the nervous manifestations of syphilis occur several years after infection, in the great majority of cases, if not in all, involvement of the cerebrospinal system took place during the secondary stage of the disease. It was at this time that there was a generalized dissemination of the spirochæte. Dreyfus has demonstrated that during this stage more than 50 per cent. of cases of syphilis showed some evidence of involvement of the cerebrospinal fluid frequently without giving rise to symptoms. It was reasonable to assume, therefore, that the infecting agent might remain latent in the cerebrospinal fluid for years but under the influence of various contributing factors it could cause during this stage or later meningitis, paresis or the complicated clinical picture of cerebrospinal syphilis. From the histories of patients who came under his observation with tabes or other forms of cerebrospinal syphilis he was impressed with the frequency with which these patients stated that they had had months or years before ocular paralysis or other manifestations of meningitis. During the early experiments with salvarsan as a therapeutic agent Dr. Fordyce said it was thought that one or two doses of the remedy would be sufficient to control the infection and unfortunately this impression was still held by many practitioners and fostered the belief that salvarsan was not effective in the treatment of syphilitic conditions of the cerebrospinal system. As a matter of fact we now know that many of these cases were aggravated by one or two doses while on the other hand many of their symptoms were relieved by the persistent use of the drug. It was a common experience with him to see an aggravation of the tabetic symptoms produced by

one or two doses of the drug but by persistence in its administration the pains, crises, bladder symptoms and general nutrition of the patients were often greatly benefited. The speaker said that his own plan of treatment in these cases was to give injections of salvarsan at weekly intervals combining them with mercury at intervals of three or four days. In one case he gave 21 injections of salvarsan, about 10 grains in all, with marked alleviation of the symptoms in a patient who had come to him with the diagnosis of paresis. The Wassermann reaction in this case had not been influenced by the treatment and his cerebrospinal fluid at the last examination contained 90 cells with a positive Wassermann and globulin reaction. He was inclined to believe in this case that the intraspinal method of Dr. Swift might prove of distinct benefit. Dr. Fordyce said that he was becoming more and more convinced that salvarsan had no deleterious effect on the optic nerve. On the contrary he now had two cases under his observation where it had proved distinctly beneficial. In one of these cases the visual fields had enlarged and whereas before the treatment the patient could not count fingers before one eye she can now distinctly recognize features with this eye. In closing his remarks he again emphasized the importance of persistent treatment with salvarsan and mercury if we wish to permanently benefit these cases and influence the pathological changes in cerebrospinal fluid.

Dr. Sachs said he had listened with much interest to the paper of Drs. Swift and Ellis, and that he, with others, would hail with great satisfaction any method that would render the treatment of syphilitic diseases of the cerebrospinal system more successful than it had been heretofore. The theory upon which this method of treatment was based was surely a plausible one, and appeared to exert a direct effect on the syphilitic process in the central nervous system. Whether the change in the globulin content and cell count necessarily indicated an improvement in the patient's condition would have to be determined by a much longer experience with this method of treatment, and the results would be watched with great interest by clinicians.

Dr. Sachs said that in the treatment of syphilis of the central nervous system with salvarsan, he had been struck by several points. One was that the persistence of the Wassermann reaction, both in the blood and spinal fluid, seemed to be out of relation to the intensity of the morbid process. While he was glad to have the assurance of Dr. Fordyce that we had given the salvarsan altogether too infrequently and in too small dosage, still a word of caution was in order, lest we should go from one extreme to the other. Women, apparently, did not tolerate as large a dose as men.

Dr. Fisher said that in the early days of salvarsan he was opposed to its use in general paresis and tabes: upon the strength of more recent reports, however, he had employed it in parasymphilitic conditions to a considerable extent, and in no instance could the results be regarded as marvelous. In certain cases, of course, we could not expect it to do more than to relieve the pains and possibly some of the ocular symptoms. He had found it more effective in those cases which we had clinically designated as cerebrospinal syphilis, in which the pathological changes differed from those of general paresis or tabes, although the differential diagnosis was often obscure.

Dr. D. M. Kaplan said that in the tables shown by Dr. Swift one could observe that in the majority of the cases the cell content became

normal much sooner than the positive Wassermann disappeared. In the majority of cases, the condition was improved in spite of the fact that the Wassermann remained positive. We had come to regard a positive Wassermann as an indication of a still existing syphilis, and until it became negative we could not look upon it as a cure or even an amelioration. It seemed to him, the speaker said, that the use of a large quantity of spinal fluid tended to make the positive Wassermann a persistent factor, regardless of the fact that the other serological tests became negative.

Dr. I. Strauss asked Dr. Swift whether the results of this treatment, as shown by the tests of the cerebrospinal fluid, had been compared with those in cases that had been treated only with salvarsan. Also, whether any improvement in the objective signs had been observed following this method of treatment, or whether they only improved subjectively. We knew that tabetics were very apt to be helped by any new method of treatment. Also, whether Dr. Swift had had any cases that showed toxicity due to the continuous use of the salvarsan, and if so, how long he would wait in such a case before repeating the dose?

Dr. Swift, in closing, in reply to Dr. Sachs, stated that the warnings of Ehrlich had been heeded, and the dose of salvarsan had been reduced in treating women. The dose for women was usually one tenth of a gram less than that for men.

In carrying out the direct treatment, Dr. Swift stated that the patients usually received five or six injections at intervals of two weeks. If intravenous treatment alone was given, weekly injections were used.

In those cases where, as the result of treatment, the cerebrospinal fluid had been reduced to normal with a negative Wassermann reaction, there had been no further progression of the tabetic symptoms. From this we might expect that if these patients had been treated in a sufficiently early stage, there would have been hope of permanently arresting the disease at that time.

In answer to Dr. Strauss the speaker said they had not seen much improvement in the objective symptoms in their cases, and he knew of no instance where the knee jerks returned once they were gone.

THE NEWER HISTOPATHOLOGY OF THE CORTEX IN THE PSYCHOSES

By H. A. Cotton, M.D., of Trenton, N. J.

Dr. Cotton made some remarks on this subject, which he illustrated with the aid of colored lantern slides. He emphasized the fact that there was a general feeling that there had not been much encouragement in the study of the histopathology of the cortex in the psychoses. This he thought was a false impression. Much had been done in paresis, and the recent discoveries of Noguchi and Moore showed the necessity for persistence in the work in connection with other diseases, such as dementia præcox, to which his own pathological studies had been largely limited.