	Positive.	Negative.	Total.
Alcoholism	1	30	31
Heat exhaustion	1	1	2
Syphilis	18	2	20
Acute poisoning	1	12	13
Morphinism	1	0	1
Miscellaneous	0	94	94

In none of these diseases is there a sufficient frequency of positive tests to make one think that the positive test was due to the non-specific condition. It is of interest to note that in malaria, scarlet fever, cancer, alcoholism, and jaundice, all conditions, which in the early days of the Wassermann were supposed to invalidate the Wassermann reaction by giving false positives, in this series do not give a more frequent positive than negative. The rarity of a positive Wassermann reaction with alcoholism seems to bear out the statement of several later observers to the effect that alcohol will vitiate a positive reaction. It is interesting to note the frequency of a positive test among cardiac conditions of one sort or another—note especially the five cases of mitral diseases (stenosis and regurgitation), and the two cases of auricular fibrillation, who showed no other physical signs. In one of these cases of auricular fibrillation there was an indefinite history of syphilis. The cases of aortic disease showing the positive Wassermann reaction and no other evidence of specific disease, as can be seen from the table, are few. The fact that one out of three of the cases of erysipelas have positive Wassermann reaction is interesting, not all of the seven with positive tests showed unquestioned evidence of specific. The two cases where we diagnosed acute rheumatic fever in spite of a positive Wassermann test were cases which showed typical signs of an acute polyarthritis. The typhoid patients, of which about one in four have a positive Wassermann test, at first made us wonder whether typhoid itself would give a positive test. This was all the more striking in that the first three typhoids upon whom we did Wassermann tests reacted positively.

From a negative standpoint, it is interesting to note the fact that among 270 married men and women, in 29 families there were histories of miscarriages. Out of these 29, 8 had positive Wassermann reactions, 3 doubtful, and 18 negative.

From this brief study, it seems to the writer that one may not tell in many of the cases admitted to the medical wards in general hospitals whether or not the patient's condition may be complicated by syphilis. Surely if one medical admission out of every six has positive Wassermann reaction, the doing of this test as a routine is valuable.

TREATMENT OF CENTRAL NERVOUS SYSTEM SYPHILIS.*

By I. CHANDLER WALKER, M.D., BOSTON.

THIS paper is a summary of the treatment and its results in the first forty cases of central nervous system syphilis at the Peter Bent Brigham Hospital. These earliest cases are selected in order to rule out as well as possible remissions, relapses and temporary improvement. A period of one year in half the cases, and over a year in several others has elapsed since treatment was stopped. Cases of tabes, general paresis, cerebrospinal syphilis and syphilitic meningitis are considered; cases of purely cerebral syphilis are excluded.

This work extends over a period of two and one-half years; during the first year and a half the treatments were given by the writer, since this time and continuing through the present, by Dr. D. A. Haller. In the treatment of parasymphylis we have employed three methods,—one salvarsan alone, another the Swift-Ellis method, and a third salvarsanized serum alone intraspinally. We modified the original Swift-Ellis method as follows: maximum doses of salvarsan were given and the patient's blood was withdrawn one-half hour, rather than one hour, later; also for the intraspinal treatment, from 20 to 25 c.c. of whole serum, rather than a 40% or 50% dilution with saline was used. These modifications ought to increase the efficiency of the original technic, or should increase many times the amount of salvarsan or "whatnot" available in the serum for the intraspinal introduction in comparison to the original method. The time interval between treatments varied; usually patients were treated once a week; however, when a bad reaction followed treatment, the next week would be skipped. By occasional bad reaction is meant a severe aggravation of previous symptoms lasting more than twenty-four hours; usually there was some aggravation of previous symptoms, such as shooting pains coming on two to three hours after treatment and lasting for five or six hours; rarely any rise in temperature above 99°, rarely was morphia given. When the Swift-Ellis method was used, the patient usually spent two nights in the hospital, receiving salvarsan one day and the intraspinal serum the next. Many times, however, both salvarsan and intraspinal serum were given the same afternoon, the patient leaving the hospital next morning without any symptoms. Improvement was gauged by the patient's own feelings, by the spinal fluid cell count and by the Wassermann reaction. In the Wassermann reaction we used the cholesterinized heart extract and varying amounts of spinal fluid, different test tubes containing from 1 c.c. to 0.05 c.c. each; in this way it was easy to note resultant changes in the strength of the reaction. It might be stated that absolute reliance should not

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be put on the cell count in tabetics as we have noted that during severe paroxysms of pain in tabetics untreated and while under treatment, the cell count may be considerably higher than during a more quiescent period. However, this finding is not constant, but should be kept in mind. We have noted this variation only in tabetics.

In the first group, with salvarsan alone, we have treated seven cases of central nervous syphilis; five were tabetics, two of which had negative cell counts and negative Wassermann reactions in the spinal fluid. These two cases were quickly relieved of their pains temporarily, but required eight and ten doses before more permanent relief of pains and improvement in ataxia resulted. These cases have not relapsed. Another tabetic has had four series of six doses each in the past two years. Considerable improvement in ataxia and relief of pains followed treatment in each series, but improvement lasted for only a few months. The spinal fluid in this case is still positive in 1 c.c. amounts and the cell count is 7. This case has had much intramuscular mercury during past series of salvarsans. The other two tabetics received six doses of salvarsan, without any improvement. Of the non-tabetics, one was a case of syphilitic meningitis with a positive blood and positive spinal fluid in 0.5 c.c. amounts, a cell count of 940 (polynuclears 3, small mononuclears 62, large mononuclears 35). Patient had a chancre nine months previous and a rash seven months previous, followed by one salvarsan and three months of mercury by mouth. Patient was given four doses of salvarsan at weekly intervals, following which his spinal fluid Wassermann reaction was reduced to 1 c.c. positive with a cell count of 33, blood still positive; after two more treatments the patient was lost sight of.

The remaining case was one of cerebrospinal syphilis, with a positive blood and spinal fluid in 0.3 amounts, a cell count of 98. Following five injections of salvarsan, the spinal fluid cell count was 23, the Wassermann reaction was negative in 2 c.c. amounts, blood still positive.

Other cases have been started on salvarsan alone, but as no improvement in symptoms and laboratory findings were obtained after a few doses of salvarsan alone, these cases were then given the Swift-Ellis treatment, and these cases will be taken up now as Group 2.

In Group 2, using the Swift-Ellis method (salvarsan and serum) as we modified it, we treated 20 cases with a total of 143 intraspinal serum injections: 6 cases received four double treatments, 4 received five treatments, 5 received six treatments, 3 received ten treatments, 1 sixteen, and 1 twenty-three. These 20 cases were classified as follows: 11 tabes, 4 general paresis, 5 cerebrospinal syphilis. As previously stated, some of these cases were tried on salvarsan alone before the intraspinal serum was given, but as

no improvement resulted from the salvarsan, either symptomatically or in the cell count or in the Wassermann reaction, we then employed the Swift-Ellis method. Five tabetics were given from three to six doses of salvarsan, 1 case of general paresis was given three, and 3 cases of cerebrospinal syphilis were given respectively six, three and two doses of salvarsan without improvement. After this, to these 9 cases and the remaining 11 cases was given the Swift-Ellis modification.

In all of these 20 cases subjective symptoms, such as headache and pains, were relieved by two or three combined treatments. Ataxia responded less readily. Only one case has relapsed, and that one while under treatment. In six of these cases over a year has elapsed since treatment and in five more, nine months. No physical signs were changed, with the exception that a positive Romberg became negative in one case; in the nine cases showing ataxia this was relieved in eight and improved in one. The spinal fluid cell count in all cases excepting the one which relapsed became normal following four or five treatments. Before treatment eight of these cases had respectively a cell count of 166, 145, 128, 108, 90, 85, 80 and 63. The cell counts in the other cases averaged between 15 and 50. In 16 cases the spinal fluid Wassermann reaction was weakened by four combined treatments; in the three cases receiving ten treatments the Wassermann reaction was weakened from a positive with 0.05 c.c. to a positive requiring 0.4 c.c., and in the case receiving 16 treatments positive with 0.05 to positive with 0.6 and in the case which relapsed from 0.2 c.c. positive to 0.6 positive. All cases showed some diminution in the strength of the Wassermann reaction, and many, as noted above, showed considerable. However, none became negative in amounts greater than 0.6 c.c.

Since nine of the above cases showed little or no improvement following two or more doses of salvarsan, but did show much improvement symptomatically and a reduction in the spinal fluid cell count when the intraspinal serum treatment was used in conjunction with salvarsan, we desired to use the serum intraspinally alone on some cases. We felt justified in trying this method on cases with a negative blood Wassermann and a positive spinal fluid. We were further influenced by the scarcity of salvarsan, for if this method should prove successful, we could treat three cases with one large dose of salvarsan, that is, one case with salvarsan and two with this patient's serum.

Therefore, to a third group of 12 cases, 8 of which were tabes, 3 syphilitic meningitis, and 1 cerebrospinal syphilis, were given 150 intraspinal treatments with salvarsanized serum, the usual dose being 20 to 22 c.c. of undiluted serum, given usually at weekly intervals.

One tabetic whose symptoms were severe pains, with a spinal fluid cell count of 15 and a positive Wassermann reaction in 0.4 c.c. amounts,

was given 27 treatments in 10 months, at the end of which time the spinal fluid Wassermann was negative with 1 c.c., globulin and colloidal gold tests were also negative. The pains were relieved by the first few treatments. One year has elapsed and the laboratory findings are still negative, one cell in the spinal fluid, symptoms still absent. It might be stated that this patient got progressively worse while under salvarsan and intramuscular mercury previous to our treating him.

Another tabetic whose symptoms were pains, beginning optic atrophy, inability to walk more than a few steps even with assistance, with a cell count of 40 and 0.2 c.c. of spinal fluid positive, was given 12 treatments in 4 months. Pains were relieved, eyesight improved and ataxia improved, until now, nine months later, the patient is able to walk with a cane, to drive his horses and auto and to conduct a country medical practice. The Wassermann reaction is negative with 1 c.c.; the cell count is one, the globulin is $\pm$.

Another tabetic with pains, unable to walk more than a few steps by taking another's arm, with a cell count of 210, and 0.4 c.c. spinal fluid positive, was given 21 treatments in 10 months, then was able to work and walk without a cane; cell count normal; Wassermann reaction negative in 1 c.c. It is now 3 months since the last treatment without untoward symptoms.

Another tabetic with gastric crises and ataxia, cell count 103, 0.3 c.c. positive, was given 10 treatments, crises were relieved, ataxia slowly improved, cell count normal, 1 c.c. of spinal fluid gave a negative Wassermann. It has been 8 months since the last treatment, with no return of symptoms, and he has worked every day.

Another tabetic with pains and slight ataxia, cell count of 88, Wassermann 0.1 c.c. positive, was relieved of pains and ataxia, and the cell count was reduced to 2, following 4 treatments at weekly intervals. Seven more treatments were given at monthly intervals, following which 0.4 c.c. of spinal fluid was positive. The long interval between the latter treatments may explain the slow diminution in the Wassermann reaction.

Another tabetic with girdle pains and cell count of 20 was relieved by 3 treatments and cell count was reduced to 2; however, 7 more treatments did not influence the Wassermann reaction.

Another tabetic, with gastric crises and vomiting, was not relieved by salvarsan, but one serum treatment did relieve symptoms for 2 weeks; a second attack of crises and vomiting was promptly relieved for 3 weeks and a third attack was relieved for 3 weeks. Subsequently, 5 more treatments were given, but the attacks of crises and vomiting were not permanently relieved. The Wassermann reaction was reduced from 0.4 c.c. to 0.8 c.c. positive. Previous to serum treatment the attacks of crises were of a week's dura-

tion and came at weekly intervals; now only an occasional attack.

The remaining tabetic, with mild pains, slight ataxia, paresthesia and loss of sexual power, was given 7 treatments at varying intervals; the pains were relieved, ataxia was improved, sexual power returned and the Wassermann reaction was changed from 0.5 c.c. to 0.9 c.c. positive; at this time the blood became positive and salvarsan has been given.

Of the three cases of syphilitic meningitis, one had headache, stiff neck, positive Kernigs, interval strabismus, cell count of 550 and Wassermann reaction 0.1 c.c. positive. In two weeks he was given 3 doses of salvarsan of 0.3 gm., 0.5 gm. and 0.6 gm., respectively, 7 intramuscular mercury injections and Ki 30 grains three times a day. This treatment relieved the headache, but nothing else; cell count and Wassermann reaction unchanged. He was then given serum intraspinally without other treatment. The first treatment reduced the cells from 533 to 272, and relieved the strabismus and positive Kernigs. Five days later a second treatment reduced cell count to 100 and patient walked out of the hospital. A week later a third treatment reduced the cell count to 46. After this 14 more treatments were given at two-week intervals, and the cell count became normal and the Wassermann reaction in the spinal fluid with 1 c.c. was negative. However, the blood became positive and six doses of salvarsan were required to make the blood negative.

Another case of syphilitic meningitis in a child 3 years old, with headache, vomiting, stiff neck, positive Kernigs, opisthotonos, blood positive, spinal fluid positive with 0.1 c.c., cell count 9800, was given 0.2 gm. of salvarsan without effect. The first serum treatment reduced the cell count to 7300; second treatment reduced the cells to 2500 and the symptoms were relieved. Following this, three doses of 0.2 gm. salvarsan and 7 intraspinal serum treatments were given, also inunctions, and both blood and spinal fluid became negative, cell count normal. Four months have elapsed and patient is still normal except that deafness is unrelieved.

The other case of syphilitic meningitis, with headache, diplopia, external rectus paralysis, drowsiness, spinal fluid cell count 150, Wassermann 0.2 c.c. positive, was given 5 treatments; symptoms were relieved, cell count became normal and Wassermann reaction was not changed. Seven months have elapsed, and the patient still feels well, and has worked every day.

The case of cerebrospinal syphilis with headache, optic atrophy and early symptoms of acromegaly, was given 16 treatments, which relieved headache for 5 months; Wassermann reaction was changed from 0.3 c.c. to 0.7 c.c. positive. This is hardly a fair case on which to base judgment, as the symptoms and signs pointed strongly to one of pituitary tumor, and treatment was instigated to rule out the syphilitic involvement.

Therefore, to summarize: In those cases treated with salvarsan we used large doses; in those treated with serum intraspinally we used 20 to 25 c.c. of undiluted serum. Cases of syphilis of the central nervous system with only a positive blood react well to salvarsan; those with a positive blood and spinal fluid may react well to salvarsan alone, but they do much better when intraspinal serum is used in conjunction with salvarsan, and some who do not react to salvarsan alone do react well to the combined method. One may get improvement in general paresis from the combined treatment. Cases of syphilitic meningitis may clear up with salvarsan alone, but the combined treatment is the quickest. Cases of central nervous system syphilis with a negative blood and positive spinal fluid findings react readily to salvarsanized serum intraspinally alone, even when salvarsan has failed. The spinal fluid of the cases treated with salvarsan has become negative in two cases, whereas the spinal fluid of 7 cases treated with the serum alone has become negative. We feel that salvarsanized serum is a great asset in the treatment of syphilis of the central nervous system, and in the general run of cases we think the Swift-Ellis method is of great value and that this method in conjunction with mercury intramuscularly is the best treatment of syphilis of the central nervous system at the present time; and much improvement practically always follows such treatment.

Therapeutic and Preventive Medicine.

THE TREATMENT OF SYPHILIS.*

BY C. MORTON SMITH, M.D., BOSTON.

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SEVERAL years ago, in the out-patient department of a general hospital, a patient was sent from the Medical to the Skin Room with a note which read, "Has this patient got syphilis? If so, send her back and we will treat her."

For nearly four hundred years mercury had kept its place in the front rank of remedies for syphilis, being considered by many a true specific. Therefore, if the diagnosis was made, any one could give the treatment where a "cure" depended on "three years of mercury."

So firmly was the value of this treatment fixed in some medical minds, that if a patient suffered a relapse, or symptoms persisted, he was accused of failing to take his medicine in the manner prescribed.

When such faith in the curative power of

* Read at a meeting of the Suffolk District Medical Society, Nov. 17, 1915.

drugs exists, regardless of the natural history of the disease, there is little wonder that the promised cure of syphilis by a single injection of salvarsan appealed to many physicians not previously interested in the subject. Furthermore, the Wassermann test apparently supplied all the necessary help.

Clinical study seemed useless. With a positive blood test and the giving of sufficient salvarsan, the lesions must disappear and the patient recover.

However, a positive Wassermann is usually obtained in leprosy, the lesions of which do not respond to salvarsan, as shown by two cases recently so treated in this vicinity. Such false positives in no way detract from the value of the Wassermann test, which should be constantly employed. However, its results must be considered with the patient's history and physical examination, as an additional sign or symptom of the disease. There is still need of careful clinical training, for an early accurate diagnosis is the basis of successful treatment.

It is seldom necessary to wait for secondary manifestations, as *spirochaeta pallida* can usually be demonstrated in serum from primary sores, either with the dark field or in stained smears. The former is easier, but the latter satisfactory and reliable. We were able to demonstrate *spirochaeta pallida*, with dark field, in 96% of smears made from the last 97 primary sores examined at the Massachusetts General Hospital. The India ink method is unreliable and inexact. With this process, serum and ink are mixed on a glass slide, and a thin smear made. *Spirochaetae* do not stain with the ink, and are therefore not seen; and one must determine between various *spirochaetae*—artefacts, fibers, etc.,—by the hole they leave in the smear. The *spirochaeta dentium* may so closely resemble the *pallida* as to make the decision extremely difficult, even with a dark field. Wright's blood-stain usually gives satisfactory results. However, stained smears from the same lesion never show as large a number of *spirochaetae* as are seen with the dark field.

Patients must be taught the importance of seeking medical advice as soon as a possible primary lesion appears, and members of our profession must be properly trained and equipped for the task of making such diagnosis. Too great optimism on the part of either patient or physician may cause a costly delay.

Though there may be failure to find *spirochaetae* in a suspected sore, the Wassermann usually becomes positive before the appearance of secondary manifestations. We are thus enabled to begin medication during the primary stage, when the disease is most amenable to treatment. It seems well within the limits of conservative expectation that complete recovery will follow intensive treatment begun during the primary stage. The same is probably true of the early secondary period. By *recovery* is meant