Special Article

A REVIEW OF RECENT LITERATURE ON NEUROSYPHILIS

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The news of another edition of Nonne's "Syphilis und Nervensystem" will be received by those interested in the subject of neurosyphilis with mingled sensations of delight and tribulation. Having been for so long a classical reference book on neurosyphilis, it is necessary only to call attention to the new edition.

A new book on the subject of neurosyphilis by Wilhelm Gennerich¹ is a notable recent contribution to the study of neurosyphilis. A review of this book appeared in the October number of the ARCHIVES, and I will only say that I consider this the most important work on the treatment of neurosyphilis that has been published to date. It merits conscientious study by all who treat or outline treatment for patients with syphilis of the central nervous system.

STRAINS OF SPIROCHETES WITH PREDILECTION FOR THE NERVOUS SYSTEM

Probably, one of the most important subjects in the consideration of neurosyphilis relates to the question of whether there are strains of spirochetes which have particular predilections for the central nervous system. A. Marie and C. Levaditi² present an important contribution. In this article, of some length, they review the various theories suggesting a neurotropic strain, calling attention to the infrequency with which patients with neurosyphilis have had active skin lesions and discussing the frequency with which the mates of neurosyphilitic patients and patients infected from the same source develop neurosyphilis. This introduction to their experimental work contains a good review of the literature on the subject, but the important part of the work deals with their experimental studies. They report that in 1913 they inoculated a rabbit from the blood of a patient with general paresis. The infection took, and it was passed through three generations of rabbits. The incubation period was two or three times longer than the habitual

1. Gennerich, Wilhelm: *Die Syphilis des Zentralnervensystems. Ihre Ursachen und Behandlung*, Berlin, Springer, 1921.

2. Marie, A., and Levaditi, C.: *Special Type of Spirochete Responsible for General Paresis*, *Rev. de méd.* **37**:193, 1920.

incubation period from spirochetes obtained from primary lesions. The work was largely interrupted by the war, but since the armistice the authors have continued their work and claim to have confirmed their former findings. They also state that rabbits successfully inoculated from the blood of a parietic patient are not immune to spirochetes obtained from other sources. They thus indicate that the immunity secured from a syphilitic infection acquired through an infection by spirochetes from a parietic patient does not hold for spirochetes obtained from another source. A summary of their findings follows:

In the dermatropic strain the average incubation period is forty-two days whereas in the neurotropic the average is ninety-five days. When a second passage to an animal is made the incubation period habitually is decreased, and in the case of the dermatropic strain it is reduced to fifteen days on the average, whereas with the neurotropic strain the average incubation period is seventy-five days. Pathologically, the primary lesion differs in the two strains. The chancre from the dermatropic strain is indurated with marked ulceration at the border of the inoculation, whereas with the neurotropic strain the chancre appears as an erosion or papulosquamous lesion with slight ulceration and desquamation. The dermatropic strain leads to an endo-arteritis and peri-arteritis with intense infiltration. The neurotropic strain produces perivascular lesions with little endarteritis. In the former a great deal of new connective tissue is produced, whereas in the latter there is little. These experiments were carried out on the rabbit. The authors found that the dermatropic strain was easily transmitted to the monkey, whereas they were unable to pass the neurotropic strain to this animal. They were able to obtain a successful inoculation of the dermatropic strain with man, but in one man on whom inoculation with the neurotropic strain was attempted they were unsuccessful. These experiments of Marie and Levaditi are most illuminating, but it is doubtful whether they are entirely convincing. The inability to transmit the so-called neurotropic strain to monkey and man is open to the criticism of having been tried in only a few instances, and failure to transmit from experimental animals to monkey or man may be open to many explanations aside from that of being due to a particular or specific strain. Nor are the differences in the pathologic examination of the lesion produced easy to interpret. A slowly developing lesion would naturally give a different pathologic picture than one rapidly produced, and it must be noted that in the second passage the chancre appeared in fifteen days after the inoculation as compared with seventy-five days in the second strain. As to the time relations, it is well known that the incubation period for syphilis produced experimentally varies considerably. It is known, too, that the spirochete after being cultivated is not as virulent as when

obtained from a fresh lesion. There are, therefore, a number of considerations which make one hesitate to accept Marie and Levaditi's findings as adequate proof of the specificity of strains for general paresis. This work, however, paves the way for further experimentation and must be considered one of the important contributions to the subject.

The work of Brown and Pearce on experimental syphilis at the Rockefeller Institute has shown some interesting features in line with those of Marie and Levaditi's. They have shown the possibility of superinoculations or a successful "take" of the second inoculation of an animal that has already been infected with syphilis. This would again argue for the difference in strains. But Brown and Pearce have been chary in reporting any far-reaching conclusions concerning the immunity problem, and we must await their further study.

The question of strains of spirochetes is approached from a different point of view by Fleming.³ The author calls attention to the six surviving members in a family of eight born of healthy parents. Four acquired syphilis from different sources and developed tabes dorsalis. The fifth member of the family gave a history of gonorrhea (probably acquiring syphilis at the time) and was in an early stage of tabes. It is suggested in the light of these facts that tabes dorsalis cannot be attributed to a special strain of spirochete introduced at the initial infection; but is more probably due to the spirochete acting on tissues specially sensitized either by natural family peculiarity or by certain methods of treatment. This is the classical method of attack on the problem and is one more addition to the vast collection of facts. These facts, however, are exceptional and should not be given too much weight.

The point suggested in the last reference as to the effect of treatment in the production of syphilis of the central nervous system harks back to the problem of so-called "arsphenamin neurorecidives." It will be remembered that following the introduction of arsphenamin as a therapeutic agent there was much discussion as to whether neurosyphilis occurred with greater frequency than previously. This subject is again taken up by J. E. McDonagh,⁴ who believes that arsphenamin tends to produce early neurosyphilis. This matter is discussed at great length in Gennerich's ¹ book. He states these views:

In practically all cases of early syphilis there is an invasion of the central nervous system by the spirochete. Ordinarily the natural immunity of the person is able to overcome this involvement. Arsphen-

3. Fleming: Familial Tabes Dorsalis, *J. Neurol & Psychopath.* **1**: No. 3 (Nov.) 1920.

4. McDonagh, J. E.: Early Nervous Syphilis After Arsenobenzene, *Brit. J. Dermat. & Syph.* **32**:29, 1920.

amin, by rapidly killing a large number of organisms, reduces the immunity reaction of the person because this high active immunity is no longer needed. Thereupon the spirochetes which may have been left in the central nervous system have a chance to multiply with less opposition, and an active neurosyphilitic lesion results. This may be overcome by a continuation of treatment of the proper type. A critical discussion of Gennerich's view on this and several other points is given by Matzenauer.⁵ The whole question is still in a relatively unsatisfactory state; its final solution has not yet been reached.

CONSIDERATION OF CENTRAL NERVOUS SYSTEM IN EARLY SYPHILIS

Much attention has been given to the evidence of the early infection of the central nervous system by the spirochete. This subject was first definitely approached by Wile and Stokes in 1915. Wile and Hasley⁶ publish their observations to date. A series of 221 cases of syphilis, in which only the chancre was present in 22 per cent., presented a few deviations in the spinal fluid content. The most interesting fact in their observations is that the spinal fluid Wassermann reaction may be positive before it becomes positive in the blood.

McIver⁷ in a study of the spinal fluid of ninety-one patients with syphilis in the primary and secondary period, draws these conclusions:

1. Slight increase in lymphocytosis occurs in the majority of cases.
2. Increase in the protein does not occur as early as increase in lymphocytosis.
3. No patient gave a strong positive Wassermann reaction in the fluid using 0.6 c.c. of fluid.
4. It does not seem reasonable to conclude that the spinal fluid examination will indicate which patients will develop symptoms of central nervous system syphilis.

Cornaz⁸ found that in 35 per cent. of the cases of early syphilis, pleocytosis had occurred before the appearance of cutaneous or mucous lesions. In the exanthematous stage 14 per cent. of the cases gave a positive Wassermann reaction; 13 per cent. of patients with condylomas had positive Wassermann reactions in the fluid, and in only one of the twenty-five patients with mucous patches was the Wassermann reaction positive in the fluid.

5. Matzenauer: Zur Frage der endolumbalen Salvarsanbehandlung und über den Einfluss der Behandlung auf Immunkörperbildung und den weiteren Krankheitsverlauf der Syphilis, *Wien. klin. Wchnschr.* **32**:831-835, 1919.

6. Wile, Udo J., and Hasley, C. K.: Involvement of the Nervous System During the Primary Stage of Syphilis, Continued Study, *J. A. M. A.* **76**:8 (Jan. 1) 1921.

7. McIver: The Spinal Fluid in Primary and Secondary Syphilis, *J. A. M. A.* **73**:1765 (Dec. 6) 1919.

8. Cornaz: Study of the Cerebrospinal Fluid in Different Periods of Syphilis, *Cor.-Bl. f. schweiz. Aerzte* **48**:1584, 1918.

Nicolau⁹ studied fifty-one cases of primary syphilis prior to the appearance of secondary manifestations. In eighteen, the spinal fluid showed definite lymphocytosis. The lymphocytosis made its appearance usually in the beginning of the third week. It may, therefore, be considered, with adenopathy, as one of the earliest manifestations of a general infection. Of the eighteen patients with lymphocytosis, an inequality of the pupils was noted in eleven, whereas of thirty-three patients without lymphocytosis pupillary inequality was noted in five. Nicolau therefore concludes that inequality of the pupils is highly suggestive of cerebrospinal lymphocytosis. The lymphocytes increased with the appearance of the secondary stage. A satisfactory review of the spinal fluid findings in early syphilis is given by Klauder.¹⁰

It has been definitely shown that in many cases the cerebrospinal axis is infected by the spirochete early in the course of syphilis. Treatment of early syphilis therefore involves a consideration of the central nervous system. Nicolau,⁹ says that in only one of his series of eighteen cases with lymphocytosis in the primary stage did treatment cause the lymphocytosis to disappear. In three cases further increase was arrested. In the fourteen remaining cases, the development of the lymphocytosis was not affected by the general treatment, although this treatment was sufficiently intensive to suppress all secondary manifestations. He therefore cautions that a persistently negative Wassermann reaction obtained by treatment in the early stage, even in the absence of any secondary symptoms, is not to be depended on as indicating an abortion or cure of syphilis. There must also be evidence of nonirritation of the cerebrospinal fluid. I believe this is one of the most valuable dicta recently enunciated. It is a matter which rarely comes into the purview of the neuropsychiatrist, and too frequently the syphilologist is not sufficiently keen in considering the central nervous system. Manifestations of the central nervous system are not rare in persons who have received the so-called "abortive treatment," beginning in the primary period before the Wassermann reaction has become positive. These patients, often discharged as cured, later show symptoms of syphilis of the central nervous system.

Scott and Pearson,¹¹ in dealing with the problem of the early involvement of the central nervous system, come to practically the same conclusions as Nicolau. Scott and Pearson state that in the early period general systemic treatment may suffice but that later when

9. Nicolau: *Recherches sur le liquide cephalo-rachidien dans la periode primaire de la syphilis* (Studies of the Cerebrospinal Fluid in Primary Syphilis), *Ann. de dermat. et syph.* 7:200 (July) 1919.

10. Klauder: *Early Neurosyphilis Asymptomatica with Report of Observations and Cases*, *Am. J. Syphilis* 3:559, 1919.

11. Scott and Pearson: *Some Observations on Syphilis of the Central Nervous System*, *Am. J. Syphilis* 4:201-252, 1920.

neurologic signs have appeared intraspinal treatment is necessary. Larkin and Cornwall¹² agree a little more closely with Nicolau and state that general systemic treatment is not sufficient to produce a negative spinal fluid, but that this may be accomplished by intraspinal treatment. Gennerich is of a similar opinion and gives many interesting illustrations in his book. For the same reason Fordyce has been an active advocate of intraspinal treatment. Although not entirely in accord with these statements, I agree that in many cases in which general treatment consists of a series of six or eight injections of arsphenamin followed by mercury, the spinal fluid remains positive. However, if treatment is given more intensively and over a longer period of time, using larger doses of arsphenamin more frequently repeated than is the routine in the majority of these early cases, the spinal fluid may be brought back to normal. In cases of early involvement of the central nervous system, as shown by the spinal fluid findings, treatment which is sufficient to suppress the ordinary secondary skin manifestations may be inadequate for the sterilization of the central nervous system. Therefore the neuropsychiatrist who is interested in the prevention of neurosyphilis should take an active interest in early syphilis; if he himself is not to treat the disease at this stage, he should stimulate the syphilologist to an interest in the central nervous system.

Fildes, Parnell, and Maitland¹³ emphasize the necessity of consideration of the central nervous system in cases of syphilis, especially in the early stages. They examined 624 syphilitic men, of whom the majority were in the early stages and showed no obvious signs of syphilis of the nervous system. Eighteen per cent. showed undoubted abnormal conditions of the central nervous system. If the cases considered as doubtful were included, the percentage would be 30. There is a progressive increase in occurrence up to the secondary stage but a slight decline in the later manifest secondary and tertiary period. In men in the so-called "latent stage," there is a pronounced increase in the number affected. In this series, of all men who had been affected for more than six months and showed no symptoms, 35 per cent. had abnormal central nervous systems. The series includes a large number of patients in the first weeks of the disease, which would bring down the percentage incidence of central nervous system involvement. The onset of abnormality occurred in two cases before the Wassermann reaction had become positive in the serum. The real difficulty is a syphilitic meningitis. Polymorphonuclear leukocytes

12. Larkin and Cornwall: The Value of Laboratory Diagnosis in Neurosyphilis, *Am. J. Syphilis* **3**:76-87 (Jan.) 1919.

13. Fildes, Parnell and Maitland: The Occurrence of Unsuspected Involvement of the Central Nervous System in Unselected Cases of Syphilis. *Brain* **41**:255, 1918.

occurred frequently in the more pronounced cases. The outstanding feature was the lack of symptoms. Few men complained of disability even when the meningitis was acute enough to produce a visible opalescence in the cerebrospinal fluid. A number showed beginning retinitis.

CONGENITAL SYPHILIS

Of equal importance to the examination of the spinal fluid in cases of acquired syphilis is the examination in the cases of congenital syphilis. Kingery¹⁴ gives an interesting study of the spinal fluid in cases of hereditary syphilis. He quotes Jeans¹⁵ who examined 214 cases of congenital syphilis, combining the results of lumbar puncture and careful clinical examinations. Jeans found that approximately one third of his patients had definite involvement of the central nervous system. Kingery's fifty-two patients ranged in age from 3 weeks to 21 years. Routine punctures were made on all patients. The spinal fluid of fifteen, or 28.8 per cent., showed some deviation from the normal spinal fluid, four showed mild changes and eleven marked changes. These findings would definitely prove that the consideration of congenital syphilis should loom large in the work of the neuropsychiatrist.

Camp,¹⁶ in considering the mastic test on the cerebrospinal fluid, says that it is more reliable than the colloidal gold test. He advocates the use of both tests in the examination of the cerebrospinal fluid.

Stokes and Busman,¹⁷ in a consideration of the so-called "Wassermann-fast" cases, that is, patients whose blood Wassermann reaction does not become negative under treatment, found that 30 per cent. of these cases were neurosyphilitic. It is, therefore, obvious that one must consider the central nervous system of all patients with syphilis in whom the blood Wassermann reaction does not readily become negative under treatment.

Clinical observation of congenital syphilis has shown that various types of dystrophy suggesting disorder of the glands of internal secretion are not rare. Nevertheless, the literature is peculiarly deficient of any consideration of this subject. It is, therefore, especially pertinent to call attention to the chapter in Hazen's¹⁸ book on syphilis, in which he deals with the affections of endocrine glands both in the acquired and congenital forms of the disease. It would seem that more work on this subject is greatly needed.

14. Kingery: A Study of the Spinal Fluid in Fifty-Two Cases of Congenital Syphilis, *J. A. M. A.* **76**:12-13 (Jan. 1) 1921.

15. Jeans: Cerebrospinal Involvement in Hereditary Syphilis, *Am. J. Dis. Child.* **18**:173, 1919.

16. Camp, C. D.: The Colloidal Mastic Test on the Cerebrospinal Fluid, *Am. J. Syphilis* **4**:301-308 (April) 1920.

17. Stokes and Busman: *Am. J. M. Sc.* **160**:625 (Nov.) 1920.

18. Hazen: Syphilis, St. Louis, The C. V. Mosby Co., 1920.

Whether the vicissitudes of war had any effect on the production of syphilis of the central nervous system in syphilitic patients is a question which has been touched on, but on which there is no universality of opinion. Thus, Peghini¹⁹ states that the nervous manifestations of syphilis were more frequent and of greater gravity during the war among the fighting men than in time of peace among this group or in the civilian population. Kahn²⁰ believes that the war has been without influence on the frequency but that the interval of latency may have been shortened and in some cases the course accelerated. Herzig²¹ does not believe that it has had any positive effect. In his institution, prior to the war, about 20 per cent. of the admissions were parietic patients. During the four years of the war only 10.8 per cent. of the admissions were parietic patients. He says that the interval between the infection and the outbreak of the symptoms was the same as that given by Mattauschek and Pilcz for peace time.

Brown and Dujardin,²² in making a study of herpes zoster, have been struck by the fact that in a large lock department, that is, a clinic dealing with venereal disease, they found that herpes zoster occurred in four cases per thousand as against one case per thousand of ordinary nonsyphilitic cases compiled from general hospital wards. They naturally question whether syphilis acts as a preparation for herpes zoster.

PARTS OF NERVOUS SYSTEM AFFECTED BY SYPHILIS

Würdemann²³ calls attention to neuroretinitis syphilitica and specific inflammation of the optic nerve and contiguous retina frequently associated with papilledema. He considers this due to syphilitic toxins affecting the optic nerve. He states that ophthalmoscopic examination occasionally discloses latent syphilis. He advocates energetic treatment with arsphenamin and mercury and states dogmatically that harm is not done by this treatment. It will be recalled that it has often been stated that it is dangerous to use arsphenamin in the presence of neuroretinitis. It is, therefore, important that an ophthalmologist states dogmatically that such treatment is indicated and is not harmful.

19. Peghini: Early Manifestations of Syphilis of the Central Nervous System in Combatants, *Riforma med.* **48**:1050 (Nov.) 1919.

20. Kahn: *J. de méd. et de chir. prat.* **90**:197, 1919.

21. Herzig: War in Relation to Paresis, *Wien. klin. Wchnschr.* **32**:1207 (Dec. 11) 1919.

22. Brown and Dujardin: The Cerebrospinal Fluid in Herpes Zoster and the Relation of Herpes Zoster to Syphilis, *Brain* **42**:86, 1919.

23. Würdemann: Syphilitic Neuroretinitis, *Am. J. Ophth.* **3**:1 (Jan.) 1920.

Of similar import is an article by Davis²⁴ dealing with the arsenical treatment of syphilitic affections of the acoustic nerve. He states that auditory nerve difficulties arising during arsphenamin treatment are due to the disease and not to the treatment. He says "when properly given we may safely acquit salvarsan of producing neurotropic lesions as neurorecidives." His point of view about the production of arsphenamin neurorecidives is not in accord with that of many authors, and his statement, as that of Würdemann, must be taken as a point of view and not as decisive.

The involvement of the eighth nerve in the secondary period of syphilis is reported by Capelli and Torrigiani.²⁵ They cite seven cases in which there was a more or less rapid onset of deafness on one or both sides accompanied by dizziness with crises of vertigo. They conclude that the eighth nerve is the cranial nerve most commonly affected in the secondary stage of syphilis. It is often accompanied by neuroretinitis of the facial and oculomotor nerves. The majority of patients improve rapidly under specific treatment but a return to normal is rare.

Goeckermann, Barlow and Stokes²⁶ studied the eighth nerve in relation to acquired syphilis. The patients were given the ordinary audition tests, the Rinne, Weber and other tests. They conclude that:

1. The so-called lowered bone conduction test (reduction in conduction of sound by bone as compared with otherwise normal hearing) is positive in 78 per cent. of known syphilitics in our series.

3. The efficiency of the test varied greatly in different types of syphilis, being at its best in late cutaneous syphilis (100 per cent.), latent syphilis (80 per cent.), syphilis of the central nervous system (80 per cent.). It had almost no value in osseous lues, and the results in early syphilis were inconclusive (too few cases). A negative Wassermann test combined with a negative bone conduction test is strong evidence of the absence of syphilis.

4. The test agrees with the positive or negative diagnosis of syphilis in 67 per cent., and disagrees in 33 per cent.

5. The test was also positive in 48.7 per cent. of patients in whom syphilis could apparently be excluded.

6. It has, on the whole, therefore, only a restricted value as a diagnostic aid, owing to its high factor of error.

24. Davis: *The Diagnosis and Treatment of Syphilitic Affections of the Acoustic Nerve, with Special Reference to the Use of Salvarsan*, *The Urol. & Cutan. Rev.* **22**:631, 1918.

25. Capelli and Torrigiani: *Nuovo contributo allo studio delle lesioni del nervo acustico nella sifilide recente* (Further Contribution to the Study of Lesions of the Acoustic Nerve in Early Syphilis), *Gior. ital. d. mal ven.* **61**: 243 (Aug. 12) 1920.

26. Goeckermann, Barlow and Stokes: *The Diagnostic Value of Lowered Bone Conduction in Syphilis*, *Am. J. Syphilis* **3**:240-247, 1919.

Schaller²⁷ has made an important contribution to the pathogenesis of tabes dorsalis. In brief, he states that both cranial nerve involvement and dorsal root degenerations are conditioned by subacute inflammatory changes in the subarchnoid space by:

1. Mechanical effects: (a) fibrous constriction of the dorsal roots in Obersteiner's area, (b) root pressure from the increased cerebrospinal fluid pressure.

2. Inflammatory: direct extension of meningeal inflammation causing a meningoradiculitis.

3. Toxic: toxic products engendered by meningeal inflammation in the subarachnoid space affecting the dorsal roots. He concludes that the primary change is in the pia-arachnoid.

Gallotti and Azevedo²⁸ report their experimental work on dogs inoculated with *Trypanosome cruzi*. They found degeneration of the posterior entering roots without involvement of the ganglions or peripheral part of the nerve.

Shmookler and Rubenstone²⁹ report the finding of active spirochetes in the frontal and parietal region of the brain and in the pons and meninges in a brain removed immediately after death. No organisms were found in the spinal cord or cerebellum. As the brain tissue cooled it was more and more difficult to demonstrate the organisms, and four hours after death it was impossible. It is interesting to note that the organisms were found in the pons as well as in the cortical region.

Rossi³⁰ calls attention to the brain changes outside of the cortex in general paresis. He states that the cortex in general paralysis of the insane has been the object of more research than subjacent areas of the central nervous system, but in paresis there are numerous clinical symptoms—ataxia, dysarthria, tremor, etc.—for which no cortical pathogenesis is probable. Rossi has found in the medulla of a number of typical cases of the disease primary neuroglial overgrowth of varying degree round the upper end of the central canal, under the floor of the fourth ventricle and around the nuclei of origin of the lower cranial nerves; in particular, throughout the inferior and accessory olives a marked amount of gliosis with hypertrophy of astrocytes

27. Schaller: The Pathogenesis of Tabes Dorsalis, Arch. Neurol. & Psychiat. **1**:749 (June) 1919.

28. Gallotti and Azevedo: Contributions to the Study of the Pathogenesis of Tabes, Rev. Neurol. **32**:489, 1919.

29. Shmookler and Rubenstone: Demonstration of the Spirochaeta pallida in Nerve Tissue by Dark Field Illumination, New York M. J. **110**:107, 1919.

30. Rossi: Bulbar Neuroglia in General Paralysis and the Significance of Its Occurrence in the Bulbar Olives, Arch. ital. de biol. **69**:55.

is to be noted. Rossi emphasizes the clinical significance both of the subependymal and the olivary gliosis, sometimes amounting to actual nodular glioma formation. From the point of view of the symptomatology of the disease the presence of this process entails a functional disturbance and eventually a degenerative atrophy of bulbar mechanisms; in fact, there is bulbar ataxia as a consequence of impairment of olivo-cerebellar fibers.

TREATMENT OF NEUROSYPHILIS

The literature on the treatment of neurosyphilis is large, and it is impossible to do more than skim over some of the suggestive papers. Gennerich's book is a most elaborate consideration of the effects of treatment on various types of syphilis of the central nervous system. It may be said in general that Gennerich is an ardent advocate of intraspinal therapy for all forms of syphilis of the central nervous system. From France as well as from Germany come reports of

RESULTS OF INTRASPINAL ADMINISTRATION OF MERCURIALIZED SERUM

	No.	Clinical Result Good	Bad	Serologic Result Good	Bad
Tabes	6	4	2	1 (?)	4 (?)
General paresis.....	6	2	4	1	5
Taboparesis	2	..	2	..	2
Cerebrospinal syphilis	8	8	..	5	3
Asymptomatic neurosyphilis.....	3	1	2	..	3
Total	25	15	10	7	17 (?)

satisfactory results obtained in the treatment of neurosyphilis by the intraspinal method. Thus, Ravaut³¹ claims good results by the use of the intraspinal method in patients who have not done well on other forms of treatment. Marinesco³² says, "I have the firm conviction that the treatment of general paresis by salvarsanized serum, in vivo or in vitro, causes the question of the curability of the affections called parasyphilitic and syphilis of the central nervous system to enter into a new phase." Lafora³³ concludes that intraspinal treatment is more efficacious than intravenous in certain cases and that patients with tabes and general paresis as well as with optic atrophy are improved by intraspinal treatment.

31. Ravaut, Arbeit and Rabeau: Treatment of Neurosyphilis, Paris méd. **10**:353 (Nov. 13) 1920.

32. Marinesco: Intraspinal Treatment of Neurosyphilis, Rev. Neurol. **32**: 901 (Dec.) 1919.

33. Lafora: Traitement intra-rachidien des affections syphilitique et Parasyphilitiques de septime nerveux, Rev. Neurol. **32**:625, 1919.

Keidel and Moore³⁴ give an interesting summary of their experiences with the use of mercurialized serum given intraspinally. Their conclusions are that intraspinal therapy is a necessary and rational adjunct in the treatment of neurosyphilis in patients who fail to respond to routine antisyphilitic treatment, and that the mode of action of the intraspinal medication does not depend on increased permeability of the meninges, but that the aseptic meningitis produced by intraspinal injections of irritants may prove an untoward rather than a beneficial factor in the treatment of neurosyphilis. Table 1 summarizes their results.

A strong plea for spinal drainage in the treatment of neurosyphilis is made by Dercum.³⁵ He discusses the circulation of the cerebrospinal fluid in considerable detail. His article is devoted largely to a theoretical discussion and is of great importance. However, we are reminded of John Hunter's famous dictum, "Don't think, try," and feel that Dercum's enthusiasm for this method is premature for the amount of clinical experience with the method of drainage as compared with the result of experience with other methods.

Schroeder and Helweg³⁶ report nine cases of paresis treated by cranial subdural injections. Their results are not satisfactory.

Skoog and Menninger³⁷ treated twelve patients suffering from nonparetic neurosyphilis with intraventricular injections. They conclude that the results are encouraging considering the material; but, aside from laboratory improvement, the results reported do not seem satisfactory and no better than could have been expected from the use of arsphenamin intravenously.

Of great interest as offering a new route for the introduction of serum into the central nervous system is the work of Wegeforth, Ayer and Essick.³⁸ McCusker³⁹ reports the utilization of this route in the treatment of general paresis without drawing any therapeutic con-

34. Keidel and Moore: Treatment of Neurosyphilis by the Intraspinally Study of a Series of Cases Treated from the Point of View of Increased Permeability of the Meninges, *Bull. Johns Hopkins Hosp.* **31**:404 (Nov.) 1920.

35. Dercum, F. X.: The Functions of the Cerebrospinal Fluid, with Special Consideration of Spinal Drainage and of Intraspinally Injections of Arsphenaminized Serum, *Arch. Neurol. & Psychiat.* **3**:230 (March) 1920.

36. Schroeder and Helweg: New Investigation Into the Treatment of Dementia Paralytica by Subdural Injections of Neosalvarsan, *Hospitalstidende* **61**:945, 1918.

37. Skoog and Menninger: The Treatment and Study of Twelve Nonparetic Neurosyphilitics Treated by Intraventricular Injections of Salvarsanized Serum, *J. Nerv. & Ment. Dis.* **1**:114, 1919.

38. Wegeforth, Ayer and Essick: The Method of Obtaining Cerebrospinal Fluid by Puncture of the Cisterna Magna (Cistern Puncture), *Am. J. M. Sc.* **157**:789, 1919.

39. McCusker: Intracistern Injections of Arsphenaminized Serum in Neurosyphilis, *Boston M. & S. J.* **183**:490 (Oct. 21) 1920.

clusions, but says it is a satisfactory procedure. I can confirm this statement from my own experience. If there is any value in the arsphenamized serum in the treatment of cases of syphilis of the base of the brain this apparently is the route of election for the introduction of the serum. The serum unquestionably reaches the base of the brain as far anterior as the fifth nerve, as symptoms of fifth nerve irritation are immediately noticed when the serum is being introduced.

Neymann and Brush⁴⁰ report twenty-four cases of general paresis treated according to their method, that is, weekly intraspinal injections of serum alternating between the arsphenamized and mercurialized serum. Six of the twenty-four patients were reported as markedly improved, five returning to their occupation with the serologic findings practically negative. The average duration of the improvement was fifteen months. Six others were somewhat improved clinically and serologically; six showed no definite improvement, and six were probably made worse.

Sicard⁴¹ advocates the use of small doses of arsphenamin repeated at short intervals for satisfactory results.

Devota⁴² cites the case of a patient with tabes who was greatly relieved by the intravenous use of potassium iodid after neo-arsphenamin had failed.

Nonspecific treatment of paresis has been attempted by infecting the patient with the spirochete of relapsing fever as patients with paresis at times improve after an infection with some pathogenic organism. Plaut and Steiner⁴³ and Mühlens, Weygandt and Kirschbaum⁴⁴ have used this method. The latter authors likewise inoculated patients with the malarial plasmodium. The results are not particularly striking, and it does not seem as though this would ever become a practical method. Plaut and Steiner report that of six patients infected with the spirochetes of relapsing fever one had a remission and two were improved.

The two divergent views as to the value of treatment in general paresis are constantly appearing in the literature. Hall,⁴⁵ in reviewing

40. Neymann and Brush: Treatment of General Paresis, *Arch. Int. Med.* **28**:345, 1918.

41. Sicard: Traitement de la syphilis par les injections novarsenicales à petites doses répétées et prolongées, *Presse méd.* **28**:281.

42. Devota: Intravenous Injections of Potassium Iodide in Tabes Dorsalis, *Lancet* **196**:339, 1919.

43. Plaut and Steiner: Rekurrensimpfungen bei Paralytikern, *Neurol. Centralbl.* **38**:727-728, 1919.

44. Mühlens, Weygandt and Kirschbaum: Die Behandlung der Paralyse mit Malaria und Rekurrenzfieber, *München. med. Wchnschr.*, March 24, 1919, p. 357.

45. Hall: Paresis, a Look-Back on Recent Therapy, *Virginia M. Month.* **45**:157, 1918.

the situation, feels that nothing can be done at present to alleviate the paretic patient. On the other hand, Starkey⁴⁶ states that paresis is characterized in the beginning by a leptomeningitis which is infiltrative or exudative, and by perivascular infiltration, especially affecting the small vessels rather diffusely distributed through the cortex. Tabes is in the beginning a syringoleptomeningitis. All the symptomatology of syphilis of the central nervous system, either paresis, tabes, or cerebrospinal syphilis, may be present when the disease is still in the leptomeningitic stage, and there is no absolute method of differentiating this exudative nondestructive, curable stage from the later destructive incurable stage.

A similar point of view is expressed by Ferrand⁴⁷ as regards tabes. He states that tabes is a chronic meningomyelitis and that the meningeal reaction can be reduced by treatment, with a resultant improvement of the case.

AUTHOR'S VIEW ON TREATMENT OF NEUROSYPHILIS

The literature quoted shows that there is no uniformity of opinion concerning the value of treatment in the various types of neurosyphilis; it does not show which method is most satisfactory. The majority of reports concerning treatment are unsatisfactory, for, as a rule, few patients were treated, and usually treatment was not carried on arduously or to conform with the patient's tolerance for the drugs. In the majority of instances the patients were not followed for a long period after improvement, a criticism often made by those who hold the opinion that treatment is of little value. However, it seems that good results reported frequently and from different localities are of more significance than the failures reported. Unless the therapist has reported poorly observed or poorly controlled results, it must be accepted that results satisfactory to the patient often have been obtained. My own experience has been that when treatment is carried on intensively over a long period of time, utilizing the various methods when indicated, on the whole rather satisfactory results are obtained.

46. Starkey: *Pathology of Neurosyphilis and Its Relation to Prognosis*, *The Alienist and Neurologist* **2**:119, 1919.

47. Ferrand: *Specific Treatment of Tabes*, *Bull. méd.* **34**:960 (Oct. 30) 1920.