experiments conducted on animals. For all the frog muscle-nerve experiments having any possible medical significance, it is perfectly feasible to substitute related experiments on living human subjects. Who will deny that, for medical students, such substitution would greatly augment the value of the experiments? The data obtainable by animal experimentation in the research laboratory can be far more scientifically imparted by a few moments' intelligent discussion, or demonstration, than by several hours of crude attempts by amateurs at the same experiment. It is, moreover, as uneconomical as it is unscientific to spend two hours in learning by instrumental manipulation what could be more thoroughly comprehended by five minutes of concentrated thinking. Circulation experiments by vivisection provoke some curiosity and wonder, when similar demonstrations with mechanical models stimulate imagination, reason and judgment. There seems no limit to the illustrative devices possible to scientific ingenuity, automations imitative of practically every bodily movement and function being readily contrivable; and such models, because of their simplicity and definiteness, are much more richly illustrative than anything a student can ordinarily obtain from the anesthetized cat, dog or guinea-pig.

A few searching questions asked of the average practitioner quickly show that there is considerable need for experimental work so arranged as to illuminate the actions of muscle-groups as well as of individual muscles; and this work might well be preceded by a carefully selected series of experiments dealing with the physiology and mechanics of bones and joints. For experiments in circulation and respiration no animal experiments (capillary circulation excepted) can compare in value with the data obtainable from examinations of fellow-students, and from manipulating mechanical models. Experiments in digestion and absorption have been largely transferred to a separate department of chemistry. The special senses could well receive much more attention than the customary allotment, while the brain, with its activities as manifested in emotional and intellectual states, should be given extensive attention in laboratory investigation. No division in physiology is more important; no section is more neglected. Even "standard" text-books on physiology devote their consideration of the central nervous system to a discussion of anatomy and somatic reflexes. And, as Loeb well says:⁷

We can no more expect to unravel the mechanism of associative memory by . . . morphologic methods than we can expect to unravel the dynamics of electrical phenomena by . . . counting and locating the telephone connections in a big city.

Very little brain physiology as expressed in mental states is discoverable in any text-book. Yet such states exert a tremendous influence on all with which the physician has to deal. Therefore both their conditions and revelations need and deserve careful, serious consideration. True, such a course constitutes physiologic psychology; but who needs such a course more than the physician? Certainly society needs to have every physician trained in such a course.

Let us clear away our pedagogic cobwebs. Let us throw out from our medical curriculum everything not demonstrably applicable and, in its place, let us give a course of applied science throughout. So may our burdened curriculum be lightened, our students held

with intense interest, our graduates strengthened to grapple more adequately with their problems, and society cheered and comforted.

SUMMARY

I can do no better, in closing, than to quote the following pregnant words from O'Shea:

"In every machine there are economical as well as wasteful methods of operation, and the same must be true in principle of the brain. A given amount of force can accomplish more in promoting activities in well-organized than in poorly-organized areas." Hence "an individual should be required to perform during his learning-period those activities which he will be called on to perform most often in maturity. He must be practiced in doing as an apprentice what he will have to do as an artisan."⁸

433 Main Street.

A STUDY OF THE SPINAL FLUID IN ONE HUNDRED CASES OF SYPHILIS

INCLUDING INVESTIGATIONS FOR ARSENIC AFTER INTRA-VEINOUS ADMINISTRATION OF NEOSALVARSAN *

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ST. LOUIS

Examination of the spinal fluid has in recent years become of great value in the study of syphilis of the nervous system, particularly in the so-called parasymphilitic conditions, tabes and paresis, which we now know, through the investigations of Noguchi and others, to be not parasymphilitic but due to the invasion of the cerebrospinal system by the *Spirochaeta pallida* itself.

We undertook the investigation of the cerebrospinal fluid on account of the definite findings that can be demonstrated in it to indicate an invasion of the cerebrospinal system by the *Spirochaeta pallida*, the purpose being to determine what percentage of patients with syphilis applying for treatment at a general dermatologic clinic would show evidence of spinal invasion.

The large percentage of early syphilis reported in literature as giving evidence of meningeal disturbance encouraged us. All of the cases of syphilis, therefore, in the outpatient department of the Washington University Hospital and the Barnard Free Skin and Cancer Hospital, if the patient would submit to spinal puncture, were studied.

All of the cases in the investigation were examined in the following manner: Blood and spinal fluid were obtained simultaneously and a Wassermann reaction made on the two fluids, two separate antigens being used with increasing amounts of spinal fluid, beginning with 0.2 c.c. and increasing to 0.5 c.c. The cells in the spinal fluid were counted from undiluted fluid in the ordinary blood-counting chamber. The globulin reaction was determined by the Noguchi method. Fehling's reduction test was also performed on each fluid, as normal spinal fluid reduces Fehling's solution, owing supposedly to the presence of pyro-

8. O'Shea: Education as Adjustment, p. 264.

9. O'Shea: Education as Adjustment, p. 265.

* From the Medical Department of Washington University and the Barnard Skin and Cancer Hospital.

* Read in the Section on Dermatology of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

* Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the Transactions of the Section and in the authors' reprints.

7. Loeb: Physiology of the Brain, 1902, p. 280.

catechin. This reaction is sometimes absent, however, in inflammatory conditions.

One of the earliest investigators of the spinal fluid in syphilis is Ravaut¹ who, in 1903, affirmed that a large number of syphilitics at all periods of the disease presented a lymphocytosis in the spinal fluid which was indicative of meningeal disturbance, and in 1907 showed that a large percentage of syphilitic children showed spinal involvement. The majority of the latter presented mucous membrane and cutaneous lesions also. Ravaut² again affirmed, in 1912, that at the time of the chancre, there was no involvement of the nervous system, but that 67 per cent. of the syphilitics showing no clinical nervous symptoms had a meningeal infection, evidenced by lymphocytosis and albumin content in the spinal fluid. He believed from this that if, in the secondary period, such a positive reaction should be present, the administration of salvarsan was dangerous, as the spirochete fixed the arsenic and caused a neurotropic reaction.

Jeanselme and Chevallier³ state that the spinal fluid is negative in the chancre stage and positive in a large majority of cases in the so-called secondary period of the invasion, but that only a small percentage show involvement of the cerebrospinal system through the study of the spinal fluid in late syphilis. From their investigations these two writers affirm that there may be no clinical symptoms of meningeal involvement, with considerable cytologic evidence, or that such an involvement may cause severe headache which is relieved by lumbar puncture. They also state that syphilitics in the so-called secondary period with no eruption may show marked lymphocytosis in the fluid. From the reported findings of these investigators and others, the general opinion has been that a large percentage of early cases of syphilis show invasion of the cerebrospinal system and the prognosis depends only on a proper study of the spinal fluid. We were under this impression when we undertook the work, but have been surprised at our results, as they differ so materially from those of others.

Previous to spinal puncture, a complete physical examination of each patient was made; namely, of the viscera, fundus of the eye, pupillary and the various other reflexes, and for other symptoms of central nerve involvement. As headache is frequently a prominent early symptom of cerebral lues, careful note of this was made in each case. In all cases in which it was possible, more than one puncture was made and after each a maximum dose of neosalvarsan was administered intravenously. In four cases, after the intravenous injection of neosalvarsan a search was made for arsenic in the spinal fluid, details of which we shall give later.

REPORT OF CASES

CASE 1.—P. C.* Congenital lues. Viscera, heart and reflexes normal. Iritis of both eyes. Nov. 19, 1912: Wassermann, serum +++++, spinal fluid +++++; cell-count 54, globulin +, reduction ±. Treatment, neosalvarsan and mercury. Puncture normal; fluid clear.

CASE 5.—History 3575, B. F. S. and C. H. No history of lues obtainable. Hemiplegia of entire left side; mental aberration, exaggerated reflexes, ankle-clonus. Aug. 17, 1912: Wassermann, serum +++++, spinal fluid +++++; cell-count 60, globulin +, reduction ±. Puncture, increased pressure; fluid clear. Treatment, salvarsan and mercury. Nov. 9, 1912:

Wassermann, serum +++++, spinal fluid +++++; globulin +, cell-count 25, reduction +. Puncture normal, fluid clear.

CASE 7.—History 4212, B. F. S. and C. H. No history of infection. Early symptoms of tabes. Heart, eyes and viscera normal. Knee-reflexes sluggish. Oct. 30, 1912: Wassermann, serum +, spinal fluid ++; cell-count 20, globulin +, reduction —. Puncture normal, fluid clear.

CASE 8.—History 4282, B. F. S. and C. H. History indefinite. Late lues. Circinate ulceration of left arm. Viscera, heart, eyes and reflexes normal. Nov. 22, 1912: Wassermann, serum +++++, spinal fluid +++++; cell-count 25, globulin +, reduction ±. Puncture, increased pressure; fluid clear.

CASE 9.—History 4179, B. F. S. and C. H. Infection one year ago. No lesions at present. Viscera, heart, eyes and reflexes normal. Oct. 12, 1912: Wassermann, serum +++++, spinal fluid +++++; globulin +, cell-count 30, reduction ±. Puncture normal, fluid clear.

CASE 17.—History 4544, B. F. S. and C. H. Infection two months ago. No lesions at present. Viscera, heart and eyes normal, reflexes sluggish. March 6, 1913: Wassermann, serum +++++, spinal fluid —; cell-count 17, globulin —, reduction +. Puncture, slight increase in pressure; fluid clear. Treatment, neosalvarsan.

CASE 20, Sanatorium.—No history of infection. At present paresis. Patient confined in sanatorium. Pupils irregular; reaction sluggish; knee and Achilles reflexes absent. Viscera and heart normal. April 22, 1913: Wassermann, serum +++++, spinal fluid +++++; globulin +, cell-count 112, reduction ±. Puncture, increased pressure; fluid clear. April 22, 1913: Treatment, neosalvarsan 0.9 gm. intravenously. April 27, 1913: Puncture; spinal fluid examined for the presence of arsenic with negative result.

CASE 21, Sanatorium.—Date of infection not obtainable. Patient confined in sanatorium with paresis. Romberg's symptom present; pupils equal, reaction good. Knee and Achilles reflexes absent. Viscera and heart normal. April 22, 1913: Wassermann, serum +++++, spinal fluid +++++; cell-count 32, globulin +, reduction +. Puncture, increased pressure; fluid clear. April 22, 1913: Treatment, neosalvarsan 0.9 gm. intravenously. April 27, 1913: Puncture; spinal fluid examined for the presence of arsenic with negative result.

CASE 22, Sanatorium.—Infection fifteen years ago. No history of treatment obtainable. Patient confined in sanatorium with paresis. Pupils irregular; reaction sluggish. Achilles and knee-reflexes absent. April 22, 1913: Wassermann, serum +++++, spinal fluid +++++; cell-count 42, globulin +, reduction ±. Puncture, pressure normal; fluid clear. Treatment, neosalvarsan 0.9 gm. intravenously. April 24, 1913: Puncture; spinal fluid examined for the presence of arsenic with negative result.

CASE 23, Sanatorium.—Date of infection not obtainable. Patient confined in sanatorium with paresis. Romberg's symptom present; pupils irregular; reaction sluggish. Reflexes: Knee sluggish, Achilles absent. Viscera and heart normal. April 22, 1913: Wassermann, serum +++++, spinal fluid +++++; cell-count 62, globulin +, reduction —. Puncture, pressure increased; fluid clear. Treatment, neosalvarsan 0.9 gm. intravenously. April 24, 1913: Puncture; spinal fluid examined for the presence of arsenic with negative result.

CASE 35.—History 1545, B. F. S. and C. H. Infection fourteen years ago. Late lues; tuberculous ulcer of lower lip. Viscera, heart and eyes normal. Knee-reflexes sluggish. April 11, 1913: Wassermann, serum +++++. Treatment, neosalvarsan. April 21, 1913: Wassermann, serum +++++, spinal fluid +++++; cell-count 27, globulin +, reduction ±. Puncture, pressure increased, fluid clear.

CASE 36.—History 4051, B. F. S. and C. H. Infection eight months ago. Viscera, heart and eyes normal. Reflexes, knee and Achilles, sluggish. March 12, 1913: Wassermann, serum +++++, spinal fluid +++++; cell-count 42, globulin +, reduction ±. Puncture, pressure increased, fluid clear. Treatment, neosalvarsan and mercury. March 26, 1913: Wassermann, serum +++++.

1. Ravaut: Ann. de dermat. et de syph., 1903, p. 537.

2. Ravaut: Ann. de dermat. et de syph., 1907, p. 81.

3. Jeanselme and Chevallier: Ann. de dermat. et de syph., 1912, p. 506.

4. In the case reports abbreviations indicate: W. U.—Washington University; B. F. S. and C. H.—Barnard Free Skin and Cancer Hospital; P. C. = private consultation.

CASE 39.—History 4339, B. F. S. and C. H. Infection two months ago. Macular secondaries. Viscera, heart, eyes and reflexes normal. Dec. 23, 1912: Wassermann, serum + + + +, spinal fluid —; cell-count 12, globulin $\pm$, reduction +. Puncture normal, fluid clear. Treatment, salvarsan.

CASE 42.—History 4375, B. F. S. and C. H. Infection five years ago. Healed scars on right forearm. Viscera, heart and eyes normal. Reflexes, knee and Achilles accentuated; ankle-clonus marked on both sides. Jan. 2, 1913: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 15, globulin +, reduction —. Puncture, increased pressure; fluid clear. Treatment, neosalvarsan and mercury.

CASE 45.—History 4571, B. F. S. and C. H. Infection two months ago. Large crusted primary on lower lip; submental adenopathy. Viscera, heart, eyes and reflexes normal. March 14, 1913: Wassermann, serum + + + +, spinal fluid —; cell-count 12, globulin —, reduction +. Puncture normal, fluid clear. Treatment, neosalvarsan.

CASE 48.—Blood positive; spinal fluid negative. History 4586, B. F. S. and C. H. Infection thirteen weeks ago. Viscera, eyes and reflexes normal. Heart, second sound accentuated. March 27, 1913: Wassermann, serum + + + +, spinal fluid —; cell-count 2, globulin —, reduction +. Puncture normal, fluid clear. Treatment, neosalvarsan.

CASE 49.—History 4574, B. F. S. and C. H. Infection four years ago. No lesions. Viscera, eyes and reflexes normal. Heart, systolic murmur at third intercostal space. March 27, 1913: Wassermann, serum + + +, spinal fluid + + + +; cell-count 107, globulin $\pm$, reduction $\pm$. Puncture, increased pressure; fluid clear. Treatment, neosalvarsan.

CASE 56.—History 4282, B. F. S. and C. H. No history of infection. At present, circinate ulceration on left arm. Healed scars on both arms. Nov. 22, 1912: Viscera, heart and eyes normal. Knee-reflexes slightly accentuated. Wassermann, serum + + + +, spinal fluid + + + +; cell-count 25, globulin +, reduction $\pm$. Puncture, increased pressure; fluid clear. Treatment, salvarsan.

CASE 67.—History 4391, B. F. S. and C. H. Infection seven years ago. No lesions. Viscera, heart, eyes and reflexes normal. Jan. 11, 1913: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 34, globulin +, reduction $\pm$. Puncture normal, fluid clear. Treatment, salvarsan.

CASE 71.—History P. C. Infection eighteen years ago. Early tabes. Eyes, reaction sluggish. Reflexes, knee and Achilles, absent. Viscera and heart normal. Feb. 14, 1913: Wassermann, serum + + + +, spinal fluid + + + +; globulin +; cell-count 60, reduction —. Puncture, increased pressure; fluid clear.

CASE 72.—Blood positive; spinal fluid negative. History P. C. Infection eight months ago. No lesions. Viscera, heart, eyes and reflexes normal. Oct. 9, 1912: Wassermann, serum + + + +, spinal fluid —; cell-count 8, globulin —, reduction +. Puncture normal, fluid clear. Treatment, neosalvarsan.

CASE 75.—History 363, W. U. No history of infection. No lesions. Progressive muscular atrophy. Reflexes accentuated. Nov. 11, 1912: Wassermann, serum —, spinal fluid + + + +; cell-count 26, globulin +, reduction +. Puncture normal, fluid clear.

CASE 78.—History 334, W. U. Definite history of syphilis twenty years ago. No skin lesions. Physical examination; aneurysm of arch of aorta. Reflexes difficult to elicit. Oct. 30, 1912: Wassermann, serum —, spinal fluid —; cell-count 43, globulin +, reduction $\pm$. Puncture normal, fluid clear.

CASE 79.—History 424, W. U. History of infection nine years ago. No skin lesions. Symptoms of chronic lead-poisoning. Nov. 4, 1912: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 264, globulin +, reduction $\pm$. Puncture normal, fluid clear.

CASE 81.—History 368, W. U. Infection ten years ago. No lesions. Viscera, heart, eyes and reflexes normal. Neck rigid. Tuberculosis of cervical vertebra. Ankylosis of right knee. Dec. 6, 1912: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 32, globulin +, reduction +. Puncture normal, fluid clear.

CASE 84.—History 364, W. U. No history of infection. No skin lesions. Reflexes sluggish. Physical examination; aneurysm of ascending aorta. Aortic mitral regurgitation. Feb. 17, 1913: Wassermann, serum + + + +, spinal fluid + +; cell-count 6, globulin —, reduction +. Puncture normal, fluid clear.

CASE 86.—History 497, W. U. Infection six years ago. No skin lesions. Heart, eyes and reflexes normal. Symptoms of duodenal ulcer. March 29, 1913: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 24, globulin $\pm$, reduction +. Puncture normal, fluid clear.

CASE 87.—History 530, W. U. No history of infection. No skin lesions. Viscera, heart and eyes normal. Reflexes exaggerated. Symptoms of right hemiplegia. History of frequent miscarriages. May 9, 1913: Wassermann, serum + + + +, spinal fluid + + + +; cell-count 32, globulin +, reduction +. Puncture normal, fluid clear.

CASE 90.—History 542, W. U. No history of infection. No skin lesions. Reflexes sluggish. Optic atrophy of both eyes; pupils fixed, right larger than left. Dizziness and headache. Romberg's symptom. April 22, 1913: Wassermann, serum —, spinal fluid + + + +; cell-count 32, globulin +, reduction +. Puncture normal, fluid clear.

CASE 91.—P. C. Infection two years ago. No skin lesions. Viscera, heart and reflexes normal. Slight headaches. Pupils irregular; right larger than left; reaction both to light and accommodation. April 28, 1913: Wassermann, serum +, spinal fluid + + + +; cell-count 18, globulin $\pm$, reduction +. Puncture normal, fluid clear. Treatment, neosalvarsan and mercury.

CASE 96.—P. C. No history of infection. Mucous patches on mouth and tonsils; ulcer on uvula. Viscera, heart, eyes and reflexes normal. March 10, 1913: Wassermann, serum + + + +, spinal fluid —; cell-count 16, globulin $\pm$, reduction +. Puncture normal, fluid clear. Treatment, neosalvarsan.

CASE 99.—History 562, W. U. Infection nine years ago. No lesions. Clinical symptoms of gastric crisis. Pupils irregular, left larger than right, no reaction to light in either. Fundus normal. Knee-reflexes absent. May 19, 1913: Wassermann, serum + + + +, spinal fluid +; cell-count 19, globulin +, reduction +. Puncture, increased pressure; fluid clear.

SUMMARY

On account of the necessary length of this communication, we have concisely summed up the net results by dividing the cases into early and late: those in which infection occurred two years previously to our observation are classed as early; those in which infection occurred prior to that time as late.

Early Syphilis.—There were thirty-six of the early cases, three of which (Cases 9, 36 and 91) gave a positive serologic reaction in the spinal fluid and a high cell-count (8.3 per cent.). In Case 9 there were no clinical symptoms whatever, but the spinal fluid gave a cell-count of 30 and an increase of globulin. In Case 36, the reflexes were sluggish with no other clinical symptoms; the cell-count was 42 with an increase in the globulin content. The patient in Case 91 had an early syphilis and had had two salvarsan and two neosalvarsan injections together with adequate intramuscular mercurial treatment. The spinal puncture was incited by the sudden irregularity of pupils and headache. The fluid showed positive findings.

In none of these early cases giving a positive spinal reaction were there any active cutaneous manifestations. Four of this group of early infections gave a negative serologic reaction and a cell-count above 10 (Cases 17, 39, 45 and 96); the cell-count in these cases was 17, 12, 12 and 16, respectively, which in the presence of no clinical symptoms and a negative serologic test in the

spinal fluid, is probably of no pathognomonic significance.

Late Syphilis.—There were sixty-four of the late cases, twenty-one of which (34.4 per cent.) gave a positive serologic reaction (Cases 1, 5, 7, 8, 20, 21, 22, 23, 35, 42, 49, 56, 67, 71, 75, 79, 81, 86, 87, 90 and 99); sixteen of these showed definite clinical symptoms of cerebrospinal syphilis, ranging from headache and pupillary changes to definite symptoms of tabes and paresis (five were tabetic, four parietic and four hemiplegic), which leaves five cases with no clinical symptoms referable to the nervous system (Cases 1, 8, 49, 67 and 86). In Case 1 the patient had congenital lues with double iritis. In Case 8 the patient was apparently normal with the exception of a serpiginous ulcer of arm. In Case 49 there was a systolic murmur. In Case 67 there were no clinical symptoms whatsoever. In Case 86 the patient had symptoms of duodenal ulcer.

Of the twenty-nine patients showing cutaneous manifestations of acquired syphilis only one (Case 8) gave a positive spinal reaction (3.4 per cent.). In thirteen cases of the late group there was a cell-count in the spinal fluid above 10, with a negative serologic reaction; in seven a cell-count of 12; in one of 15; one of 17, and three of 20, all of which gave a negative globulin content except one which showed a slight increase. In Case 78, the cell-count was 43 with an increase of globulin. This patient also gave a negative Wassermann in the blood but was suffering from an aortic aneurysm, probably the result of an old cured syphilis.

Of the one hundred cases included in this report, only six had a positive spinal fluid⁵ with no clinical symptoms of involvement of the central nervous system. One of these was congenital, two visceral and one showed late cutaneous lesions.

During the course of our investigation, we were quite anxious to determine whether, if some of the spinal fluid was removed and an intravenous injection of neosalvarsan followed immediately, the fluid removed would not be replaced with a fluid surcharged with arsenic. To determine this we selected four cases of paresis. In each of these a spinal puncture was made and 10 c.c. of fluid removed immediately after which a full dose of neosalvarsan was administered intravenously. Within forty-eight hours, in two of these cases puncture was again made; and in the remaining two, in ninety-eight hours. The fluid was then examined for the presence of arsenic by the Gutzeit and Marsh methods fully controlled, with negative results in all four cases.

From the number of cases included in this report, one is not justified in being dogmatic, but the study seems to demonstrate that (1) only a comparatively small percentage of those infected by the *Spirochaeta pallida* give serologic and cytologic evidence of cerebrospinal invasions, and (2) when such an invasion does occur there are usually early clinical manifestations of it, which substantiate clinical observation.⁶

Before closing we wish to thank Dr. George Dock of the Washington University for his kindness in allowing us to use some of his cases from the wards, and also, Dr. Walter Fischel and Dr. H. N. Lyon of the Barnard Free Skin and Cancer Hospital, for the physical examinations of the patients from that institution.

ABSTRACT OF DISCUSSION

DR. F. G. HARRIS, Chicago: It has been shown that in a large number of cases of secondary syphilis there is involvement of the spinal fluid. The percentage of cases in which this occurs differs according to the reading of different observers, but we know that it is comparatively large. The cerebrospinal axis is affected early, in my experience, and these are the cases that later develop tabes and paresis and cerebrospinal syphilis. The spinal fluid is a true secretion, and our antisiphilitic remedies circulating in the blood have little effect on it, as they do not reach it. As long as a case of syphilis shows a positive reaction of the cerebrospinal fluid, it should still remain under treatment.

DR. DAVID LIEBERTHAL, Chicago: The assertion made by some that any case of syphilis in which the cerebrospinal fluid shows a positive Wassermann will, if left untreated, eventually develop into tabes or paresis or cerebrospinal syphilis is too broad. We have lost sight of the fact, apparently, that there is a natural healing process in connection with syphilis. If we review the statistics of cases of syphilis, treated and untreated, we shall find quite a large number of the latter in which the patients never developed any of these nervous affections. We are not in a position to prove that those cases showing a positive reaction in the cerebrospinal fluid will develop paresis or tabes; this can only be proved or disproved in the course of time. The authors stated that under the administration of neosalvarsan, the findings in the cerebrospinal fluid improved. I believe that mercury gives still better results. I use both salvarsan and neosalvarsan, but not to the exclusion of mercury. I do not limit my time of treatment of syphilitic patients to three years or to five years or even longer, and I advise them to keep themselves under observation for the rest of their lives, even in those cases in which the Wassermann has been negative for a year or longer.

DR. H. G. IRVINE, Minneapolis: I should like to call attention to the fact that these late syphilitic manifestations are very resistant to treatment. I should like to ask Dr. Buhman what his results have been in changing the positive Wassermann to a negative by treatment.

DR. M. L. LEIDINGSFELD, Cincinnati: I should like to ask Dr. Buhman if these cases have been followed by subsequent spinal puncture. If so, with what result? Dr. Buhman's work exercises a therapeutic control over selected cases that would be otherwise entirely lacking. The therapeutic efficacy of salvarsan can hardly be questioned in these cases. Mercury may effect some good here and there. Four hundred years of experience has shown that it utterly fails in the vast majority of instances. Syphilis shows one peculiarity in that it often directs its influence against one special system, and I believe that for that reason we often see a positive cerebrospinal fluid, when the nervous system is attacked, and a negative blood Wassermann.

DR. H. H. HAZEN, Washington, D. C.: It has been noticed that an intravenous injection of salvarsan is often followed by a positive Wassermann in the blood in from seventeen to forty-eight hours. Will Dr. Buhman tell us if this is also true of the cerebrospinal fluid?

DR. RUDOLPH BUHMAN, St. Louis: In reply to Dr. Harris I would say that in our work the blood and cerebrospinal fluid are obtained simultaneously, and that all the cases that did not give a positive blood or spinal-fluid reaction were thrown out. I cannot make any definite statement as to the effect of treatment on a positive spinal-fluid reaction, as I do not think that sufficient time has elapsed between the first and succeeding spinal punctures to draw any positive conclusions. In three of the cases, however, in which there was definite involvement of the nervous system, with positive blood, spinal-fluid and cytologic findings, the patients received five or six injections of salvarsan, and at the end of a year the findings were still practically unchanged with the exception of a lower cell-count. I have had no experience with the provocative treatment of the spinal fluid, but I have had experience with this treatment of the blood.

5. Positive spinal fluid, meaning a positive Wassermann reaction in the fluid with a cell-count above 10 and an increase of the globulin content.

6. In those patients on whom subsequent spinal punctures were made after intravenous injection of salvarsan and neosalvarsan there was no material change noted in the spinal fluid in the large majority of cases. We hope to report on this later.