The Journal OF Nervous and Mental Disease

An American Journal of Neuropsychiatry, Founded in 1874

ORIGINAL ARTICLES

SPINAL DRAINAGE FOLLOWING INTRAVENOUS ARSPHENAMINE*

BY C. BURNS CRAIG, M.D.,

ASSOCIATE PHYSICIAN, N. Y. NEUROLOGICAL INSTITUTE

AND

L. BEVERLEY CHANEY, M.D.,

CLINICAL ASSISTANT, N. Y. NEUROLOGICAL INSTITUTE

The cerebrospinal fluid is a derivative of the blood plasma. "It is not an ordinary filtrate, such as lymph, since it is almost free from proteins, in health."¹ Because of this, McClendon² called it an "ultrafiltrate" of the blood, as microscopic colloid particles are restrained from entering the cerebrospinal fluid. The transudation occurs almost wholly in the choroid plexuses of the fourth, third and lateral ventricles of the brain.³ In health, this fluid is a watery solution of inorganic salts similar to those of the blood plasma, with a trace of coagulable protein and glucose, and has a specific gravity of 1.0075.⁴ The dialysing membrane, the choroid plexus, consists of the capillary wall and a layer of ependymal cells. It has a peculiarly selective activity, and to foreign chemicals in the blood it is impermeable under ordinary conditions, chloroform and hexamethylenamine being the only consistent exceptions yet determined.

Because of this physiological obstacle the attempt to treat syphilis of the central nervous system with maximum effect by the introduction of medication into the blood would seem to be hopelessly blocked. Indeed, the investigations of numerous workers to determine the presence of arsenic in the spinal fluid after intravenous injection of arsphenamine would seem to further this conclusion.

* From the N. Y. Neurological Institute.

Sicard and Block⁵ recovered arsenic from the spinal fluid in three of ten cases after intravenous arsphenamine. Camp⁶ found a questionable trace of arsenic in one of seventeen cases in spinal fluid removed from fifteen minutes to fourteen hours after intravenous arsphenamine. Ravaut⁷ discovered arsenic in the spinal fluid of six of thirty-three cases treated with arsphenamine intravenously. Benedict⁸ detected arsenic in the spinal fluid of four of a large series of cases similarly treated by Sachs, Straus and Kaliski. Engman, Buhman, Gorham and Davis⁹ report four cases of general paresis treated intravenously with 0.9 grams of neoarsphenamine and negative results in tests for arsenic in the spinal fluid in all. Hall¹⁰ reports two positive findings of arsenic in the spinal fluid out of eight cases treated intravenously with the arsenical preparations. Hall administered to a series of seven cases by the Ravaut intraspinal method, 3 mgm. of arsphenamine, and later tested the spinal fluid for arsenic. After ten hours he found it present in four cases and absent in three. In another series of ten cases similarly treated the fluid was removed after twenty-four hours, and he found it present in one case and absent in nine.

Of 123 spinal fluids examined by Rieger and Solomon,¹¹ following intravenous administration of arsphenamine, 38 showed appreciable amounts of arsenic, the maximum number of positive findings and the maximum concentration being one hour after injection. Findings before one half hour were negative. These writers remark that "in general, those patients consistently showing the larger amounts of arsenic in their fluids made the more rapid improvement." The clinical findings of Rieger and Solomon¹¹ on the rapid removal of arsenic from the spinal fluid after intravenous arsphenamine, and of Hall,¹⁰ after intraspinal administration of arsphenamine, correspond with the experimental work done on the introduction of chemicals into the spinal canal. They are taken up by the arachnoidal villi and rather rapidly removed through the venous channels of the dura.¹²

A certain small percentage of the cases of syphilis of the nervous system are unquestionably benefited by the intraspinal method of administration. We have used this method for a period of years, and it is doubtful that the spirochaeticidal power of the arsenic thus applied is the sole cause of the improvement. It may act as a local irritant, rousing the sluggish forces of nature to combat, or it may be that the withdrawal of the spinal fluid is a factor, permitting a fresh supply of new fluid to escape from the choroid plexus into the containing cavities of the cerebrospinal fluid. The rather exacting technical difficulties involved in the intraspinal method are disadvantageous to the physician, but are inconsiderable compared with the root-pains, sometimes inaugurated in the patient, which can be

likened only to the severest pains of tabetic crises, and because of them many patients are deterred from continuing treatment.

Investigations concerning the removal of chemicals from the arachnoid space as performed with phenolsulphonephthalein show that when injected into the lumbar space it appears in the urine in from four to ten minutes in health¹³ and from twelve to sixty-eight minutes in paresis, and from twenty-five to one hundred and four minutes in catatonic dementia praecox.¹⁴

From their work with phenolsulphonephthalein in hydrocephalus, Dandy and Blackfan¹⁶ conclude that the spinal fluid passed directly into the blood. The dye appeared in the blood in three minutes and in the urine in six minutes following introduction into the lumbar subarachnoid space. They state that the dye appeared in the cerebral ventricles within a few minutes. This observation could not be confirmed by Weston,¹⁴ who found that the dye was not found in fluid drawn from the cisterna magna at any time up to five hours after it had been injected into the lumbar subarachnoid space. The absorption of the dye took place from the lumbar region. He further found that in recent cadavers immediately after death no dye was recoverable from the thoracic region of the spinal canal after introduction into the lumbar space.

So it would seem that, at best, the introduction of the existing arsenical preparations into the lumbar subarachnoid space is merely a local application to the adjacent structures, and is in no sense applicable as a therapeutic measure to disease of the cord higher up or of the brain. It is physiologically unscientific.

Dercum¹⁵ states that simple drainage alone done by Gilpin and Earley produced "striking results." "Marked improvement followed, an improvement which was more pronounced than that observed in the Swift-Ellis method; doubtless because the drainage was more thorough." Again, "in a number of cases we have practiced drainage alone, and always with improvement." No case records are cited. Be that as it may, in 1915 Fisher,¹⁶ and later Barbat,¹⁷ suggested drainage of the spinal canal following the intravenous injection of arsphenamine in the treatment of syphilis of the nervous system.

It seems highly desirable, if possible, to create an increased concentration of the spirochaeticidal remedy in the cerebrospinal fluid in view of the "canalicular system" which Mott¹⁸ describes as "surrounding the cells and vessels of the brain" and "in direct communication with the subarachnoid space." By the withdrawal of spinal fluid a deficiency of fluid and lowered pressure is created in the containing cavities, thereby stimulating the choroid plexus to replace from the blood the deficit. Now, if, at the time of this activity, the blood in the plexus is charged with medication, the probability of

some of it being carried over into the cerebrospinal fluid would seem to be enhanced. Further, it would seem logical that a greater quantity of medication would be transferred, than under ordinary conditions when the arachnoid of the spinal tube is distended at all points with the normal amount of fluid.

Gilpin and Earley¹⁹ published in 1916 an article with report of three cases, two of which had been drained seven times and one case six times, with fair success. In 1918, Barbat²⁰ reported that by withdrawing all the fluid that would run from a lumbar puncture, within twenty minutes after intravenous arsphenamine, he could find arsenic in the spinal fluid of twenty-five out of twenty-six cases the following day. This percentage of positive findings of arsenic in the spinal fluid is far in excess of those of the investigators who withdrew small amounts of fluid. A recent article in which the average number of spinal drainages per case was five, the authors admit, is not conclusive.²¹ Such a limited number of treatments with arsphenamine by any method is inconclusive.

Under abnormal conditions all are familiar with the saturation in a few hours of large dressings, following wounds penetrating the cranial meninges. An attempt to estimate the amount of spinal fluid poured out in twenty-four hours, following a shell-fragment puncture of the meninges, showed an average of 150 c.c.²² Numerous observations particularly common to the neurological surgeon establish the existence of a capacity to produce cerebrospinal fluid in considerable quantity and rather rapidly. That the spinal tube is refilled overnight after drainage of 50 to 80 c.c. is reasonable to suppose, as no deleterious effects are produced. Curiously enough, headache which may follow the withdrawal of 10 c.c. has been less frequent in our experience after complete drainage. The patient is, of course, kept in bed for twenty-four hours following the puncture.

Since the arsenic of arsphenamine becomes rapidly fixed in the body cells following injection into the blood stream, it was thought desirable to initiate the increased flow of cerebrospinal fluid while the maximum amount of arsenic was in solution in the blood. This period would be immediately after the intravenous injection. For Adler and Wetmore²³ found, following the administration of 0.6 gm. of arsphenamine intravenously, that 80 per cent had disappeared from the blood stream in one hour and 98 per cent in three hours, and that the concentration, then, was 0.25 to 0.50 mgm. per c.c. Therefore, as soon as the arsphenamine solution had been introduced into one of the veins of the arm, the patient rolled over on his side and a lumbar puncture was done immediately. All lumbar punctures were done with the patient lying on the side. All the spinal fluid that would run out was withdrawn, until it began to drip very slowly, five or six drops per minute. It rarely ceased to drop

entirely. The amount collected varied greatly with the same individual, the minimum being 15 c.c. and the maximum 80 c.c.

The blood and spinal fluid analyses were done in the laboratory of the Neurological Institute under the direction of Dr. O. S. Hillman, and the personal factor was constant, as all analyses were done by Miss Ruth Shivitz, to both of whom we are deeply indebted.*

The laboratory methods were as follows: Both with the blood serum and cerebrospinal fluid, two antigens, namely, crude alcoholic and cholestrinized, guinea pig heart were used. Fixation was done by the ice box method for four hours. Amboceptor was titrated against complement, and sensitized cells were used. No difference was noted in the cerebrospinal fluid reaction to the two antigens.

Globulin was estimated by the following method: 0.5 c.c. of spinal fluid was boiled with three drops of 5 per cent butyric acid. This was stratified upon 0.5 c.c. of saturated neutral ammonium sulphate solution and the tube allowed to stand a half hour before reading.

Cells were counted in the Fuchs-Rosenthal counting chamber with Nonne's cerebrospinal fluid strain.

The standard method of preparing colloidal gold was followed.

Of twenty-five cases of syphilis of the nervous system treated with intravenous arsphenamine followed by spinal drainage, those to be reported are typical examples. The average case of cerebrospinal syphilis responds so readily to simple intravenous treatment that it is rarely necessary to institute drainage. For this reason only tabetic and paretic cases are cited.

Case No. 1. Diagnosis, *Tabes Dorsalis*. April, 1920. Female, 46 years old, married. She had married at 18 years and had one miscarriage; divorced her husband after eighteen months because of dissolute character, and remarried four years ago.

The onset of the present illness four years ago was marked by indistinctness of vision, general weakness, and gradual loss of weight. At present, the patient complains of weakness and shakiness of legs, sharp shooting pains in the legs, staggering, inability to climb stairs, numbness and stiffness in the feet, girdle sensation, constipation and dysuria. She is unable to walk alone, but uses a cane and is supported on the one side by her sister and on the other by her husband. The gait is markedly ataxic. There is a slight internal squint of both eyes and the pupils are of pinpoint size and fixed. The finger-nose test displays moderate ataxia and the heel-knee test very marked ataxia. The knee and ankle jerks are gone, and the muscle-joint sense in the toes is greatly disturbed.

* We wish to thank Dr. E. G. Zabriskie for permission to use such clinical material on his service, as we desired, also Dr. C. Lester Wood, and Dr. Patrick M. Carroll for assistance in carrying out the treatments.

Treatment and serology follow:

1920	Neo-arsphen gm.	C. S. Fluid with- drawn c.c.	Serum Wasser- mann	C. S. F. Wassermann			Cells c.m.	Globulin Excess
				2 c.c.	1 c.c.	0.4 c.c.		
Apr. 23	0.6	40	4+	4+	4+	2+	44	1+
Apr. 30	0.6	15	4+	4+	4+	2+	13	1+
May 7	0.6	15		4+	4+	2+	12	1+
May 14	0.6	50		4+	4+	2+	13	3+
May 19	0.6	45		4+	3+	1+	10	2+
May 26	0.6	35		4+	3+	2+	8	2+
June 9	0.6	50		4+	3+	1+	3	1+
July 2	0.6	50		4+	3+	1+	3	1+
July 14	0.6	35		4+	2+	2+	3	—
July 22	0.6	40		4+	2+	1+	2	1+
July 28	0.6	35		4+	2+	1+	0	1+
Aug. 5	0.6	45	—	4+	4+	1+	0	1+
Oct. 15	0.6	50	—	3+	2+	1+	0	1+
Oct. 29	0.6	50		3+	1+	1+	0	1+
Nov. 5	0.6	50		4+	2+	1+	0	1+
Nov. 12	0.6	50		3+	1+	1+	0	1+
Nov. 26	0.6	60		3+	1+	1+	4	1+
Dec. 3	0.6	40		1+	—	—	0	1+
Dec. 10	0.6	50		2+	1+	—	3	1+
Dec. 17	0.6	50		2+	—	—	4	1+
Jan. 28	0.6	50	—	1+	—	—	3	1+
Aug. 5, 1920, Gold, Sol., IIII000000.								

January, 1921. The patient has been practically transformed. She has gained 21 pounds in weight, now weighing 153 pounds. Whereas she was a dependent invalid, she now does all her own housework, marketing and shopping alone in any part of the city, mounting and descending the elevated and subway stairs and getting on and off buses. She is free from pain, but has paresthesia in the feet at times. The pupillary, ocular and tendon reflex signs are unchanged. The ataxia of the upper extremities is almost nil and has so ameliorated in the lower extremities that she can walk a straight line with only rare evidence of ataxia and Romberg's sign is scarcely perceptible.

Case No. 2. Diagnosis, Tabes Dorsalis. April, 1920. T. R. Q., male, 41 years old, married. Patient had a chancre fifteen years ago. For two years the patient has suffered from numbness in the feet, more marked in the left, urinary urgency, and attacks of stabbing pains in the legs and thighs and pectoral region, so severe, of late, as to prevent sleep. The pupils are unequal and react to light fairly promptly. The tendon reflexes at the knees and ankles are absent. The gait is ataxic and Romberg's sign is positive. Tests of sense of position in the upper and lower extremities are inaccurately performed. The patient has a mild aortic insufficiency.

April, 1921. The patient is working as an automobile salesman and is quite active. There is a slight residual ataxia evident in an occasional slight misstep with the left foot. Station is more secure. The reflex signs, tendon and pupillary, are unchanged. Aortic signs

Treatment and serology follow:

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells Globulin	
	Neo- arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.	c.m.	Excess
Dec. 10	0.6	40	4+	4+	4+	4+	2	1+
Dec. 17	0.6	50						
Dec. 21	0.6	40		4+	2+	1+	3	1+
1921								
Jan. 11	0.6	40		4+	4+	3+	0	1+
Jan. 21	0.6	40		4+	4+	2+	3	—
Feb. 1	0.6	30		4+	2+	1+	3	1+
Feb. 12	0.6	40		4+	4+	2+	3	—
Feb. 26	0.6	30		4+	3+	1+	0	1+
Mar. 11	0.6	40		4+	2+	1+	4	1+
Mar. 25	0.6	50	2+	4+	2+	1+	0	±
Apr. 8	0.6							
Apr. 26	0.6	40		2+	1+	1+	3	1+
May 14	0.6	40		4+	2+	1+	0	1+
May 28	0.6	40		3+	1+	—	0	1+
May 14.	Gold Sol., 5524331100.							

May, 1921. The patient's improvement has been very gradual. He has gained thirty pounds in weight since December. In walking he now uses but one cane, and can go up and down stairs. He still makes an occasional uncertain step. Strength has greatly improved. Recently he walked a mile and a half. Urinary control is now normal. The hypotonus of the knees is less evident. The reflex signs are unchanged.

Case No. 4. Diagnosis, Tabes Dorsalis. March, 1920. C. G., male, 36 years old, married. The patient denies having a chancre, but admitted having gonorrhea one year prior to marriage, fifteen years ago. His wife had no pregnancy. The onset of present illness, two months ago, was ushered in with urinary retention, staggering gait, pressure in abdomen and "general nervousness."

Recently he has had shooting pains in the legs, urgency of urination, and failing sexual potency. The patient presents decided insecurity in the Romberg position, ataxic gait, moderate incoördination in finger to nose and heel to knee tests, and absent knee and ankle jerks. The pupils are irregular, the right is sluggish and left does not respond to light.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells Globulin	
	Neo-arsphen gm.	with-drawn c.c.	Serum-mann	2 c.c.	1 c.c.	0.4 c.c.	c.m.	Excess
Apr. 14	0.6	45	4+	4+	4+	4+	296	1+
Apr. 24	0.6	50		4+	4+	2+	109	1+
Apr. 30	0.6	40	4+	4+	3+	2+	40	1+
May 6	0.6	30	4+	4+	3+	2+	76	1+
May 11	0.6	45	2+	4+	2+	1+	51	1+
May 18	0.6	30		4+	4+	2+	55	1+
Oct. 1	0.6	30		4+	4+	2+	28	1+
Oct. 5	0.6	50		4+	2+	1+	0	1+
Apr. 14, 1920. Gold Sol., 2555554310								

June, 1920. Patient shows marked improvement in gait and station. He can run up stairs. He can also use the pedals of an auto.

November, 1920. The patient shows continued improvement. He has complete control of the sphincters. He can almost succeed in walking a straight line, but missteps occasionally. There is moderate swaying in Romberg position. The finger to nose test is accurate. The reflexes remain unchanged. He has been able to keep at his work as a chauffeur, working ten hours a day.

Case No. 5. Diagnosis, Tabes Dorsalis. March, 1920. H. C., male, 39 years old, married. Venereal infection is denied. The onset of the present illness, two years ago, was marked by lightning pains, dimness of vision, and impotence. He now complains of occasional pains in the legs, slight unsteadiness in walking and numbness in the feet.

Physical examination reveals irregular, fixed pupils, slight temporal pallor of the discs, absent knee and ankle jerks, and very slight unsteadiness in the Romberg station. No other ataxia can be demonstrated. To date the patient has received thirty intravenous treatments of arsphenamine, with a certain amount of improvement but without change in the serology.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells Globulin	
	Neo-arsphen gm.	with-drawn c.c.	Serum Wassermann	2 c.c.	1 c.c.	0.4 c.c.	c.m.	Excess
Apr. 2	0.6	20	1+	4+	4+	4+	46	2+
Apr. 16	0.6	40		4+	4+	1+	24	1+
Apr. 25	0.6	25		3+	2+	1+	10	1+
July 1	0.6	60		2+	2+	1+	16	—
July 8	0.6	50	—	3+	2+	1+	8	1+
July 15	0.6	50		2+	1+	—	6	—
July 22	0.6	45		1+	1+	1+	5	—
Aug. 5	0.6	65		1+	—	—	0	—
Nov. 1	0.6	35	—	—	—	—	0	—
1921								
Feb. 10	0.75	45	—	—	—	—	0	—

February, 1921. The patient is quite recovered. He is without complaint. This is not a euphoric state, as he is leading a very active life. Among other activities he plays several sets of tennis twice a week. Physical signs are the same as one year ago.

Case No. 6. Diagnosis, *Tabes Dorsalis*. March, 1920. M. H., male, 32 years old, single. Syphilis is denied; gonorrhea is admitted ten years ago.

The onset of the present illness, two years ago, was marked by pain in the legs, unsteadiness in walking and standing, failing sexual power, and double vision. There was gradual increase in all the symptoms to such an extent that he is unable to walk unsupported. He is unable to get up and down stairs, is incontinent of urine, is impotent, suffers sharp pains in legs, has a girdle sensation and has drooping of the right eyelid.

Examination shows marked ataxia and incoördination of all the extremities. The patient is unable to stand with the eyes closed even when feet are widely separated. He is unable to walk twenty-five feet and keep in a path a yard wide. In the finger-to-nose test there is extreme ataxia and dysmetria. He often misses the face entirely when trying to touch the nose. He is equally as ataxic in the lower extremities. The knee and ankle jerks are absent and there is loss of postural and vibratory sense in the toes and feet. Argyll-Robertson pupils and partial paralysis of right third and left sixth cranial nerves are present.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo-arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
Apr. 9	0.6	40	4+	4+	4+	4+	73	3+
Apr. 16	0.6	20		4+	4+	4+	44	2+
Apr. 23	0.6	30		4+	4+	4+	33	1+
Apr. 30	0.6	40		4+	3+	2+	6	1+
May 7	0.6	25		4+	4+	2+	9	1+
May 18	0.6	30		4+	4+	2+	8	3+
May 21	0.6	15		4+	4+	2+	8	1+
May 28	0.6	30		4+	2+	1+	6	1+
June 22	0.6	40		4+	3+	1+	4	1+
June 29	0.6	40		4+	2+	1+	14	2+
July 2	0.6	25		4+	3+	1+	0	1+
July 7	0.6	30		4+	3+	1+	0	1+
July 20	0.6	20		3+	1+	—	2	1+
July 30	0.6	40		4+	2+	1+	R.B.C.	1+
Aug. 3	0.6	25	4+	4+	4+	2+	2	1+
Sept. 28	0.6	30		4+	4+	3+	38	1+
Oct. 4	0.6	25		4+	4+	4+	12	1+
Oct. 11	0.6	35		4+	4+	2+	6	1+
Oct. 18	0.6	35	4+	4+	4+	4+	3	1+
Oct. 25	0.6	30		4+	4+	4+	4	1+
Oct. 31	0.6	40		4+	4+	4+	6	1+
1921								
Feb. 1	0.6	45		4+	4	4+	108	2+
Feb. 8	0.6	30		4+	4+	4+	21	2+
Feb. 15	0.6	40		4+	4+	4+	36	1+
Mar. 1	0.6	35		4+	4+	2+	13	1+
Mar. 8	0.6	30		4+	4+	2+	6	1+
Mar. 15	0.6	45	4+	4+	4+	2+	17	1+

Wide variations in the colloidal gold curve, have been noted in numerous cases, during treatment. As an example of this variation, that of this case is cited below. The significance of this variable chemical reaction is not obvious.

Apr. 9, 1920. 4554332200; Apr. 30, 1920. 1112221000; May 18, 1920. 1222110000; June 22, 1920. 1122110000; June 29, 1920. 2434321110; July 2, 1920. 1111100000; June 1, 1921. 2233311000.

June, 1920. The patient has improved in many respects. The gait is more secure, but still ataxic. The flail-like swinging of left leg has practically ceased. The finger-to-nose test is executed with only slight dysmetria and ataxia, whereas there was formerly an inaccuracy from three to five inches. There is still ptosis of right eyelid and weakness of left external rectus, some wobbling on the heel-to-knee test, positive Romberg sign and slight loss of postural sense in both great toes. The reflexes are unchanged.

March, 1921. There has been progressive improvement since treatment began, one year ago. The patient has been steadily at work for some months, and has little difficulty in walking. He is free from pain except at rare intervals. When pain recurs it is very slight. Examination now shows ability to stand in the Romberg position with eyes closed, but with considerable swaying. The gait shows only slight ataxia. The finger-to-nose and heel-to-knee tests are executed almost perfectly. The ptosis of the right eyelid

has disappeared, but there is slight paresis of left external rectus. Sensation is normal. The Argyll-Robertson pupils and absent knee and ankle jerks are unchanged.

Case No. 7. Diagnosis, *Tabes Dorsalis*. August, 1919. A. R., male, 39 years old, married. Patient suffered a chancre twenty years ago, for which he took mercury and iodides for two years. He remained well until September, 1918, when he began having pains and stiffness in right knee and left arm, stabbing pain in muscles of legs and unsteadiness in walking. The symptoms grew gradually worse during the past year. No sphincter disorder or loss of sexual power was complained of.

The patient presents the following signs: ataxic station and gait; absent knee and ankle jerks; unequal, irregular and sluggish pupils; pedal incoördination; loss of postural sense in toes, and hypalgesia in radicular areas in the legs. Prior to drainage the patient had received sixteen intravenous treatments.

Treatment and serology were as follows:

	C. S. Fluid			C. S. F. Wassermann			Cells Globulin	
	Neo-arsphen gm.	with-drawn c.c.	Serum Wassermann	2 c.c.	1 c.c.	0.4 c.c.	c.m.	Excess
1920								
Mar. 15	0.6	40	—	4+	4+	4+	152	3+
Mar. 22	0.6	30						
Mar. 29	0.6	50		4+	3+	2+	56	1+
Apr. 8	0.6	20		2+	1+	—	11	—
June 2	0.6	30		2+	2+	1+	11	—
June 9	0.6	60		3+	1+	1+	32	1+
1921								
Mar. 29	0.6	30		4+	2+	1+	0	±
Mar. 15, 1921. Gold Sol., 1224333300.								

June, 1920. The patient has been at work six weeks as a mechanic and feels quite well. He has an occasional pain with change of weather. The insecure station and ataxic gait have disappeared, and sensory examination shows only slight postural disorder in toes. The reflexes and pupils remain as first noted.

February, 1921. The patient remained well until a few weeks ago, when he noticed a return of pain in the legs. This disappeared after a dose of calomel. The only treatment since June, 1920, has been thirty mercurial rubs. No objective sensory disorder can be demonstrated; otherwise the examination is the same as noted in June, 1920.

Case No. 8. Diagnosis, *Tabes Dorsalis*. September, 1920. A. S., male, 35 years old, married. Venereal infection is denied. The duration of the present illness is about two years. He complains of difficulty in walking and "no feeling in the legs and feet." He suffers frequently with severe pains in legs, inability to hold the urine, and, at times, difficulty in starting urination.

With great difficulty the patient can walk with the aid of two

canes. The feet are lifted high and thrown forward in a flaccid ataxic gait. There is hypotonus of legs with genu recurvatum. The patient is unable to stand in the Romberg position. When attempting the heel-to-knee test he frequently lets the heel fall on the shin; then again it falls far above the patella. The knee and ankle jerks are absent. The pupils are irregular, unequal and rigid to light. Postural and vibratory sense are lost in the feet, and there is definite hypalgesia corresponding to lower lumbar and upper sacral distribution.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo- arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
Oct. 2	0.6	15	4+	4+			13	1+
Oct. 9	0.6	30		3+			10	1+
Oct. 16	0.6	20		4+			11	1+
Oct. 23	0.6	35		4+			10	±
Oct. 30	0.6	20		2+			2	1+
Nov. 13	0.6	45		4+	3+	1+	31	2+
Nov. 20	0.6	40		3+	1+	1+	3	±
Nov. 27	0.6	40		3+	1+	1+	3	1+
Dec. 14	0.6	30		2+	1+	—	2	—
Dec. 21	0.6	45		3+	1+	1+	3	1+

December, 1920. The patient states that he has less pain and he thinks he is not so uncertain in his walking. The dead feeling in his feet has improved. Objectively no change can be noted. He is as ataxic as on previous examination. There is probably slight improvement in deep muscle and joint sensibility.

Case No. 9. Diagnosis, *Tabes Dorsalis*. September, 1920. W. W., male, 42 years old, married. The patient denies venereal infection. His wife has never been pregnant. The duration of the present illness is four years. The patient complains of unsteadiness and difficulty in walking. He has frequent lightning-like, stabbing pains in the arms and legs. He complains of a girdle sensation around the abdomen and inability to hold the urine.

Patient is unable to stand in the Romberg position with eyes open or closed. His gait is staggering, ataxic and on a broad base. Manual and pedal incoördination is so marked that he frequently missed his face entirely when trying to bring finger to nose, and when an attempt is made to locate the knee with the heel he misses the point from three to six inches. The deep reflexes in upper and lower extremities are abolished. There is paresis of the right sixth and left third cranial nerves. The pupils are unequal and do not react to light. Postural sense is lost in the toes and greatly diminished in ankles and knees.

The patient has received fifty intravenous treatments before drainage was instituted. Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo- arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
Sept. 30	0.6	15		4+	4+	4+	44	2+
Oct. 7	0.6	15		4+	4+	4+	20	2+
Oct. 21	0.6	15		Bloody				
Oct. 29	0.6	15		4+	4+	4+	21	2+
Nov. 4	0.6	30		4+	4+	4+	9	1+
Nov. 11	0.6	35		4+	4+	4+	5	1+
Dec. 7	0.6	30		4+	4+	4+	13	1+
Dec. 17	0.6	25		4+	4+	4+	29	1+
Dec. 24	0.6	35		4+	4+	4+	16	1+
Dec. 31	0.6	30		4+	4+	4+	8	1+
1921								
Feb. 4	0.6	15		4+	4+	4+	89	1+
Feb. 11	0.6	25		4+	4+	4+	6	1+
Feb. 18	0.6	35		4+	4+	4+	10	1+
Feb. 26	0.6	15		4+	4+	4+	16	1+
Sept. 30, 1920.	554432	1000						
Feb. 18, 1921.	5555543	200						

December, 1920. The patient is greatly improved. He seldom has any pain. His gait is greatly improved. Paresis of the left third cranial nerve has disappeared. The right external rectus still is parietic. He has gained weight and states he can work all day as a transit man, but he cannot set his transit over the tack.

March, 1921. For the past six weeks the patient has been more uncertain in his movements. He had to give up his work as a surveyor and take an office job. He complains of pain on damp, cold days. He feels better, but there is equally as much ataxia as on first examination. The reflexes and sensations are unchanged.

Case No. 10. Diagnosis, Tabes Dorsalis. May, 1920. J. M., male, 48 years old, married. The patient had a chancre twenty-five years ago. His wife was never pregnant. During the present illness of seven years' duration there has been gradual progression of unsteadiness in standing and walking. He suffers from pains in legs and difficulty in urination. The examination shows marked Romberg and ataxic gait, bilateral hypotonus of legs, marked pedal incoordination, absent knee and ankle jerks and Argyll-Robertson pupils.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo- arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
May 13	0.6	45	4+	4+	4+	4+	58	1+
May 21	0.6	40	4+	4+	4+	4+	44	1+
May 27	0.6	22	4+	2+	2+	2+	26	1+
June 4	0.6	25	4+	2+	1+		8	—
							R.B.C.	
June 11	0.6	30	4+	4+	2+	2+	0	1+
June 18	0.6	35	4+	2+	2+	2+	6	—
July 27	0.6	25	4+	4+	2+	2+	15	1+
Aug. 3	0.6	30	4+	2+	1+	1+	13	1+
Aug. 10	0.6	25	4+	4+	2+	2+	24	2+
Aug. 10.	Gold Sol.,	11100000000						

January, 1921. Patient states that he feels better generally and that there is very decided decrease in the severity and frequency of pain in the legs, and that he has a sense of greater security in walking. Ataxia in gait is still obvious. The reflex and pupillary signs are unaltered.

Case No. 11. Diagnosis, Tabo-Paresis. May, 1920. P. C., male, 34 years, married. The patient suffered a chancre twelve years ago which was treated locally.

The present symptoms, shooting pains in the legs, difficulty in urination and muscular fatigue, were first noticed four months ago. He became irritable and excitable. Examination shows slight ataxia of gait and station; very slight incoördination of upper extremities; absent knee and ankle jerks, and Argyll-Robertson pupils.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo- arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
May 25	0.6	30	1+	4+	4+	4+	31	1+
June 2	0.6	35		4+	4+	3+	33	1+
June 8	0.6	20		4+	3+	1+	22	1+
June 15	0.6	45		4+	2+	1+	11	1+
June 22	0.6	30		1+	1+	—	12	1+
June 29	0.6	35	2+	2+	1+	1+	6	1+
Sept. 28	0.6	30		4+	3+	1+	15	1+
Oct. 5	0.6	35		4+	4+	2+	15	2+
Oct. 12	0.6	30		4+	4+	2+	9	1+
Oct. 19	0.6	35		4+	4+	2+	5	1+
Oct. 26	0.6	50		4+	4+	1+	13	1+
Nov. 9	0.6	45	4+	2+	1+	—	9	1+
Nov. 16	0.6	40		3+	1+	1+	9	1+
Dec. 21			4+					
1921								
Feb. 11	0.6			4+	4+	2+	12	1+
Feb. 16	0.6	35		4+	4+	2+	8	1+
Feb. 23	0.6	45		4+	4+	4+	40	1+
Mar. 1	0.6	30		4+	4+	4+	8	1+
Mar. 11	0.6	40		4+	4+	4+	13	1+
Mar. 19	0.6	35		4+	4+	4+	4	1+
May 24	0.6	35		4+	4+	2+	3	1+
June 1	0.6	30		4+	2+	1+	5	1+

June 22, 1920. Gold Sol., 5555543210; Feb. 11, 1921. Gold Sol., 5555532110;
Feb. 23, 1921. Gold Sol., 5555543110; Mar. 1, 1921. Gold Sol., 5555332100;
Mar. 11, 1921. Gold Sol., 5555421100; Mar. 18, 1921. Gold Sol., 5555431000;
May 5, 1921. Gold Sol., 5554311000; June 1, 1921. Gold Sol., 5555421000.

February, 1920. The patient states that the pain is greatly diminished and that control of sphincters is normal. The physical examination is as noted above, and in addition there is a very slight facial and labial tremor; memory is defective, and there is an attitude of indifference regarding his illness. He cannot repeat test phrases.

May, 1921. The condition of the patient seems stationary. He is able to conduct a small shop despite his moderate excitability and memory disorder for recent events. He cannot remember test

phrases correctly, but there is no slurring of speech. The physical signs are unaltered. The labial and lingual tremors are not always perceptible.

Case No. 12. Diagnosis, *General Paresis*. May, 1920. J. S., male, 50 years, single. Patient had a chancre in 1904. He took mercury and iodide for two years. He complains of shooting pains in arms and legs and impotence of three years' duration. He shows active knee and ankle jerks, irregular pin-point pupils, fixed to light, slurring speech, tremors of face and tongue, failing memory and poor judgment, flights of ideas and euphoria.

Treatment and serology were as follows:

1920	C. S. Fluid			Serum			Cells Globulin c.m. Excess	
	Neo-arsphen gm.	with- drawn c.c.	Wasser- mann	C. S. F. 2 c.c.	Wassermann 1 c.c.	0.4 c.c.		
May 11	0.6	35	4+	4+	4+	4+	3	1+
May 18	0.6	25		4+	4+	2+	12	1+
May 25	0.6	30		4+	3+	2+	0	1+
June 2	0.6	40	4+	4+	4+	2+	13	1 ⁺
June 9	0.6	25		3+	3+	2+	13	1+
June 16	0.6	45		4+	4+	2+	10	1+
July 27	0.6	30		4+	3+	1+	5	1+
Aug. 10	0.6	30		4+	2+	—	8	1+
Sept. 28	0.6	25		4+	4+	2+	24	1+
Oct. 2	0.6	20	—	4+	3+	1+	12	1+
Oct. 9	0.6	20		4+	3+	1+	12	1+
Oct. 16	0.6	30		4+	2+	1+	9	1+
1921								
Feb. 4	0.6	25	1+	4+	4+	2+	22	1+
Feb. 23	0.6	40		3+	1+	1+	10	1+
Mar. 11	0.6	30	—	4+	2+	2+	25	1+

Mar. 11, 1920. Gold Sol., 1122110000; Mar. 11, 1921. Gold Sol., 3222211000.

April, 1920. The patient presents practically the same picture as on admission a year ago. He is little concerned over his illness. There is decided lack of attention and loss of insight. His speech is of parietic type. He is quiet and uncommunicative. Gradual deterioration has been evident.

Case No. 13. Diagnosis, *General Paresis*. September, 1920. C. McK., male, 44 years old, married. The patient denied having had syphilis, but admitted having had gonorrhea some years ago. The present symptoms are of one year's duration. There has been progressive deterioration of memory and increasing irritability and impatience. Ordinarily he is quiet and taciturn, but displays periods of great excitement and anger, without cause. He has become unable to continue his occupation, playing the piano in an orchestra. He is careless in his habits and occasionally soils himself.

Examination shows a slight swaying in the Romberg position. The gait is slightly ataxic. The finger-nose and heel-knee tests are well performed. There is marked tremor of the face, tongue and hands. The knee and ankle jerks are hyperactive. The deep

reflexes in the upper extremities are active and equal. The Kleppel-Weil sign is present in both hands. No disturbance of sensation could be determined. The pupils are irregular and do not react to light. Speech is slurring and there is stumbling in test phrases. The patient is jovial and manifests a juvenile amusement at the tests. Memory for recent events is very poor. Emotional outbursts are frequent.

Treatment and serology were as follows:

1920	C. S. Fluid			C. S. F. Wassermann			Cells c.m.	Globulin Excess
	Neo-arsphen gm.	with- drawn c.c.	Serum Wasser- mann	2 c.c.	1 c.c.	0.4 c.c.		
Oct. 1	0.6	40	4+	4+	4+	4+	129	2+
Oct. 8	0.6	40		4+	4+	4+	28	2+
Oct. 15	0.6	40		4+	4+	4+	16	2+
Oct. 22	0.6	50		4+	4+	4+	16	2+
Oct. 29	0.6	30		4	4+	4+	6	2+
Nov. 5	0.6							
Nov. 12	0.6							
Nov. 26	0.6	45		4+	2+	—	4	2+
Dec. 4	0.6							
Dec. 10	0.6	35		4+	4+	2+	4	1+
Dec. 17	0.6	30		4+	4+	2+	6	2+
1921								
Jan. 7	0.6	45		2+	1+	1+	3	2+
Jan. 14	0.6	35		4+	4+	2+	3	1+
Jan. 21	0.6	35		4+	4+	2+	5	2+
Oct. 8.	Gold Sol., 5555555332							

November, 1920. The patient manifests a certain insight into his condition and expresses a degree of concern regarding it. His wife states that he is less irritable and less restless, and that he sleeps better. He is coöperative with the physician and his conduct exemplary.

January, 1921. No substantial improvement has taken place since that noted above. He is less irritable and emotionally more stable, but has deteriorated intellectually. The tremors, reflex changes and other physical signs are as originally noted.

In forming opinions concerning therapy in syphilis of the nervous system, one may expect favorable results only in cases in which disordered function is due to perivascular exudate. Where degeneration of nervous tissue has occurred, naturally no improvement will follow treatment. The majority of cases, when first applying for treatment, are pathologically of mixed type, combining exudation and parenchymatous degeneration. There is no positive clinical method of determining the degree of each state except by pushing anti-syphilitic therapy to the limit. To be sure, certain serological and physical findings are suggestive, but not absolute. General paresis and tabes dorsalis of long standing without efficient treatment present the largest proportion of parenchymatous deterioration of nervous tissue. In cerebrospinal syphilis and early tabes the exuda-

tive pathology predominates, and in them the most favorable results may be expected from treatment. It is the exudative pathological condition which may be remedied. And it is in the perivascular and perineural spaces that the cause of the exudative inflammatory reaction, the spirochaete, must be attacked. Perhaps the beneficial feature of spinal drainage is not an increased quantity of arsenic in the cerebrospinal fluid, but the fact that a lowered pressure in the cavities surrounding the central nervous system permits a dilatation of the capillaries, with consequent increase in the quantity of medication-bearing blood in the parts. For, it is in the perivascular and perineural spaces that the spirochaete must be attacked.

In many cases the serological changes do not parallel the clinical improvement. Even when the spinal fluid Wassermann is persistently fixed, progressive clinical improvement may have occurred.

As a result of this piece of clinical research, of which some of the results appear above, and our experience during the past ten years in treating syphilis of the nervous system with the various arsenical preparations by the simple intravenous administration, by the several intraspinal methods and by combinations of these with mercurial treatment, we have arrived at the following conclusions:

1. No single method of treatment is applicable to all cases.
2. The intravenous administration of arsphenamine is the method of choice.
3. Spinal drainage after intravenous administration of arsphenamine is not a hazardous procedure.
4. Drainage will benefit some cases which have arrived at a position of inertia under intravenous administration alone.
5. As satisfactory clinical and serological results may be obtained by intravenous arsphenamine and drainage as are produced by the intraspinal method and without the severe root-pains frequently set up by the latter method.

BIBLIOGRAPHY

1. L. H. Weed. Development of the cerebrospinal spaces in the pig and in man. Wash. 1917. Carnegie Institute. Vol. 5, No. 14. Contributions to Embryology.
2. J. F. McClendon. The formation and composition of the cerebrospinal fluid. J. A. M. A. 70:977, April 6, 1918.
3. W. D. Halliburton. The possible function of the cerebrospinal fluid. Brain Vol. 39, page 213, Oct. 1916.
4. W. Mestrezat. Le liquide cephalo-rachidien normale et pathologique. Paris. A. Maloine, 1912.
5. Sicard and Block. Bull. et men. Soc. Med. d. hop de Paris Series 3 p. 894; compt. rend. Soc. de biol. 1910: 69:624.
6. C. D. Camp. Note on the examination of the cerebrospinal fluid for arsenic following the administration of Salvarsan. THE JOURNAL OF NERVOUS AND MENTAL DISEASE. Vol. 39, page 807. Dec. 1912.

7. P. Revaut. Les reactions nervouses tardives. *La Presse Médicale*. Vol. 20, page 181. March 1912.
8. B. Sachs, I. Straus, D. J. Kaliski. Modern methods of treatment of syphilis of the nervous system. *Amer. Jour. Med. Sc.* Vol. 148, page 693. Nov. 1914.
9. M. F. Engman, R. Bahman, F. D. Gorham, R. H. Davis. A study of the spinal fluid in one hundred cases of syphilis. *J. A. M. A.* Vol. 61, page 735. Sept. 6, 1913.
10. G. W. Hall. The presence of arsenic in the spinal fluid. *J. A. M. A.* Vol. 64, page 1384. April 24, 1915.
11. J. B. Reiger and H. C. Solomon. The circulation of arsenic in the cerebrospinal fluid. *J. A. M. A.* 71:15. July 6, 1918.
12. L. H. Weed, P. Wegeforth, J. B. Ayer, L. D. Felton. The production of meningitis by release of cerebrospinal fluid. *J. A. M. A.* Vol. 72, page 190. Jan. 18, 1919.
13. H. G. Mehrrens, H. F. West. The absorption of phenolsulphonephthalein from the subarachnoid space in diseases of The Central Nervous System. *Arch. Int. Med.* Vol. 20, page 575. Oct. 1917.
14. P. G. Weston. Phenolsulphonephthalein absorption from the subarachnoid space in Paresis and Dementia Praecox. *Am. Arch. Neur. & Psych.* 5, 58. Jan. 1921.
15. W. E. Dandy and E. D. Blackfan. An Experimental and Clinical Study of Internal Hydrocephalus. *J. A. M. A.* 61, 2216. December 20, 1913.
16. G. C. Fisher. A preliminary report on a new method of treatment for cerebrospinal syphilis. *Illinois Med. Jour.* Vol. 27, page 380. May 1915.
17. J. H. Barbat. Preliminary report on the finding of arsenic in the cerebrospinal fluid following intravenous administration of Neo-Salvarsan. *Calif. State Journal Med.* Vol. 13, No. 11, page 438. Nov. 1915.
18. F. W. Mott. The cerebrospinal fluid. *Lancet*, 1910, Vol. 2, page 1. July 2.
19. Gilpin and Early. Drainage of the cerebrospinal fluid as a factor in the treatment of Nervous Syphilis. *J. A. M. A.* 66, 260. Jan. 22, 1916.
20. J. H. Barbat. Permeability of the meninges to arsenic in Paresis and Tabes. *J. A. M. A.* Vol. 70, No. 3, page 147. Jan. 19, 1918.
21. J. H. Stokes and E. D. Osborne. Relative effectiveness of various forms of treatment in Neurosyphilis. *J. A. M. A.* 76, 108. Mar. 12, 1921.
22. C. B. Craig. Meningitis due to shell wound. *JOUR. NERV. & MENT. Dis.* Vol. 47, page 100. Feb. 1918.
23. H. M. Adler and A. J. Wetmore. *Boston Med. & Surgical Jour.* 171:900. 1914.