

GENERAL PARALYSIS TREATED BY INTRAVENTRICULAR INJECTION OF ARSPHENAMIN

REPORT OF THE NECROPSY FINDINGS IN A CASE *

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Following the discovery of the *Treponema pallidum* in the brain in cases of general paralysis, and encouraged by the reported favorable results obtained in the treatment of neurosyphilis by the intraspinal injection of arsphenamin as advocated by Swift and Ellis and by Ogilvie, many men began to treat general paralysis with arsphenamin, administering the drug either by the intravenous or intraspinal method. The results obtained are now well known to those who have followed the evolution of therapy of neurosyphilis since the introduction of arsphenamin. Failing to obtain as favorable results from the use of arsphenamin in paresis as from its employment in the more benign forms of neurosyphilis, and stimulated by the results from animal experimentation, Hammond and Sharpe¹ introduced a method of injecting arsphenamin into the ventricles of the brains of the cases of general paralysis, hoping to get the drug more closely to the site of the pathologic process. They reported a series of cases which showed clinical improvement following this mode of treatment. Many observers were impressed with these results, and Neymann and Brush,² in their analysis of the different forms of treatment of paresis, spoke very favorably of this method.

The following case is of interest as it is the first case which has received this form of therapy, and has been studied clinically as well as at the postmortem examination.

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* Presented before the New York Neurological Society, Oct. 1, 1918.

1. Hammond, G. M., and Sharpe, Norman: The Treatment of Paresis by Injections of Neosalvarsan into the Lateral Ventricle, J. A. M. A. **65**:2147 (Dec. 18) 1915.

2. Neymann, C. A., and Brush, N. H.: The Treatment of General Paresis, Arch. Int. Med. **22**:245 (August) 1918.

REPORT OF CASE

History.—H. F., a man aged 40, was born in New York City of German parentage. He was graduated from the public school. He married in 1905 and has one living child; no miscarriages. He drank early in life, but he was a good provider for the family. He was of a happy disposition and was well liked by his friends. He has had several attacks of rheumatism. No knowledge of any venereal diseases. Worked satisfactorily as a carpenter. In December, 1915, he showed the first evidence of the disease, becoming forgetful. He continued to work until the middle of 1916, when his memory became so poor that he had to discontinue his work. At the same time he became irritable, showed speech defect, and began to manifest unsteadiness in walking. He later became grandiose in his statements, saying that he was a millionaire, etc. He finally became very restless and was sent to the Post-Graduate Hospital for treatment.

Clinical Course.—In March, 1917, he received one intraventricular injection of arsphenamin, through a trephined opening in the skull. Subsequently he was transferred to Bellevue Hospital, where he was characterized by the physicians as being simple, childish, dull in speech; wandered about in an aimless manner; was very irritable; was expansive in his statements; his pupils were small and irregular and did not react to light; knee jerks were increased.

Examination.—He was admitted to the Manhattan State Hospital on May 16, 1917. An examination in this institution revealed considerable mental deterioration; he said he was a carpenter and that he was feeling fine, and that he had to go to work. He did not know when he was married. He was disoriented. He had no memory on immediate past. He did small calculations very poorly. His speech showed considerable defect. He could not interpret what he had read. He had no insight. He expressed grandiose ideas. His judgment was poor. Physically, he showed good nutrition. Pupils were irregular, unequal and reacted very sluggishly to light. Spinal fluid showed positive globulin, 54 cells, and a ++++ Wassermann reaction.

Subsequent History.—He soon began to soil himself and became quite ataxic. He was very euphoric in the latter part of May, and his speech became so defective as to be hardly understood. On June 27 he developed convulsions and died on the following day.

ANATOMIC SUMMARY

Necropsy performed fifteen hours postmortem. The remains of a well developed, and of a moderately well preserved man appearing about 40 years of age. Rigor mortis was present in all extremities. Excepting slight abrasions over the sacrum and over the right knee, there was nothing of significance noticed in the skin of the body. Over the junction of the parietal and frontal bones, just to the left of the midline, a distinct depression of the scalp was seen. This was due to a defect in the subjacent bone evidently caused by a trephined area in the skull, 3 by 2 cm. in size. The scalp at this area was adherent to the subjacent dura. The calvarium stripped with considerable ease, and left a pale dura beneath it. Immediately beneath the trephined area in the skull there was a semicircular incision in the dura; the

resultant flap in the dura was half the size of a 5-cent piece. The edge of the flap was adherent to the subjacent pia-arachnoid by only very thin fibrous tissue, and it could readily be lifted from the underlying tissue. The dura as a whole appeared quite pale, and over the anterior

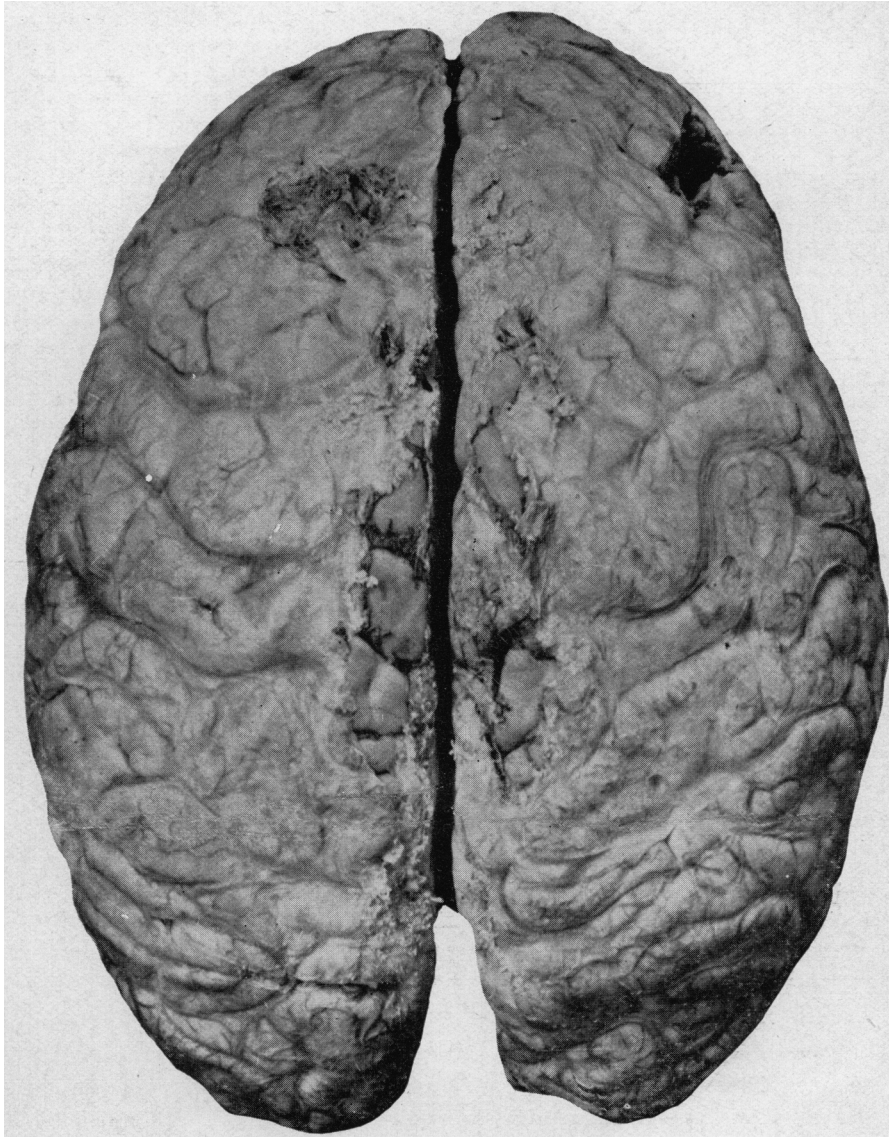


Fig. 1.—Note thickened pia and characteristic appearance of exudate. Left hemisphere more involved than right. The defect in the right frontal lobe was caused by removal of a section for fixation in alcohol. The pia-arachnoidal flap is in the plane of the arrow.

third of the brain, most marked over the frontal poles, it was decidedly puckered and redundant. There was no pathologic condition found in the dura. The vessels in the dura were of the normal size and

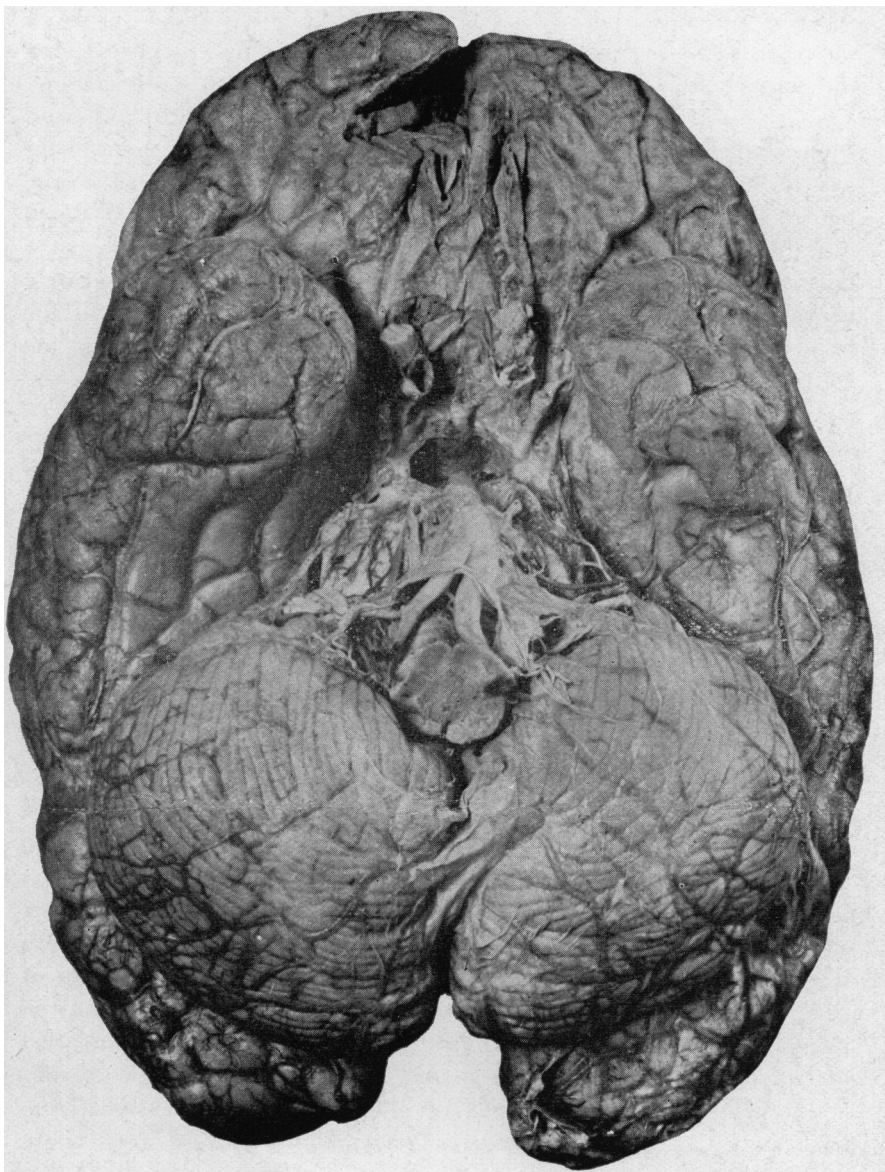


Fig. 2.—Note exudate on the base of the brain. Lesion is greater on the left side. Note exudate over the left side of the cerebellum. The defect in the right gyrus rectus was caused by removal of section for fixation in alcohol.

appearance. On incision of the dura and arachnoid an excessive amount of cerebrospinal fluid escaped.

The brain weighed 1,175 gm. It was of medium size, and its consistency was about normal. The pia over the anterior two-thirds of the brain showed a characteristic milky cloudiness and thickness; over the posterior third of the brain the pia was fairly clear and glistening. The base of the brain, especially over the interpeduncular spaces, showed thickened and clouded pia. The pia over the left hemisphere was decidedly more thickened and evidently more involved than the pia over the corresponding parts of the right hemisphere. The pia over the cerebellum, and also in the ponto-cerebellar angles, was of a milky, clouded appearance. On lifting the flap of dura immediately beneath the trephined area in the skull there appeared a part of the brain cortex, evidently due to the adhesion of the dural flap to the subjacent pia-arachnoid. Characteristic granulations were seen in the gyri recti and in the ventricles, especially on the floor of the fourth ventricle. There was considerable atrophy in the frontal lobes, the convolutions being well rounded out and the sulci and fissures were quite wide and shallow. The large vessels, namely, the basilar, internal carotids, and the cerebrals were quite normal in their macroscopic appearance. No hemorrhagic areas were noticed.

Sections from the superior frontal, precentral, paracentral and occipital convolutions, from the gyrus rectus, and from the lobule immediately beneath the trephined area, and from the medulla and cerebellum were examined microscopically. The pia showed considerable edema; there was present the characteristic lymphoid and plasma cell infiltration, especially about the pial vessels; numerous mast cells were also seen; the exudate was greater in the sections from the left hemisphere. The neuroglia layer was thicker than normal, and throughout the cortex there was noted an increase in neuroglia cells; in several places there were typical pictures of satellitosis. The cortex showed considerable disorganization; there was much edema; the cells were found in all stages of degeneration and characteristic pictures of cloudy swelling and granular degeneration were noticed, especially in the sections from the left hemisphere. The perivascular exudation of lymphoid and plasma cells was quite striking. Numerous mast cells and a small number of rod cells were also noted. The sections from the cerebellum and from the occipital lobule showed very slight pathologic changes as compared with the sections from the other regions studied. The sections from the left hemisphere showed more edema, greater exudation and a more advanced cortical disorganization than the sections from the right hemisphere. The spinal cord showed nothing of significance macroscopically; but microscopically,

considerable degeneration was noticed in the fibers of the posterior columns stained by the Marchi method. Sections from the right optic nerve showed many lymphoid and a few mast cells running through the nerve. The other cranial nerves showed no significant changes macroscopically. The internal ears were opened and found in normal condition.

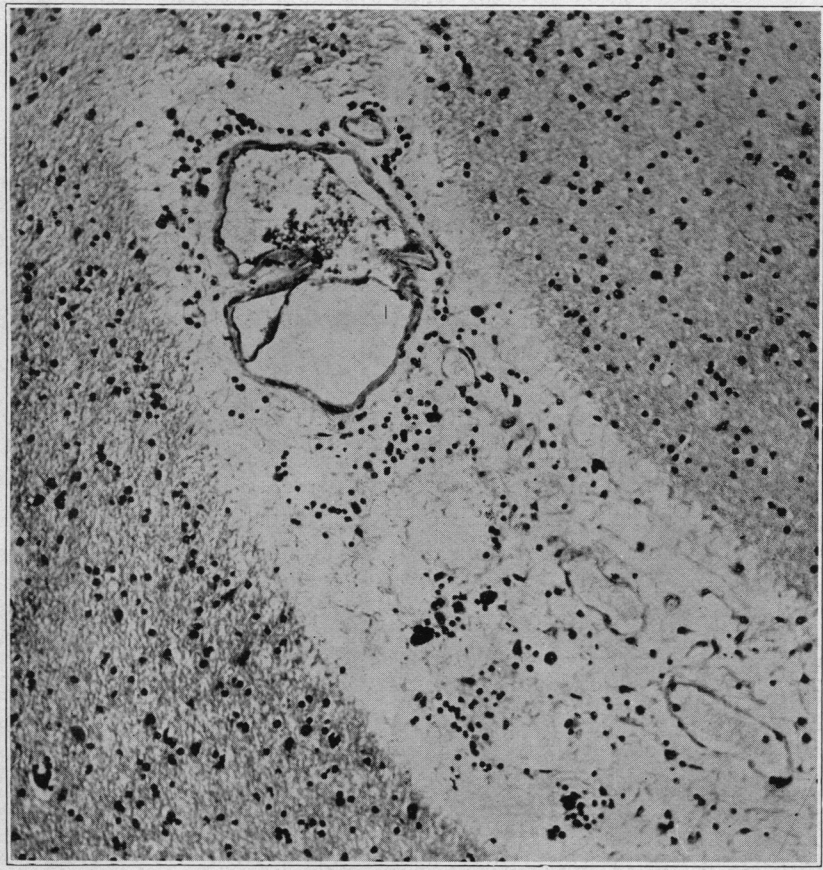


Fig. 3.—Note infiltration of pia with lymphoid and plasma cells; considerable edema of pia is present. Note increase in neuroglia cells in the adjacent cortex.

The *pituitary* gland did not present anything of significance. The *thyroid* gland was of normal appearance; the alveoli were distended with colloid and the cells were definitely flattened. The *thorax* was externally symmetrical; the sternum stripped with ease; the costal cartilages were not calcified. Both pleural cavities were free from fluid, but each contained moderately dense adhesions in the apices.

The *right lung* weighed 580 gm. and the left 560 gm.; the apices showed definitely healed tuberculous nodules which had been partly replaced by calcium salts, and between these nodules there were numerous strands of connective tissue; the posterior portions of the lower lobes showed distinct edema and bronchopneumonic patches.

The *pericardium* was free from fluid and adhesions. The *heart* weighed 330 gm.; it was covered on its anterior surface by a very

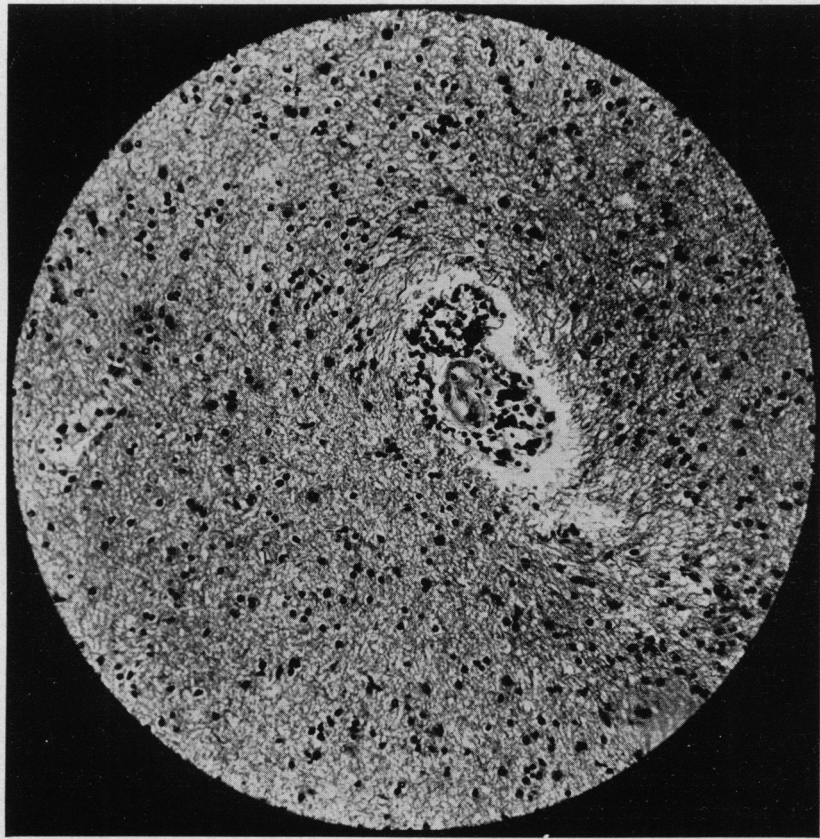


Fig. 4.—Note the perivascular exudation of lymphoid and plasma cells around two small cortical vessels. There is also seen an increase in neuroglia cells in the cortex.

thick fat pad; it was of normal size and consistency; all valves were compensating and their cusps were quite delicate; the papillary muscles were normal in appearance; the coronaries were patent. The *aorta* presented a characteristic picture; the arch was definitely dilated; there was a decided loss of elasticity in the entire aorta; throughout the thoracic portion there were numerous linear scars and pearly nodular

elevations; the abdominal portion was relatively free and only an occasional yellow-colored ulcerated area was seen; microscopically, the intima presented a fairly normal appearance; the media was infiltrated with many lymphoid and plasma cells which in places were grouped and assumed a picture which was highly suggestive of miliary gummas, the adventitial vessels showed perivascular exudations of lymphoid and plasma cells.

The *abdomen* was scaphoid; the panniculus adiposis was of medium size and of normal color; the peritoneal cavity was free from fluid; the omentum extended into the pelvis and in the left hypochondrium it was adherent to the peritoneum by thin but firm adhesions. The appendix was entangled in a mass of adhesions; it had an injected inflammatory appearance. The *stomach* was distended with gas and was otherwise of a normal appearance; the rest of the intestinal tract showed nothing of importance. The *spleen* weighed 130 gm.; it was of a normal size and appearance, and of a slightly increased consistency. The *liver* weighed 1,450 gm.; it was somewhat larger than normal, and its color was definitely yellow and its consistency was diminished; microscopically, the cells showed a condition of fatty infiltration and cloudy swelling. The gallbladder was distended with bile; all ducts were patent. The *pancreas* showed nothing remarkable. The *adrenals* were of normal size and consistency, and on section presented a normal cell layer arrangement.

The right *kidney* weighed 110 gm. and the left 140 gm.; the right appeared normal, but the left kidney showed a few adhesions between the capsule and the cortex, and the cut section presented a rather boiled appearance. The ureters showed nothing remarkable; the bladder was contracted. The genitals appeared normal.

ANATOMIC DIAGNOSIS

Trephined opening in the skull, diffuse meningo-encephalitis, bilateral bronchopneumonia and pulmonary edema, syphilitic aortitis, chronic appendicitis and fatty liver.

SUMMARY

A man, aged 40, married, who had one living child, a negative family history, but an alcoholic personal history, who had no knowledge of any venereal disease, began to show lapses of memory in December, 1915, which increased in severity so that he was obliged to discontinue his work as a carpenter in the middle of 1916; he then became irritable, showed speech defect and became ataxic; in March, 1917, he received one intraventricular injection of arsphenamin through a trephined opening in the skull. He was admitted to the Manhattan State Hos-

pital in May, 1917, when he showed disorientation, poor memory, expressed grandiose ideas; showed marked speech defect, pupils were unequal and reacted very sluggishly to light, and the spinal fluid showed positive globulin, 54 cells, and a positive Wassermann reaction. He soon began to soil himself, became very euphoric and died following a convulsion. The postmortem examination showed the characteristic lesions of general paralysis in the brain; namely, a thickened pia showing a characteristic milky exudate in the anterior two-thirds, atrophy of the anterior poles of the cortex, lymphoid and plasma cells infiltration into the pia, neuroglia increases, cortical disorganization and perivascular exudation of lymphoid and plasma cells, many mast cells and a few rod cells, granulations on the floor of the ventricles, syphilitic aortitis and bilateral bronchopneumonia and pulmonary edema; the lesions in the left side of the brain which received the arsphenamin were more intense than those in the right side.

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I am indebted to Dr. M. B. Heyman for allowing me to present and publish this case, and to Dr. F. C. Wood for the photomicrographs.