THE ALBUMEN CONTENT OF THE SPINAL FLUID IN ITS RELATION TO DISEASE SYNDROMES¹

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The routine examination of the spinal fluid as it is followed in the European and American clinics is an effort to determine the presence or absence of globulin in clinically appreciable quantities, of an increase in the cellular content, and the Wassermann reaction. A fluid negative to all these tests is declared negative, i. e., normal. It is the purpose of this paper to establish the fact that the presence or absence of an *increase* in the normal albumen content is an essential part of a spinal fluid examination and moreover that this constituent, or rather group of constituents, plays a rôle in the pathology of the nervous system of a peculiar and important character.

In the first large book devoted to the chemistry of the cerebro-spinal fluid, Mestrezat² gives an account of the history of the researches along this line as well as his own experience. He has found that the albumen content when increased always denotes organic disease. He gives an interesting and important account of the various disease syndromes in which this group of constituents is increased, and in particular lays stress upon the meningeal affections. He likewise speaks of the increase found in the syphilogenous diseases, general paresis, tabes, but here, like all the authors, his attention is directed mainly to the globulin increase. An important finding of Mestrezat's, but which he dismisses rather carelessly, is the increase of albumen found in "chronic alcoholism" (a very indefinite term), lead poisoning, etc. With his findings, as far as I have gone, I thoroughly agree, and I have to add some observations which my experience leads me to believe are of fundamental clinical importance.

¹ Read before Boston Society of Psychiatry and Neurology, November 20, 1913. Being contributions of the Psychopathic Hospital, Boston, Mass., 1914. Taunton State Hospital papers, 1914, I.

² W. Mestrezat, *Le Liquide Cephalo Rachidien*, Paris, Maloine, 1912, p. 223, etc.

For a year I have included in my routine examination of spinal fluid, a clinically quantitative estimation of albumen. Into a narrow test tube, one with a bore of about 6 mm., 2 c.c. of spinal fluid measured by a graduated pipette is dropped. The fluid is heated short of the boiling point and then 6 drops of a $33\frac{1}{3}$ per

FIG. 1. Illustrates the appearance of the spinal fluid immediately after the test. The degree of cloudiness or opalescence is shown. The difference between the normal, for example, that entitled dementia præcox, and the abnormal, designated as general paresis, etc., is well shown.

cent. aqueous solution of trichloroacetic acid is dropped into the warm liquid (Mestrezat). In the normal fluid there is at once a diffuse but not marked cloudiness which gradually settles in thirty minutes or thereabouts into a flocculent precipitate just covering the bottom of the tube. Where there is distinct increase there is a dense cloud which almost immediately becomes flocculent and

settles to a height of perhaps .5 cm., from the bottom of the tube. A very short experience is sufficient to enable one to recognize the difference between the normal amount and any decided increase (Figs. 1 and 2). If, then, the same sized tubes are used with the same quantities of the reagents, a permanent record can be kept by simply sealing the tubes and storing them away. While this method is not chemically accurate, it suffices for present clinical purposes.

FIG. 2. The same tubes and fluids one hour later. The precipitate has settled and the differences are well shown.

The following statements cover the results of my investigation. One hundred cases of general paresis have had their spinal fluids examined for Wassermann reaction, cell count, globulin and albumen. Eight cases of general paresis have been treated by the Swift-Ellis intradural treatment for periods ranging from two to eight months, and in some cases as many as ten lumbar punc-

tures have been performed, and an examination of the spinal fluid has been instituted each time. Six cases of Korsakoff's disease, two cases of brain tumor, and over one hundred miscellaneous conditions (dementia præcox, manic depressive, cerebral organic disease, etc.) have been studied. The patients were examined either at the Psychopathic Department, Boston State Hospital, or at the Taunton State Hospital, and I hereby thank the authorities of these hospitals for their kindly assistance.

1. *Incidence of albumen* as compared with other findings in general paresis, with special reference to fluctuations in treated cases.

It may be stated without reserve that there is always a very marked increase of albumen in general paresis. This increase is three or four times the normal amount. This increase parallels the globulin increase as follows:

If the globulin content be expressed in terms of 1 +, 2 +, or 3 +, then the albumen can usually be expressed in the same proportion, 1 +, 2 +, or 3 +. Usually, too, an increased cell count goes with a large amount of albumen but *not so constantly* as the globulin increase. The intensity of Wassermann reaction seems to bear about the same relationship to the albumen increase as does the cell count.

In the cases treated by Dr. R. R. Rupp and myself³ by the Swift Ellis salvarsanized serum method, the following points are important.

(a) The Wassermann reaction is the first reaction to disappear and is the most variable.

(b) The cell count increase approaches closely to the Wassermann reaction in variability. This, however, may be due in part to the technical difficulties of accurate cell counts, but is certainly not altogether due to this difficulty.

(c) The globulin content varies to a less extent than either the Wassermann reaction or the cell count.

(d) The albumen content varies least of all.

That is to say that the variations occurring during treatment (either because of it or coincidentally) show that albumen increase is a more constant sign of the paretic process than any of the other signs, and has a certain independence of their occurrence. Moreover, in two untreated cases, where general paresis

³ Myers, Boston Med. and Surg. Journal, Sept. 18, 1913.

was suspected, and the first spinal fluid specimen gave a negative Wassermann reaction, while the second gave a positive, the albumen content was practically the same in each specimen.

2. In one case of cerebro-spinal syphilis (Psychopathic Hospital, case No. 11823) with facial palsy, ophthalmoplegia externa, etc., following the initial lesion by three months, treatment finally brought about a negative Wassermann reaction, a normal cell count, a very slight globulin increase and a decided improvement clinically, but the albumen increase was *marked* even upon discharge. The significance of this to me is that the man was not cured.

3. In Korsakoff's disease (six cases). This disease throws into striking relief the significance of the total protein increase as evidenced by the test under question. To cite a couple of cases will perhaps be the simplest way of bringing out the point to be emphasized.

Case No. 12009, Psychopathic Hospital, showed on entrance multiple neuritis, external ophthalmoplegia, amyosis to blue light, confabulation, recent memory defect, etc. Wassermann reaction in blood and spinal fluid negative, no globulin, no increase in cell count, *albumen distinctly increased*. Repeated punctures over a period of four months have shown the same findings, except that the albumen content is now less marked (Fig. 3).

Case No. 12038, Psychopathic Hospital (kindness of Dr. Cook), showed on entrance clinical signs of Korsakoff's disease. Spinal fluid showed no cell increase, negative Wassermann reaction, no globulin, but a marked albumen increase. On discharge to another hospital, with clinical symptoms showing only the mild dementia of old Korsakoff's disease, there was only a slight increase, if any, of the albumen content. That is to say, the restitution brought about, or was accompanied by, a reduction of the albumen to the normal.

The next two cases tend to show that the neuritic symptoms bear less relation to the albumen content than do the mental symptoms.

Case No. 19562, Taunton State Hospital, is a man whose disease is of two years standing. There never have been neuritic symptoms but there is a decided history of alcoholism, a marked memory loss, and a delusional state of mild character. No signs of organic disease. Wassermann reaction in blood and spinal

fluid negative. Eyegrounds normal. At present no cells in spinal fluid, very slight globulin increase, distinct albumen increase (Fig. 3).

Case No. 20266, Taunton State Hospital, a woman whose disease of one year's duration. At onset hallucinations of sight and hearing and restlessness. Later, confabulation, memory loss, and multiple neuritis. At present no confabulation, good insight, but a mild dementia and distinct multiple neuritis (absent re-

FIG. 3. These tubes are from one case of Korsakoff's disease and from left to right the specimens pass from earlier to later. The first specimen is shown in Fig. 1 as "Recent Korsakoff."

flexes, atrophy, foot drop, etc.). Wassermann reaction in spinal fluid negative; globulin 0; no cells. *Albumen, very slight, if any increase.* Wassermann reaction in blood positive but the clinical signs and symptoms preclude nervous syphilis and indicate that the syphilitic infection was only incidental.

The first of these two cases has marked mental symptoms and no neuritis, shows albumen increase; the second with reverse symptoms shows no decided increase. The conclusion, which, of course, needs more cases to substantiate it, points toward the increase as due to the brain change.

Two cases of tumor of the brain, one of which was a gumma, showed interesting spinal fluid findings, particularly in relation to albumen.

Case No. 1449, Psychopathic Hospital, had choked disk, convulsions, aphasia, and focalized dullness and tenderness over right parietal region. Wassermann reaction in blood serum, first examination was negative; second positive; spinal fluid, negative to Wassermann reaction, globulin very slight, 6 cells, marked albumen increase. Operation by Dr. Harvey Cushing revealed inoperable gumma.

Case No. 20782, Taunton State Hospital, having as evidence of tumor Jacksonian epilepsy of left hand and arm, occasional grand mal, inability to stand or walk, exaggerated reflexes, with Babinski's phenomenon on left, markedly choked disks, gave the following findings—Wassermann reaction in blood and spinal fluid negative on two occasions. In the spinal fluid, globulin very slight, 70 cells, and the heaviest precipitation of albumen that I have seen in any case (Figs 1 and 2).

At the present time I am not prepared to discuss the findings in other diseases. Dr. Cook of the Psychopathic Hospital has reported to me that in a case of cyst of the brain, so diagnosed because of the focalized symptoms with history of hemorrhage and no symptoms of pressure, he has found decided increase in albumen, very slight increase in globulin and 6 cells. Wassermann reaction negative in blood and spinal fluid. My own experience with cerebral hemorrhage and allied conditions is not of a nature to permit definite statements except that I have seen cases with moderate increase in albumen and no other pathological findings.

Looking over the facts as above detailed, the following general conclusions present themselves.

1. That in the full fledged general paresis, the relationship of albumen, globulin, cells and Wassermann is quite constantly one of parallelism but that in the remissions the Wassermann reaction disappears first, the cell count and globulin increase diminish next,

and the albumen most constantly remains at a high level of increase. This points toward a conclusion which is merely a forward deduction—namely, that in the pre-paretic stage the albumen increase is probably the first sign of disease.

(a) In Korsakoff's disease, in certain cases of tumor, and in other organic diseases there is a dissociation of albumen and globulin in this sense, that there is either marked increase of albumen without globulin or that a marked increase of albumen, say 3 +, is accompanied by a globulin increase of, say, only 1 +.

(b) These two series of facts lead to the further conclusion, that the increase of albumen is a primitive reaction of the nervous system and is the first as well as the most constant of the present known chemical and biological changes to appear in the spinal fluid. Tests to ascertain its presence should be part of the routine spinal fluid examination and its exact measurement and significance constitute a task worthy of neurological research.