THE CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS*

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Since the introduction of the colloidal gold test of Lange,¹ numerous reports have appeared in the literature of examinations of the cerebrospinal fluid of large numbers of patients with neurologic diseases of all types.

Characteristic results have been obtained only in neurosyphilis, and the findings of the various types of this disease are now well known. However, the so-called "paretic" gold curve, at first supposed to be pathognomonic of general paralysis, at least within the group of syphilitic disorders, has been obtained in a number of other conditions, among which are lead poisoning, tuberculous meningitis, brain tumor and multiple sclerosis. In the first three of these conditions the curve has not appeared with any regularity, but in the last named it seems to be more than an occasional finding. For this reason, it has been thought worth while to survey the material from this clinic and review the literature, with the object of determining if definite changes in the spinal fluid occur with any regularity in multiple sclerosis.

Textbooks on neurology make scant comment on this point. Such statements as do occur indicate nothing of a characteristic nature. Current literature is also lacking in definite information. In various reports of long series of neurologic and psychiatric cases in which the colloidal gold test has been employed on the spinal fluid, a few cases of multiple sclerosis appear, but the results obtained present no uniformity. Jaeger and Goldstein² report, in a few cases of multiple sclerosis (number not stated), a "slight" colloidal gold reaction, there being a faint color change in the first four or five tubes. Three of four cases reported by Eskuchen³ were completely negative with the Wassermann and colloidal gold tests. The remaining case, which had been regarded as one of multiple sclerosis for years, was at once

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1. Lange: Berl. klin. Wchnschr. **49**:897, 1912; Ztschr. f. Chemotherap., **1**:44, 1913.

2. Jaeger, R., and Goldstein, M.: Ztschr. f. d. ges. Neur. u. Psych. **23**:219, 1913.

3. Eskuchen, K.: Ztschr. f. d. ges. Neur. u. Psych. **25**:486, 1914.

diagnosed as cerebrospinal syphilis in spite of a negative Wassermann reaction in the blood and spinal fluid, because examination disclosed a pleocytosis, positive globulin and paretic colloidal gold curve in the fluid alone.

Flesch⁴ reports eight cases, one case completely negative, one case in which the colloidal gold test was slightly positive and other tests were negative, and six cases with the colloidal gold reaction of a paretic type, in which the precipitation was limited more strictly to the first few tubes than is the case in paresis. Kaplan⁵ reports two cases, one serologically completely negative, the other with a paretic colloidal gold curve as the only positive finding. In a later paper,⁶ reporting eighteen cases, seventeen were negative, and one gave complete precipitation of the gold in the first two tubes.

In this clinic, Miller and his co-workers⁷ called attention to the presence of a paretic colloidal gold curve in the three cases of multiple sclerosis which they investigated. These cases are included in the present report.

Oetiker⁸ reports two cases, one case with the globulin slightly positive and other findings negative, and one case in which there was no pleocytosis or globulin reaction, but the gold showed partial precipitation in the first five tubes, reaching as high as 3 plus. In Robertson's⁹ case, the colloidal gold curve, instead of being paretic in type, showed a "verschieben nach oben," a reaction in the last tubes, reading 0000003355. Lowrey¹⁰ reports one case with a paretic gold curve.

As regards pleocytosis, Rotstadt,¹¹ in an exhaustive article on the cells of the cerebrospinal fluid, states that in 75 per cent. of his cases of multiple sclerosis (number not given) there was no pleocytosis.

These citations illustrate the status of the subject in the literature. It is obvious that nothing characteristic has been found so far. Of these forty cases, fourteen gave paretic gold curves, twenty-five were completely negative and one case was atypical. Because of the small number of cases reported and the lack of uniformity in the results obtained, it was thought worth while to examine the material from this clinic.

4. Flesch, N. E.: *Ztschr. f. d. ges. Neur. u. Psych.* **26**: 318, 1914.

5. Kaplan, D. M.: *J. A. M. A.* **62**:511 (Feb. 11) 1914.

6. Kaplan, D. M.: *Ztschr. f. d. ges. Neur. u. Psych.*, **27**:246, 1915.

7. Miller, Brush, Hammers and Felton: *Bull. Johns Hopkins Hosp.* **26**:391, 1915.

8. Oetiker: *Ztschr. f. klin. med.* **82**:246, 1916.

9. Robertson, W. E.: *Boston M. & S. J.* **174**: 136, 1916.

10. Lowrey: *J. Nerv. & Ment. Dis.* **46**:186 (Sept.) 1917.

11. Rotstadt, J.: *Ztschr. f. d. ges. Neur. u. Psych.* **31**:228, 1916.

TABLE 1.—RESULTS OF SEROLOGIC EXAMINATION IN CASES OF PROBABLE MULTIPLE SCLEROSIS

Case No.	No. of Cells	Globulin		Wassermann			Gold Chlorid Curve	Diagnostic Possibilities Suggested Other Than Multiple Sclerosis	Final Diagnosis Made before Laboratory Examination	
		Ross-Jones	Pandy	Blood	Cerebrospinal Fluid					
					0.25 C.c.	0.5 C.c.				1.0 C.c.
36353	4	0	+	0	0	..	5 5 5 5 5 5 5 2 1 0	Peripheral neuritis.....	Multiple sclerosis	
35531	21	+	++	0	+	1	2	5 5 5 5 5 5 2 1 0 0		Multiple sclerosis
34895	Bloody	+	+	0	0	0	...	5 5 4 3 8 1 1 0 0 0		Multiple sclerosis
34890	7	+	+	0	0	0	...	5 5 5 5 5 5 4 2 2 0		Multiple sclerosis
34504	4	+	+	0	0	0	...	5 5 5 5 5 5 4 2 2 0	Neurosyphilis.....	Multiple sclerosis
33638	3	0	0	0	0	0	...	4+4+4+4+3 8 2 0 0		Multiple sclerosis
37549	70	++	++	0	0	0	...	5 4+4+4+4+2 1 0 0		Multiple sclerosis
P. M.	27	++	++	0	0	0	0	5 5 5 4 3+3 2 1 0	Cord tumor; Erb's disease.....	Multiple sclerosis
36361	3	++	++	0	0	0	0	5 5 5 5 5 5 5 4 2 0		Multiple sclerosis
39125	6	++	++	0	0	0	0	5 5 4 4 4 3 1 0 0 0		Multiple sclerosis
38606	7	++	++	0	0	0	0	5 5 5 4 4 3 2 1 1 0		Multiple sclerosis
39141	9	++	++	0	0	0	0	5 5 5 5 1 0 0 0 0 0		Multiple sclerosis
39275	4	++	++	0	0	0	0	4 5 5 5 5 5 4 2 0 0		Multiple sclerosis
39271	6	0	++	0	0	0	0	5 5 5 5 5 4 2 2 1 0	Neurosyphilis.....	Multiple sclerosis
40953	5	++	++	0	0	0	0	4 5 5 5 3 2 1 0 0 0		Multiple sclerosis
41353	5	++	++	0	0	0	0	5 4+4 3 1 0 0 0 0 0		Multiple sclerosis
41986	2	++	++	0	0	0	0	5 5 5 5 5 2 6 0 0 0		Multiple sclerosis
40021	1	++	++	0	0	0	0	5 5 5 3 1 0 0 0 0 0		Multiple sclerosis
38831	14	++	++	0	0	0	0	3+3+3+1 0 0 0 0 0		Multiple sclerosis
36724	8	++	++	0	0	0	0	1 1 3 3 3 1 0 0 0 0	Hereditary ataxia.....	Multiple sclerosis (?)
37131	6	++	++	0	0	0	0	1 2 2 3 3 1 1 0 0 0	Combined sclerosis; brain tumor.....	Multiple sclerosis (?)
39680	7	++	++	0	0	0	0	1 2 2 3 3 4 3 0 0 0	Disseminated myelitis.....	Multiple sclerosis (?)
39805	6	++	++	0	0	0	0	0 0 0 0 1 0 0 0 0 0		Multiple sclerosis (?)
40054	15	0	++	0	0	0	0	1 1 2 2 1 0 0 0 0 0	Tabes (syphilitic ulcers ?).....	Multiple sclerosis (?)
41359	12	0	0	0	0	0	0	0 0 0 1 0 0 0 0 0 0	Spastic paraplegia (cause ?).....	Multiple sclerosis (?)
38748	3	0	0	0	0	0	0	1 1 2 2 1 0 0 0 0 0		Multiple sclerosis
35606	2	0	0	0	0	0	0	2 2 2 2 2 1 1 0 0 0		Multiple sclerosis
P. 913	89	0	+	0	0	0	0	0 0 0 0 0 0 0 0 0 0	Encephalomyelomacia disseminata multiplex.....	Multiple sclerosis (?)

Since the introduction of the colloidal gold reaction, there have been in Johns Hopkins Hospital twenty-eight cases in which complete serologic examinations were made, and in which the clinical diagnosis was either certainly or probably multiple sclerosis. The results are presented in Table 1.

Examination of Table 1 reveals the fact that in sixteen cases there was a pleocytosis, considering any cell count larger than five to be abnormal. In twenty-five cases globulin was detected, the amount being large in ten cases. Blood and spinal fluid Wassermanns were completely negative, except for one doubtful reaction with 1.0 c.c. of spinal fluid (which can be regarded as a nonspecific reaction). The gold curve was paretic in type eighteen times; syphilitic three times and negative seven times.

These figures become more striking when the validity of the clinical diagnosis is considered. It will be noted from Table 1 that the definite diagnosis of multiple sclerosis had been made without reserve twenty times before the laboratory examinations were made, and that it was questionable in the remaining eight cases, in which it was made solely as the best possibility. It is without the scope of this paper to discuss the clinical aspects of the disease. Suffice it to say that the diagnosis is often by no means made easily, and that in many cases, unless the patient is observed over long periods of time, it must remain in doubt. Taking these facts into consideration, Table 2 shows the number of cases in which pathologic findings occur in the two groups.

TABLE 2.—SEROLOGIC FINDINGS IN TWO GROUPS OF CASES

Diagnosis	Number of Cases	Pleocytosis of More than 5 Cells	Globulin			Wassermann		Gold Curve			
			Strongly Positive	Positive	Negative	Positive	Negative	Paretic	Syphilitic	Atypical	Negative
Multiple sclerosis...	20	8	9	9	2	0	20	18	0	0	2
Possible multiple sclerosis.....	8	8	1	6	1	0	8	0	3	0	5

Thus, in twenty cases of multiple sclerosis, a paretic gold curve, together with a positive globulin reaction, appeared in eighteen cases, or 90 per cent. This average is high enough to exclude the assumption of a merely occasional accidental finding of such a curve, and leads to the suspicion that in the other eight cases, diagnosed as being probably multiple sclerosis, the diagnosis is at fault, rather than the negative findings.

Excluding the rare cases of lead poisoning, tuberculous meningitis, etc., in which a paretic gold curve has occasionally been found, there are, therefore, only two diseases in which this type of curve occurs

with constancy, parenchymatous neurosyphilis and multiple sclerosis. There is usually no cause for confusion between these two, the diagnosis of neurosyphilis being in most cases clear enough from history, symptoms and clinical findings. If these fail to establish a definite diagnosis, one can fall back on the blood and spinal fluid Wassermann reactions. One or both of these will be positive in neurosyphilis; in fact, whenever a paretic gold curve is found in syphilis, the spinal fluid Wassermann is, so far as is known, always positive, with the single exception of long treated cases, in which the Wassermann becomes negative before the colloidal gold test.

As for the explanation of this reaction it is probably, as Felton¹² suggests, "an estimation of the albumin globulin content of the cerebrospinal fluid, rather than a specific reaction for any one lesion of the nervous system." This, of course, leaves unexplained why in neurosyphilis, multiple sclerosis and certain isolated cases of other nervous lesions, the albumin globulin content should be altered to the particular proportions necessary to produce a paretic gold curve.

SUMMARY

1. The cerebrospinal findings in twenty-eight cases of multiple sclerosis are reported.

2. In twenty of these cases the diagnosis is clinically certain; in the other eight cases it is clinically doubtful.

3. In the first group, the findings are (a) negative blood and spinal fluid Wassermann (all cases); (b) pleocytosis (eight cases); (c) positive globulin (eighteen cases); (d) paretic gold curve (eighteen cases). In the second group the findings are the same, except for the gold curve, which is syphilitic in three cases and negative in five cases.

4. Together with the clinical evidence, it is believed that the spinal fluid picture is fairly constant, and that, other things being equal, such a picture is a strong argument in favor of a diagnosis of multiple sclerosis. In its absence the diagnosis becomes at least doubtful.

12. Felton, L. D.: *Trans. A. M. A., Sect. Path. & Physiol.*, 1917, p. 73; *Bull. Johns Hopkins Hosp.* **30**:242 (Aug. 1) 1919.