Electrophoretic Fractionation of Serum Protein in Multiple Sclerosis.* (21158)

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Aberrations in blood proteins in multiple sclerosis have been reported previously. Swank, Franklin and Quastel(1) have observed abnormal chromatograms of plasma proteins in the acute phase of multiple sclerosis, and Putnam(2) found lowered fibrinogen and an increase in the euglobin fraction. In an investigation of a series of neurological disorders, with no information as to the specificity of the disease, Fisk, Chanutin and Klingman(3) found a decrease in the plasma albumin concentration in this general grouping. In contrast, numerous investigators of whom Dobin and Switzer(4) are the most recent, have reported no abnormal plasma protein findings. In view of the lack of any definitive investigation of serum proteins in this syndrome employing electrophoresis, it was considered advisable to obtain such information.

Methods and apparatus. Fasting blood samples were obtained from patients where a diagnosis of multiple sclerosis had been made by the neurological consulting staff of the Veterans Administration Hospital. The cases were selected at random, with the exception that the older age group was omitted, and our patient population ranged from 27-41 years. Normal subjects were obtained from the laboratory and resident staff. Twenty-seven patients and 16 controls were studied, and since no correlation was observed between the disease state and the findings both quiescent and acute cases are grouped together.

The electrophoretic separation was carried out in a Perkins-Elmer Model No. 38 Tiselius apparatus after preliminary comparisons with the Klett apparatus had substantiated the observations of Moore and White(5) that the 2 instruments gave results that were in good agreement. Determinations were carried out in a veronal buffer at pH 8.6 and 0.1 ionic strength, after 24-hour dialysis against the buffer at 3°C, at a protein concentration of approximately one percent. Fractionation was completed after 70 to 80 minutes. Initial and final boundaries were obtained by the Longsworth scanning technic(6). Area and mobility measurements were made on the ascending boundary. Since all mobility measurements were within normal limits the data have been omitted.

Protein determinations were obtained by the micro-Kjeldahl method and nitrogen values converted to protein using 6.25 as a factor.

Results. A statistical analysis of the results obtained are presented in Table I. A comparison of the normal and pathological groups reveals that the latter show a diminished albumin component and a concomitant increase in the α_2-globulin component. The albumin fraction averaged 55.0% in the multiple sclerosis cases and 60.2% in normals, while the α_2-globulin component averaged 12.4% and 8.9% in the respective groups, the P value in both cases being less than 0.001, showing a high degree of significance for the differences. The other globulin components showed no significant differences between the two groups. Because of the diminished albumin and increased α_2-globulin component in the pathological group the A/G ratio was decreased in this group, averaging 1.25 as compared to the normal value of 1.52. This difference was statistically significant ($P < .001$).

Protein determinations showed average values of 7.36 and 7.20 for the multiple sclerosis patients and normals respectively, the differences not being statistically significant.

In addition to the quantitative variations found in the pathological group, a qualitative difference in the α_2-globulin component was also observed. In 15 of the 27 patients, the α_2-globulin component exhibited a "double"

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TABLE I. Statistical Data of Results of Serum Protein Fractionation in Multiple Sclerosis.

	Total protein, g/100 ml		Electrophoretic distribution of protein fractions											
			Albumin, %		α_1-globulin, %		α_2-globulin, %		β-globulin, %		γ-globulin, %		A/G	
	Path.	Normal	Path.	Normal	Path.	Normal	Path.	Normal	Path.	Normal	Path.	Normal	Path.	Normal
Mean	7.36	7.20	55.0	60.2	4.9	4.7	12.4	8.9	14.7	14.4	13.1	11.7	1.25	1.52
Stand. deviation	.73	.43	4.71	2.35	.27	.23	2.81	1.26	2.60	1.63	3.82	2.58	.25	.15
Stand. error of mean		.19		1.08		.08		.62		.64		.98		.06
t value		.85		4.81		.003		5.60		.46		1.43		4.43
P		.40		<.001		—		<.001		.65		.25		<.001

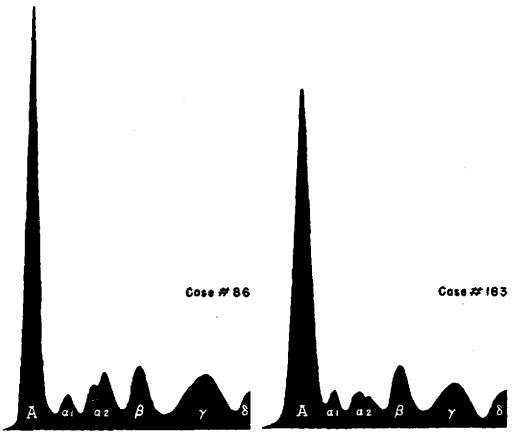

FIG. 1. Electrophoretic patterns of 2 cases of multiple sclerosis showing "double" α_2-globulin peak (ascending boundary).

α_2-globulin peak, not commonly demonstrated in normal patterns. Two examples of this "double" peak are illustrated in Fig. 1. No correlation between the existence of this heterogeneity in the α_2-globulin component and its magnitude was observed. Our lowest α_2-globulin value in the patient group exhibited this disturbance in the peak.

Discussion. Deviations from the normal electrophoretic pattern of blood proteins have been demonstrated in a variety of pathological conditions. Changes in all components in disease states have been recorded, and though an increase in γ-globulin in an inflammatory process, presumably due to antibody production, is fairly general, other changes are less well characterized. Some rationale for a hypoalbuminemia has also been evolved, but changes in the α- and β-globulin components are non-specific and less well understood. The high degree of association of lipid material in these 2 protein types might implicate some aberration in lipid metabolism with an abnormality in these components, but as pointed out earlier, such correlations have not been established. Some of our own results on cholesterol and total phospholipids(7), provide no evidence for any abnormal blood levels of these fractions in this syndrome.

Despite the extensive application of electrophoretic technics to disease states the neurological disorders have not been generally investigated, and it is of interest that an atypical

pattern is obtained in this study. Routh and Paul(8) in a similar study on anterior poliomyelitis obtained electrophoretic patterns which bear some similarity to our cases of multiple sclerosis. The similar distribution of protein fractions in these 2 dissimilar types of neurological lesions is to be noted, and the systemic change manifested by an increased a_2-globulin fraction, exhibits a uniformity which may be significant, and such studies should be extended to other types of neurological disturbances. The fact that a biochemical aberration can be demonstrated in the blood in neurological disorders is of some importance in further investigations on the behavior of nervous tissue. While this aberration is probably secondary in nature, the causative elements of such a finding should not be ignored.

Summary. 1. Electrophoretic fractionation of serum proteins in 27 cases of multiple sclerosis showed an increase in the a_2-globulin moiety with a concomitant reduction in the albumin component. This resulted in a lowered A/G ratio in the pathological cases. These differences were statistically significant. 2. In 15 out of the 27 cases an electrophoretic heterogeneity in the a_2-globulin fraction was observed which was characterized by a "double" peak.

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Association of Group A Streptococci with an Outbreak of Cervical Lymphadenitis in Mice. (21159)

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In October, 1953 a suppurative involvement of the neck was observed in Princeton mice by Dr. Alice E. Moore at the Sloan-Kettering Institute. These animals had been injected subcutaneously some weeks earlier with bacteriologically sterile suspensions in connection with her work on the suppression of tumor growth by viruses. Since the cervical reaction was in no way related to the activity of the injected agents a number of the affected mice were brought to the laboratories of animal pathology at the Rockefeller Institute for examination. The Princeton strain, which was originally established in these laboratories, has been under observation for many years. The mice used by Dr. Moore were obtained, however, from a commercial colony.

The signs of disease were unlike any previously observed in Princeton mice. The under surface of the neck showed eroded areas, with loss of hair and matting of the hair by a sticky exudate. In some animals the cervical lymph nodes were prominent and palpable. The mice were sickly in appearance and several that were held under observation died within a few days.

Fifteen of the diseased mice were killed and autopsied. The diagnosis in all of them was purulent cervical lymphadenitis. It resembled the condition originally described in guinea pigs by Boxmeyer(1) and sometimes known as "lumps" but was less progressive. In advanced cases one or more of the abscessed cervical nodes ruptured, releasing a semi-fluid purulent exudate. Its volume was evidently increased by subsequent involvement of the