ELECTROPHORESIS OF SERA IN MULTIPLE SCLEROSIS AND OTHER NEUROLOGICAL DISEASES

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It is a well established fact that in a large percentage of cases the cerebrospinal fluid gamma globulin is increased in multiple sclerosis but the serum gamma globulin is not raised. Changes in albumin and alpha and beta globulin concentrations have been reported by Bernsohn and Cochrane (1954) and by Volk, Saifer, Rabiner, and Oreskes (1955).

In the present investigations a comparison has been made of the serum proteins of 11 normal subjects, 28 patients with multiple sclerosis, and nine patients having other organic disease of the nervous system.

Method

Electrophoresis was performed on an Antweiler micro apparatus, using veronal buffer pH 8.6, $I = 0.1$, as described by Geissen, Schuler, and Schuster (1950). The normal controls ranged in age from 21 to 40 years, and the multiple sclerosis patients from 23 to 53 years, 13 being under 35 years. The duration of the disease was from a month to 15 years, and the average duration four and a half years. In 22 of the cases the disease was active.

Results

The mean values and standard deviations for the protein fractions in normal sera and sera of patients with multiple sclerosis are given in Table I. The

TABLE I
ELECTROPHORETIC ANALYSIS OF NORMAL SERA AND OF SERA IN MULTIPLE SCLEROSIS

	Albumin		Globulin					
			Alpha ₂		Beta		Gamma	
	Mean %	S.D.	Mean %	S.D.	Mean %	S.D.	Mean %	S.D.
Normals (11)	63.4	2.7	7.7	1.5	13.0	2.6	15.9	2.7
Multiple sclerosis (28)	58.2	3.6	11.0	2.4	13.9	2.7	16.9	2.8

normal values are similar to those published by other workers (Bierring and Nielsen, 1952). Statistical analysis shows that for the multiple sclerosis patients the mean value of albumin concentration is

significantly decreased and the alpha₂ globulin significantly increased ($P < 0.001$ in both cases). The mean concentrations for beta and gamma globulin, however, are not significantly different from the normal means ($P = 0.3$ in each case).

In order to determine whether there was any relationship between the concentration of serum alpha₂ globulin and the duration of the disease or the age of the patient, the multiple sclerosis patients were divided into two groups according to whether the duration was less than two years or more, and also according to age, over or under 35 years (Tables II and III). In both instances the difference

TABLE II
RELATIONSHIP BETWEEN ALPHA₂ GLOBULIN CONCENTRATION IN SERA IN MULTIPLE SCLEROSIS AND DURATION OF DISEASE

Duration of Disease	Mean Concentration % Total Protein	Standard Deviation	No. of Cases
Less than 2 years	11.3	2.2	11
More than 2 years	10.9	2.6	17

TABLE III
RELATIONSHIP BETWEEN ALPHA₂ GLOBULIN CONCENTRATION IN SERA IN MULTIPLE SCLEROSIS AND AGE OF PATIENTS

Age of Patient	Mean Concentration % Total Protein	Standard Deviation	No. of Cases
Under 35 years	10.8	2.4	13
Over 35 years	11.2	2.5	15

in the mean values of alpha₂ globulin were not significant ($P = 0.5$). The Lange gold curve was positive in the cerebrospinal fluid of 13 of the patients; the mean values of serum alpha₂ globulin of patients having positive and negative Lange gold reactions are shown in Table IV. There is no significant difference between these means ($P = 0.8$).

A comparison between the normals and the group of nine cases of organic disease of the nervous system (Table V) shows that the means of albumin, alpha₂, and beta globulins are significantly different

TABLE IV

RELATIONSHIP BETWEEN ALPHA₂ GLOBULIN CONCENTRATION IN SERA IN MULTIPLE SCLEROSIS AND CEREBROSPINAL FLUID LANGE GOLD TEST

Lange Gold Test	Mean Concentration % Total Protein	Standard Deviation	No. of Cases
Positive	11.1	2.7	13
Negative	10.9	2.2	15

TABLE V

ELECTROPHORETIC ANALYSIS OF NEUROLOGICAL SERA

Disease	Albumin (%)	Globulin		
		Alpha ₂ (%)	Beta (%)	Gamma (%)
Tabes dorsalis	59	12	13	16
Chronic peripheral neuro- pathy	52	14	19	15
Chronic encephalomyelo- radiculitis (inactive) ..	64	12	15	9
Polyneuritis	56	16	13	15
Intracranial aneurysm— ankylosing spondylitis ..	53	13	19	15
Haematomyelia	57	15	15	13
Brain-stem vascular lesion ..	55	10	15	20
Cervical spondylosis—pneu- monia—angina pectoris ..	54	17	18	11
Paraplegia—diabetes melli- tus—arteriosclerosis ..	50	12	22	16
Mean ..	55.3	13.0	16.5	15.2
Standard deviation ..	5.0	2.5	2.7	3.3
Normal Series Mean ..	63.4	7.7	13.0	15.9
Standard deviation ..	2.7	1.5	2.6	2.7

from the normal means ($P < 0.001$). The gamma globulin concentration is not significantly different from the normal value ($P = 0.5$).

Discussion

The disease was active in 22 of the multiple sclerosis patients, but only 12 of these had raised alpha₂ globulin concentration, *i.e.*, more than two standard deviations above the normal mean. Also, of the six patients in whom the disease was inactive, four had increased alpha₂ globulin concentration. There is, therefore, no correlation between the alpha₂ globulin concentration and the activity or duration of the disease, the age of the patient, or the results of the Lange gold reaction on the cerebrospinal fluid.

It is interesting to compare these results with those reported by Bernsohn and Cochrane (1954), who found the mean values of albumin decreased and alpha₂ increased in a series of 27 cases of multiple sclerosis. The duration of the disease is not stated, but the age of the patients ranged from 27 to 41 years. Also Volk and others (1955) reported a

significant difference in the mean values of albumin, alpha₂, and beta globulin in a series of 43 cases of multiple sclerosis. In this series, however, the average duration of the disease was 18 years.

Increased alpha₂ globulin concentration has been reported in other pathological conditions. Longworth, Shedlovsky, and MacInnes (1939) found increases in nephrosis and fevers, while Flynn (1954) reported increases in cases of high fever, tissue destruction, nephrotic syndrome, collagen disease, and malignant disease. The 28 patients with multiple sclerosis studied were all in-patients, and with one exception none were febrile or had other complications while in hospital. The only cases of infection were four patients with chronic tonsillitis and three with infected teeth. In each case electrophoresis was performed before the tonsillectomy or dental extraction. One patient had a history of recurrent thrombophlebitis and developed an attack at the site of the venepuncture carried out to obtain the specimen of blood for this study. It is evident, therefore, that the increased alpha₂ globulin and decreased albumin concentrations found in the sera of some of the multiple sclerosis patients are not due to fever, urinary, or other complications. These changes are not, however, specific for multiple sclerosis as they occur in other neurological diseases.

Summary

An increase in serum alpha₂ globulin and a decrease in albumin concentrations can occur in the early and later stages of multiple sclerosis. These changes cannot be correlated with the activity or duration of the disease, the age of the patient, or the Lange colloidal gold reaction on the cerebrospinal fluid and they are not specific for multiple sclerosis.

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