EUGLOBULIN IN LEPROSY *

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In developing their biochemical diagnostic test for malaria, which is a quantitative estimation of serum euglobulin, Proske and Watson (8) obtained from this laboratory a number of sera from ambulatory leprous patients representing the various types and stages of progression of the disease. Their purpose was to compare the results of the test on leprous patients with those obtained in other diseases and in normal persons. The high values noted in the sera of leprous patients, led Proske, in a personal letter to this hospital, to suggest that a further study of the euglobulin content of serum in leprosy might be of interest. It has been shown (7, 9) that changes in the serum proteins have occurred in the sera of leprous patients and have consisted, in the main, of a reduction in the albumin fraction with an increase in the globulin fraction, this being more pronounced in patients in whom the disease is progressing. Clinical improvement was generally accompanied by a decrease in the percentage of globulins with a corresponding increase in albumin. Since a study of the serum euglobulin has not been made in leprosy (as far as the writer is aware), it was thought that a study might be of value.

The 150 cases selected were of various types, state of progression, and activity of leprosy, and their sera were analyzed for total proteins, albumin, globulin, and euglobulin. As controls, the sera of 12 presumably normal persons, employees of this institution, were used.

ANALYTICAL METHODS

Approximately 10 cc. of blood was drawn from a cubital vein. The blood was allowed to clot and was centrifugalized, and the serum was removed immediately; all analyses were made the day the blood was withdrawn. The euglobulin was determined by the method of Proske and Watson (9). The procedure is based on the fact that proteins possess a chromogenic property which can be measured quantitatively against the color produced by pure tyrosin in the presence of a phenol reagent. This chromogenic value is constant for a given protein, and the intensity of the color produced can be used as a measure of the amount of protein examined. The euglobulin is precipitated from the serum by the addition of 13.5 per cent sodium sulphate solution, according to the method of Howe. The tyrosin chromogenic index (TI) is determined by comparison with standards prepared from pure tyrosin

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(Pfanstiehl). Total proteins were determined by a micro-Kjeldahl method; albumin was determined by the Howe method quoted by Hawk (3), and globulin by subtracting the albumin from the total protein. Proske and Watson (8) point out that a tyrosin-euglobulin coefficient has not as yet been worked out for reporting the results of the test in terms of milligrams of euglobulin per 100 cc. of serum. Hence the total protein, albumin, and globulin, in the present paper, are reported in percentages.

The average figures for total protein, albumin, and globulin in our controls agree with findings in a previous report (9); the tyrosin index for euglobulin in our controls ranges between 60 and 100, which is slightly higher than those reported by Proske and Watson, who reported 50 to 80.

EUGLOBULIN—TYROSIN INDICES

*Stage of Progression**

	80-100	100-200	200-300	300-400	400-500
Arrest.		14	3		
I. E.			1		
A. E.	2	12	7		
I. M. A.		2	1		
A. M. A.	1	7	35	22	6
A. F. A.		3	15	10	9
Total	3	38	62	32	15

*Stage of Activity***

Arrest.		14	3		
Stny.		2	2		
Imp.	3	12	10	3	1
Retg.		10	47	29	14
Total	3	38	62	32	15

* Arrest. —Arrested
I.E. —Inactive, early
A.E. —Active, early
I.M.A. —Inactive, moderately advanced
A.M.A. —Active, moderately advanced
A.F.A. —Active, far advanced.

** Arrest. —Arrested
Stny. —Stationary
Imp. —Improving
Retg. —Retrograding

In the entire group the results show that of the 150 cases, 147 had tyrosin indices above normal. Of these, the albumin-globulin ratio was below normal in 123 of the cases, the remaining 24 cases having a normal albumin-globulin ratio. The initial protein values in all cases ranged from 4 to 11.6 per cent; 20 of the 150 cases were above 8 per cent, the upper limit of normal. Initial albumin values ranged from 1.8 to 5.3 per cent; the globulin determinations varied from 1.2 to 7.9 per cent; the albumin-globulin ratio ranged from 0.3 to 3.3.

The tyrosin indices show variations between the groups into which the cases have been divided. In the patients who are active, moderately advanced, and active far advanced, the findings reveal higher tyrosin indices. This is also true of the cases showing retrogression. However, it is interesting to note that the tyrosin indices were increased in the 24 cases who had a normal total serum protein as well as a normal albumin-globulin ratio. Three cases were normal throughout.

It is believed that globulin is increased usually at the expense of the albumin fraction in many infectious conditions or toxic states. A hyperglobulinemia is an almost constant finding in leprous patients who are active and retrograding; and clinical improvement is usually coincident with a decrease of globulin, but seldom returns to normal. From the results of this study, the increase in globulin is chiefly in the euglobulin fraction.

Bodansky (2) states: "Luck has shown that the liver proteins may be separated into several fractions, globulin II, euglobulin, pseudoglobulin, and albumin, and all of these participate equally in the function of storage." Some (5, 6) have considered that the liver is the main source of much of the globulin and that infections impair the manufacture of serum proteins in the liver despite the fact that protein intake may be maintained. Whipple (10), in his interesting article on "Hemoglobin and Plasma Proteins," formulates briefly the plasma protein metabolism by stating that food proteins yield the amino-acids absorbed from the intestinal tract and that the amino-acids are synthesized in the liver cells (and elsewhere) into plasma proteins. These plasma proteins (and amino-acids) supply the protein requirements of the body cells.

In a previous study in this laboratory (1) the serum bilirubin was determined qualitatively and quantitatively and found to be positive in 138 out of 200 cases studied. The qualitative was of the delayed type, showing the possibility of early hepatic lesions. Hopkins *et al.* (4) have shown that disease of the liver is common in leprosy, and in reports of autopsies on 96 cases of leprosy at this institution liver damage was noted in almost all cases. In view of these findings, hepatic dysfunction and liver damage might be an important etiologic factor in the disturbed protein metabolism noted in leprosy, although no evidence has been obtained of the existence during life of symptoms of disease of the

liver. Euglobulins are also increased in malaria (8), but it is felt that malaria could be ruled out because clinical manifestations of malaria infection were not present during the periods this work was being conducted.

Summary

Sera from 150 leprous patients representing the various stages of progression and activity of the disease, were examined for euglobulin, total proteins, albumin, and globulin.

The tyrosin index for euglobulin was found to be above normal in 147 of the 150 cases. The greatest variation was found in active, advanced leprosy. The albumin-globulin ratio was below normal in 123 of the 147 cases. The tyrosin index was above normal in 24 cases who exhibited a normal total protein as well as a normal albumin-globulin ratio.

It is suggested that hepatic dysfunction and liver damage might be an etiologic factor in the disturbed protein metabolism noted.

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