ELECTROPHORETIC CHANGES IN THE SERUM PROTEIN PATTERN OF A PATIENT WITH TYPHUS FEVER[1]

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In an earlier communication (1) attention was called to the marked depressions of albumin: globulin ratios that frequently occur in the course of louse-borne typhus fever. Serum globulin concentrations in a number of cases were found to be higher than 5 grams per 100 ml. Because of the consistent rise in serum globulins in this disease, possibly a feature of the immune response, it was of interest to determine which globulin components were increased and to observe the sequence of changes associated with the clinical course.

The electrophoretic analyses to be described were made on serum samples taken from a patient with clinically typical severe typhus fever, included in the group previously reported. It will be seen that the depression of his albumin: globulin ratio was associated with a striking increase in the γ globulin component.

PROCEDURE

Sera were stored in sterile tubes at 4° C. without preservative. After the collections were complete they were brought from Egypt to New York City, refrigerated in transit.

The electrophoretic analyses were made in diethylbarbituric acid buffer (μ 0.1, pH 8.6) as previously described (2).

OBSERVATIONS AND DISCUSSION

A. S. M. (No. 2501), a 21-year-old Egyptian man, was admitted to the Typhus Commission ward on the third day of disease, acutely ill. There was no history of previous typhus, nor had he received anti-typhus vaccine.

During the first three weeks of hospitalization he had a sustained high fever. Delirium, vomiting, and a typical rash were present during the first week; intractable diarrhea during the second, and attacks of bronchial asthma during the third. In the latter part of his febrile course, dysarthria appeared with periods of emotional depression, increased tendon reflexes, spasticity of extremities, and adiadokokinesis. These neurological signs gradually disappeared during the subsequent five weeks of convalescence. At the time of discharge on the fifty-ninth day of disease, he was underweight, but the physical examination in other respects was normal.

On the fifth day of disease the Weil-Felix and complement fixation reactions were negative. On the forty-seventh day these tests were positive in dilutions of 1/320 and 1/1280 respectively.

OBSERVATIONS AND DISCUSSION

The results of electrophoretic analysis and the associated clinical data are charted in Figure 1.

The total protein, low during the early febrile stage, rose to abnormally high values in convalescence.

The relative proportion of albumin, and with it the albumin to globulin ratio, was found to be markedly depressed even on the fourth day of disease. Similar, but lesser, early depressions of albumin have been observed in patients with malaria (3) and with scarlet fever (4). Presumably this is a non-specific reaction to an acute febrile illness.

The relative proportion of α_1 globulin was not significantly disturbed; α_2 globulin showed a slight sustained increase. The practical absence of change in these components contrasts with the conspicuous increase found in patients with scarlet fever (4).

β globulin was on the low side of normal throughout the illness.

Most interesting is the early marked elevation of γ globulin. If it be assumed that the patient had a normal distribution of serum protein components prior to illness, this phenomenon would appear to indicate that there is a considerable release of γ globulin protein during the acute reaction to typhus infection. It would seem unlikely that the increase in γ globulin on the fourth day of disease could have been due to production of

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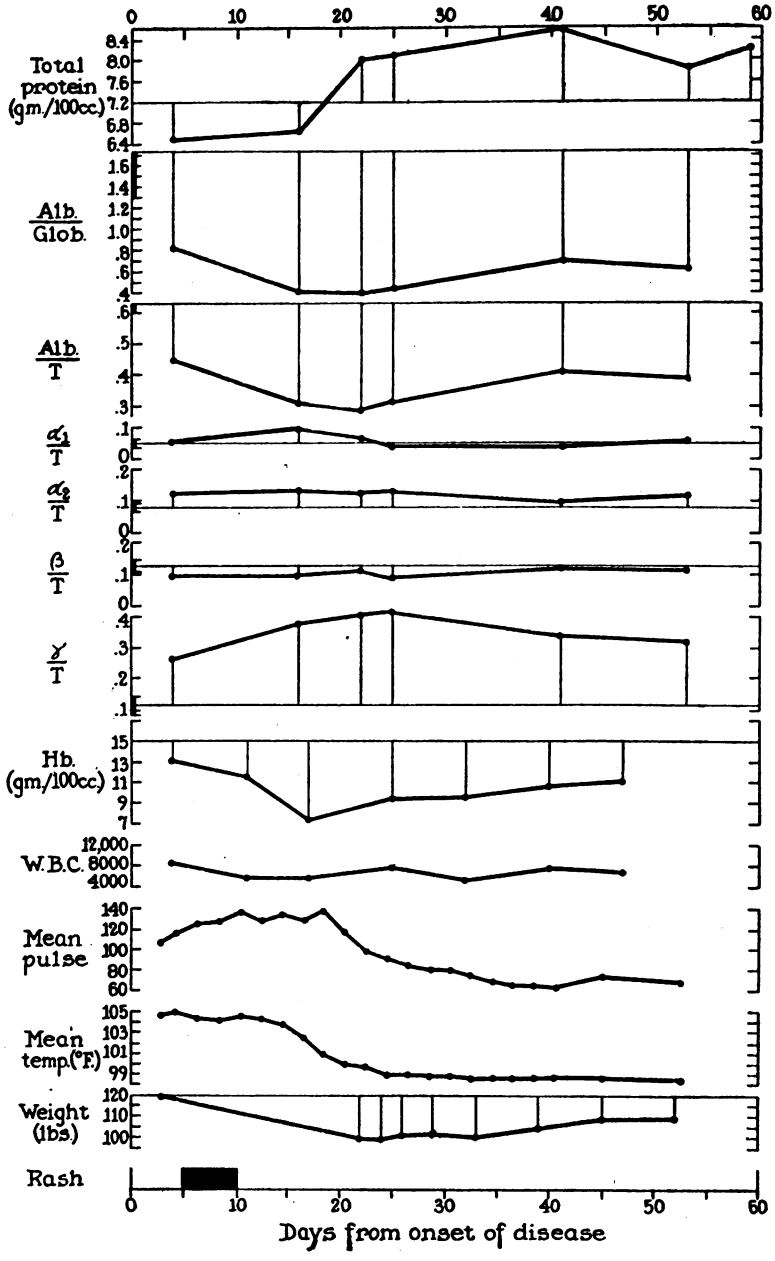

FIG. 1. ELECTROPHORETIC AND CLINICAL DATA DURING THE COURSE OF TYPHUS FEVER

From above downwards the ordinates show total protein concentration, the albumin: globulin ratio (measured electrophoretically), the fraction of the total protein (T) included in the different electrophoretic components, and the clinical data indicated. Horizontal lines show normal values, with the range of one standard deviation about the normal indicated by the heavy vertical brackets.

specific antibodies at that early date in a person without previous exposure to the antigens concerned. The available data, moreover, indicate that at least some of the antibodies which appear in the course of typhus fever were not then present, since the Weil-Felix and complement fixation tests were negative at that time, although later positive in high dilutions. It would further appear probable that protective antibodies were not present in significant concentration on the fourth day since the patient continued to be severely ill for over two weeks subsequently.

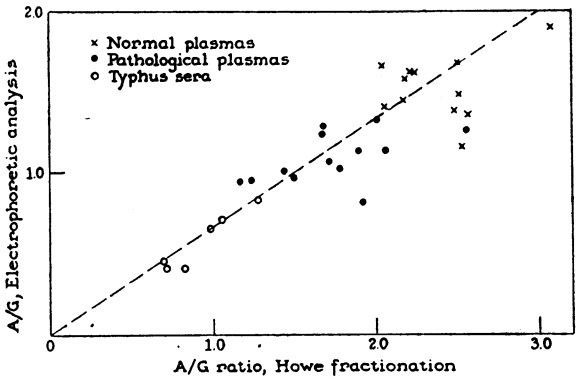

FIG. 2. CORRELATION OF ALBUMIN: GLOBULIN RATIOS MEASURED BY ELECTROPHORETIC ANALYSIS AND BY HOWE SODIUM SULFATE FRACTIONATION

Open circles show the new data.

The exceptionally low albumin: globulin ratios encountered in these sera presented an opportunity to extend the previously reported (2) correlation between the ratios determined by electrophoretic analysis and by the customary Howe sodium sulfate fractionation. It may be observed in Figure 2 that the newer data (open circles) approximate the same line drawn to fit earlier values. It would thus appear proper to infer from the more extensive study on typhus fever serum proteins (1) that the marked depressions observed in albumin: globulin ratios by salt fractionation would imply comparable abnormalities in the electrophoretic ratios.

SUMMARY

1. The relative proportion of albumin and the albumin: globulin ratio were markedly reduced on the fourth day of typhus fever and through the convalescence.

2. The α and β globulins were practically unaffected.

3. γ globulin was increased to a striking degree on the fourth day and to an even greater extent in convalescence.

4. A previously described relation between the albumin: globulin ratios determined electrophoretically and by salt fractionation was found to remain valid for the lower ratios encountered in this study.

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