results from premature fusion of sutures of the cranial vault. It is of most significance when it occurs during the period of rapid brain growth. Although the condition has been recognized for a considerable time no review of an unselected series of cases has been reported.

A review of 37 cases shows the condition to be relatively common in Africans; the incidence and clinical features have been discussed, and it is concluded that the disease is much less malignant than hitherto thought. Only raised intracranial pressure leading to papilloedema or other consequent symptoms is regarded as an unequivocal indication for operation, but this complication must be remembered, particularly where multiple sutures are involved. The only other indication for operation is the correction of deformity, and this only in the first few weeks or months of life.

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The new Factories Act, 1959, makes it obligatory for an industrial first-aid-er to have prescribed qualifications. What these qualifications will be has not yet been laid down, but it is probable that regulations will shortly be made requiring first-aid-ers to hold a valid certificate of one of the ambulance associations. At present only six out of 10 industrial first-aid-ers hold valid Red Cross, St. John or St. Andrew certificates, according to a survey which details the first-aid provision in 244 companies with up to 1,000 employees. Of the firms examined 70% had all male first-aid-ers and only 10% all female, mostly in firms with a single first-aid-er. The number of first-aid-ers under 30 and over 60 is small, and the most common age is in the forties. Sixty per cent. of all first-aid-ers received their training from the St. John Ambulance Association, 10% from the Red Cross, and 5% from the St. Andrew Ambulance Association. More than half the firms questioned experience difficulty in recruiting first-aid-ers, but of these only 22 provide training facilities of any sort. In fact, three-quarters of the companies make no practical effort to help with training, although nearly half provide some type of incentive for a first-aid-er to become qualified. Sixty per cent. make no payment at all to first-aid-ers; among the other 40% annual payments range from 30s. to £40. (*First Aid in the Smaller Company*, Industrial Welfare Society.)

SERUM PROTEINS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Of the diagnostic tests for systemic lupus erythematosus, the L.E. cell phenomenon, the differential agglutination, Coombs, Wassermann, and paratoluene sulphonic acid tests all depend upon protein abnormalities. Nevertheless, the serum proteins in systemic lupus erythematosus have received comparatively scant attention in the literature and little information is available regarding their diagnostic value.

There is general agreement that while the total serum protein level may be normal, the serum albumin is often reduced and hyperglobulinaemia is frequent. Unfortunately, reports of serum protein electrophoretic studies in systemic lupus erythematosus relate to small series of patients. Probably because of this and because some authors have failed to make comparisons between the absolute figures and those of normal controls, further findings are conflicting. Smith (1954) found an increased α_2 -globulin in six patients with "little or no evidence of renal disease," and a reduced level in four patients with nephropathy. Baptista *et al.* (1956) and Reiner (1950) also found that the α_2 -globulin level tended to be high, but Walker and Benditt (1950) and Sunderman and Sunderman (1957) report normal levels without mentioning their relationship to proteinuria. The β -globulin level has been reported to be normal (Reiner, 1950; Smith, 1954; Sunderman and Sunderman, 1957) or reduced (Walker and Benditt, 1950; Baptista *et al.*, 1956). All workers seem agreed that the α_1 -globulin level is normal in systemic lupus erythematosus and that the γ -globulin is usually increased, though Baptista *et al.* (1956) are alone in finding the latter change less frequently than the increase in α_2 -globulin.

The present study was undertaken to define the serum protein changes in systemic lupus erythematosus, to ascertain whether these changes could be of diagnostic or prognostic value, and to correlate the changes with disease activity and manifestations.

Materials and Methods

Total protein estimations and electrophoretic studies were done on 71 blood specimens from 31 patients with systemic lupus erythematosus. In every case the clinical picture was compatible with this diagnosis, which had been confirmed by the demonstration of the L.E. cell phenomenon.

The total protein estimations were made on serum, using the biuret method (Gornall *et al.*, 1944).

Electrophoretic studies were done on the same sera, using a technique similar to that described by Flynn and De Mayo (1951). 0.02 ml. of serum was applied to a 3-in. (7.5-cm.) wide strip of Whatman paper No. 1, and

the separation performed in a veronal buffer (pH 8.6) (ionic strength 0.05) for 16 hours. The applied potential was 2.5 volts/cm. length of strip. The strips were dried for 15 minutes at 100° C., stained for 10 minutes with light green (Gurr), and repeatedly rinsed in 2% acetic acid until a white background was obtained. After drying, the strips were rendered translucent by oiling (Grassmann *et al.*, 1951).

The scanning was done with an electrodensitometer (Laurence, 1954) and the absolute values of each protein fraction were calculated from the total protein result and the results of planimetry on the electrophoresis curves after extrapolating each segment of the curve to the baseline. No correction was made for differences in staining by the different protein fractions.

In order to provide a normal range of values, sera from 12 healthy young adults were similarly examined. These results are summarized in Table I.

TABLE I.—Summary of Serum Protein Values (g./100 ml.) from 12 Healthy Young Adults

	Total Proteins	Albumin	Globulin			
			α_1	α_2	β	γ
Mean	7.3	3.7	0.3	1.0	1.0	1.3
Standard deviations (S.D.)	0.38	0.39	0.1	0.16	0.19	0.25
Mean $\pm$ 2 S.D.	6.5-8.1	2.9-4.5	0.1-0.5	0.7-1.3	0.6-1.4	0.8-1.8

All statistical comparisons were made by using Student's "t" test.

Results

Untreated Systemic Lupus Erythematosus without Proteinuria

Two factors influencing the serum proteins in systemic lupus erythematosus are, firstly, the effect of the disease process, and, secondly, in those patients with nephropathy, the loss of protein in the urine. In order to get a clearer picture of the protein changes due to the disease process itself, serum protein results from 18 untreated patients without persistent proteinuria were analysed separately. The actual protein values are listed

TABLE II.—Results of Initial Protein Estimations (g./100 ml.) on 25 Patients with Systemic Lupus Erythematosus Grouped as Follows:

Patient	Total Proteins	Albumin	Globulin			
			α_1	α_2	β	γ
18 Untreated Patients without Persistent Proteinuria						
E. B.	8.7	3.1	0.4	1.4	1.0	2.8
G. D.	7.0	3.4	0.2	0.6	0.7	2.1
G. G.	7.7	3.5	0.3	0.9	0.7	2.2
P. G.	8.0	4.2	0.2	0.5	0.7	2.3
G. Gr.	8.8	3.7	0.1	0.4	1.0	3.6
J. G.	9.0	1.5	0.2	0.3	0.5	6.5
B. H.	8.4	3.8	0.3	0.7	0.8	2.8
R. J.	7.4	3.3	0.1	0.5	0.6	2.9
D. L.	7.3	3.1	0.4	0.4	0.8	2.5
J. L.	7.4	2.8	0.4	0.6	0.8	2.7
C. M.	9.0	2.5	0.3	1.2	0.9	4.1
S. M.	7.2	3.3	0.2	0.6	0.8	2.3
K. M.	9.2	3.9	0.3	0.6	0.6	3.9
H. R.	8.2	3.2	0.4	1.1	1.1	2.5
A. S.	5.6	2.9	0.3	0.4	0.5	1.5
E. S.	9.5	4.3	0.5	1.0	1.4	2.3
E. St.	8.0	2.4	0.6	0.7	0.7	3.7
P. S.	7.7	2.7	0.4	0.8	1.0	2.8
5 Untreated Patients with Persistent Proteinuria						
R. N.	5.4	1.5	0.2	0.8	0.4	2.6
E. O.	7.6	2.7	0.6	0.9	0.4	3.0
K. O.	4.6	1.1	0.4	1.0	0.8	1.3
Y. S.	6.0	1.7	0.4	0.8	0.5	2.6
J. W.	8.7	3.6	0.2	1.0	0.4	3.4
2 Patients Inadequately Controlled on Steroids and with Persistent Proteinuria						
J. Q.	5.5	1.7	0.5	1.5	0.7	1.2
E. T.	6.2	2.2	0.3	1.2	1.1	1.5

in Table II, but for convenience the results in these 18 patients are summarized in Fig. 1 for comparison with the healthy controls. The systemic lupus patients without proteinuria showed raised total proteins, low albumin, low α_2 -globulin, low β -globulin, and markedly raised γ -globulin levels as compared with the healthy

FIG. 1.—Serum protein results from 18 patients with systemic lupus erythematosus without proteinuria and from 7 patients with systemic lupus erythematosus and proteinuria, compared with those of 12 healthy controls. Statistical comparisons have been made between the patients without proteinuria and the healthy controls and between the patients with proteinuria and those without. Where a significant difference exists this is indicated in the bottom line.

controls. As can be seen from Fig. 1, all of these changes reached the 5% level of significance, but the elevation of the γ -globulin was much more significant.

There was no correlation between any of the initial clinical features and the serum protein changes.

The correlation between disease activity, as judged from the temperature, sedimentation rate, and clinical features was only fair, there being a tendency for the severely ill patients to have particularly low serum albumin and exceptionally high serum γ -globulin levels. Also in individual cases clinical improvement was usually accompanied by a return of the serum protein changes towards normal.

Though the changes in the whole group are of great interest, in practice, where one is concerned with an individual case, it is of more value to know the incidence of deviations from the normal range, which is taken as two standard deviations above and below the mean for the healthy controls and is shown in Table I. From Table II it will be seen that of the 18 patients with untreated systemic lupus erythematosus and without persistent proteinuria 5 had a serum albumin level below the normal limit, 10 had a low serum α_2 -globulin, and only 2 had a low β -globulin level. A single patient had a serum α_2 -globulin value above the upper normal limit, and, of much more interest, 17 of the 18 patients had a raised γ -globulin level. In only one patient were the serum albumin, α_2 -globulin, β -globulin, and γ -globulin levels all outside the normal limits.

Effect of Proteinuria

The initial serum protein values of five untreated patients with persistent proteinuria, together with those of two patients already receiving small doses of steroid therapy and still showing clinically active disease, were

analysed separately (Fig. 1) to ascertain how the proteinuria modified the serum protein pattern. When the serum proteins of this group were compared with those of the 18 patients without persistent proteinuria, the following significant differences emerged (see Fig. 1). The total proteins and the serum albumin were even lower and the α_2 -globulin was higher. The γ -globulin was lower, but this did not reach statistically significant levels. When compared with the healthy controls the serum α_2 -globulin in the patients with proteinuria was normal but the γ -globulin was still significantly raised.

The absolute protein values for the seven patients with proteinuria are listed in Table II, and it will be noticed that six patients had a serum albumin below the lower normal limit, only one patient had a serum α_2 -globulin slightly above the upper normal limit, four patients had a β -globulin below the normal lower limit, and only four had a γ -globulin above the upper normal limit. It was those patients with very heavy proteinuria who showed very low serum albumin and normal serum γ -globulin levels. Electrophoresis on a concentrated urine specimen from one of these patients showed that the urinary protein was mainly albumin, but there was also a little β -globulin and some γ -globulin (Fig. 2).

Effect of Therapy

In nine patients multiple protein estimations were made both before and during steroid therapy. In eight patients the serum albumin rose rather slowly towards normal, but in two of these patients, on whom frequent studies were made, normal values were reached only after 10 weeks' therapy, which was long after clinical suppression of the disease had been achieved. The α_2 -globulin and β -globulin levels fluctuated but also tended to rise slowly during therapy. In all cases without proteinuria the γ -globulin fell within a few days, but only in two patients did it reach the upper normal range, and this occurred only after several months' therapy, during much of which time both patients had been in clinical remission. Fig. 3 shows the albumin and γ -globulin changes in one of these patients.

FIG. 2.—Tracings of electrophoretic patterns on serum and urine (concentrated 10 $\times$) from a patient with systemic lupus erythematosus and severe nephropathy. These tracings, which were not used in quantitative estimations, are somewhat distorted, as the sensitivity of the densitometer had to be increased to record the low protein concentrations.

Similar trends were observed in five patients who

were already on steroid therapy at the time of first testing and who had further tests.

Discussion

The almost constant change in the serum proteins in cases of systemic lupus erythematosus uncomplicated by proteinuria is a considerable increase in the γ -globulin fraction, and this is often accompanied by less constant and less marked but probably significant reductions in the serum albumin, and α_2 -globulin and β -globulin fractions. The large increase in the serum γ -globulin more than compensates for the reductions in the other components, so that the total protein value is normal or raised.

The cause of these changes is a matter for speculation. The increased γ -globulin is so constant as to suggest that it is a rather fundamental part of the

FIG. 3.—Serum albumin and γ -globulin levels from a patient with systemic lupus erythematosus correlated with temperature, sedimentation rate, and treatment.

disease process. It is known that this increased γ -globulin fraction contains many abnormal proteins, including those responsible for various positive serological reactions sometimes found in systemic lupus erythematosus. These include the L.E. cell phenomenon (Haserick et al., 1950), complement-fixation tests against human tissue antigens (Gajdusek, 1958), the Wassermann reaction (Coburn and Moore, 1943), and paratoluene sulphonic acid test (Wilkinson and Rees, 1958). Whether the Coombs and haemagglutinating factors in systemic lupus erythematosus are γ -globulins has yet to be demonstrated. Nevertheless, some of these reactions are probably antibody-antigen phenomena, and the raised serum γ -globulin is but the biochemical expression of a raised antibody level, much of which may be auto-antibody.

The reduction in albumin, α_2 -globulin, and β -globulin is much less constant and less marked, and may well be a non-specific result of a severe systemic illness with decreased protein anabolism, or increased protein katabolism.

When nephropathy supervenes the serum albumin falls further and the γ -globulin sometimes falls towards or into the normal range, presumably because of urinary loss, as was demonstrated in one of our patients. This urinary loss of γ -globulin undoubtedly includes L.E. factor, for this has been demonstrated in the urine (Korting and Schmitz, 1952), and we have noticed that in patients with proteinuria and a normal γ -globulin level the L.E. cells are demonstrable only with difficulty and in scanty numbers. On the other hand, the α_2 -globulin rises to normal levels when proteinuria is present. This is found in the nephrotic syndrome whatever the aetiology, and presumably represents selective retention by the damaged kidney of the high molecular weight α_2 -globulin.

It seems likely that the reason we have rarely found actual increases in the serum α_2 -globulin, as has been reported by other workers, is because we have expressed the protein values in absolute figures and not as percentages, which in this instance, at least, would be misleading.

Even though the serum protein changes in systemic lupus erythematosus are not specific they have diagnostic value in a negative sense. This disease is most unlikely in a patient with a normal serum γ -globulin level in the absence of considerable proteinuria. Unfortunately, changes in the other protein fractions are too slight and too inconstant to be helpful.

In systemic lupus erythematosus the serum proteins probably have little prognostic value, for though those patients with a very low albumin and a normal or only slightly raised γ -globulin level did progress to an early death, this can be forecast from the invariable presence of severe nephropathy.

Summary

The total serum proteins and electrophoretic fractions were measured in a group of patients with systemic lupus erythematosus and compared with the results obtained from a healthy control group.

Eighteen untreated patients with systemic lupus erythematosus but without persistent proteinuria showed statistically significant increases in the total protein and γ -globulin levels and reductions in the albumin, α_2 - and β -globulin levels that were probably significant. The raised γ -globulin was quantitatively the most striking change, and was above the upper normal limit in 17 of the 18 patients.

Seven patients with systemic lupus erythematosus and persistent proteinuria (five were untreated, two were on small doses of steroids) were compared with the 18 patients without proteinuria and showed significantly lower total protein and albumin levels and a higher α_2 -globulin level. The γ -globulin level was lower, but not significantly so. The α_2 -globulin level in the patients with proteinuria was not different from that of the healthy controls, but the γ -globulin was still significantly raised.

Therapeutically induced remissions were accompanied by a reversal of the serum protein changes towards normal, but it was exceptional for the γ -globulin actually to reach normal levels.

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TUBERCULOSIS IN THE FAMILY

BY

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Recent years have seen a fall in the mortality and the incidence of all forms of tuberculosis in children and adults, and it is sometimes assumed that tuberculosis is becoming a relatively unimportant disease. The fall in tuberculous morbidity, however, is much slower than the fall in mortality, and tuberculosis remains among the most important of communicable diseases. In children the source of infection is now almost always an adult contact with pulmonary tuberculosis. The observations described here on tuberculous children and the adults in contact with them indicate the continuing significance of this aspect during a time when many changes are occurring in the management of tuberculosis and in the type of disease seen. The cases described were observed over a period of seven and a half years between 1951 and 1958. The district covered by the two chest clinics and the hospital group is primarily residential, and the overall incidence of tuberculosis is not unduly high. The type of tuberculous disease seen in 87 children under 14 who were treated in the paediatric department is shown in Table I. The disease was classified as primary or disseminated. *Primary* was taken to include mediastinal adenitis with or without segmental collapse, pleural effusion, cervical adenitis, abdominal adenitis, primary cutaneous lesions, and positive tuberculin tests in children under 4 years of age. *Disseminated* included meningitis, miliary tuberculosis, bone and joint disease, renal disease, and adult-type pulmonary disease.

TABLE I.—Type of Tuberculous Disease in 87 Children

Primary Disease (62 Cases)		Disseminated Disease (25 Cases)	
Bronchial adenitis only	27	Meningitis only	10
" " with		" " with miliary	4
segmental collapse	11	Miliary only	2
Pleural effusion	9	Bone and joint	6
Cervical adenitis	7	Renal	1
Abdominal	3	Adult-type pulmonary	2
Cutaneous	2		
Aged 3 and under with positive tuberculin test	3		