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*VII. A Note on the Proteins in Acute Nephritis***

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THE PLASMA PROTEINS IN RELATION TO BLOOD HYDRATION

VII. A NOTE ON THE PROTEINS IN ACUTE NEPHRITIS

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The preceding paper (1) of this series dealt with the serum proteins in chronic nephritis of the nephrotic type. A close relation was established between the concentration of protein in the serum and the occurrence of edema. Evidence was presented to show that the serum protein reduction which involves only the albumin fraction was chiefly the product of two factors, loss of serum albumin in the urine and malnutrition.

In this paper a similar analysis will be made of the serum proteins in acute nephritis. The total serum proteins were determined 85 times on 38 patients; in 55 instances in 22 cases the albumin and globulin fractions were separately determined. The ages of the patients ranged from 2 to 60 years. The infections which preceded and were presumably the etiological factors provoking nephritis, as well as the outcome of the disease, are tabulated below.

Antecedent infection	Number of cases				
	Total	Died	Cured	Improved	Unimproved
Scarlet fever	6	2	2	2	0
Tonsillitis and other upper respiratory infections	16*	2	7*	5	2
Rheumatic fever	4	0	3	1	0
Lobar pneumonia	5	1	1	2	1
Empyema	1	1	0	0	0
Autohemoagglutination	1	1	0	0	0
Unknown	5	1	3	0	1
	38				

* One of these patients also had severe impetigo contagiosa.

The great majority of patients who have been labelled "improved" probably recovered completely, but could not be followed long enough to make this certain. Of the "unimproved" there is reason to believe that

most or all died or developed the chronic form of the disease. The second group, "tonsillitis or upper respiratory infections," is chiefly composed of patients with hemolytic streptococcus infections. Some of them probably belong in the scarlet fever category, but escaped because they presented no exanthematous lesions. The disease in one of the patients in the scarlet fever group began after a sore throat which was unaccompanied by any rash. Because her sister had scarlet fever, the hemolytic streptococci recovered from the throat of the patient were tested and found to be of the scarlet fever variety.

The disturbances of the serum proteins appear to be related neither to the ages of the patients nor to the etiological agents concerned in the production of the disease.

Figure 1 shows the level of the serum proteins, protein fractions and the oncotic pressure in all observations, and the relation of each one of these factors to the occurrence of edema. As in the chronic nephrotic forms of the disease edema was always present when the total protein concentration was less than 4 per cent and, with one exception, when albumin was below 2.20 per cent. On the other hand, it often occurred when the protein and albumin concentrations were above 5 per cent, and occasionally even when they were well within the normal limits. The natural inference to be drawn from the figure is that while oncotic pressure is quite as influential in the production of edema in acute nephritis as it is in the chronic nephrotic condition, some additional factor is active in the acute condition. Moore and Van Slyke (2) and others (3, 4) have reported similar observations.

In Figure 2 the same phenomenon has been illustrated in a different manner. In this figure the abscissae represent the length of time which has elapsed since the onset of nephritic symptoms, the ordinates the serum protein concentration. Solid circles indicate edema. Near the onset of the disease edema is found often enough when the serum proteins are high. As the disease progresses, however, edema disappears unless the proteins fall. It is, of course, impossible to draw sweeping conclusions from such semi-statistical treatment of the data. The majority of the patients who maintained a high protein level throughout the disease recovered rapidly. Therefore, towards the right of the figure, the hollow circles at high levels represent chiefly convalescent or recovered cases, the solid circles at low levels cases that failed to improve or passed through a long nephrotic stage. The development of serum protein deficiency in the latter may be only evidence of advance of the disease; the disappearance of edema in the former, evidence of recovery. The records of certain individual cases in the series make this explanation unsatisfactory.

Number 68285, male, aged 48, was admitted on the 17th day of the disease with a profuse albuminuria, blood pressure of 150/110 and a blood nonprotein nitrogen of 39 mgm. per 100 cc. He had moderate subcutane-

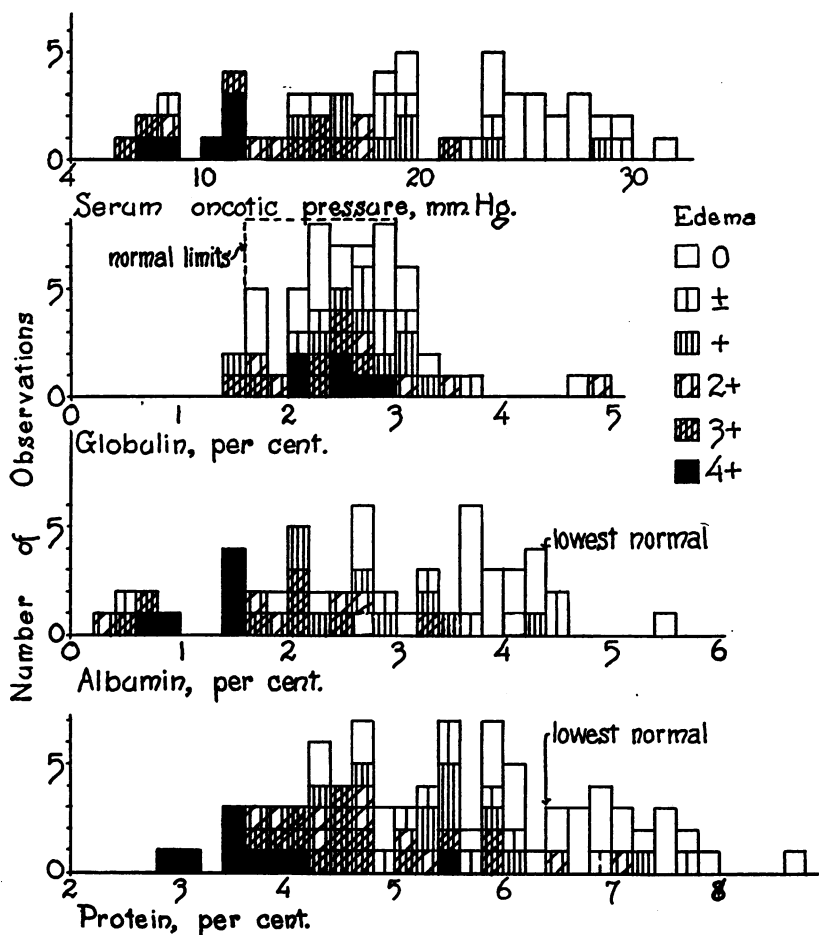


FIG. 1. THE RELATION OF SERUM PROTEINS TO EDEMA IN ACUTE NEPHRITIS

Estimation of the degree of edema is quite rough. ± indicates slight puffiness of the eyes, or slight swelling of the feet noticed by ambulatory patients at the end of the day; + represents persistent, demonstrable swelling of the feet; 2 +, more extensive subcutaneous edema; 3 +, subcutaneous edema and serous effusions; 4 +, extreme general anasarca.

Oncotic pressure was calculated from the serum protein values by the factors of Govaerts (6): $(5.5 \times \text{per cent albumin}) + (1.4 \times \text{per cent globulin}) = \text{oncotic pressure in mm. Hg.}$

ous edema, but diuresis had already actively begun. The serum proteins were 6.18 per cent, albumin 3.84 per cent. The edema showed no tendency to recur although the serum protein as late as the 46th day was only 5.92 per cent, with only 3.69 per cent of albumin. Meanwhile the blood pressure had fallen to normal, but the proteinuria continued undiminished. In this case edema appeared and disappeared in the course of the disease without relation to the serum proteins, which never fell far below the normal limits.

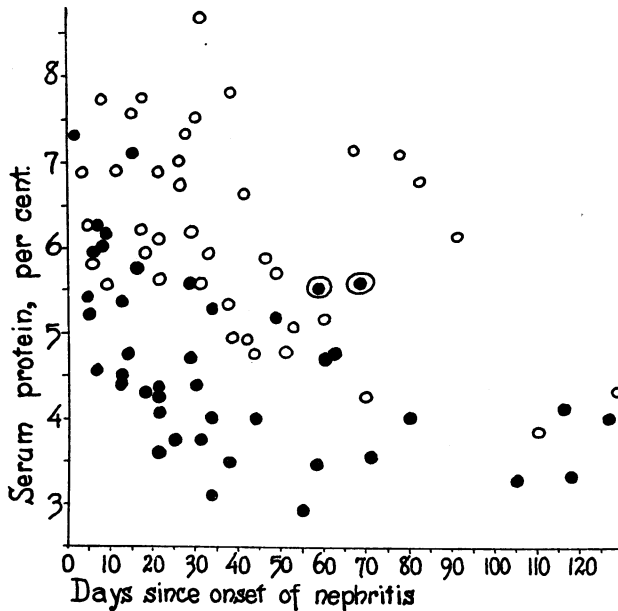


FIG. 2. THE RELATION OF SERUM PROTEINS AND EDEMA TO THE DURATION OF THE DISEASE.

Solid dots represent patients with edema; open circles—patients without edema; ringed dots—patients with distinct evidence of heart failure with edema.

In several cases proteins at the first examination were found somewhat reduced and rose later in the course of the illness, while proteinuria and other evidences of nephritis continued. In these instances edema disappeared as it does in nephrosis cases when the protein in its upward course approached 5 per cent.

If Starling's theory of edema production is accepted, the appearance of edema with a normal serum oncotic pressure must be due either to increased vascular permeability, which permits proteins as well as a protein-free filtrate to pass through the capillary walls, or to increased capillary blood pressure. There can be little doubt, in view of the retinal lesions, the hypertension and other circulatory changes, that the patho-

logical manifestations of acute nephritis are not confined to the kidney, but involve the general vasculature of the body. It is probably to these vascular disturbances that the edema is to be referred. Whether increased vascular permeability or increased hydrostatic pressure is chiefly responsible for the exudation it is still impossible to say. Available analyses of serous effusions from acute nephritic patients reveal only slightly higher concentrations of proteins—about 0.6–0.7 per cent—than are usually found in similar effusions from nephrosis patients ((5, 7) and authors' unpublished data). These are not so high as those found in effusions in heart failure. Unfortunately these determinations have not been made at the inception of the disease.

In this connection attention may be called to the two solid circles which have been distinguished by rings. These two are exceptions to the general rule that edema persists in late stages of the disease only when the proteins are greatly reduced. Both patients had distinct evidences of heart failure, in one of them associated with hemolytic streptococcus septicemia.

The causes of albumin reduction, when this occurs, seem to be the same as those which are operative in the chronic nephrotic forms of nephritis: drainage of serum albumin into the urine and malnutrition, in the sense of protein starvation. Anorexia, nausea, vomiting and digestive disturbances are among the commonest symptoms and are assisted in their destructive work by the infection which so commonly accompanies at least the early stages of the disease. In this series when the patients were able to take diets containing adequate amounts of protein and high calories serum albumin failed to fall or rose if it was low. It fell only when digestive disturbances or the restrictive efforts of physicians limited diets. The value of such restrictions is quite doubtful unless it be assumed that malnutrition and consequent edema are desirable aims of therapy. At least limitation of protein and calories should be practised only over short periods in selected cases.

A further point, to which attention has been called by previous observers, is brought out in Figure 1, the relative frequency of high globulin values. These are presumably referable, not to the renal lesion, but to the infectious process from which it originates and with which it is associated. There is no demonstrable relation between the concentration of globulin and the occurrence of edema.

CONCLUSIONS

Serum proteins have been determined 85 times in 38 cases of acute nephritis.

Edema was regularly found when the protein concentration was below 4 per cent; but was sometimes present in the early stages of the disease when protein and albumin were within or just below the normal limits.

In the early stages of the disease edema appears to be due partly to vascular disturbances which increase the hydrostatic pressure or the permeability of the capillaries.

Serum albumin reductions, when they occur, seem to be referable to leakage of albumin into the urine and malnutrition.

Serum globulin in acute nephritis is frequently above normal.

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