

## THE PLASMA PROTEINS IN RELATION TO BLOOD HYDRATION

### III. THE PLASMA PROTEINS IN MALNUTRITION

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In previous publications from this laboratory it has been shown that patients with diabetes severe enough to cause extreme under-nutrition and evidences of protein starvation regularly have reduced plasma proteins (1). Furthermore patients with the types of nephritis which are characterized by a tendency to edema of non cardiac origin, profuse albuminuria and low plasma proteins (chronic parenchymatous nephritis of the old terminology, nephrosis or nephrotic glomerular nephritis of Volhard and Fahr) also show distinct evidences of protein starvation (2). When given diets sufficiently rich in protein these patients retain large amounts of nitrogen over long periods, without developing any increase in the non protein nitrogen concentration of the blood. Since the early report further cases have been studied and previous observations have been confirmed. Such an ability to store nitrogen has only been observed in patients who have previously suffered protein starvation. We have, therefore, been forced to the conclusion that nephrosis is characterized by protein starvation and believe that this may play an important part in preventing the restoration of the normal plasma protein concentration.

The association of low plasma proteins with evidences of protein starvation in two entirely unrelated conditions has led to the investigation of patients with malnutrition due to various causes which would presumably lead to protein starvation. The results of these studies appear in the table.

For the determination of plasma or serum proteins the techniques described in the previous papers of this series were employed. Blood was withdrawn with a syringe from an artery or from a vein (without the production of venous stasis) and immediately transferred to a centrifuge tube under oil, without contact with air. The oil was displaced by the blood from the tube and the latter was tightly stoppered. After centrifugation the serum or plasma was removed and analyzed for total nitrogen by the regular Kjeldahl procedure. A sample of the whole blood or the serum was also analyzed by the Folin and Wu procedure for non-protein nitrogen.  $(\text{total N} - \text{non-protein N}) \times 6.25 = \text{protein}$ . For the most recent studies serum was employed; earlier plasma was used for analysis. Plasma was obtained by collecting the blood in a centrifuge tube the walls of which had been coated with enough neutral, dried potassium oxalate to make a concentration of 0.2 per cent when the tube was filled with blood.

Although the number of cases studied is comparatively limited, it includes such a variety of unrelated conditions and the results are so consistent that it seems warranted to present them and to advance the tentative hypothesis that low plasma proteins are found in patients suffering from severe malnutrition with serious depletion of the protein stores of the body and may be considered an indication of previous protein starvation in patients without obvious cardiac disease or nephritis of the hypertensive type. In the latter conditions, reduction of the proteins of the plasma which are not easily explained as the result of undernutrition may be frequently encountered.<sup>1</sup>

It must be emphasized that conditions that cause malnutrition also frequently lead to dehydration. The latter may, by producing hemoconcentration mask the plasma protein reduction. Such effects of hemoconcentration were demonstrated during diabetic acidosis (1) and are well illustrated in cases 46584 and 9002 of this study.

The term "plasma" proteins has been used throughout this discussion, although in some of the more recent studies, as indicated in the table, serum and not plasma was employed for the analyses. Serum is preferable for two reasons. It has been frequently demonstrated, most recently by Eisenman (7) from this laboratory, that the addition of oxalate to blood causes contraction of the blood cells and the passage of fluid from the cells to the plasma. Fibrinogen appears to differ from the other proteins of the plasma in both func-

<sup>1</sup> Unpublished studies.

TABLE 1  
*Plasma proteins in malnutrition*

Case number	Date	Plasma proteins* <i>per cent</i>	Diagnosis and remarks
8169	August 31, 1922	5.89	Pernicious anemia. Red blood cells 0.8 million. Pitting edema of legs
	June 2, 1923	6.57	Red blood cells 0.65 million. Pitting edema of legs
33106	October 14, 1924	5.42	Pernicious anemia. Red blood cells 0.60 million. Generalized subcutaneous edema, ascites and double hydrothorax
33372	May 29 1924	3.68	Advanced pulmonary tuberculosis. General anasarca
35686	January 19, 1925	5.87s	Tuberculous pneumonia. Marked under-nutrition
35966	February 16, 1925	5.63s	Advanced disseminated pulmonary tuberculosis. Edema of legs
54894	September 2, 1926	6.04s	Abscess of lung. Marked emaciation. Examination of blood when general condition was beginning to improve
29239	February 18, 1924	5.98	Esophageal carcinoma with almost complete obstruction
	March 1, 1924	5.89	After gastrostomy, when patient was improving
26690	December 28, 1923	5.52	Carcinoma of ascending colon with almost complete obstruction. After the administration of fluids
46584	December 22, 1925	5.87s	Carcinoma of stomach with complete obstruction of pylorus. Before saline treatment, when patient was extremely dehydrated
	December 23, 1925	4.69s	After subcutaneous administration of saline
	December 26, 1925	4.11	Three days after gastroenterostomy
8834	April 27, 1926	5.80s	Duodenal ulcer with complete pyloric obstruction. Before treatment
9002	June 3, 1926	7.17s	Strangulated intestinal hernia with complete intestinal obstruction. Before treatment
	June 7, 1926	5.73	when patient was extremely dehydrated, and after he had received saline
22798	September 20, 1923	4.89	Extensive burns of trunk and extremities in an old man. Fluids had been forced to the point of producing edema
46876	November 24, 1925	4.90s	Mild diabetic with arsenical dermatitis which proved fatal. Patient was almost entirely unable to eat

TABLE 1—*Concluded*

Case number	Date	Plasma proteins*	Diagnosis and remarks
		<i>per cent</i>	
34753	June 16, 1926	3.44s	Intestinal tuberculosis with severe diarrhea and extreme emaciation. Pitting edema of legs and feet
	July 1, 1926	3.56s	
54174	June 9, 1926	3.56s	Bacterial endocarditis. Quite wasted
22114	July 2, 1923	5.52	Adenoma of uterine cervix. Cachexia. Secondary anemia. Red blood cells 1.10 million
35608	January 5, 1925	5.28s	Lobar pneumonia. Severe secondary anemia of unknown origin. Red blood cells 2.70 million. Patient had been losing weight and strength for 2 months before onset of pneumonia
48373	September 13, 1926	3.69s	Boy, aged 6 years. General peritonitis from perforated appendix had led to an anastomosis between jejunum and colon and side tracking the intermediate portions of the gut. Under these conditions he had become extremely wasted and emaciated and had developed generalized subcutaneous edema and ascites
51600	August 14, 1926	4.99s	Chronic pulmonary tuberculosis, bilateral and extensive. Moderate albuminuria. Patient presented slight anemia and was apparently in a fair state of nutrition

\* For protein determinations marked s serum and not plasma was employed.

tion and origin. It is definitely increased, independently of the other proteins, by inflammatory or carcinomatous conditions. If only total proteins are determined such fibrinogen increases may partially or entirely mask reductions of albumin and globulin.

The frequency of edema in these patients is worthy of note. Cachectic or nutritional edemas have been long recognized and have been ascribed by several investigators (3, 4) to protein starvation. Although there is no direct relation between the occurrence of edema and the degree of plasma protein reduction, the latter, by reducing the colloidal osmotic pressure of the plasma (5, 6), must play at least

a contributory part in the production of edema just as it does in nephrosis.<sup>2</sup>

#### CONCLUSIONS

Low plasma proteins have been found consistently in patients who, from a variety of causes, have developed severe malnutrition. It is suggested that reduction of the plasma proteins in individuals without obvious cardiac disease or nephritis of the types associated with hypertension and uremia, is an indication of previous protein starvation and at least a contributory cause of cachectic and starvation edemas.

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<sup>2</sup> Knack and Neumann (*D. med. Woch.*, 1917, xliii, 901) found low refractive indices in the sera of patients with famine edema. This is the only attempt to estimate serum proteins in this condition that we have been able to find in the literature.