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Abstract. A series of plasma and ascitic fluid specimens withdrawn from patients with cirrhosis, and a series from one patient over a seven-week period prior to his death, were subjected to electrophoretic analysis. The results indicate a qualitative similarity between plasma and ascitic fluid protein patterns. In most instances, the ascitic fluid contained more albumin, alpha$_1$ and gamma globulins than the plasma, whereas the plasma was richer in alpha$_2$ and beta globulins and fibrinogen. Based on the molecular weights of the protein fractions, the values indicate that selective protein enrichment of ascitic fluid may be related to the molecular size of the protein components.

The variations in the plasma proteins in cirrhosis of the liver have been the stimulus for considerable investigative work. Since Gilbert and Chiray (1907) reported a diminution of total protein in cirrhosis with ascites, and Grenet (1907) observed similar changes in cirrhosis without ascites, the problem has been approached from many angles. Using the chemical precipitation method of Howe (1921), investigators such as Salvesen (1929), Abrami and Wallich (1929), Wiener and Wiener (1930), Peters and Eisenman (1933), and Turner and Bockus (1937), noted a reduction in the albumin and an increase in the globulin of the plasma in cirrhosis.

Meyers and Keefer (1935) found that a high protein diet was not effective in restoring plasma proteins to normal. They observed that the ascitic fluid contained a greater proportion of albumin to globulin than did the plasma and felt that this loss of albumin was significant in the production of edema. Post and Patek (1942) traced the changes in plasma proteins throughout the course of the disease and concluded that the trend of changes in the albumin value was of prognostic significance, in so far as a rise in this fraction followed improvement. A high protein intake produced no consistent rise in albumin, although the nitrogen balance was positive. Thorn *et al.* (1946) were able to produce diuresis proportional to the amount of edema by the intravenous administration of salt-poor concentrated human serum albumin solution. A rise in the plasma albumin attended this procedure.

Kendall (1937) demonstrated an altered plasma protein relationship in this disease by immunologic methods emphasizing the alpha

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globulin fraction. This fraction was also consistently elevated in all the cases studied by Stacy (1945).

In contrast to the numerous studies of the plasma proteins in cirrhosis by chemical precipitation methods, electrophoretic technique has not been extensively applied to this problem. Luetscher, in 1941, reported the protein components of three pairs of plasma and ascitic fluids in cirrhosis in an electrophoretic study of plasma and serous effusions. An electrophoretic analysis of the serum of twelve patients with cirrhosis was included in an investigation by Gray and Barron in 1943. Popper *et al.* (1950) investigated the correlation between electrophoretic and chemical partitions of serum proteins. The following year this group in two separate investigations, Popper *et al.* (1951) and Franklin *et al.* (1951), reported a study of the electrophoretic serum protein fractions in hepatobiliary disease, and a comparison of serum and plasma electrophoretic patterns in liver disease.

Although the protein content of ascitic fluid has been the subject of a few investigations, the technique of electrophoresis has been sparingly applied to this problem. The present paper is concerned with the electrophoretic analyses of a series of plasma and ascitic fluid samples from patients with cirrhosis. It includes a series of samples withdrawn from the same patient over a seven-week period prior to his death.

Experimental

Plasma and ascitic fluid samples were withdrawn from the patients at approximately the same time whenever paracentesis was necessary. Plasma was diluted with three parts of a barbiturate buffer of pH 8.6 and ionic strength 0.1, whereas fluid samples were diluted to a protein concentration of 1.5 to 2.0 per cent. Electrophoresis was conducted in the Tiselius apparatus by passing 25 milli-amperes of current through the cell for 120 minutes. All of the results in this paper were obtained from descending patterns.

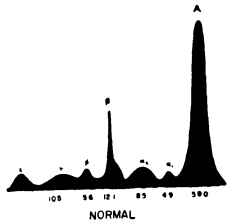
Results

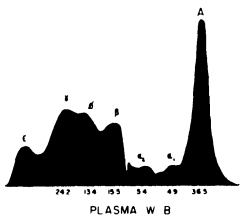
Typical results obtained from an electrophoretic analysis of plasma and ascitic fluid pairs are shown in Table 1. Values for normal plasma and the approximate molecular weights of the protein fractions are included for comparison. Table 2 presents a series of values obtained from plasma and ascitic fluid pairs withdrawn at approximately weekly intervals for seven weeks prior to the death of a patient (W.B.) with cirrhosis. The electrophoretic patterns of plasma and ascitic fluid from this and another patient and from normal plasma are illustrated in Figure 1.

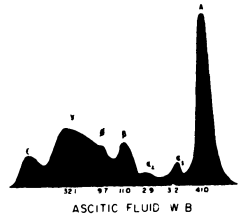
Discussion

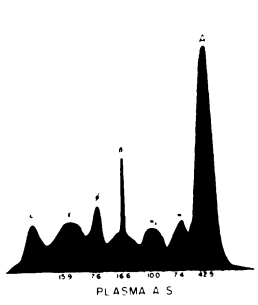
The patterns for plasma and ascitic fluid (W. B.), Figure 1, are typical for severe cirrhosis. Various stages of the disease are represented in Table 1, although each patient had in common the development of ascites. There is no orderly progression of the disease evident in the seven-week series of specimens in patient W. B., Table 2. Since this series covered the last weeks of the patient's life, it may be reasonable to classify these results as pre-terminal findings.

Several interesting comparisons might be made between the plasma and fluid samples in Tables 1 and 2. There is a marked









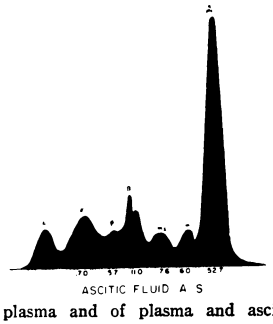


Figure 1. Electrophoretic patterns of normal plasma and of plasma and ascitic fluid in cirrhosis.

Table 1

Electrophoretic Analyses of Plasma and Ascitic Fluid in Cirrhosis

Patient	Specimen	Alb.	α_1	α_2	β	ϕ	γ
E. P.	Plasma	32.6	3.9	14.4	20.5	11.2	17.4
	Fluid	47.9	6.6	7.7	15.3	3.7	18.8
M. J.	Plasma	36.1	6.0	12.0	12.2	8.2	25.5
	Fluid	41.2	5.6	7.1	10.6	5.4	30.7
J. J.	Plasma	42.7	8.2	13.7	15.9	8.6	10.9
	Fluid	50.7	5.7	8.4	17.7	2.7	14.8
S. W.	Plasma	24.6	8.0	8.5	23.8	17.1	18.0
	Fluid	35.0	9.0	8.1	16.1	6.3	25.6
A. S.	Plasma	42.5	7.4	10.0	16.6	7.6	15.9
	Fluid	52.7	6.0	7.6	11.0	5.7	17.0
M. F.	Plasma	33.2	12.1	7.6	27.2	9.8	10.1
	Fluid	39.6	12.6	12.3	15.5	4.7	15.3
Average Normal Plasma		59.0	4.9	8.5	12.1	5.6	10.2
Approximate Molecular Weights		69,000	200,000	300,000	1,300,000	400,000	156,000

Table 2

Electrophoretic Analyses of Plasma and Ascitic Fluids in Cirrhosis Patient, W. B.

Date	Specimen	Alb.	α_1	α_2	β	ϕ	γ
7/10	Plasma	36.5	4.9	5.4	15.5	13.4	24.2
	Fluid	41.0	3.2	2.9	11.0	9.7	32.1
7/15	Plasma	31.9	3.6	4.1	17.1	14.9	28.4
	Fluid	35.1	3.6	4.7	12.1	8.6	35.9
7/23	Plasma	30.9	3.8	3.8	12.9	17.7	30.8
	Fluid	37.2	4.6	3.7	12.3	11.5	30.7
7/31	Plasma	32.7	2.7	4.5	18.9	17.6	23.6
	Fluid	37.7	3.8	3.3	15.7	16.6	22.9
8/5	Plasma	29.9	2.9	5.2	12.4	16.5	33.1
	Fluid	34.2	3.2	4.8	14.5	11.6	31.6
8/18	Plasma	34.6	4.6	7.4	12.3	13.0	28.1
	Fluid	37.3	6.1	3.4	13.9	8.9	30.3
8/26	Plasma	32.9	5.7	5.6	16.4	14.1	25.2
	Fluid	39.0	2.7	2.4	15.7	6.8	33.4

similarity of protein component distribution in the plasma and ascitic fluid specimens drawn at the same time from any patient. The specimens in cirrhosis demonstrate a marked reduction in albumin and increase in beta and gamma globulins and fibrinogen compared to normal plasma. As seen from the approximate molecular weights of the protein components of plasma in Table 1, albumin, and γ and α_1 globulins are the smallest molecules, whereas α_2 and β globulins and fibrinogen are the largest. The data indicate that there is always more albumin in the ascitic fluid than in the plasma drawn at the same time. There is also more α_1 and γ globulin on the average in the fluid than in the plasma. On the other hand α_2 and β globulin and fibrinogen are consistently higher in the plasma than in the fluid. These findings are in agreement with those reported by Luetscher (1941) on three pairs of plasma and ascitic fluid samples, although it is difficult to compare the α globulin since at that time it was not divided into α_1 and α_2 globulins. The most obvious explanation for these results is the difference in molecular weight. Albumin is the smallest followed by γ and α_1 globulins, whereas α_2 and β globulins and fibrinogen are the largest molecules. The smaller molecules would pass more readily through membranes during the formation of ascitic fluid while the larger molecules would tend to remain in the plasma.

The fact that the fluid patterns are very similar to those of the plasma suggests an equilibrium between the plasma and ascitic fluid proteins in a normal individual. In cirrhosis, when abnormal quantities of ascitic fluid are formed, this equilibrium may be disturbed and a dynamic state exist in which the molecular weights of the plasma proteins exert an influence on their passage from the plasma to the fluid.

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