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Electrophoretic Analysis of the Proteins of Body Fluids in Various Disease States

J. I. Routh and W. D. Paul[1]

Abstract. Plasma, serum, and body fluid specimens (pleural fluid, ascitic fluid, synovial fluid, edema fluid, hydrocele fluid, cyst fluid, lymph, bile, and subdural fluid) from patients with heart disease, carcinoma, liver disease, and arthritis, were subjected to electrophoretic analysis. A decrease in plasma albumin and an increase in globulin components occurred in the disease conditions. In most instances the albumin and gamma globulin were higher, the α_1 globulin the same, and the α_2 and β globulin and fibrinogen in lower concentration in the fluid than in the corresponding plasma specimen. The distribution of the protein components between the plasma and fluid is explained on the basis of their molecular weights.

For the past several years our laboratory has been interested in the protein composition of body fluids other than plasma or serum. Abnormal increases in normal body fluid commonly occur in cardiac conditions, carcinoma, liver disease and arthritis. Leutscher (1941) first reported electrophoretic analysis of pleural fluid in cardiac patients. A more extensive study of pleural fluid, ascitic fluid, and edema fluid in heart cases was carried out by Keller and Spang (1953). The average albumin content of these fluids was higher than that of the corresponding serum specimens, whereas the fluid gamma globulin content was lower than that of the serum. In studies of serum and plasma proteins in liver disease in our laboratory (Franklin et al., 1951), ascitic fluids were often drawn and simultaneously analyzed. A comparison of plasma and ascitic fluid proteins in a series of specimens obtained in terminal cirrhosis has recently been published (Routh and Paul, 1960). The electrophoretic patterns of proteins in synovial fluid and serum in rheumatoid arthritis have been studied by Perlmann et al. (1954) and Schmid and MacNair (1956). Perlmann divided the fluids into three groups—those with more albumin than the serum, those with approximately equal concentrations of albumin, and those with less albumin than the serum. In the first group the fluid gamma globulin concentration was less than that of the serum, but in the last two groups it was higher than that of the serum.

The present paper is concerned with further electrophoretic studies of fluids and plasma in heart disease, liver disease, and arthritis. A series of fluid-plasma pairs obtained from patients with carcinoma and a group of uncommon body fluids are also included.

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Experimental

Patients with abnormal accumulations of body fluids accompanying a disease process served as subjects of this investigation. Pleural fluid, edema fluid, subdural fluid, hydrocele fluid, ascitic fluid, synovial fluid, cyst fluid and lymph specimens were obtained. In most instances a plasma sample was obtained at the time the fluid was withdrawn. Whenever the total protein content was adequate all specimens were diluted to approximately 1.5 per cent protein with a barbiturate buffer, pH 8.6 and ionic strength of 0.1. The solutions were dialyzed at 5°C for three days with daily change of buffer in preparation for electrophoresis. The Tiselius apparatus was used for electrophoretic analysis during which 25 milliamperes of current were passed for 120 minutes under standardized conditions established in our laboratory. The analytical results reported in this investigation were obtained from descending patterns.

Results

Heart Disease

Patients with this classification included those diagnosed as having arteriosclerosis, cardiac hypertrophy, cardiac failure, cardiac decompensation, superior vena cava thrombosis, or rheumatic heart disease. Plasma and pleural fluid were obtained from most patients, as well as an occasional ascitic fluid or urine specimen. The results of electrophoretic analysis of typical fluids are shown in Table 1.

Carcinoma

These patients had carcinoma of the lung, stomach, or ovary; generalized carcinoma; or chronic myeloid leukemia. Plasma and pleural fluids were the main specimens collected from this group. Examples of the protein composition of these fluids are shown in Table 2.

Liver Disease

Patients with Lannecs cirrhosis frequently form large volumes of ascitic fluid which must be tapped. Results of electrophoretic analysis of typical plasma-ascitic fluid pairs from these patients are presented in Table 3.

Arthritis

The volume of synovial fluid often increases in patients with rheumatoid arthritis and osteoarthritis. Typical results of the electrophoretic analysis of plasma and synovial fluid specimens are shown in Table 4.

Uncommon Fluids

A miscellaneous group of fluids, including edema fluid, hydrocele fluid, cyst fluid, lymph, bile, and subdural fluid, was collected. The analytical results are reported in Table 5.

Discussion

Considerable variations in plasma and pleural fluid components occurred in heart disease (Table 1). Patients W. P. and E. P. exhibited minor changes in plasma proteins compared to normal plasma, and pleural fluid components were similar to those in the plasma. Much more extensive changes occurred in patients G. M. and J. B. in both plasma and pleural fluids. In general, the plasma in heart disease showed a marked decrease in albumin and an increase in all globulin components. The pleural fluid specimens always contained more albumin, and in all but two instances more gamma globulin, than the corresponding plasma specimens. The α_1 globulin values were similar, whereas the other globulin components were lower in the fluid than the plasma. These values are similar to those reported by Keller and Spang (1953) with the important exception that the average gamma globulin of all their fluids was less than the average serum values.

Patients with carcinoma of the lungs, stomach, and ovary formed abnormal quantities of pleural fluid (Table 2). The protein components of the fluid reflected the changes in the plasma that resulted from the disease. The plasma variations in carcinoma consisted of a marked decrease in albumin, accompanied by increases in all the globulin fractions. The pleural fluid albumin and gamma globulin were almost always higher in concentration than in the corresponding plasma. The α_1 globulin fraction was similar in the fluid and plasma, but the other globulin components were in higher concentration in the plasma.

The electrophoretic analyses of plasma and ascitic fluid in liver disease (Table 3) yielded results similar to those reported earlier from this laboratory (Routh and Paul, 1960). Marked decreases of albumin and increases of gamma globulin and other globulin components were found when plasma in disease was compared to normal plasma. The ascitic fluid components showed a pattern similar to those reported above for heart disease and carcinoma when compared to plasma drawn at the same time.

For many years patients with rheumatoid arthritis have been studied in our laboratory, and investigations of plasma and serum proteins by electrophoretic technique have been reported (Routh and Paul, 1950). The values shown in Table 4 for the protein components of plasma in this disease are similar to those reported by other investigators (Ropes et al., 1954). The synovial fluid components however, do not completely agree with any of the three groups classified by Perlmann et al. (1954). The great majority of specimens exhibited more albumin and a large increase in gamma globulin over their corresponding plasmas. The average α_1 globulin concentration was similar in plasma

and fluid, and the other globulin components were in lower concentration in the fluid.

Table 5 presents data on fluids which are not commonly analyzed. No definite pattern was apparent when the protein components of these fluids were compared to serum or plasma drawn at the same time. In general, the albumin content of the fluids was higher than the plasma or serum but no constant relationship was observed between gamma globulins or other globulins in the fluids and those in the plasma or serum. The outstanding observation based on the data in this table is the widespread distribution of the globulin components in the various fluids.

A consideration of the approximate molecular weights of the protein components (Table 5) may assist in an explanation of the fairly constant pattern of results in heart disease, carcinoma, liver disease, and arthritis. Albumin and gamma globulin are the smallest molecules, which may explain their ease of passage into the various fluids. A molecular weight of 200,000 appears to be a balance point where equal quantities of the component (α_1 globulin) will pass into the serum or remain in the plasma. The α_2 and β globulins and fibrinogen molecules are so large that they tend to pass the membranes with greater difficulty, thus producing a greater concentration in the plasma.

The results obtained in this investigation further emphasize the probability that an equilibrium exists between the protein components of plasma and normal pleural and ascitic fluids. In the disease conditions studied the permeability of the membranes separating these fluids may be altered to upset this equilibrium and to allow passage of proteins, depending on their molecular size.

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Table 1. Electrophoretic analyses of plasma and fluids in heart disease.

Patient	Specimen	Diagnosis	Alb.	α_1	α_2	β	ϕ	Υ
J. B.	Plasma	Cardiac Decomp.	17.9	7.3	10.8	42.4	17.7	3.9
	Pleural Fluid		33.5	27.7	17.0	15.4	...	6.4
O. F.	Plasma	Hyper. Heart	36.5	9.8	8.1	16.0	10.7	18.9
	Pleural Fluid		43.3	8.8	9.9	11.0	2.7	24.4
H. H.	Plasma	Cardiac Failure	31.8	8.2	15.6	17.0	10.3	17.1
	Pleural Fluid		48.1	5.8	7.9	13.9	5.1	19.2
G. M.	Plasma	Cardiac Failure	12.1	8.5	13.2	9.5	18.5	38.2
	Pleural Fluid		23.2	11.3	7.2	7.8	16.3	34.2
W. P.	Plasma	Sup. ven. cav.	51.3	6.5	11.4	14.4	7.3	9.1
	Pleural Fluid	Thrombosis	66.4	5.7	6.7	10.6	0.9	9.7
E. P.	Plasma	Cardiac Decomp.	52.7	6.7	7.3	15.0	5.6	12.7
	Pleural Fluid		59.4	9.4	6.0	12.1	2.0	11.1
G. R.	Plasma	ASHD	34.7	11.0	13.3	16.4	11.9	12.7
	Pleural Fluid		39.4	9.3	3.4	23.1	7.0	17.8
A. S.	Plasma	Rheumatic Heart	42.5	7.4	10.0	16.6	7.6	15.9
	Pleural Fluid		52.7	6.0	7.6	11.0	5.7	17.0
	Ascitic Fluid		48.5	6.9	8.0	14.5	6.9	15.2
Average Normal Plasma			59.0	4.9	8.5	12.1	5.6	10.2
Average 13 patients, 20 plasmas			29.7	8.7	11.1	17.1	10.0	13.4
Average 13 patients, 27 pleural fluids			48.5	9.1	8.6	13.6	4.5	15.7

Table 2. Electrophoretic analyses of plasma and fluids in carcinoma.

Patient	Specimen	Diagnosis	Alb.	α_1	α_2	β	ϕ	Υ
J. A.	Plasma	General Carcinoma	27.6	14.3	22.4	10.6	16.3	8.8
	Pleural Fluid		43.1	5.9	5.6	10.8	22.8	11.8
R. B.	Serum	Carcinoma of Ovary	26.8	11.2	30.7	11.4	...	19.9
	Pleural Fluid		37.2	13.3	17.5	9.3	5.5	17.2
J. B.	Plasma	Carcinoma of Stomach	31.1	6.8	6.9	17.5	18.7	19.0
	Ascitic Fliud		31.8	14.2	7.6	14.4	6.7	25.3
R. K.	Plasma	Bronchiogenic	40.0	7.5	18.6	13.2	7.5	13.2
	Pleural Fluid	Carcinoma	50.2	7.6	14.8	11.9	...	15.5
M. L.	Plasma	Carcinoma of Ovary	44.2	6.3	16.4	17.2	9.6	6.3
	Pleural Fluid		63.8	8.6	8.0	9.1	3.6	6.9
E. P.	Plasma	Myeloid	42.1	12.3	5.8	23.3	6.9	9.6
	Pleural Fluid	Leukemia	46.9	14.9	9.6	14.6	3.4	10.6
G. T.	Plasma	Bronchiogenic	30.2	12.0	14.8	15.8	14.0	13.2
	Pleural Fluid	Carcinoma	41.4	11.8	10.3	14.9	6.1	15.5
B. W.	Plasma	Carcinoma of Stomach	33.7	8.8	14.0	14.0	15.2	14.4
	Pleural Fluid		39.6	10.2	9.8	10.5	9.3	20.6
Average Normal Plasma			59.0	4.9	8.5	12.1	5.6	10.2
Average 11 patients, 12 plasmas			35.2	10.1	14.9	16.1	11.0	12.7
Average 11 patients, 13 fluids			45.1	10.2	10.2	12.8	7.0	14.7

Table 3. Electrophoretic analyses of plasma and ascitic fluid in liver disease.

Patient	Specimen	Diagnosis	Alb.	α_1	α_2	β	ϕ	γ
C.	Plasma	Cirrhosis	28.2	4.5	14.6	29.1	...	23.6
	Ascitic Fluid		38.0	9.7	5.2	11.0	13.1	23.1
E. H.	Plasma	Cirrhosis	35.5	9.7	13.6	17.9	9.5	13.7
	Ascitic Fluid		40.6	10.9	10.3	17.7	7.6	12.9
E. M.	Plasma	Cirrhosis	40.8	4.7	7.2	6.4	11.1	29.8
	Ascitic Fluid		45.2	6.5	5.6	10.6	9.7	22.4
R. M.	Plasma	Cirrhosis	37.6	9.8	12.5	16.8	12.4	10.9
	Ascitic Fluid		44.3	9.4	2.5	17.1	15.3	11.3
A. R.	Serum	Cirrhosis	34.7	10.5	15.5	11.8	3.7	23.8
	Ascitic Fluid		36.5	12.4	11.7	13.5	8.2	17.7
L. S.	Plasma	Cirrhosis	32.5	7.5	8.7	14.5	9.8	27.0
	Ascitic Fluid		46.3	7.1	6.4	8.9	7.9	23.4
N. S.	Plasma	Obstruct.	34.9	7.5	29.6	6.8	10.4	10.8
	Ascitic Fluid	Jaundice	37.6	11.2	22.1	13.2	...	15.9
A. Y.	Plasma	Cirrhosis	33.2	6.0	6.6	11.4	12.0	30.8
	Ascitic Fluid		38.4	6.8	8.4	8.4	3.2	34.8
Average Normal Plasma			59.0	4.9	8.5	12.1	5.6	10.2
Average 15 patients, 21 plasmas			34.2	6.4	10.1	16.0	11.3	22.0
Average 15 patients, 21 fluids			40.7	6.9	7.1	13.4	8.1	23.8

Table 4. Electrophoretic analyses of plasma and synovial fluid in arthritis.

Patient	Specimen	Diagnosis	Alb.	α_1	α_2	β	ϕ	Υ
F. A.	Plasma	Rheu. Arthritis	43.0	11.3	18.0	11.3	7.3	9.1
	Synovial Fluid		49.8	11.4	13.6	8.3	6.3	10.6
J. D.	Plasma	Rheu. Arthritis	48.7	6.6	13.6	9.8	7.7	13.6
	Synovial Fluid		52.8	4.4	9.7	11.5	2.2	19.4
M. F.	Plasma	Rheu. Arthritis	39.4	5.5	17.5	20.2	8.9	8.5
	Synovial Fluid		52.3	8.4	9.3	16.2	1.9	11.9
H. F.	Plasma	Rheu. Arthritis	43.6	6.6	18.2	8.8	11.9	10.9
	Synovial Fluid		53.0	5.7	7.3	13.4	3.7	16.9
O .H.	Plasma	Rheu. Arthritis	43.5	5.2	12.0	11.5	11.8	16.0
	Synovial Fluid		49.1	8.1	9.5	12.3	3.5	17.5
V. H.	Plasma	Rheu. Arthritis	39.5	9.7	21.8	7.4	8.6	13.0
	Synovial Fluid		46.7	4.4	6.2	11.0	5.3	26.4
F. M.	Plasma	Rheu. Arthritis	44.4	7.3	9.4	9.6	9.4	19.9
	Synovial Fluid		50.3	7.0	7.0	10.5	3.2	22.0
C. W.	Plasma	Hyper. Arthritis	45.2	6.0	9.4	15.7	10.6	13.1
	Synovial Fluid		59.1	4.5	6.9	15.0	3.0	11.5
Average Normal Plasma			59.0	4.9	8.5	12.1	5.6	10.2
Average 14 patients, 15 plasmas			40.9	7.8	15.7	12.6	9.0	14.0
Average 14 patients, 17 synovial fluids			42.6	7.5	8.9	11.7	5.3	24.0

Table 5. Electrophoretic analyses of plasma and uncommon body fluids.

Patient	Specimen	Diagnosis	Alb.	α_1	α_2	β	ϕ	Υ
W. D.	Plasma	Pamphigus	46.8	6.6	16.3	12.1	7.9	10.3
	Blister Fluid	Vulgaris	56.0	8.0	12.0	10.0	2.0	12.0
C. F.	Plasma	Cystic Dis.	32.9	14.9	15.3	11.0	18.0	7.8
	Liver Cyst Fluid	of Liver	60.2	19.3	5.9	9.1	2.2	3.3
N. G.	Plasma		48.2	5.8	4.7	22.6	6.3	12.4
	Hydrocele Fluid		41.3	6.2	12.8	7.1	7.3	25.4
V. G.	Plasma	Thrombocytopenia	53.6	8.3	6.8	15.4	7.1	8.8
	Urine	Purpura	65.8	12.3	3.1	9.2	1.7	7.9
W. H.	Plasma	Infect.	51.7	4.8	10.1	15.1	6.0	12.3
	Lymph	Arthritis	58.3	8.5	6.1	14.0	...	13.1
R.	Serum		58.6	7.3	17.2	10.7	1.4	4.8
	Subdural Fluid		56.0	8.7	9.8	15.0	2.8	7.7
A. Y.	Plasma	Cirrhosis	33.2	6.0	6.6	11.4	12.0	30.8
	Edema Fluid		43.4	5.6	5.6	10.5	4.2	30.7
S. H.	Rt. subdural fl.		77.3	5.4	5.4	7.9	...	4.0
	Left subdural fl.		81.5	4.7	4.4	6.5	...	2.9
V. Mc.	Cyst Fluid	Mulheim duct cyst	63.9	10.9	9.1	6.2	3.4	6.5
W.	bile	Liver disease	38.3	3.2	4.7	7.8	11.0	35.0
Approximate Molecular Weights			69,000	200,000	300,000	1,300,000	400,000	156,000