injections of gamma globulin† may have been responsible for the increases in plasma levels which occurred in the 2 patients with low values.

Summary. Multiple electrophoretic determinations of the plasma proteins of 23 patients with pneumococcic pneumonia or meningitis have been made in relation to the duration of the infection and the importance of antecedent factors. Hypoproteinemia, due largely to significant progressive hypoalbuminemia, together with early increases in alpha-globulins and fibrinogen have been observed. Malnutrition, chronic alcoholism, cirrhosis and chronic passive congestion of the liver were found associated with more severe degrees of hypoalbuminemia. Diminished plasma albumin levels were seldom restored to normal within a month from the onset of the infection. The effects of intramuscular injections of immune human gamma globulin were investigated, with inconclusive results.

† Dr. W. Addison Clay assayed the protective power of gamma globulin in type 27 pneumococcic peritonitis in 40 mice and found a reduction of gross mortality from 95 to 55%. By serial dilutions the protective power was estimated to be of the order of one ten thousandth of that of immune rabbit serum.

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Effects of Albumin on Hypoalbuminemia in Pneumococcic Pneumonia.

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A previous report[1] confirmed the findings of others that patients with pneumococcic infection exhibit hypoalbuminemia within the first 2 weeks of the infection. Results obtained by electrophoresis of plasma proteins showed depression of albumin concentrations to as low as 1.4 to 1.8 g%, and that normal concentration was not often established within a month after the infection. Such marked hypoalbuminemia was considered to be the result of protein loss in exudate and urine in addition to protein break-down and malnutrition during the acute phase of the illness. Because of this hypoalbuminemia the effects of intravenous albumin therapy were investigated. This report presents the metabolic changes as well as some of the secondary effects of such therapy on cardio-respiratory functions.

Patients and procedures. During 1947 eight patients with severe pneumococcic lobar pneumonia were selected, and in addition to the routine chemotherapy of the infection 2 were controls, and 6 were treated with albumin. Observations on still another patient are included because of a fatal outcome following albumin therapy. The 6 albumin-treated patients and one control were placed on a special liquid diet† of known nitrogen content a day or two after the restoration of normal temperature following the febrile reaction. Twenty-four hour urinary collections were made to determine urinary nitrogen ex-

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1 Bruce, R. A., Alling, E. L., and Barnett, A. D., PROC. SOC. EXP. BIOL. AND MED., 1948, **69**, 398.

† The diet consisted of 1200 ml of powdered whole milk, eggs, yeast, and sugar in addition to orange juice. There was 17.7 g of nitrogen in this mixture. To satisfy some patients, the amount of diet had to be increased to 2400 ml volume.

TABLE I.
Results of Albumin Administration in Patients with Pneumococcic Lobar Pneumonia.
A. Effects on Plasma Albumin Levels and Protein Metabolism.

Patient	Day of illness when alb. was started	Plasma albumin conc., g/100 ml			Protein intake, g		Apparent retention in protein during period of observation, g
		Before	After	1 wk later	Dietary	Alb. i.v.	
J.S.	Control	2.65	2.85	2.88	542	—	62
C.M.	"	3.20		3.24	*	—	—
D.P.	5	2.48	3.46	3.48	611	100	245
W.D.	10	2.68	3.74	3.91	743	100	—
A.M.	7	2.51	3.64	3.78	743	100	244
S.W.	11	1.58	3.19	3.23	472	125	151
E.E.	9	1.25	2.26	—	890	125	598
C.S.	7	2.54	4.01	3.32	986	170	363

*This patient was permitted an unrestricted diet, hence the nitrogen intake could not be determined.

B. Effects on Plasma Globulin Levels.

Patient	Alpha-1		Alpha-2		Beta		Fibrinogen		Gamma	
	b*	a	b	a	b	a	b	a	b	a
J.S.	.66	.52	1.33	1.19	.79	.95	.95	.89	.58	.75
C.M	.58	.58	1.10	1.24	.87	.92	.97	.88	.60	.96
D.P.	.69	.51	1.29	.92	.92	.75	.72	.45	.80	.58
W.D.	.67	.46	1.21	.91	1.02	.95	.67	.58	.99	.74
A.M.	.64	.47	.98	.76	.73	.82	.71	.50	.60	.82
S.W.	.60	.47	.99	.86	.91	.93	.82	.92	1.01	1.14
E.E.	.65	.58	.95	.88	.82	.71	.93	1.23	1.06	1.18
C.S.	.48	.35	.95	.70	1.09	.87	.93	.50	.70	.68

*"b" represents the concentration before the albumin was administered, and "a" represents the concentration after the albumin.

cretion, whereas the fecal nitrogen excretion was estimated to be 1.0 g per diem. Such a simplified nitrogen balance study was maintained for 5 to 7 days during which time the treated patients received 25 g (100 ml) of salt-poor human albumin‡ intravenously daily for 4 to 6 days. Venous blood samples for plasma electrophoresis were obtained the morning before, the morning after, and again a week after the course of albumin. The technic of electrophoresis was the same as previously described.[1,2] Electrophoresis of the plasma was done on the second control patient who was permitted an unrestricted hospital diet *ad libitum*. Serial determinations of pulse rate, blood pressure, venous pressure, respiratory rate, breath-holding time, cardiac output (ballistocardiographic method§), and pulmonary capacities including total and vital capacity as well as residual air were made before and after the administration of albumin intravenously in 5 patients.

Metabolic results. Table I summarizes the changes in concentration of the various plasma protein fractions and the alteration of nitrogen balance resulting from the infusion of albumin in 6 patients with pneumonia. The treated patients exhibited increments in albumin concentration of 0.98 to 1.61 g% following the administration of 100 to 170 g of albumin over 4 to 6 days, and in most instances these increments were maintained over the following week of observation. In contrast the controls showed but slight change in albumin levels. Furthermore, the treated patients retained more protein than could be accounted for by the amount of albumin

‡ The salt-poor human albumin was furnished through the kindness of Mr. R. B. Clark, by the Cutter Laboratories, Berkeley, Calif.

2 Zeldis, L. J., Alling, E. L., McCoord, A. B., and Kulka, J. P., *J. Exp. Med.*, 1945, **82**, 157.

§ Courtesy of Dr. H. R. Brown, Jr., of Department of Medicine.

alone. The magnitude of this protein retention is apparently dependent upon the dietary protein ingested, as well as the albumin administered. The patient (S.W.) who showed the least retention of protein, received only limited quantities of the special liquid diet for 2 days due to a misunderstanding of the orders. Contrariwise the patient (E.E.) who retained 598 g of protein during the period of observation was the one who requested and ingested more than the prescribed amount of the diet.

In addition to the changes in albumin concentration in the treated patients, there were reductions in the globulin fractions, especially the alpha-globulins (Table I). The mechanisms‖ of these alterations in the various fractions of the plasma proteins are not clear from these studies. Suitable isotope studies yielding accurate data on rates of protein turn-over will be needed to determine whether there is impaired synthesis or utilization, of the albumin and globulins under such conditions of stress.

Cardio-respiratory results. One patient, clinically considered to have chronic pulmonary disease, basilar pneumonia and shock, was given 25 g of albumin intravenously. Within 3 hours this patient developed acute pulmonary edema. Electrocardiogram showed left bundle branch block and ischemic type of T waves. Before definitive therapy could be instituted the patient died. Autopsy showed coronary arteriosclerosis, cardiac dilatation and hypertrophy, myocardial scars and pulmonary edema. Thus, the cause of the shock probably was due to coronary artery disease, and the administered albumin evidently contributed to pulmonary congestion. By electrophoresis the plasma albumin concentration was initially 2.0 g%. Because of this experience the secondary cardio-respiratory effects of albumin were investigated in all patients subsequently treated. Before any albumin therapy, each patient was found to have hypotension with systolic blood pressure ranging between 88 and 104 mm of mercury. Following the infusion of albumin, the effects were quite variable, even in the same patient on consecutive days. The trend of changes, however, were a slowing of the pulse together with increased blood pressure, stroke volume and cardiac output. The venous pressure often rose, but not above 12 cm of water. One patient (C. S.), who had had a myocardial infarction several months previously, showed no signs of cardiac dilatation or pulmonary congestion. The breath-holding time was often increased. Finally, the observed reductions in pulmonary volumes immediately after albumin therapy were indicative of pooling of blood within the lungs.

Summary. Six patients recovering from the acute febrile reaction of severe pneumococcic lobar pneumonia were given salt-poor human albumin intravenously. Electrophoretic analyses of the plasma proteins showed significant increases in the albumin concentration, together with reduction in globulins, particulary alpha-globulin, following this therapy. Simplified nitrogen balance studies showed retention of more protein than could be accounted for by the amount of albumin alone. Another patient with shock related to serious heart disease succumbed from pulmonary edema shortly after the administration of albumin. The secondary cardio-respiratory effects of albumin therapy were investigated in 5 patients.

‖ There was no significant increase in plasma volume by the Evans blue technic in the patient who received 150 g of albumin (the authors are indebted to Dr. L. A. Kohn for this observation). By urinary chromatography there was no significant change in renal excretion of amino acids in another patient treated with albumin. (The authors are indebted to Dr. C. Dent of Department of Pathology for this observation.)