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Effect of the Intravenous Administration of Human Serum Albumin on Renal Function.*

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The intravenous infusion of concentrated human serum albumin often produces a transient diuresis in patients with nephrosis and Laennec's cirrhosis.[1,2] It has not been definitely shown that this diuresis is related to an increase in the oncotic pressure of the blood, since the immediate result of albumin administration is an increase in plasma volume and, therefore, of total circulating protein but with little or no change in the albumin or total protein concentration of the plasma.[3] The possibility exists that the administration of albumin may be followed by an alteration in renal function. We have attempted to study the immediate effect of the rapid injection of a large amount of albumin on glomerular filtration rate and renal blood flow.

Methods. The clearance techniques of Smith, Goldring and Chasis[4] have been followed, using inulin and sodium para-aminohippurate (PAH). In addition, samples of renal venous blood have been obtained by the catheterization procedure of Warren, Brannon, and Merrill,[5] and compared with simultaneous samples from the femoral artery for PAH content. The fraction of PAH extracted from the blood during passage through the kidney has been determined by the formula: $Ext_{pah} = A\text{-}RV/A$, where A and RV represent the concentration of PAH (mg %) in arterial and renal venous blood. Renal plasma flow (RPF) has been determined from the clearance and extraction of PAH ($RPF = C_{pah}/Ext_{pah}$) and this value adjusted by the hematocrit reading to obtain the renal blood flow. Glomerular filtration rate was estimated from the inulin clearance (C_{in}), and the filtration fraction (FF) from the ratio C_{in}/RPF. It will be noted that this derivation of the filtration fraction differs from that usually reported, where it is calculated from the inulin and PAH clearances alone, and since the actual renal plasma flow is always greater than the PAH clearance, our values for FF are, therefore, lower than those commonly accepted.

Following two control clearance periods 300 cc of a 25% solution of salt-poor human serum albumin† were injected intravenously in from 10 to 25 minutes. The bladder was then emptied, the urine discarded, and the experiment continued for three additional periods. Three normal subjects, three patients with hypertension, one patient with chronic glomerulonephritis without edema, and one patient with the nephrotic syndrome of subacute glomerulonephritis have been studied in this manner. In addition, similar clearance studies without catheterization of the renal vein have been performed on 2 normal subjects and one patient with the nephrotic syndrome.

Results. An immediate increase in plasma volume after the injection of albumin was indicated by a fall in the hematocrit reading of all subjects. In all but one of the subjects, (J.M.) there was an immediate increase in both the inulin and PAH clearances. In the 8 subjects from whom samples of renal venous blood were obtained, a decreased PAH ex-

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1 Thorn, G. W., Armstrong, S. H., Jr., Davenport, V. D., Woodruff, L. M., and Tyler, F. H., *J. Clin. Invest.*, 1945, **24**, 802.

2 Thorn, G. W., Armstrong, S. H., Jr., and Davenport, V. D., *J. Clin. Invest.*, 1946, **25**, 304.

3 Luetscher, J. A., Jr., *J. Clin. Invest.*, 1944, **23**, 365.

4 Smith, H. W., Goldring, W., and Chasis, H., *J. Clin. Invest.*, 1938, **17**, 263.

5 Warren, J. V., Brannon, E. S., and Merrill, A. J., *Science*, 1944, **100**, 108.

† Obtained from the American Red Cross.

traction was found after albumin administration, so that the actual renal plasma flow showed a greater rise than would be indicated from the PAH clearance alone. The fall in PAH extraction in patient J.M. more than compensated for the slight decrease in PAH clearance, so that he also showed an increased plasma flow. Since the renal plasma flow rose more than the filtration rate, there was a fall in the filtration fraction of all subjects. In spite of the marked drop in hematocrit readings, there was an increase in renal blood flow in all subjects.

The average increase in filtration rate for the 11 subjects was 13% of the initial value. The control filtration rates of the 2 patients with the nephrotic syndrome (G.W. and M.B.) were below normal, 66 and 77 cc/min., and following albumin, these rose to 110 and 129 cc/min., increases of 67 and 68%. The increases in renal plasma flow ranged from 35 to 106%, averaging 58% for the group of 8 subjects in which it was measured. A significant increase in the rate of urine flow was seen in only one patient, G.W., who had nephrosis and massive edema. All of the subjects were undergoing a water diuresis at the time of study, however, to facilitate the clearance determinations.

The individual data are tabulated in Table I. Fig. 1 illustrates the changes produced in a patient with nephrosis. Fig. 2 demonstrates the individual variations in the degree and duration of the decreased PAH extraction, and includes 6 additional subjects in whom PAH extraction was determined at intervals for similar periods of time but to whom no albumin was given. These control subjects demonstrate that water diuresis and renal vein catheterization do not in themselves cause changes in PAH extraction.

Discussion. Although the number of patients studied is too small to allow generalization, several factors of interest may be noted. It is apparent that the administration of albumin is followed by definite changes in renal hemodynamics, and any attempt to explain the diuretic action of albumin must take this into consideration.

These studies also emphasize the danger of

TABLE I.
Determinations of Renal Function Before and After the Injection of 75 Grams of Albumin.

Pt.	Diagnosis	C_{IN} Before	C_{IN} After	C_{PAH} Before	C_{PAH} After	% Ext. PAH Before	% Ext. PAH After	RBF Before	RBF After	FF Before	FF After
H.K.	Normal	123	131	622	915	—	—	—	—	—	—
B.W.	”	143	150	692	850	—	—	—	—	—	—
M.A.B.	”	165	189	863	1123	82.7	71.2	1921	2429	.15	.13
W.W.	”	112	124	741	1001	90.4	78.3	1456	2110	.14	.10
R.A.	”	130	138	638	764	81.0	61.0	1401	1995	.17	.11
M.S.	Hypertension	109	112	375	491	87.3	74.3	700	994	.25	.15
E.F.	”	100	103	542	693	82.5	73.7	1177	1450	.15	.11
B.H.	”	36	39	145	154	58.0	43.6	247	398	.21	.13
J.M.	Chronic nephritis	56	32	265	240	64.0	45.1	636	783	.14	.05
M.B.	Nephrotic syndrome	77	129	498	841	—	—	—	—	—	—
G.W.	” ”	66	110	444	757	90.0	75.0	816	1604	.13	.11

All figures are the averages of at least 2 clearance periods. Clearances have been corrected to 1.73 sq.m. surface area.

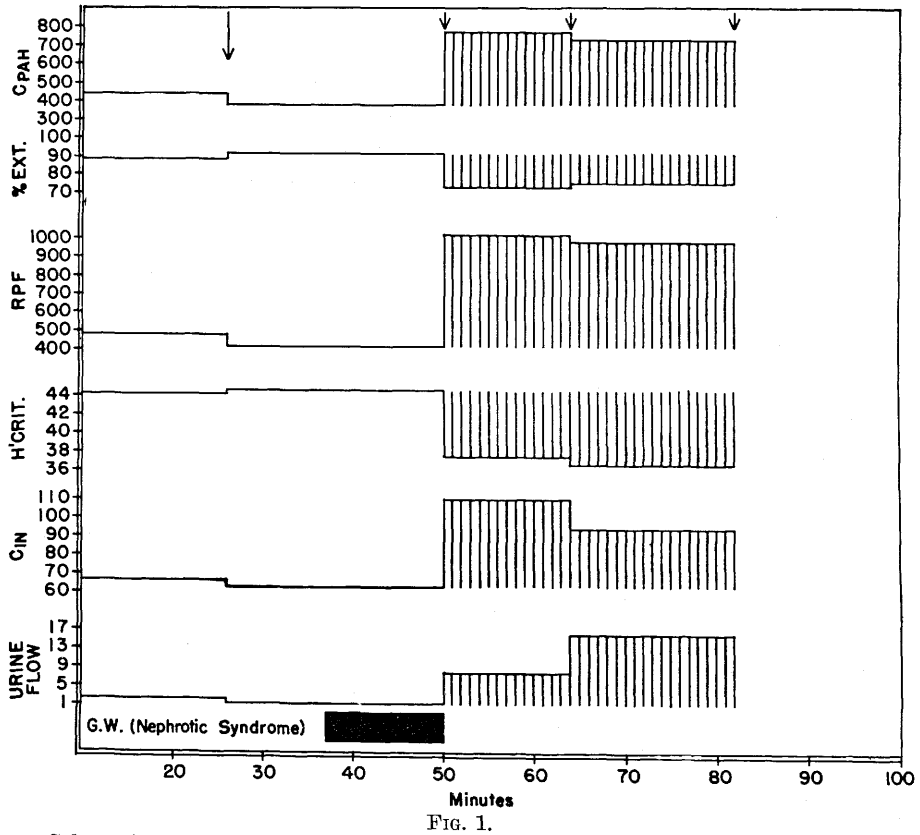

FIG. 1.

Schematic representation of the effects of albumin administration. The black bar represents the duration of injection of 75 g of albumin. The arrows indicate the end of each clearance period.

studying the effect of a substance on renal blood flow by means of the PAH clearance alone. The effect of the substance on the tubular extraction of PAH must also be determined. Since albumin actually increased the urinary excretion of PAH in the experiments reported here, a decreased extraction would have appeared unlikely. The data show that conclusions as to the extraction of PAH drawn from the rate of excretion of PAH may be in error.

There are several possible explanations for the decreased extraction of PAH. Functional impairment of the cells of the proximal convoluted tubules must be considered. It is conceivable that the injection of albumin led to its increased filtration and subsequent reabsorption, thereby over-loading the transfer mechanism of the tubular cells. A more likely explanation, however, is that accessory vascular channels were opened to accommodate the increased volume of blood perfusing the kidney, analogous to changes which have been observed in cutaneous vessels during saline infusions.[6] Morphologic studies have demonstrated the presence of juxta-medullary arterio-venous communications in the human kidney;[7] diversion of a portion of the renal blood flow through this pathway could account for the decreased extraction of PAH and the decreased filtration fraction observed. It is possibly significant that the 2 patients with advanced renal disease (J.M. and B.H., represented by the lowermost lines in Fig. 2)

[6] Altschule, M. D., Freedberg, A. S., and McManus, M. J., *Arch. Int. Med.*, 1947, **80**, 491.

[7] Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., and Prichard, M. M. L., *Studies of the Renal Circulation*, Chap. IV, Charles C. Thomas, Springfield, 1947.

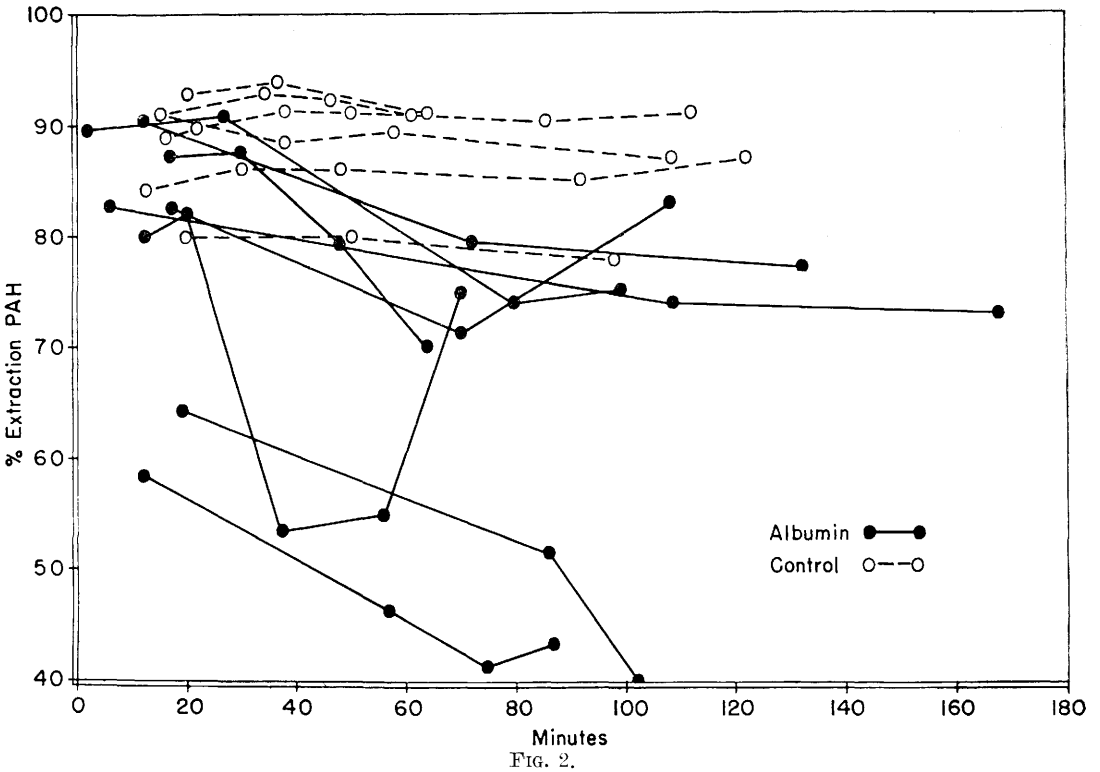

FIG. 2.

The fall in PAH extraction after albumin. Each point represents the simultaneous collection of arterial and renal venous samples.

showed the greatest and most prolonged fall in PAH extraction following albumin, since juxtamedullary shunts are most prominent in the granular, contracted kidneys of chronic nephritis and nephrosclerosis.[7]

The apparent decrease in the extraction of PAH might be due to a change in the rate of its acetylation. Determinations of total as well as free PAH after albumin have eliminated this possibility.

Summary. 1. The rapid intravenous infusion of 75 g of human serum albumin produced a consistent increase in glomerular filtration rate and renal blood flow. These changes were accompanied by both an increased clearance and a decreased tubular extraction of sodium para-aminohippurate. 2. In 2 patients with the nephrotic syndrome of chronic glomerulonephritis the administration of albumin increased the filtration rate from low to normal levels, and in one of these patients produced a marked diuresis. 3. A possible mechanism for the decreased tubular extraction of PAH accompanying an increased renal blood flow is presented.