THE EFFECT OF AN ARTERIOVENOUS FISTULA ON RENAL HEMODYNAMICS AND ELECTROLYTE EXCRETION [1]

By FRANKLIN H. EPSTEIN,[2] ROBERT S. POST, AND MARION McDOWELL[3]

(From the Department of Cardiorespiratory Diseases, Army Medical Service Graduate School, Washington, D. C.)

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Patients with a compressible fistula between peripheral artery and vein provide a unique opportunity to study the reactions of the body to certain abrupt changes in the circulation. As has been said of the patient with congestive heart failure (1), the subject with an arteriovenous fistula is literally bleeding into his large veins. Opening or closing a fistula causes an immediate and marked change in peripheral resistance and a shift in the distribution of blood inside the vascular tree. This in turn elicits numerous compensatory adjustments (2–4).

It was of interest to examine the behavior of the kidneys in this situation for two reasons. First, the renal circulatory pattern in patients with arteriovenous fistulas has not been described. Secondly, it has been suggested that the kidneys retain or excrete sodium in response to alterations in the "effective" distribution of blood (5, 6). The present study permitted this hypothesis to be tested. The data presented show that glomerular filtration rate, renal blood flow and renal venous pressure do not change when a fistula is closed or opened, but demonstrate that the renal excretion of sodium is augmented when an arteriovenous shunt is compressed.

METHODS

Subjects were 17 young male casualties of the Korean war, treated on the Vascular Surgery Service of the Walter Reed Army Hospital. Each patient had a large arteriovenous fistula in the neck, shoulder, arm or leg, created by a penetrating wound received one and a half to five months previously. The diameters of the shunts as estimated at operation varied from 3 millimeters to 20 millimeters. No patient exhibited the signs or symptoms of congestive heart failure.

Patients were studied in the morning, in the postabsorptive state, while lying supine. After awaking, they were not permitted to get up and walk about before being wheeled in the supine position to the laboratory at 8 A.M. In all except four instances the subjects drank 240 cc. of water or hypotonic (0.14 per cent) saline every hour or half hour from 6:00 A.M. until the conclusion of the procedure, in order to insure a copious flow of urine. In seven experiments, including all those with initial urinary flows of less than 4.0 cc. per minute and collection periods of less than 20 minutes, urine was collected through an indwelling multi-eyed urethral catheter and the bladder was rinsed with distilled water and air. In the other studies, in which relatively high urinary flows and long collection periods minimized errors in the collection of urine, patients were permitted to stand briefly and void voluntarily. Clearances of inulin (7) and para-aminohippurate (8) were determined during constant infusion following a priming dose. Renal blood flow was calculated from the clearance of para-aminohippurate and venous hematocrit. In nine patients the clearance of endogenous creatinine was determined using a modification of the analytical technique of Bonsnes and Taussky (9). Concentrations of sodium and potassium in serum and urine were determined with a flame photometer. The method of Schales and Schales (10) was used to determine chloride in the urine of two patients. At intervals of two to five minutes throughout the procedure arterial pressure was measured with a sphygmomanometer and the pulse was counted for 30 seconds at the wrist. The mean blood pressure was arbitrarily taken to equal diastolic pressure plus ⅓ of the pulse pressure (11). All data were analyzed for significance by the Fisher "t" test.

Following a *"CONTROL"* period of at least 30 minutes, consisting of two or more clearance periods, the fistula was occluded by direct manual pressure over the fistula itself or the artery proximal to it, in such a fashion as to eliminate the characteristic bruit and to produce a definite elevation in diastolic blood pressure and slowing of the cardiac rate. *"COMPRESSION"* was maintained for 20 to 50 minutes while one to four collections of urine were made. After this the fistula was released and measurements were continued for another 20 to 50 minutes of *"RECOVERY."* After operative repair of the fistula, the same procedure was repeated in 12 patients, substituting pressure over the operative site or the opposite artery for compression of the previously existing fistula.

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[2] Captain, M.C. Present address: 1st General Dispensary, Fort Richardson, Alaska.

[3] Major, M.C.

RESULTS

1. *Blood pressure and pulse rate* (Table I)

Acute occlusion of an arteriovenous fistula in every instance caused an immediate and sustained increase in diastolic blood pressure, averaging 15 mm. Hg. Systolic pressure rose less or not at all, and in four patients, actually fell slightly. During compression, therefore, the calculated mean arterial pressure increased, and the pulse pressure diminished in every case. The average rise in mean arterial pressure was 11 mm. Hg, with values ranging from 4 to 20 mm. Hg. In general, those patients with the largest arteriovenous communications, as estimated by the surgeon at the time of operation, demonstrated the most marked elevation of mean blood pressure when their fistulas were compressed. The cardiac rate of all patients slowed when the fistula was compressed and became more rapid when the shunt was released (Nicoladoni-Branham sign) (12, 13).

2. *Renal hemodynamics* (Tables I and II, Figure 1)

In all subjects except two (H. B. and F. R.) the clearance of inulin or endogenous creatinine was within normal limits. Renal blood flow was normal in all but one patient (R. J.), who had a bifid ureter demonstrated by intravenous pyelography, but no other evidence of renal disease. These values were not changed significantly by surgical repair of the fistula. Acute occlusion and release of an arteriovenous shunt produced no

TABLE I

Summary of data obtained in the seventeen patients studied pre-operatively

Patient	Location of fistula	Procedure	Duration *minutes*	Number of periods	B. P. *mm. Hg*	Mean press. *mm. Hg*	Pulse rate *beats/min.*	G.F.R.* *cc./min. per 1.73 m.²*	R.B.F. *cc./min. per 1.73 m.²*	Urine flow *cc./min.*	$U_K V$† *mEq./min.*	$U_{Na} V$†† *mEq./min.*	E/F_{Na}‡
		Control	44	3	91/53	66	88	146	1040	1.5		0.151	0.007
1. G. B.	Femoral	Compression	36	3	99/67	78	72	142	1100	2.3		0.295	0.014
		Recovery	48	3	97/57	70	85	132	1033	1.6		0.171	0.008
		Contr.	40	3	94/62	73	77	129	1080	5.2	0.051	0.231	0.011
2. G. M.	Femoral	Compr.	50	5	95/70	78	71	127	1110	3.1	0.045	0.394	0.020
		Recov.	26	3	97/69	78	78	126	1058	3.3	0.042	0.310	0.016
		Contr.	59	2	120/69	86	73	126	1098	5.0		0.320	0.015
3. R. C.	Femoral	Compr.	31	1	121/82	95	58	132	1065	4.4		0.512	0.022
		Recov.	31	1	121/64	83	76	148	1185	2.4		0.331	0.013
		Compr.	30	1	121/84	96	54	138	1082	3.7		0.392	0.016
		Contr.	113	2	119/73	88	77	*117*		17.9	0.035	0.199	0.012
		Compr.	32	1	117/80	92	59	*111*		19.5	0.021	0.318	0.021
		Recov.	60	2	117/69	85	77	*100*		11.6	0.022	0.209	0.021
		Contr.	31	2	112/41	65	109	112	1023	3.0		0.218	0.014
4. W. G.	Femoral	Compr.	21	2	105/65	78	94	117	1082	4.6		0.287	0.018
		Recov.	33	3	115/45	68	109	109	1098	3.3		0.180	0.012
		Contr.	41	3	104/41	62	75	117	648	6.7		0.160	0.009
5. R. J.	Sub-clavian	Compr.	33	2	108/76	87	52	104	554	5.2		0.200	0.013
		Recov.	44	4	111/48	69	76	113	660	5.2		0.158	0.009
		Contr.	38	3	134/53	80	69	143	830	2.1	0.029	0.298	0.012
6. J. C.	Femoral	Compr.	44	3	130/80	97	56	129	831	2.6	0.024	0.321	0.014
		Recov.	35	3	136/51	79	70	134	755	2.0	0.022	0.260	0.011
		Compr.	10	1	143/88	106	58	125	816	3.5		0.343	0.016
		Contr.	51	2	102/61	75	69	103	742	3.9		0.115	0.007
7. G. S.	Carotid	Compr.	39	1	108/78	88	49	110	875	6.8		0.202	0.011
		Recov.	41	1	105/59	74	71	97	723	3.4		0.091	0.008
		Contr.	72	3	131/80	97	76	111	785	13.0		0.370	0.023
8. J. F.	Brachial.	Compr.	31	1	127/88	101	64	97	653	13.6		0.313	0.023
		Recov.	51	2	123/78	93	77	121	760	14.9		0.324	0.019
		Compr.	36	3	118/84	95	77	108	704	1.2		0.196	0.012
		Recov.	33	3	117/78	91	85	111	686	1.1		0.180	0.011
		Compr.	36	3	125/92	103	74	102	655	1.1		0.223	0.014

TABLE I—*Continued*

Patient	Location of fistula	Procedure	Duration *minutes*	Number of periods	B. P. *mm. Hg*	Mean press. *mm. Hg*	Pulse rate *beats/min.*	G.F.R.* *cc./min. per 1.73 m.²*	R.B.F. *cc./min. per 1.73 m.²*	Urine flow *cc./min.*	U_KV† *mEq./min.*	$U_{Na}V$†† *mEq./min.*	E/F_{Na}§
		Contr.	32	3	104/64	77	71	137	1327	3.2		0.071	0.003
9. W. T.	Carotid	Compr.	46	4	108/73	85	66	131	1158	4.2		0.114	0.006
		Recov.	31	3	103/67	79	99	116	1245	1.3		0.122	0.007
		Contr.	87	2	105/60	75	70	*118*		5.6	0.144	0.280	0.015
10. D. B.	Popliteal	Compr.	45	1	111/68	82	62	*128*		2.6	0.190	0.514	0.026
		Recov.	45	1	115/63	80	72	*116*		5.2	0.178	0.368	0.020
		Contr.	29	1	98/52	67	62	*120*		8.5	0.135	0.132	0.006
11. J. T.	Thoraco-	Compr.	30	1	99/66	77	56	*116*		5.3	0.113	0.184	0.009
	acromial	Recov.	60	2	97/59	72	61	*117*		4.1	0.108	0.152	0.007
		Contr.	135	4	116/45	69	78	*105*		7.8	0.075	0.127	0.008
12. E. B.	Femoral	Compr.	28	1	121/73	89	65	*94*		8.5	0.088	0.273	0.020
		Recov.	58	2	124/52	76	79	*111*		4.8	0.078	0.235	0.015
		Contr.	69	3	111/56	72	66	*100*		8.7	0.095	0.110	0.008
13. A. D.	Femoral	Compr.	20	1	114/73	87	50	*100*		9.6	0.103	0.147	0.011
		Recov.	30	1	114/58	73	68	*91*		6.1	0.087	0.123	0.010
		Contr.	57	2	116/45	69	76	*78*		9.8		0.252	0.023
14. H. B.	Popliteal	Compr.	29	1	113/62	79	56	*72*		13.5		0.345	0.034
		Recov.	20	1	118/48	71	78	*77*		8.4		0.250	0.023
		Contr.	50	2	126/76	93	63	*140*		12.6		0.182	0.009
15. H. F.	Popliteal	Compr.	20	1	132/82	99	54	*137*		11.1		0.228	0.012
		Recov.	28	1	125/75	92	65	*143*		6.0		0.228	0.011
		Contr.	65	2	100/52	68	85	*146*		7.9		0.079	0.004
16. W. R.	Femoral	Compr.	31	1	100/58	72	68	*144*		7.0		0.099	0.005
		Recov.	32	1	98/52	67	80	*151*		6.7		0.079	0.004
		Contr.	120	4	112/57	75	66	*82*		5.4	0.038	0.046	0.004
17. F. R.	Femoral	Compr.	26	1	111/78	89	58	*89*		7.1	0.036	0.085	0.007
		Recov.	26	1	116/61	79	71	*83*		5.6	0.029	0.042	0.004
		Contr.			111/59	76	76	118	926	6.8	0.075	0.185	0.011
Mean		Compr.			112/74**	87**	62**	115	913	7.0	0.077	0.267**	0.016**
		Recov.			113/61**	78**	78**	115	920	5.1	0.071	0.200**	0.012**

* Italicized figures indicate clearances of endogenous creatinine. All other values in this column are clearances of inulin.

** Indicates "highly significant" change from the preceding value ($P < 0.01$).

† U_KV = Urine concentration of potassium in mEq./cc. × Urine volume flow in cc./min. = milliequivalents of potassium excreted in the urine per minute time.

†† $U_{Na}V$ = Urine concentration of sodium in mEq./cc. × Urine volume flow in cc./min. = milliequivalents of sodium excreted in the urine per minute time.

§ $E = U_{Na}V$. F_{Na} = Plasma concentration of sodium in mEq./cc. × Glomerular filtration rate in cc./min. = mEq./min. of sodium filtered by the glomeruli. Hence E/F_{Na} represents the ratio of excreted to filtered sodium.

consistent or significant change in the clearances of inulin, endogenous creatinine chromogen, or PAH; the filtration fraction, therefore, was also unaffected. The venous hematocrit was similarly unaltered. The left renal vein was catheterized in six patients (patients 12 to 17, Table I), in order to measure its pressure directly. Renal venous pressure was within normal limits (6 to 10 mm. Hg) (14) and was unaltered by temporary closure or opening of the arteriovenous fistula.

Since renal blood flow remained essentially unchanged when a fistula was occluded, despite a rise in the mean arterial pressure perfusing the kidneys, the total renal vascular resistance must have increased. If the data of Table I are analyzed according to the concepts of Gomez (15) it is apparent that this was accomplished largely by an increase in renal "afferent" arteriolar resistance.

3. *Excretion of electrolytes and water*

In contrast to the relative constancy of renal blood flow and glomerular filtration rate, the excretion of sodium increased significantly ($P <$ 0.01) when the fistula was compressed in every

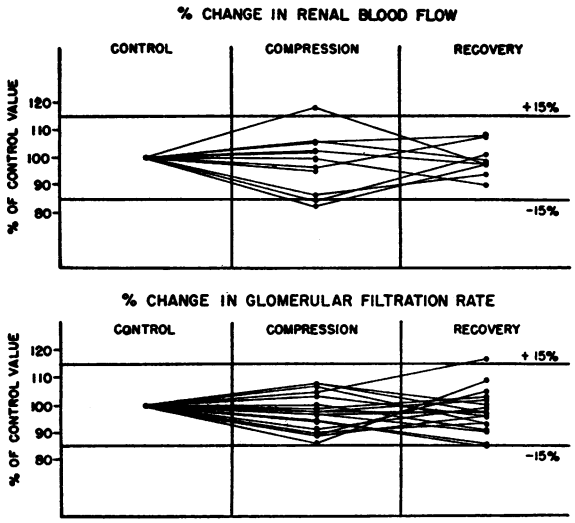

FIG. 1

TABLE II

Comparison of pre- and post-operative glomerular filtration rate and renal blood flow

Pt.	GFR* cc./min./1.73 m.² pre	GFR* cc./min./1.73 m.² post	RBF cc./min./1.73 m.² pre	RBF cc./min./1.73 m.² post
G. B.	146	137	1,040	1,194
P. M.	129	113	1,080	1,008
R. C.	126	133	1,098	1,455
W. G.	112	102	1,023	874
R. J.	117	112	648	635
J. C.	143	129	830	914
G. S.	139	112	923	1,030
J. F.	111	126	785	810
Mean	128	120	928	990

* Clearances of inulin. Each value represents the average of three collection periods.

There is no consistent or significant difference between the values before and after repair of an A-V fistula.

experiment except one (Table I, Figure 2). The increase ranged from 0.020 milliequivalents per minute to 0.234 milliequivalents per minute and the average rate of sodium excretion during the period of compression was 144 per cent of control. The effect could not be quantitatively correlated with the size of the shunt as estimated at operation or with the magnitude of the response of the blood pressure to occlusion. An augmented excretion of sodium was apparent in urine collected 10 to 15 minutes after occlusion of the fistula and continued throughout the compression period. After the fistula was released, sodium excretion fell toward control values in all but two instances. In two patients the urinary excretion of chloride was measured and found to parallel that of sodium. Following surgical repair of the

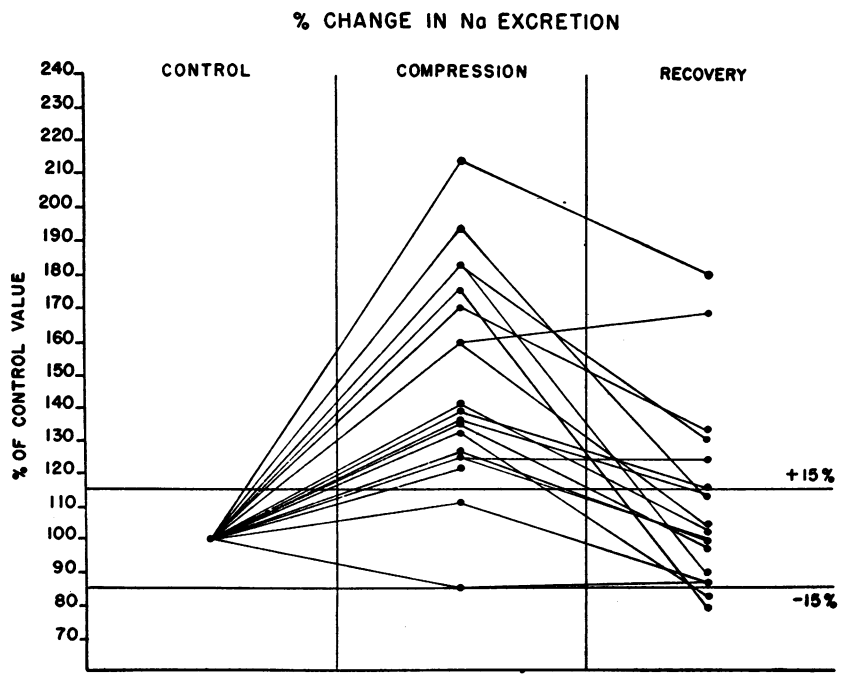

FIG. 2

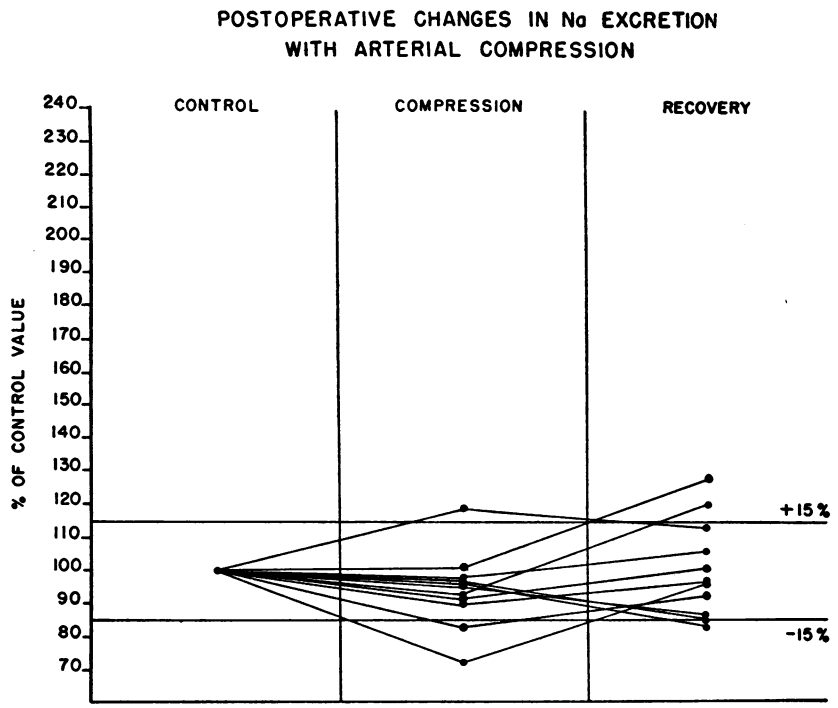

FIG. 3

fistula (Figure 3), renal excretion of sodium was unchanged by manual occlusion of an artery at the operative site or in the opposite limb, a procedure which did not produce significant changes in cardiac output or arterial pressure (16).

The renal excretion of potassium, studied in six patients, was not consistently altered by temporary closure or release of an arteriovenous shunt.

The flow of urine increased in 12 of 19 experiments when the fistula was closed, and diminished during the recovery period in 16. Interpretation of these findings is complicated by the fact that most of the patients had been drinking and were in positive water balance, and by the well-known tendency for urinary flow to fall off toward the end of a long and sometimes tiring procedure (17).

DISCUSSION

It is pertinent to review briefly the effects upon the general circulation of closing and opening an arteriovenous fistula and to consider how they might influence the kidneys. When an arteriovenous shunt is occluded, the arterial tree is emptied more slowly and less completely, and mean arterial pressure rises. Pressures in the great veins, the right atrium, and the pulmonary vessels tend to fall as these regions become less distended with blood (3, 18–21). Cardiac output is decreased as the heart rate slows and stroke volume diminishes. When the fistula is opened, blood pours from arteries into veins. Despite an increase in cardiac output (3, 4, 19, 22–24), the arteries become less distended, and mean systemic arterial pressure falls, while the great veins become more swollen and pressures in the right atrium and pulmonary artery may increase (3, 18–20).

The effects of sudden changes in renal vascular pressures, similar to those occurring in the present experiments, on renal hemodynamics, urinary flow and electrolyte excretion have been extensively studied in isolated kidneys and anesthetized animals, and have recently been discussed in detail (25–27). The kidneys of such preparations, whether or not the renal nerves are intact, exhibit a remarkable ability to maintain a constant rate of blood flow and glomerular filtration, in the face of wide variations in mean arterial perfusing pressure. Renal blood flow and filtration rate were similarly unaffected in the present study by the changes in mean arterial pressure accompanying closure and release of an arteriovenous

fistula, so that in contrast to the reported response of other vascular beds (3, 28, 29), the renal vascular resistance regularly increased when a peripheral fistula was occluded and decreased when it was opened. Presumably this is a manifestation of the "autonomy" of the renal vasculature expressed, in intact subjects (30–32) as in the isolated kidney, primarily through changes in afferent renal arteriolar resistance.

When an arteriovenous fistula is occluded, arterial pulse pressure is diminished at the same time that the excretion of sodium is augmented. A narrowed pulse pressure was thought by Hooker (33) and Gesell (34) to result in antidiuresis and retention of chloride. More recently it has been shown by Selkurt (35) and by Goodyer and Glenn (36) that alterations in renal arterial pulse pressure *per se* are not necessarily followed by changes in the excretion of sodium. On the other hand, an increase in the mean arterial pressure perfusing one kidney has been reported by Selkurt to induce a unilateral diuresis of salt and water without greatly changing the glomerular filtration rate (35). In all subjects of the present study, the increase in sodium excretion produced by closing a fistula was accompanied by an elevation of the calculated mean arterial pressure. However, the increase in pressure was always much smaller than that required in Selkurt's experiments to bring about the change in sodium excretion. Furthermore, the changes in sodium excretion from patient to patient could not be correlated with the magnitude of the response of the blood pressure.

The fraction of filtered sodium rejected by the tubules and appearing in the urine (E/F_{Na}) increased in all patients except one when flow through the fistula was shut off. In the absence of a consistent increase in the clearance of inulin or endogenous creatinine, the increase in renal excretion of sodium might be construed to be the result of altered tubular behavior toward this ion, presumably because of changes in nervous, hormonal or intrinsic renal influences. Unfortunately present techniques for the measurement of glomerular filtration are not accurate enough to rule out completely the possibility that an undetected increase in the filtration of sodium might have occurred to account for the observed increment in sodium excretion.

The present findings might be considered an example of the regulatory role of the kidneys in opposing distortions in the volume and distribution of the fluids of the body. It has long been realized that renal excretion of salt and water must be conditioned by the volume of body fluids, as well as by their tonicity (37), and it has been reasoned that renal excretion or retention of sodium may be related to some function of the volume of the circulating blood (38). Others have suggested that diuresis may be stimulated by an increase, and depressed by a reduction, in the cardiac output (39). Studies of the effects of posture on diuresis support the view that the effective distribution of blood rather than its total volume is important in influencing renal behavior (6, 40, 41). The great veins (42), the right heart and pulmonary artery (43), the cranial cavity (44), the "cephalad portion of the body" (45), and the arterial pressoreceptors (46) have all been proposed as possible sites for the initiation of afferent impulses designed to modify renal excretion of salt or water. Since the distribution of blood in the vascular tree of a patient with an arteriovenous communication is altered acutely when the shunt is occluded or released, the present study provides additional information by which to evaluate these hypotheses. The data suggest that an increase in arterial pressure or arterial filling may initiate a chain of events culminating in an increased renal excretion of sodium. If this were true, the experimental creation of a large arteriovenous fistula might be expected to promote the renal retention of salt, at least until a new equilibrium is established. This sequence of events has in fact been observed (47, 48).

It is interesting to list the circulatory states, chronic as well as acute, in which the kidneys tend to retain sodium. Dehydration (49), hypoproteinemia (50, 51), and hemorrhage (52, 53) are associated with a diminution in total blood volume. In quiet standing (6), venous congestion of the limbs (54, 55), partial occlusion of the superior or inferior vena cava (56), and portal hypertension (57), filtration from the capillaries is increased and in addition blood is pooled in the peripheral veins, away from the general circulation. Acute (58) and chronic (59, 60) constrictive pericarditis, constriction of the pulmonary artery (61, 62) and congestive heart failure are characterized by distention of the central veins with blood which

the heart is unable to pump efficiently into the aorta. In some of the above conditions the volume of blood in the central veins is reduced; in others these vessels are engorged. In all, however, there exists a tendency toward inadequate filling of the systemic arterial tree, either because of a diminished total blood volume or an altered distribution of blood within the vascular system. The latter may have its origin either in pooling or shunting of blood in the periphery or in failure of the heart as a pump. The changes in sodium excretion, described in the present communication, which accompany occlusion or release of an arteriovenous fistula, are consistent with the hypothesis that renal excretion or retention of sodium is conditioned by the degree of filling of some portion of the arterial tree.

SUMMARY

Occlusion of an established arteriovenous fistula results in an increased renal excretion of sodium. This accompanies the well-known rise in diastolic arterial pressure and slowing of the cardiac rate, despite no change in glomerular filtration rate, renal blood flow or renal venous pressure. The latter values are usually normal and are not altered significantly by surgical repair of the fistula. The data suggest that renal excretion of sodium may be conditioned by the degree of filling of some portion of the arterial tree.

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