

samples from the right and left internal jugular bulbs do not differ appreciably on the two sides in subjects at rest. These data also suggest that adequate mixing of blood from the two cerebral hemispheres may occur in the presence of unilateral cerebral disease. They are not in agreement with the findings reported by Ferris and his colleagues(2); this discrepancy remains unresolved. These data would also cast doubt on the assumption that accurate differential values for metabolism of the cortex and lower portions of the brain can be adduced from bilateral internal jugular bulb samples(5,14).

Summary and conclusions. 1. The values

for cerebral blood flows, arterial-cerebral venous oxygen and glucose differences were not significantly different on the two sides in 18 simultaneous bilateral observations in 12 subjects. 2. Three subjects with unilateral cerebral disease also had similar values on the two sides. 3. The assumption that blood obtained from one internal jugular bulb is representative of mixed cerebral venous blood appears to be correct.

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Diurnal Variations of Renal Function in Congestive Heart Failure. (17978)

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(Introduced by Homer W. Smith)

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Employing a constant intravenous infusion technic, Sirota, Baldwin and Villarreal(1) have examined the diurnal variations of renal function in normal subjects. These studies reveal a significant decrease in urine flow during sleep, resulting primarily from increased tubular reabsorption of water, with only a slight and questionably significant decrease in glomerular filtration rate from 12 midnight to 4 a.m. The renal plasma flow did not vary significantly throughout the 24 hour period. The present report is concerned with similar studies in patients with congestive heart failure.

Methods. Simultaneous endogenous creatinine chromogen, inulin and p-aminohippurate clearances were determined during 4 to 6 hour periods throughout 24 hours in 10 male subjects in congestive heart failure. In

6 subjects sodium excretion was also followed. In 5 subjects cardiac failure was associated with rheumatic heart disease, in 4 with arteriosclerosis, and in 1 with cor pulmonale. Six of these patients at the time of study had persistent or increasing peripheral edema in spite of complete bed rest, low salt diet and complete digitalization. Of the other 4, 2 were edema-free and 2 were undergoing diuresis, spontaneous in 1 case and in the other as a result of digitalization. With the exception of 1 individual (E.), mercurial diuretics were withheld for a minimum of 5 days prior to study. The test substances were administered by means of a constant delivery pump at an approximate rate of 0.3 cc./min. Five per cent glucose in distilled water was used as the diluent.§ Analytical methods and details of technic in continuous 24 hour clearance studies have been reported previously(1).

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§ PAH dissolved in 5% glucose solution forms a reaction product in which the p-amino group is covered. This product apparently has a low clearance, as indicated in the low extraction ratios of PAH-glucose mixtures(2). For this reason all data on C_{PAH} are deleted from the report.

Urine sodium was determined with the Perkin-Elmer internal standard flame photometer.

Results. Data on day (D) and night (N) values of urine flow, inulin U/P ratio, inulin clearance (C_{IN}), endogenous 'creatinine' chromogen clearance (C_{CR}) and sodium excretion are recorded in Table I. The night value in each case represents the mean value obtained for the periods corresponding roughly to the sleeping hours for that individual; the day values are the means of all other observations.

Discussion. While the number of patients studied in this series is small, certain conclusions appear to be warranted. In the group with persistent edema the urine flow either remained constant or increased, in contradistinction to the decrease in urine flow which occurs during sleep in normal subjects. In all the edematous subjects, the filtration rate increased to some extent (6 to 35%) during sleep, whereas in normal subjects this function remains unchanged or decreases(3). In normal subjects the nocturnal decrease in urine flow is almost wholly attributable to increased reabsorption of water. The data suggest that the increase in filtration rate may be causally related to increased urine flow in three subjects (J.Me., F. and G.), but the problem does not permit accurate analysis at this time. This reversal of the diurnal variation in urine flow and filtration rate pattern in patients with persistent edema does not appear to be directly related to the level of glomerular filtration since it occurred in J.Me. with a day-time filtration rate of 92 cc/min and in F. with a day-time filtration rate of 47.9 cc/min.

The reversal of diurnal pattern was not observed in 2 patients with left ventricular heart failure but without peripheral edema (J.T. and A.D.), or in 2 patients undergoing diuresis spontaneously (J. Ma.) or in consequence of digitalization (T.P.).

Chloride(4-7) and sodium(7-8) excretion

typically decrease in normal subjects during sleep. In contrast, 2 of our 3 subjects with edema showed a marked increase in sodium excretion at night (N/D ratio of 1.54), and the third showed a slight increase (N/D ratio of 1.05), as did J. Ma. who was undergoing spontaneous diuresis. A.D., who was edema-free, and T.P., who was digitalized, showed reduced excretion of sodium at night.

It is not possible at the present time to establish a cause and effect relation between filtration rate and sodium excretion in either normal subjects or subjects in congestive failure, since other factors affecting tubular reabsorption of sodium remain unanalyzed.

There was no correlation in these patients between the presence of edema and the absolute level of the filtration rate. Four of the 6 patients with edema had filtration rates above the critical level of 70 to 80 cc suggested by Merrill and Cargill(9), while one of the edema-free patients had a filtration rate of only 56.6 cc. The highest filtration rates, 111 and 121 cc, were observed in the 2 patients with edema who were undergoing diuresis.

Brod and Sirota(10) report that the C_{CR}/C_{IN} ratio averages close to 1.0 in normal subjects, exceeding 1.0 in patients with renal disease. In all our patients in congestive failure with edema, and in 2 undergoing diuresis, this ratio was significantly below 1.0. Despite this discrepancy between the absolute values of C_{CR} and C_{IN} , the N/D ratios for C_{IN} and C_{CR} were almost identical, indicating that C_{CR} , although not a reliable measure of the absolute value of the filtration rate, is useful for following changes in this function over short periods.

Summary. 1. Diurnal variations of renal

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TABLE I.
Renal Function During Waking and Sleeping Hours in 10 Subjects with Congestive Heart Failure. Clearance Data Are Corrected to Body Surface Area of 1.73 sq. m.

Patient	Age	Diagnosis	Avg urine flow, cc/min.		Avg inulin U/P ratio		Average clearance				Avg sodium excretion, μ Eq/min.		N/D ratios				C _{CR} /C _{IN}	
			Day	Night	Day	Night	Inulin, cc/min.		Creatinine, cc/min.		Day	Night	Urine flow	Inulin U/P	C _{IN}	C _{CR}		
							Day	Night	Day	Night						C _{CR}		C _{CR}
J.Me	49	RHD	.31	.46	260	244	92	107	72	79			1.48	.94	1.16	1.10	.77	
A.	39	"	.40	.38	262	286	100	106	65	69			.95	1.09	1.06	1.06	.65	
F.	49	"	.49	.69	101	81	48	55	37	42	2	4	1.40	.80	1.15	1.13	.77	
E.*	42	"					94	111	69	79					1.17	1.15	.75	
G.	52	CP	.36	.54	82	64	36	48			22	34	1.50	.78	1.35	1.54		
J.	59	ASHD	.67	.63	173	171	92	103	75	83	68	72	.93	.99	1.12	1.05	.81	
Edema-free or during diuresis																		
J.T.†	52	RHD	.48	.50	156	144	74	74	70	71			1.03	.92	1.00	1.01	.95	
A.D.†	68	ASHD	.45	.34	145	145	57	52	59	57	33	24	.76	1.00	.91	.97	1.06	
T.P.†	60	"	2.52	2.36	51	45	111	101	82	83	270	243	.94	.88	.91	1.01	.78	
J.Ma§	67	"	.81	.72	186	196	121	123	98	95	83	103	.89	1.05	1.02	.97	.79	

RHD = Rheumatic heart disease.

CP = Cor pulmonale.

ASHD = Arteriosclerotic heart disease.

* Urine flow and inulin U/P ratios are not recorded in this subject because of the administration of a mercurial diuretic the day before study.

† Free of peripheral edema. Left ventricular heart failure was present, as manifested by dyspnea, orthopnea and basilar pulmonary rales.

‡ Undergoing rapid diuresis following digitalization.

§ This patient was studied during slow spontaneous diuresis.

|| Values to nearest whole number.

function were studied by means of a constant infusion technic in 10 subjects with congestive heart failure. 2. In contrast to normal subjects, urine flow, sodium excretion and filtration rate increased during sleep in 6 patients with persistent peripheral edema. Four subjects with congestive heart failure who were edema-free or undergoing diuresis

showed a diurnal pattern with respect to urine flow and filtration rate similar to that seen in normal subjects. 3. The endogenous 'creatinine' chromogen clearance is substantially lower than the inulin clearance in patients with congestive heart failure and edema.

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Effect of Certain Amines on the Blood Pressure of Normotensive and Hypertensive Rats.* (17979)

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Differences in the usual degree of response of the blood pressure to various pressor substances in experimental hypertension have been described (1,2). Tyramine, epinephrine, pitressin, and renin appear to be more vasoactive in hypertensive dogs and rabbits than in normotensive animals. In the present investigation the pressor responses of isoamylamine, phenethylamine, tyramine, arterenol, and epinephrine have been studied in normal rats and rats with experimental renal hypertension. It was found that the degree of pressor response in the two groups varied with the amine tested. In hypertensive rats isoamylamine showed less, phenethylamine and tyramine the same, and arterenol and epinephrine more effect on blood pressure than in normotensive rats.

Method. Albino rats, of approximately 200 g, were anesthetized by intraperitoneal injection of sodium pentobarbital (4.5 mg per 100 g body weight). By a flank incision the left kidney was isolated and the renal artery freed from the vein. A copper wire,

0.48 mm in diameter, was placed along the artery and a nylon ligature tied tightly around both the artery and the wire. When the wire was removed the artery was left partially constricted. About 70% of the operated animals developed an elevation of systolic blood pressure as measured by a photoelectric plethysmograph, the hind leg being occluded by a pneumatic cuff. After a period of at least 3 weeks to allow for recovery from operative trauma, the hypertensive rats were used for pressor assay. The rat, either hypertensive or normotensive, was again anesthetized and a tracheotomy performed to maintain a patent airway. The right femoral artery was exposed and a saturated solution of novocaine applied to it to prevent constriction. A curved 23 gauge needle connected to a Hamilton optical manometer was inserted into the artery through a small incision. The left femoral vein was isolated and cannulated for the intravenous administration of the substance to be studied. After stabilization, this preparation exhibited levels of blood pressure which were constant within the limits of ± 5 mm Hg for over 2 hours. The minimal quantity of each amine necessary to produce a pressor response in the normotensive rat was determined.

Results. The following amounts of free base, in gammas per 100 g body weight of rat, produced a "minimal" reproducible pres-

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