STUDIES OF UREA EXCRETION. IV: *Relationship Between Urine Volume and Rate of Urea Excretion by Patients with Bright's Disease*

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STUDIES OF UREA EXCRETION. IV.

Relationship Between Urine Volume and Rate of Urea Excretion by Patients with Bright's Disease

By EGGERT MÖLLER, JOHN F. McINTOSH and DONALD D. VAN SLYKE

(From the Hospital of the Rockefeller Institute for Medical Research, New York)

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Previous papers from this hospital (2, 6) have shown that until the urine volume reaches a certain augmentation limit, averaging about 2 cc. per minute, the rate of urea excretion by a normal man increases in direct proportion to the square root of the urine volume, but that when the urine volume attains this limit urea excretion attains its maximum, equal per minute to the urea content of 60 to 90 cc. of blood, and is unaffected by further increase in urine volume.

In order to ascertain the manner in which these relationships are affected in Bright's disease we have determined the hourly blood urea clearances (defined in a preceding paper (6)) of a number of patients with this disease in whom maximum changes in urine volumes were induced by regulating the water intake. Results from six typical cases are reported in this paper. The experimental technique was identical with that outlined in the paper on normal subjects (6). In each case experiments on two or more days were performed in order to obtain the desired amount of data, but the days were sufficiently close together, and the condition of each patient sufficiently stable, to permit a fair degree of assurance that the renal function in each subject was practically unchanged during the period.

In most of the experiments on patients Jac., Cic., Val., and Wol., cutaneous blood was taken and the urea content estimated with the micro-gasometric method of Van Slyke (7), while in some of the shorter experiments on these four patients and in all the experiments on patients Chi. and Gia. venous blood was drawn and its urea content estimated with the aeration method of Van Slyke and Cullen (8).

In two cases, patients Val. and Wol., it was impossible to get urine

TABLE 1

Data of cases

Case	Blood pressure	Size of heart	Eye grounds	Hemoglobin as O_2 capacity	Red blood corpuscles	White blood corpuscles	Plasma proteins				Blood urea	Plasma creatinine	Plasma non-protein N	Urine protein (Esbach)	Diuresis (ca.)	Specific gravity	Sediment	Phenolsulfonephthalein test in two hours	Mean standard blood $\frac{U}{B\sqrt{V}}$ urea, clearance corrected to body size
							Albumin	Globulin	Total protein	A/G ratio									
				volumes per cent	*millions per cu. mm.*	*per cu. mm.*	*per cent*	*per cent*	*per cent*		*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*grams per liter*	*cc.*			*per cent*	
1 Chi. Hospital No. 5335	100/70	Normal	Normal	13.2	4.98	5,500	3.34	2.32	5.66	1.44	15	1.3	34	0.3	1,000	1013–1017	+++ RBC, + hyaline and granular casts, no DRG*	70	62
2 Jac. Hospital No. 5699	134/85	Slightly increased	Normal	20.2	5.31	6,100	1.71	2.11	3.82	0.81	20	1.9	41	4	1,000	1012–1018	+ RBC, + WBC, +++ hyaline casts, ++ granular casts, + DRG		22
3 Cic. Hospital No. 5644	115/80	Normal	Normal	20.1	4.50	8,900	1.70	2.24	3.94	0.76	22	1.9	29	6	1,200	1010–1014	+ RBC, + WBC, +++ hyaline casts, + granular casts, + DRG	35	18
4 Val. Hospital No. 5446	145/75	Somewhat increased	Normal	12.0	4.39	7,300	2.11	1.92	4.03	1.10	40	3.0	32	6	1,600	1010–1018	++ RBC, ++ WBC, ++ RBC casts, ++ granular casts, no DRG		

5 Gia. Hospital No. 5338	120/75	Normal	Normal	14.0	3.11	8,200	2.41	2.43	4.84	0.99	80	5.1	87	ca. 1	1,600	1010–1016	++ RBC, ++ WBC, + hyaline casts, + granular casts, no DRG	
6 Wol. Hospital No. 5731	145/90	Normal	Normal	14.2	3.97	6,200	3.87	2.57	6.44	1.50	55	2.4	62	2	1,400	1006–1010	+ RBC, ++ WBC, + hyaline casts, + granular casts, no DRG	

* DRG = double refractive globules.

volumes as low and as high respectively as desired, although many attempts on different days were made. This was due to the loss of the power of concentration and of dilution respectively in these two patients.

The laboratory findings in our 6 cases of Bright's disease are given in table 1. The terms of classification are those used by Addis (1).

CASE HISTORIES

Case 1. Chi. Hospital No. 5335. Boy, 13 years old. When 7 years old he had acute glomerulonephritis, now relapse with hematuria and some edema.

TABLE 2

Correction factors for body size

Case			Age	Weight	Height	Body surface area observed	Weight ideal for height and age	Area ideal for height and age	Correction factor	
Name	Number	Hospital number							$\frac{1.73}{\text{Area observed}}$	$\frac{1.73}{\text{Area ideal}}$
			years	*kgm.*	*cm.*	*sq.m.*	*kgm.*	*sq.m.*		
Chi.	1	5335	13	38	145.9	1.30*	37.5	1.29*	1.33	1.34
Jas.	2	5699	24	56	173.0	1.66	66.8	1.79	1.04	0.97
Cic.	3	5644	24	48	163.4	1.50	59.8	1.65	1.15	1.05
Val.	4	5446	24	59	176.0	1.73	69.2	1.84	1.00	0.94
Gia.	5	5388	24	64	175.0	1.79	68.3	1.83	0.97	0.95
Wol.	6	5731	16	38	155.0	1.31	46.9	1.43	1.32	1.21

* Calculated from the table of Benedict and Talbot for children: Carnegie Trust Wash. Publ. No. 302, 1921, p. 61.

Surface areas of other patients are calculated by Du Bois' formula.

No loss of ability to excrete urea or phthalein. *Course of the disease:* After 6 weeks sent home with no edema, only a trace of albuminuria, and a slight microscopic hematuria. Seen 6 months and one year later, when the hematuria had quite disappeared, while the slight albuminuria persisted. Other findings normal.

Case 2. Jac. Hospital No. 5699. Man, 24 years old. One year ago, tonsillitis followed by albuminuria and marked edema. This cleared up gradually in 6 months, but after chrysarobin treatment for psoriasis severe relapse set in with edema, ascites and hydrothoras. *Course of the disease:* Edema and anasarca cleared up completely in one month. Seen 6 months later, there was then no edema and only a few red cells and casts in the urine.

Case 3. Cic. Hospital No. 5644. Man, 24 years old. Syphilis found 6 years ago, since then repeated treatment with salvarsan and mercury. One

year ago edema and ascites began, both still present. Renal function diminished. Wassermann reaction negative. *Course of the disease:* Edema nearly disappeared after 3 months. Seen 6 months later, when the condition was unchanged as at discharge from hospital.

Case 4. Val. Hospital No. 5446. Man, 24 years old. The last year some edema, hematuria and dyspnea on exertion have been present. Now only slight edema. Diminished ability to excrete urea and phthalein. *Course of the disease:* After 3 months, hematuria much decreased and the blood hemoglobin content somewhat increased. Seen 3 months later, when the condition was unchanged.

Case 5. Gia. Hospital No. 5338. Man, 24 years old. Tonsillitis, bronchitis and pleurisy 8 months ago, followed by marked edema, ascites, oliguria and hematuria. Now no ascites, only slight edema, no hematuria; but dyspnea on exertion. Marked loss of renal function. Unusual normal blood pressure and normal heart, despite advanced renal disease and function loss. *Course of the disease:* Died 9 months later in uremia. Histological diagnosis: Chronic glomerulonephritis.

Case 6. Wol. Hospital No. 5731. Scarlet fever 6 years ago. During the convalescence albuminuria appeared and has been present since then. 10 months ago, moderate edema, nausea and vomiting set in and hypertension was found. Since then the condition has somewhat improved. On admission only a trace of edema and a little nausea were present. Phthalein excretion in 2 hours was 25 to 31 per cent. *Course of the disease:* During 3 months, nausea and edema disappeared. Five months later the patient was re-examined. Although he was subjectively well, progress towards uremia was indicated by a blood creatinine of 4.8 mgm. per cent and a blood urea nitrogen of 56 mgm. The data recorded in table 3 were obtained 6 weeks after the first admission.

RESULTS AND DISCUSSION

The results are given in table 3 and in figures 1 to 6. The clearance values are corrected for body size, by calculating them from observed V values multiplied by the factor $\frac{1.73}{\text{sq. m. ideal area}}$, as described in the preceding paper (6). The correction factors are given in table 2.

As in the normal subjects reported in the foregoing paper, the same effect of a given urine volume on urea excretion was observed, whether the volume had been reached through increase or decrease.

For 5 of the 6 patients the position of the augmentation limit has

TABLE 3

Data concerning urea excretion

	Time	V Urine volume	V cor. Urine volume corrected for body size by factor $\frac{1.73}{\text{Area}}$ from table 2	U Urine urea nitrogen	B Blood urea nitrogen	$\frac{UV \text{ cor.}}{B}$ Observed clearance*	$\frac{U\sqrt{V \text{ cor.}}}{B}$ Calculated standard below clearance (for V) augmentation limit	Per cent of average normal clearance
		cc. per minute	*cc. per minute*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*cc. blood per minute*	*cc. blood per minute*	*per cent*
Exp. No. A 12. Chi. 8:50 a.m., 100 cc. of water. Venous blood	9–11	0.97	1.30	413	7.5	71.6	62.7	116
Exp. No. A 13. Chi. 8:40 a.m., 100 cc. of water. Venous blood	9–11	0.67	0.90	678	10.1	60.0	63.6	118
Exp. No. A 14. Chi. 8:20 a.m., 100 cc. of water. Venous blood	9–11	0.41	0.55	1019	11.9	96.9	63.4	117
Exp. No. A 15. Chi. 8:20 a.m., 100 cc. of water. Venous blood	9–11	0.21	0.28	966	11.1	24.4	46.2	85
Exp. No. A 16. Chi. 8:20 a.m., 100 cc. of water. Venous blood	9–11	0.30	0.40	828	7.0	47.6	75.0	139
Exp. No. A 17. Chi. 8:20 a.m., 100 cc. of water. Venous blood	9–11	0.28	0.38	1005	10.1	37.4	61.0	113
Exp. No. A 18. Chi.	9–10	6.50	8.71	282	30.4	80.9*		108*
6 a.m., 20 grams urea and 300 cc. of	10–11	6.92	9.27	240	27.0	82.4*		110*
water. 7, 8, 9, 10, and 11 a.m., 300 cc. of water each time. Venous blood	11–12	4.50	6.03	336	25.1	80.7*		108*

Exp. No. 10. Jac.	9–10	0.65	0.63	737	27.4	17.0	21.4	40
7 a.m., 15 grams urea. 8 a.m., dry breakfast. 1:05 p.m., dry lunch. Cutaneous blood	10–11	0.77	0.75	800	Lost			
	11–12	0.72	0.70	729	27.7	18.2	22.0	41
	12–1	0.70	0.68	705	25.1	19.1	23.1	43
	1–2	0.58	0.56	681	27.5	14.1	18.6	34
	2–3	0.67	0.65	704	24.7	18.4	22.9	42
Exp. No. 10-a. Jac.	10–11	0.33	0.32	335	9.9	11.0	19.1	35
9 a.m., 100 cc. of water. Venous blood	11–12	0.50	0.49	345		17.0	24.2	45
Exp. No. 13. Jac.	9–10	0.70	0.68	800	32.3	16.8	20.4	38
7 a.m., 15 grams, urea. 8 a.m., breakfast with 500 cc. of water. 12 noon, lunch with 1000 cc. of water. 2, and 3 p.m., 300 cc. of water each time. Cutaneous blood	10–11	0.77	0.75	749	30.0	18.6	21.6	40
	11–12	0.70	0.68	742	27.5	18.6	22.3	41
	12–1	3.10	3.01	269	27.3	29.8*		40*
	1–2	5.33	5.17	155	24.4	32.8*		43*
	2–3	6.17	5.98	131	23.0	34.1*		45*
	3–4	6.57	6.37	122	21.8	35.6*		47*
Exp. No. 17. Jac.	9–10	0.60	0.58	700	24.0	17.0	22.3	41
7 a.m., 15 grams urea with 50 cc. of water. 7:30 a.m., dry breakfast. 12:35 p.m., lunch with 800 cc. of water. Cutaneous blood	10–11	0.77	0.75	712	25.6	20.7	24.0	44
	11–12	0.82	0.80	690	24.0	22.8	25.6	47
	12–1	0.72	0.70	658	24.6	18.6	22.4	41
	1–2	2.42	2.35	305	21.4	33.5*		44*
	2–3	2.73	2.65	278	22.9	32.2*		43*
	3–4	2.03	1.97	336	21.2	31.3	22.3	41
Exp. No. 18. Jac.	10–11	4.33	4.20	137	18.0	32.0*		43*
7:30 breakfast with 1000 cc. of water. 9 and 10:30 a.m., 500 cc. of water each time. Cutaneous blood	11–12	4.08	3.96	130	18.0	28.6*		38*
	12–1	5.17	5.02	104	17.2	30.3*		40*
Exp. No. 20. Cic.	9–10	0.73	0.77	904	39.3	17.6	20.1	37
7 a.m., 15 grams urea. 7:30 a.m., dry breakfast. 1:05 p.m, lunch with 100 cc. of water. Cutaneous blood	10–11	0.78	0.82	809	35.2	18.9	20.8	38
	11–12	0.67	0.70	790	32.4	17.1	20.5	38
	12–1	0.58	0.61	787	32.8	14.7	18.8	35
	1–2	0.92	0.97	518	33.5	15.0	15.2	28

TABLE 3—*Continued*

	Time	V Urine volume	V cor. Urine volume corrected for body size by factor $\frac{1.73}{\text{Area}}$ from table 2	U Urine urea nitrogen	B Blood urea nitrogen	$\frac{UV \text{ cor.}}{B}$ Observed clearance*	$\frac{U\sqrt{V \text{ cor.}}}{B}$ Calculated standard below clearance (for V) augmentation limit	Per cent of average normal clearance
		cc. per minute	*cc. per minute*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*cc. blood per minute*	*cc. blood per minute*	*per cent*
Exp. 20-a. Cic.	10–11	0.37	0.39	384	16.2	9.1	14.8	27
9 a.m., 100 cc. of water. Venous blood	11–12	0.60	0.63	386		15.0	19.0	35
Exp. 20-b. Cic.	10–11	0.50	0.53	347	15.2	11.9	16.6	31
9 a.m., 100 cc. of water. Venous blood	11–12	0.35	0.37	270		6.6	10.8	20
Exp. 20-c. Cic.	10–11	1.27	1.33	198	12.1	21.7	18.9	35
9 a.m., 100 cc. of water. Venous blood	11–12	0.92	0.97	299		23.8	24.3	45
Exp. No. 22. Cic.	9–10	1.92	2.02	354	36.6	19.4*		26*
7:30 a.m., breakfast with 15 grams urea	10–11	1.87	1.96	344	35.1	19.2*		26*
and 1000 cc. of water. 11:50 a.m.,	11–12	1.83	1.92	345	34.5	19.2*		26*
lunch with 1000 cc. of water. 1:20	12–1	2.17	2.28	349	34.6	22.9*		31*
and 2:05 p.m., 500 cc. of water each	1–2	4.17	4.38	209	37.0	24.7*		33*
time. Cutaneous blood	2–3	4.50	4.73	230	35.4	30.7*		41*
	3–4	4.83	5.07	185	33.8	27.8*		37*
Exp. No. 14. Val.	9–10	1.10	1.03	244	21.8	11.6	11.3	21
8 a.m., breakfast with 100 cc. of water.	10–11	0.97	0.91	265	19.4	12.4	13.1	24
12 noon lunch with 1000 cc. of water.	11–12	0.90	0.85	285	18.9	12.9	13.9	25
1:40 p.m., 500 cc. of water. Cutane-	12–1	2.17	2.04	135	22.1	12.5*		17*
ous blood	1–2	5.08	4.78	57	20.5	13.2*		18*
	2–3	6.37	5.99	50	19.6	15.2*		20*
Exp. No. 14–a. Val.	10–11	1.87	1.76	222		14.9*		21*
9 a.m., 100 cc. of water. Venous blood	11–12	0.88	0.83	361	26.1	11.5	12.6	23

Exp. No. 19. Val.	9–10	1.02	0.96	419	29.6	13.6	13.9	26
7:30 a.m., dry breakfast. 1 p.m., dry	10–11	0.90	0.85	429	29.2	12.4	13.5	25
lunch. Cutaneous blood	11–12	0.70	0.66	473	29.5	10.6	13.0	24
	12–1	0.70	0.66	492	30.2	10.8	13.2	24
	1–2	0.87	0.82	417	29.1	11.7	13.0	24
	2–3	0.80	0.75	418	28.5	11.1	12.7	24
Exp. No. 21. Val.	9–10	0.83	0.78	499	32.9	11.9	13.4	25
7:30 a.m., dry breakfast. 12:05 p.m.,	10–11	0.97	0.91	466	30.8	13.8	14.4	27
lunch with 1000 cc. of water. Cutane-	11–12	1.00	0.94	469	31.3	14.1	14.5	27
ous blood	12–1	1.53	1.44	321	30.2	15.3*		20*
	1–2	3.42	3.21	131	29.3	14.4*		19*
	2–3	1.27	1.19	306	29.8	12.2*		16*
Exp. No. 23. Val.	9–10	0.78	0.73	520	32.1	11.9	17.7	33
7:30 a.m., dry breakfast. 12 noon lunch	10–11	0.83	0.78	504	30.8	12.9	14.4	27
with 1000 cc. of water. Cutaneous	11–12	0.77	0.72	495	30.5	11.7	13.8	26
blood	12–1	1.70	1.60	285	30.6	14.9*		20*
	1–2	4.08	3.83	121	30.2	15.3*		20*
	2–3	2.20	2.07	203	30.0	13.9*		19*
Exp. A-19. Gia.	11–1	2.29	2.17	234	50.2	10.2*		14*
Admitted to hospital 10:30 a.m. Venous blood								
Exp. A-20. Gia.	9–11	1.54	1.46	247	46.2	7.9	6.47	12
Fasting. Venous blood								
Exp. A-21. Gia.	9–11	0.75	0.71	304	38.2	5.7	6.72	12
8:15 a.m., 100 cc. of water. Venous blood								
Exp. A-22. Gia.	9–11	0.90	0.85	305	34.0	7.6	8.29	15
8:25 a.m., 100 cc. of water. Venous blood								
Exp. A-23. Gia.	9–11	0.93	0.88	319	39.9	7.1	7.52	14
8:20 a.m., 100 cc. of water. Venous blood								

TABLE 3—*Concluded*

	Time	V Urine volume	V cor. Urine volume corrected for body size by factor $\frac{1.73}{\text{Area}}$ from table 2	U Urine urea nitrogen	B Blood urea nitrogen	$\frac{UV \text{ cor.}}{B}$ Observed clearance*	$\frac{U\sqrt{V \text{ cor.}}}{B}$ Calculated standard below clearance (for V) augmentation limit	Per cent of average normal clearance
		cc. per minute	*cc. per minute*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*cc. blood per minute*	*cc. blood per minute*	*per cent*
Exp. A-24. Gia. 8:20 a.m., 100 cc. of water. Venous blood	9–11	1.02	0.97	269	34.8	7.4	7.61	14
Exp. A-25. Gia. 8:20 a.m., 100 cc. of water. Venous blood	9–11	0.80	0.76	314	35.3	6.8	7.76	14
Exp. A-26. Gia. 9:05 a.m., 100 cc. of water. Venous blood	9–11	1.04	0.99	339	37.0	9.0	9.10	17
Exp. A-27. Gia. 8:25 a.m., 100 cc. of water. Venous blood	9–11	0.97	0.92	388	44.6	8.1	8.36	15
Exp. A-28. Gia. 8:30 a.m., 100 cc. of water. Venous blood	9–11	0.97	0.92	362	39.4	8.4	8.82	16
Exp. A-29. Gia.	9–10	2.17	2.06	362	71.9	10.3*		14*
6 a.m., 30 grams urea and 500 cc. of	10–11	3.37	3.20	268	70.4	12.2*		16*
water. 7, 8, 9, 10, and 11 a.m., 500 cc. of water each time. Venous blood	11–12	4.17	3.96	209	69.0	12.1*		16*
Exp. A-30. Gia. 8:25 a.m., 100 cc. of water. Venous blood	9–11	1.17	1.11	435	49.9	9.7	9.19	17

Exp. No. 24. Wol.	9–10	2.33	2.82	141	27.8	14.3	8.52	16
7:30 a.m., breakfast with 1000 cc. of	10–11	1.98	2.40	142	27.4	12.5	8.14	15
water. 9:30 a.m., 500 cc. of water.	11–12	1.53	1.85	147	27.0		7.42	14
12:05 p.m., lunch with 1000 cc. of	12–1	1.37	1.66	141	27.9	8.5	6.52	12
water. Cutaneous blood	1–2	2.93	3.55	123	27.5	16.0	8.42	16
	2–3	2.63	3.18	126	26.2	15.4	8.58	16
Exp. No. 24-a. Wol.	10–11	1.17	1.42	383	45.2	11.9	10.10	19
9 a.m., 100 cc. of water. Venous blood	11–12	0.67	0.81	425		7.6	8.47	16
Exp. No. 27. Wol.	9–10	2.38	2.88	126	25.5	14.3	8.39	16
7:30 a.m., breakfast with 1000 cc. of	10–11	1.77	2.14	122	23.2	11.3	7.69	14
water. Cutaneous blood	11–12	0.80	0.97	43	24.2	6.3	6.23	12
Exp. No. 30. Wol.	9–10	2.12	2.57	110	22.5	12.5	7.83	14
8:30 a.m., breakfast with 1000 cc. of	10–11	1.93	2.33	109	21.9	11.7	7.61	14
water. 9:50 a.m., 250 cc. and 11:20	11–12	1.43	1.73	118	24.6	8.2	6.32	12
a.m., 500 cc. of water. 11:50 a.m.,	12–1	1.67	2.02	109	21.0	10.5	7.39	14
lunch with 500 cc. of water. 1:10 p.m.,	1–2	1.97	2.38	103	22.3	10.9	7.13	13
300 cc. of water. Cutaneous bood	2–3	1.97	2.38	93	23.1	9.7	6.22	12
Exp. No. 30-a. Wol.	10–11	0.75	0.91	164	21.4	7.0	7.30	14
9 a.m., 100 cc. of water. Cutaneous blood								
Exp. No. 30-b. Wol.	9–10	2.08	2.52	151	37.4	10.0	6.40	12
6 a.m., 300 cc. of water and 15 grams	10–11	2.08	2.52	147	35.9	10.3	6.49	12
urea. 7, 8, 9, 10, and 11 a.m., 300 cc.	11–12	2.47	2.99	134	35.2	11.3	6.58	12
of water each time. Cutaneous blood								

* Clearance figures marked * represent maximum clearance values determined when V was above the augmentation limit of the subject. For augmentation limits see table 4.

TABLE 4

Summary of data concerning urea excretion

Subject	Diagnosis	Body weight	Augmentation limit. Urine volume per minute	Standard blood clearance, $\frac{U}{B}\sqrt{V}$ (from points below augmentation limit)						Maximum blood clearance $\frac{UV}{B}$ cor. from points above augmentation limit					
				Number of observations	Maximum	Minimum	Average	Probable deviation from average		Number of observations	Maximum	Minimum	Average	Probable deviation from average	
		kgm.	*cc.*		*cc. blood per minute*	*cc. blood per minute*	*cc. blood per minute*	*cc. blood per minute*	*per cent of average*		*cc. blood per minute*	*cc. blood per minute*	*cc. blood per minute*	*cc. blood per minute*	*per cent of average*
Chi.	Glomerulonephritis stage I	38	1.72	6	74.0	46.2	62.0	±6.2	±10.1	3	82.4	80.7	81.3	±0.6	±0.8
Jac.	Glomerulonephritis stage I	56	2.11	15	25.6	18.6	22.1	±1.2	±5.6	9	35.6	28.6	32.1	±4.4	±13.8
Cic.	Nephrosis	48	1.65	11	24.3	10.8	18.2	±2.5	±13.5	7	30.7	19.2	23.4	±3.1	±13.2
Val.	Glomerulonephritis stage III	59	1.07	16	17.7	11.3	13.7	±0.9	±6.7	10	15.3	12.2	14.2	±0.8	±5.6
Gia.	Glomerulonephritis stage III	64	1.97	10	9.19	6.47	7.98	±0.6	±7.9	4	12.2	10.2	11.2	±0.7	±6.6
Wol.	Glomerulonephritis stage III	38	?	21	10.10	6.22	7.51	±0.7	±9.2						
Average			1.74						±8.8						±8.0
Probable deviation from average	cc. per minute		±0.36												
	per cent of average		±20.5												

been calculated as in the preceding paper. The results are given in table 3. For the sixth patient (Wol.) such a calculation was not possible because of his failing ability to put out large volumes of water.

The points determined after previous ingestion of urea are indicated on the charts by black discs, those determined on the days when no urea had been given, by hollow circles. It is apparent from figures 2 and 3 that the results are not to any important degree influenced by urea ingestion.[1]

Two facts are at once apparent from the figures. The first is that the urea excretion curves of these patients in five cases out of six are much lower than any observed normal curve. The second is that the pathological curves resemble the normal ones in that, when urea excretion is plotted against the square root of urine volume, each curve is composed of 2 straight lines, an ascending line showing urea excretion increasing with urine volume over the lower ranges of the latter, and a horizontal line, at higher volume ranges, representing maximum excretion. These two lines intersect, as in normal subjects, at an augmentation limit. In the case of patient Wol., only the sloping first part of the curve remains, diminution of power to excrete water had rendered unattainable the urine volumes represented on all or nearly all of the horizontal part. In patient Val., on the other hand, most of the ascending part is lost through loss of power of concentration. Only enough remains to suggest the bend of the curve at the augmentation limit.

[1] Addis (Arch. Int. Med., 1922, xxx, 378) considers it essential to place the kidneys under strain by administration of urea and water in order to force them to maximum effort, whereby functional deficits should be revealed that would otherwise escape notice. The idea is logical, and is supported by Addis' results with partially nephrectomized animals. We have accordingly expected to find some patients in the initial stages of declining renal function, who would still show normal standard and maximum clearances under ordinary living conditions, but would reveal deficits in the maximum clearance when fed urea and water under the conditions of Addis' test. This expectation has, however, never been realized. In observations on patients with the various types of Bright's disease, with all variations in renal function from normal to practically zero, we have not yet encountered one in whom the conditions of the Addis test revealed a functional deficit when the blood urea clearance, determined without urea feeding, did not do so, nor have we seen any in whom the degree of deficit found was significantly increased by imposing the conditions of the Addis test.

In figure 7 the same urea excretion curve as the one given in figure 5 has been plotted on logarithmic paper. In the logarithmic curve variations in height are proportional to *percentage* changes, rather than absolute changes, in the data plotted. In a uremic case, the clearance values are all so low that variations on them are inconspicuous, when plotted on an ordinary scale, as in figure 5. But when plotted logarithmically, as in figure 7, they are as evident as the clearance variations of a normal subject.

The values for the augmentation limits, given in table 4, are on the whole somewhat lower than those found for normal subjects in the preceding paper (6). The average figures for nephritic and normal subjects are 1.73 and 2.13 cc. per minute respectively. The decrease in augmentation limit is hardly great enough to justify the conclusion that it represents an effect of the disease. It is not very significant compared with the relatively great fall in the *level* of the curves observed in cases with damaged renal function.

In each case there is, compared with the normal, a fall of nearly equal proportions in the level of the ascending line and in that of the horizontal line reached at the augmentation limits, with relatively small change in the limit. Consequently the standard blood urea clearance, indicated by the height of the ascending line at $V = 1$ cc. per minute, and the maximum clearance, indicated by the height at the augmentation limit and beyond, show in these cases approximately equal percentage diminutions below the normal. The similarity in the significance of results by the maximum and standard clearance determinations is also indicated by the agreement between the percentages of normal values shown by the two clearances for each individual, indicated by the figures with and without stars. respectively in the last column of table 3.

In table 4 the variations for the standard and maximum clearances in each patient are given. The table shows that, as previously found with normal individuals, the average variation in a given subject is slightly greater for the standard clearance than for the maximum clearance.

In figure 8 all the curves are presented, with scales indicating the per cent of normal standard and maximum clearance observed in each case. It is apparent that both clearances tend to show about the same percentage fall in cases with renal deficiency.

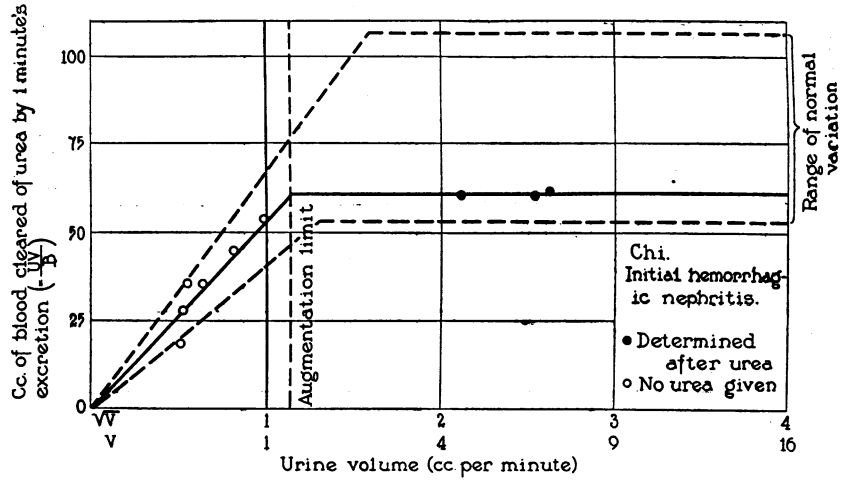

FIG. 1. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT CHI.

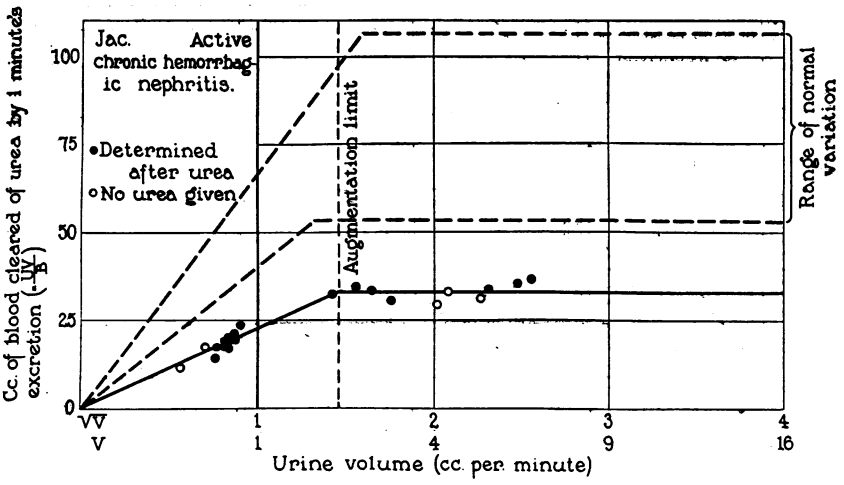

FIG. 2. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT JAC.

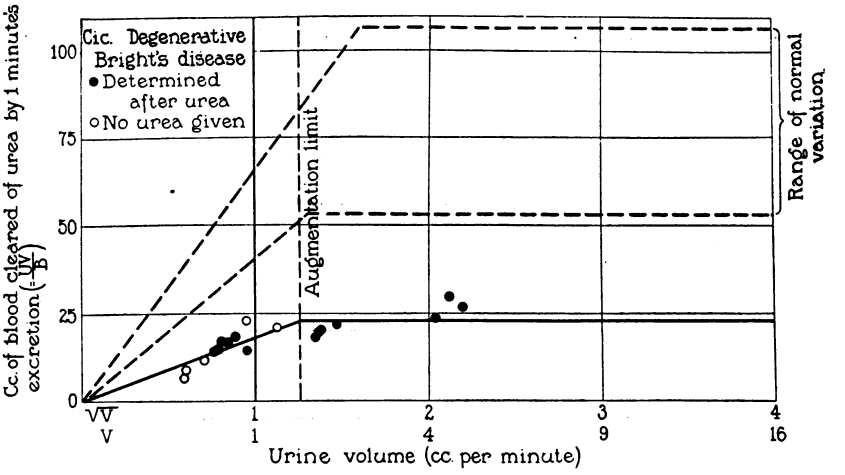

FIG. 3. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT CIC.

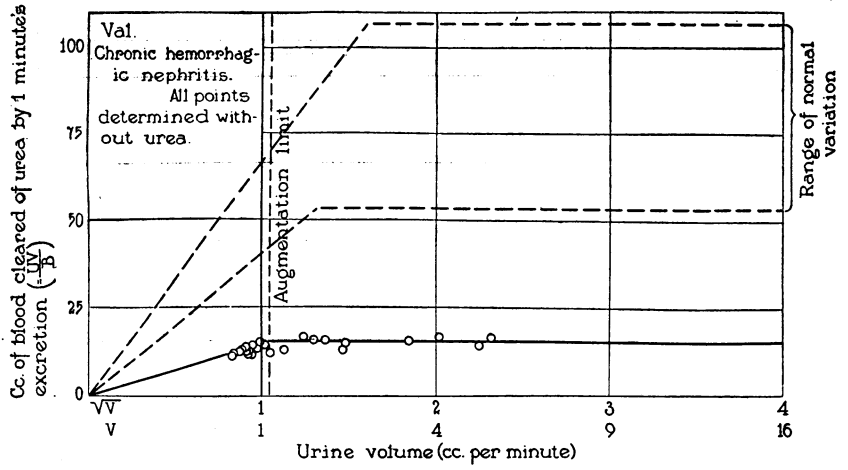

FIG. 4. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT VAL.

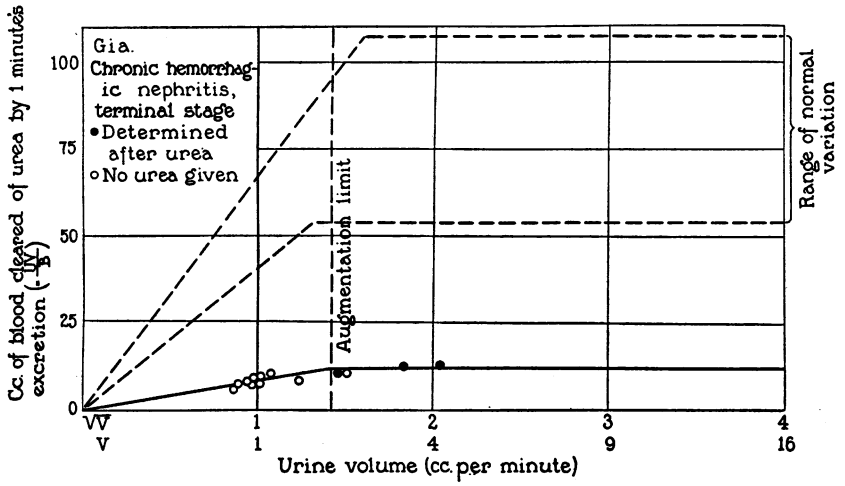

FIG. 5. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT GIA.

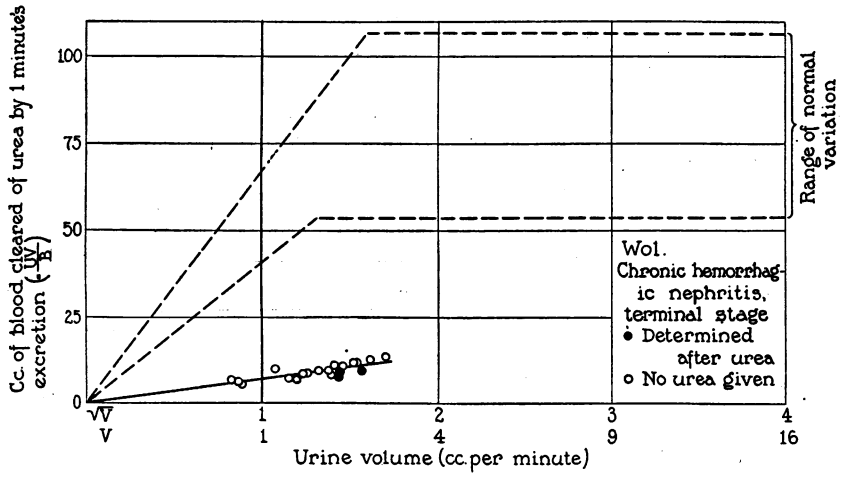

FIG. 6. BLOOD UREA CLEARANCE CURVE, CORRECTED FOR BODY SIZE, OF PATIENT WOL.

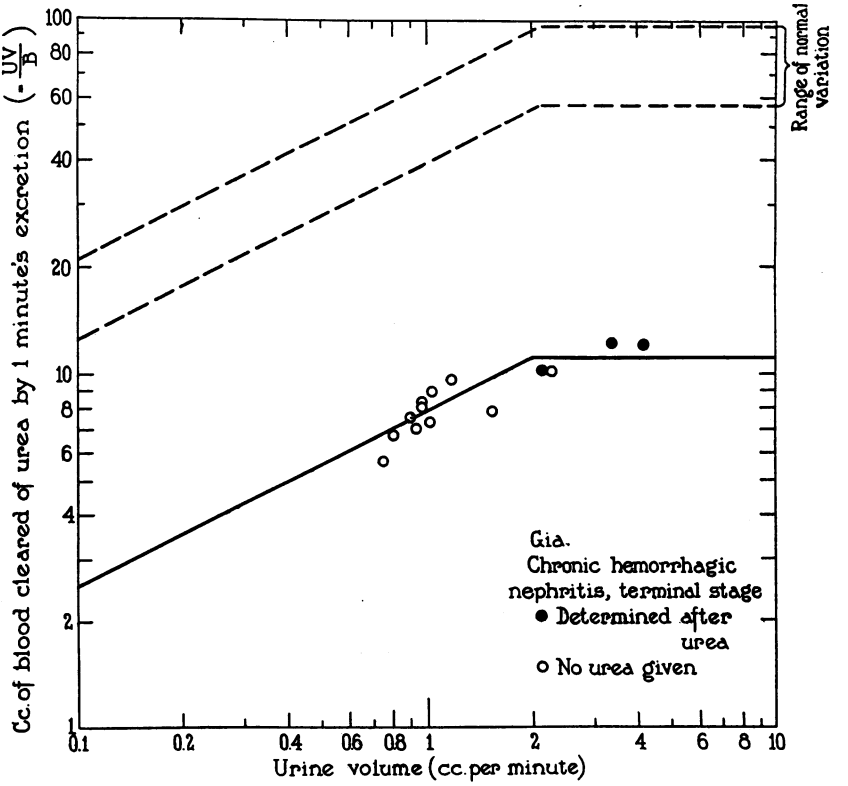

FIG. 7. THE SAME UREA CLEARANCE CURVE AS THE ONE GIVEN IN FIGURE 5 BUT HERE PLOTTED ON LOGARITHMIC PAPER

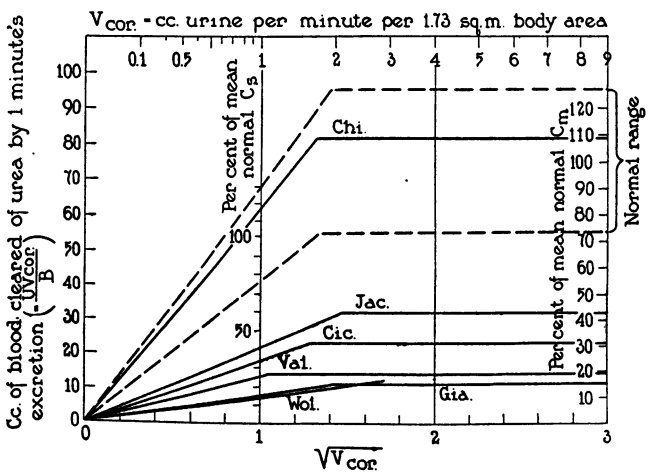

FIG. 8. CURVES OF THE SIX PATIENTS, SHOWING RELATIVE EFFECTS OF RENAL DEFICIENCY OF EACH ON STANDARD AND MAXIMUM CLEARANCES

Of the 5 cases with urea excreting power, as indicated by the blood urea clearances, consistently reduced to from 40 to 12 per cent of the average normal, all except one (Gia.), showed at times blood urea nitrogen below the maximum (23 mgm. per cent) found by MacKay and MacKay (4) in normal subjects. These results confirm the conclusion of these authors (3), that more than half the functioning tissue of the kidneys may be destroyed before the blood urea rises above normal limits.

In subjects with such renal loss the blood urea may, in fact, even be less than the normal average. Thus in experiments 10-a and 20-c blood urea nitrogen of only 10 to 12 mgm. per 100 cc. is seen, despite the fact that both subjects showed only about 40 per cent of mean normal excreting power. Such results indicate the uncertainty attending interpretation of normal blood urea values in nephritic patients if the urea excretion rate is not also taken into consideration. It has in fact been common on our wards to find consistently normal blood ureas in nephritic patients who have lost 40 to 60 per cent of their renal function. Such patients are likely, either by choice or direction, to take diets low in protein: and if they consume half as much as a given normal subject, other factors being equal, they will show about normal blood urea content. If, in addition, they drink more water, they may have even less blood urea than many normal subjects. In the cases to be presented in a later paper there are numerous examples of this fact.

SUMMARY

1. Data are presented showing the relationship between urine volume and urea excretion in 6 patients with Bright's disease, in stages varying from an acute case with normal urea excreting ability to an advanced chronic case with only one-eighth of normal urea excreting power.

2. The rate of urea excretion in these patients was found to vary with blood urea content and urine volume in the same manner as in normal subjects.

3. The standard blood urea clearance, representing the cubic centimeters of blood cleared of urea by 1 minute's excretion when urine volume is 1 cc. per minute, and the maximum clearance, with

urine volumes above the augmentation limit of about 2 cc. per minute, proved to be equally sensitive as indicators of renal function in these nephritics.

4. Our data confirm MacKay and MacKay (3) in showing that loss of renal function may exceed 60 per cent before the blood urea content rises above the highest level observed in normal subjects. Unless the excretion rate is also considered, the blood urea, taken alone, may fail to reveal diminishing renal ability until the latter has reached an advanced stage.

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