A COMPARISON OF THE CREATININE AND UREA CLEARANCE TESTS OF KIDNEY FUNCTION

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The urea clearance test developed by Möller, McIntosh and Van Slyke (1) has one disadvantage, namely, that maximum and standard clearances are only comparable by reference to the average normal value for each or by multiplying the standard clearance by a constant. In addition the standard clearance, involving the square root of the urine volume, is difficult to interpret. The creatinine clearance test, developed by Rehberg (2), is not subject to these objections, since the excretion of creatinine is independent of urine volume. It therefore seemed worth while to compare the creatinine and urea clearances as a test of renal function, to determine if there was sufficient practical advantage in the creatinine test to compensate for the added technical difficulties.

Rehberg presented evidence that led him to believe that the creatinine clearance represented the volume of glomerular filtrate, and on this assumption calculated the quantities of urea and chloride reabsorbed. Rehberg's conception has been accepted by Wyschegorodzewa (3), Bergwall (4), and others (5, 6); questioned by Cope (7) and Ekehorn (8); and denied by Shannon, Jolliffe and Smith (9). The evidence at present available does not, in our opinion, justify unreservedly accepting the creatinine clearance as equal to the volume of glomerular filtrate, and while this lessens the value of the test as a tool in the study of renal physiology, it need not detract from its usefulness as a practical test of kidney function.

METHODS

Hospital patients were kept in bed for the period of the test. Dispensary patients and normal subjects were allowed to sit in a chair or engage in light laboratory work. Some tests were made after fourteen hours' fast, the majority after a light breakfast which MacKay (10) found had no effect on the urea clearance. Three to five grams of creatinine were given by mouth an hour to one and one-half hours before the beginning of the test. At the beginning of the test, the bladder was emptied as completely as possible and a sample of venous blood obtained. Approximately an hour later, but timed to the nearest minute, the bladder was again emptied as completely as possible and a second sample of blood obtained. If there was any doubt whether the subject could empty the bladder, he was catheterized. All blood analyses were made on serum.

Urea nitrogen in urine and serum was estimated by the gasometric method of Van Slyke (11); in a few instances by Van Slyke and Cullen's (12) method. All analyses were made in duplicate. Creatinine in urine and serum was estimated by Rehberg's (13) modification of Folin's method, using a colorimeter with Bürker optical system.

The ingestion of three to five grams of creatinine increases the plasma concentration to 5 to 10 mgm. per cent. This decreases the effect of substances other than creatinine in plasma which give the Jaffe reaction, as well as making the estimation more certain. Since Behre and Benedict (14) and Gaebler (15) have doubted the existence of creatinine in normal blood, and since Gaebler could recover only a relatively small fraction of the creatinine added to blood, it was felt that the creatinine analyses had to be examined before any reliance could be placed on the calculation of creatinine clearance by the formula $UV/B = C$. By the method used in these experiments the average recovery of creatinine added to serum in amounts equivalent to 0.5 to 15.0 mgm. per 100 cc. was 93.5 per cent in 15 experiments, the extremes being 80 and 124 per cent. Table I shows

TABLE I

Comparison of creatinine clearances calculated from total chromogenic substances and from ingested creatinine only

Name	Before ingestion		After ingestion		Creatinine clearance †	
	Serum "creatinine"	Creatinine excreted	Average serum creatinine	Creatinine excreted		
	mgm. per cent	*mgm. per minute*	*mgm. per cent*	*mgm. per minute*	*A*	*B*
J. M. H.	1.27*	1.42*	9.63	12.72	132	134
			8.31	10.30	124	126
			12.22	12.50	102	101
White.	0.95	1.37	6.16	10.05	163	166
Wilson.	1.08	1.59	8.28	8.08	106	100
Letcher.	1.01	.89	9.20	11.05	120	124

* Average of 4 determinations.

† *A*—clearance calculated from total chromogenic substance in serum and urine.

B—clearance calculated from ingested creatinine only, subtracting value of chromogenic substances normally present in serum and average rate of excretion of creatinine before ingestion.

that there is no difference in the clearance calculated on total chromogenic substances in serum and urine after ingestion of creatinine and in the clearance calculated on ingested creatinine only. Gaebler and Keltch (16) have shown that all the chromogenic material adsorbed on Lloyd's reagent and released again is indistinguishable from creatinine. Therefore, a clearance calculated on the material released from Lloyd's reagent should be higher than that calculated on total chromogenic substances when no creatinine has been fed, since other substances account for a considerable fraction of the value obtained for " creatinine " in normal serum. After ingestion of creatinine, the clearances calculated before and after the use of Lloyd's reagent should show much less difference. Table II shows that

TABLE II

Comparison of creatinine clearances calculated from total chromogenic substances and from material released from Lloyd's reagent with and without ingestion of creatinine

Experimental number and condition		Urine volume	Total "creatinine"			Released from Lloyd's		
			Serum	Urine	Clearance	Serum	Urine	Clearance
		cc. per minute	*mgm. per cent*	*mgm. per cent*	*cc. per minute*	*mgm. per cent*	*mgm. per cent*	*cc. per minute*
1.	No	6.84	1.01	131	89	.84	136	111
2.	creatinine	7.07	1.30	20	109	.96	18	133
3.	ingested	7.75	1.32	18	106	.87	14	125
4.	Creatinine	7.72	9.63	165	132	9.03	159	136
5.	ingested	1.95	12.22	642	102	10.99	600	106
6.		9.35	6.16	108	164	6.02	101	157

this is the case. These experiments led us to believe that with serum concentrations of creatinine above 5 mgm. per cent, the creatinine clearance could be calculated on total chromogenic substance present in serum and urine without significant error.

In order to estimate the range of creatinine clearance in normal individuals under conditions of hospital and office practice, 59 clearances on 59 apparently healthy individuals were tabulated. In 45 of these, only a single test was made. In 14, from 2 to 21 clearances were determined. For these, the first clearance determined was tabulated. The range in these 59 observations was from 87 to 232 cc. per minute, the mean 144 cc. per minute with a standard deviation of 36 cc. When repeated tests are made of the same individual, there is a similar wide dispersion, but the limits for all clearances which we have obtained from normal individuals are only slightly wider. Nor apparently does any normal individual tend to have a constantly high or low clearance.

For this reason, it seemed proper to include all our observations (130) of normal individuals where no recognized unusual factor, such as administration of a drug or exercise, was present to show the normal chance distribution of clearances. If this be done, the range is from 70 to 238 cc. per minute, the mean 148 cc. per minute with a standard deviation of 34 cc. A frequency polygram of these observations shows a decided skewness, but not sufficient to make unreasonable the belief that the chances of a single clearance of a normal adult falling between 80 and 216 are about 24:1. (Fig. 1).

McIntosh, Möller and Van Slyke (17) found that more constant normal values for urea clearance were obtained if a correction was made for surface area. This seems reasonable for Taylor, Drury and Addis (18) were able to show that kidney weights in rabbits varied in proportion to surface area rather than to body weight. To avoid an error greater than ± 5 per cent in using the formula $UV/B = C$, body size can be neglected only in adults between 164 and 176 cm. in height. We have corrected the creatinine clearance values by the factor $(1.75/A)$ where A is surface area

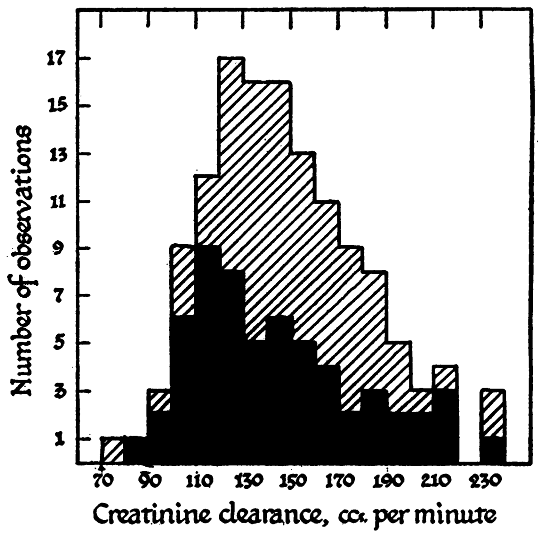

FIG. 1. FREQUENCY POLYGRAM OF 130 CREATININE CLEARANCE VALUES ON 59 NORMAL ADULTS

The solid area includes only the first observation made on each person.

in square meters. This amounted to more than 10 per cent in 5 instances. The average of the corrected clearances is 145 ± 34 cc. per minute, and the dispersion practically the same as for the uncorrected values. Since other unknown factors produce a much greater variation in clearances done on the same individual at different times than the amount of the correction for surface area, we feel that this correction is unnecessary in the case of adults except possibly for those of extreme heights. We have not applied the correction in the patients studied.

From our experience with normal subjects and patients suffering from various diseases, we have come to believe that creatinine clearances below 60 cc. per minute (41 per cent of average normal) are definitely abnormal, and those between 60 and 80 cc. per minute (41 to 54 per cent average normal) doubtful but significant if a repeated test is in the same range.

This is a lower normal limit than Holten and Rehberg (19) use. They found the clearance always above 100 cc. per minute in normal individuals when tested between 10 and 11 a.m. But in 89 clearances reported by Rehberg of himself where experimental conditions were more varied regarding posture and fluid intake, the clearance was 9 times between 80 and 100 cc. per minute, and twice between 60 and 80 cc. per minute, so that a patient cannot be said to have diminished renal function on the basis of a single creatinine clearance test between 60 and 100 cc. per minute.

The maximum urea clearance in 56 observations of 25 normal individuals ranged from 38 to 112 cc. per minute, with an average of 74.68 cc. per minute, and a standard deviation of 17.57 cc., identical with the average of 75 cc. per minute found by Möller, McIntosh and Van Slyke. The range in our subjects is somewhat greater than the extremes of 52.2 and 103.8 cc. per minute which they found. The mean standard urea clearance in 39 observations of 26 persons was 51 cc. per minute with a standard deviation of 10.11 cc. The range was from 30 to 67 cc. per minute. This is the same range found by Möller, McIntosh and Van Slyke (28.3 to 69.3 cc. per minute) while the mean is but slightly lower. Thus in the case of normal individuals creatinine and urea clearances have about the same degree of dispersion. The creatinine clearance is always numerically greater than the maximum urea clearance, although when the standard urea clearance is calculated using the square root of urine volume, the numerical value may be greater for urea than for creatinine clearance. In estimating reduction of kidney function we have used 148 cc. per minute as the average normal creatinine clearance, and 75 cc. and 54 cc. per minute as the average normal maximum and standard urea clearances.

A comparison of creatinine and urea clearances has been made 116 times on 93 patients with Bright's disease and certain other conditions (Tables III, IV and V). We have followed Addis's classification (20) of Bright's disease but have used the term acute instead of initial hemorrhagic Bright's disease. Patients with degenerative Bright's disease, of whom relatively few were examined, have been grouped with the miscellaneous cases in Table V. We have not had the opportunity of examining any patient in whom the diagnosis of "cryptic" degenerative Bright's disease (pure lipoid nephrosis) seemed proper. Cases 107–624 and 151–532 presented a typical picture at the time of some examinations, but had had hematuria some time previously. Both clearance tests frequently show marked reduction in kidney function before there is any elevation of blood urea nitrogen, decrease in two hour phenolsulphonphthalein output, or fixation of specific gravity. This was shown for the urea clearance by Van Slyke and his associates (21) and for creatinine by Holten and Rehberg (19). We have not found the decrease more constant or more marked in one test than the other. Just as in normal persons, the creatinine clearance is always numerically greater than the maximum urea clearance; the

TABLE III

Creatinine and urea clearances in patients with hemorrhagic Bright's disease

Hospital number	Sex	Age	Date	Stage of disease	Blood pressure	Phenolsulphonphthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years			*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
146–625	F	14	May 17, 1932	Acute	110/70	80	16.5	32.8	44	55	37	
146–212	M	33	January 28, 1932	Acute	140/100		33.6	51.0	68	94	64	
136–555	M	20	January 26, 1933	Acute	135/80	55	10.0	32.8*	61	83	56	
148–341	M	55	October 26, 1932	Acute	140/80	30	25.3	33.3	44	80	54	
150–822	F	27	February 23, 1933	Acute	115/80		9.8	92.5	123	166	112	
139–831	M	42	June 25, 1931	Acute	190/120	20	34.9	12.7*	24	39	26	
			August 27, 1931	Latent	140/90	70	14.0	21.9*	41	69	47	
			December 22, 1932	Latent	120/80		18.0	36.9	49	88	59	
			January 5, 1933	Latent			9.7	34.2	46	73	49	
			January 19, 1933	Latent			21.7	43.2	58	95	64	
			January 23, 1933	Latent			34.4	22.3*	41	66	45	
			January 30, 1933	Latent			9.2	27.8	37	73	49	
150–571	M	38	January 4, 1933	Chronic active	180/100	68	18.2	21.4	29	41	28	
146–216	M	52	April 26, 1932	Chronic active	130/80	30	26.6	16.6*	31	86	58	
107–624	M	15	January 12, 1932	Chronic active	115/70		8.5	62.2	83	206	139	
			April 25, 1932	Chronic active	115/45	67	79.8	9.1*	17	30	20	
149–975	F	38	November 21, 1932	Chronic active	140/100	48	24.2	29.1*	54	89	60	
139–722	M	45	October 8, 1931	Chronic active	115/80	20	28.8	14.6	19	28	19	
149–916	F	24	November 22, 1932	Chronic active	160/110	50	17.6	33.4	45	77	52	
150–097	M	32	November 29, 1932	Chronic active	105/70	65	21.1	18.8*	35	62	42	
			December 9, 1932	Chronic active		70	14.2	50.0*	93	95	64	

TABLE III—(*Continued*)

Hospital number	Sex	Age	Date	Stage of disease	Blood pressure	Phenol-sulphon-phthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years			*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
151–107	F	35	February 10, 1933	Chronic active	120/70	58	16.0	44.0*	82	79	53	
118–347	M	54	October 2, 1931	Chronic active	130/80	60	7.5	67.0	89	88	60	
			November 2, 1931	Chronic active	140/100	50	11.3	34.9	47	47	32	
142–123	M	51	September 28, 1931	Chronic active	155/85	60	19.0	24.4	33	70	47	
144–018	F	28	December 8, 1931	Chronic active	165/90	65	14.9	24.6*	46	53	36	
142–730	M	34	October 2, 1931	Chronic active	185/110	40	14.0	18.2*	34	47	32	
			October 10, 1932	Chronic active	205/135	10	30.3	13.8*	26	29	20	
			January 4, 1933	Terminal	190/130	10	28.6	14.9	20	20	14	March 1, 1933
86–642	F	31	October 28, 1932	Chronic active	110/80	25	24.0	11.9	16	28	19	
			January 25, 1933	Chronic active			24.7	9.3	12	26	18	
145–429	M	43	March 1, 1932	Latent	135/80	70	14.0	101.0	135	149	101	
0–343–184	F	59	April 6, 1933	Latent	160/100		8.9	67.0	81	126	85	
134–772	M	52	July 20, 1931	Terminal	160/110		12.4	21.5*	40	46	31	November 28, 1932
89–697	M	22	February 4, 1932	Terminal	180/110	5	111.0	3.9*	7	6	5	May 6, 1932
145–811	M	49	March 28, 1932	Terminal	140/70	5	188.0	0.6*	1	0.5	0.34	April 1, 1932
117–565	F	20	October 19, 1931	Terminal	150/110	10	52.4	3.8*	7	8.0	5.0	February 21, 1933
151–508	F	27	March 3, 1933	Terminal	260/150	10	70.0	5.5*	10	12.0	8	March 4, 1933
147–812	F	49	July 26, 1932	Terminal	110/60	5	119.0	0.9*	2	0.4	0.3	July 28, 1932

* Standard clearances.

TABLE IV

Creatinine and urea clearances in patients with arteriosclerotic Bright's disease

Hospital number	Sex	Age	Date	Blood pressure	Phenol-sulphon-phthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years		*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
0–348–091	F	41	April 6, 1933	220/140		13.5	46.8	62	116	78	
105–700	M	41	January 19, 1933	260/160	30	13.2	41.7*	77	111	75	
126–997	M	54	October 6, 1931	150/110	50	14.2	34.8	46	98	66	June 28, 1932
145–997	M	29	• April 7, 1932	200/130	52	16.9	31.8*	59	98	66	
			July 29, 1932	230/170	25	31.9	26.8*	50	47	32	August 27, 1932
149–734	F	60	November 23, 1932	140/80		15.4	44.8*	83	91	62	
0–339–644	M	62	January 17, 1933	200/100	55	20.0	37.8*	70	81	55	
150–795	F	28	January 18, 1933	198/130	56	22.5	72.6	97	78	53	
143–350	F	38	May 17, 1932	240/150	40	29.1	34.6	46	73	49	December 15, 1932
87–720	F	30	November 9, 1932	300/165	55	15.2	29.4	39	71	48	
135–951	F	44	January 12, 1933	275/154	30	20.1	34.5*	64	65	44	
149–462	F	55	November 8, 1932	235/155	40	16.5	13.7*	25	59	40	
150–053	F	56	November 29, 1932	200/100	70	19.6	16.4*	30	59	40	
143–048	M	43	June 28, 1932	150/90		23.1	15.8*	29	55	37	
138–277	F	49	January 2, 1931	170/95	40	20.5	40.4*	75	55	37	
			October 14, 1932	180/100	10	36.4	3.2*	6	7	5	
			January 10, 1933	165/90	10	47.0	5.1*	9	12	8	
121–988	M	41	July 16, 1932	190/125	55	20.3	10.3*	19	52	35	

TABLE IV (*Continued*)

Hospital number	Sex	Age	Date	Blood pressure	Phenol-sulphon-phthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years		*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
151–530	M	52	March 6, 1933	220/30	50	22.8	23.4*	43	45	30	
141–842	M	56	June 28, 1932	260/140	25	29.8	19.2*	36	45	30	
125–983	M	52	September 2, 1932	170/120	40	17.4	28.1*	52	40	27	
144–079	F	38	October 11, 1932	225/145	33	35.0	11.2*	21	35	24	November 9, 1932
150–478	M	39	January 9, 1933	220/135	25	40.6	15.4*	29	34	23	
			March 14, 1933	245/150	15	53.5	8.1*	15	13	9	
142–341	F	38	September 2, 1931	170/116	5	18.0	25.6	34	32	22	
142–324	M	55	September 25, 1931	240/140	5	74.1	29.2*	54	32	22	September 27, 1931
146–857	M	30	July 6, 1932	220/160	10	109.0	0.7*	1	11	7	
			July 23, 1932			49.7	18.6	25	27	18	August 2, 1932
148–705	F	48	August 31, 1932	245/150	18	49.4	16.5	22	21	14	December 30, 1932
149–634	M	44	November 8, 1932	200/160	5	105.7	12.9	17	18	12	November 20, 1932
149–237	M	58	October 5, 1932	260/130	10	57.4	5.2*	10	15	10	December 11, 1932
125–448	F	43	September 24, 1932	150/90	10	76.3	17.5*	32	11	7	
			October 13, 1932	160/110		46.9	5.0*	9	7	5	
150–929	F	60	January 22, 1933	170/80		156.0	3.8*	7	7	5	January 23, 1933
134–806	F	32	July 22, 1931	230/140	5	61.5	4.1*	8	7	5	August 19, 1931
144–535	F	45	January 7, 1932	230/110		131.5	1.7*	3	4	3	January 8, 1932
146–471	M	56	May 19, 1932	160/100		232.0	0.3*	0.6	3	2	May 19, 1932
91–504	F	43	June 9, 1932	250/170	3	118.0	3.6*	7.0	3	2	June 18, 1932
147–168	F	40	June 17, 1932	230/110	5	88.9	1.7*	3.0	2	1.4	June 29, 1932
141–832	M	47	July 31, 1931	235/130		163.0	0.2*	0.4	0.6	0.4	August 5, 1931

* Standard clearances.

TABLE V

Creatinine and urea clearances in patients with degenerative Bright's disease and certain other diseases

Hospital number	Sex	Age	Date	Diagnosis	Blood pressure	Phenolsulphonphthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years			*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
150–775	F	23	January 12, 1932	Degenerative Bright's disease and eclampsia	155/100	55	12.5	23.7*	44	56	38	
			March 20, 1933	Degenerative Bright's disease			13.7	31.3	42	77	52	
151–532	M	41	March 6, 1933	Degenerative Bright's disease	150/95	42	26.1	29.6	39	41	28	
151–057	F	21	February 1, 1933	Degenerative Bright's disease and eclampsia	165/120		60.4	17.5*	32	21	14	
			April 3, 1933	Degenerative Bright's disease	158/100	50	13.4	25.2*	47	61	41	
149–975	F	38	December 29, 1932	Diabetes and arteriosclerosis	150/90	35	27.3	33.0*	61	131	89	
149–793	M	53	January 21, 1933	Diabetes and arteriosclerosis	150/100	26	32.2	18.1	24	32	22	
0–320–284	M	43	January 14, 1933	Diabetes and arteriosclerosis	240/140		19.7	19.6*	36	51	34	
131–380	F	49	January 27, 1932	Diabetes and arteriosclerosis	230/130	40	9.1	42.0*	78	65	44	
136–525	M	28	October 25, 1930	Diabetes insipidus	130/85		11.0	38.5	51	104	70	
			August 15, 1932	Diabetes insipidus			15.0	43.5	58	79	53	August 27, 1932

TABLE V (*Continued*)

Hospital number	Sex	Age	Date	Diagnosis	Blood pressure	Phenol-sulphon-phthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years			*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
133–845	M	23	August 22, 1932	Essential Hypertension	160/110	80	8.1	103.0	137	119	80	
149–816	F	67	November 28, 1932	Carcinoma of stomach and arteriosclerosis	125/70		56.4	11.8*	22	44	30	November 30, 1932
149–535	M	64	December 5, 1932	Carcinoma of bronchus	110/70		15.0	21.1*	39	74	50	
122–258	F	66	June 10, 1932	Carcinoma of stomach	170/90		6.5	14.5*	27	28	19	June 21, 1932
146–484	M	75	May 6, 1932	Carcinoma of prostate	110/55	10	16.9	28.7*	53	81	55	May 9, 1932
149–077	F	52	November 25, 1932	Carcinoma of pancreas and jaundice	90/60		7.0	37.0*	69	20	14	November 30, 1932
146–070	M	50	April 7, 1932	Pneumonia	110/65		19.2	63.5	85	88	59	
142–587	M	26	September 12, 1931	Pneumonia	125/75		41.4	30.0*	56	145	98	September 14, 1931
142–828	M	36	September 25, 1931	Pneumonia	130/70		15.0	62.0*	115	155	105	September 27, 1931
145–644	M	27	March 11, 1932	Pneumonia	95/60		19.5	76.0*	141	231	156	March 18, 1932
150–738	M	51	January 12, 1933	Pneumonia	110/80		65.0	8.3*	15	38	26	January 13, 1933
143–756	M	36	November 16, 1931	Pneumonia			183.0	9.45	13	23	16	November 18, 1931
144–053	M	71	December 8, 1931	Pyelonephritis	125/80	5	137.0	3.5	5	5	3	December 18, 1931
147–549	F	34	July 19, 1932	Pyelonephritis	108/78	20	73.5	7.0*	13	9	6	August 24, 1932
85–756	F	70	March 13, 1933	Pyelonephritis	130/76	Trace	175.0	0.8*	1.5	2	1.4	March 18, 1932

TABLE V (*Continued*)

Hospital number	Sex	Age	Date	Diagnosis	Blood pressure	Phenolsulphonphthalein	Blood urea nitrogen	Urea clearance	Per cent of normal	Creatinine clearance	Per cent of normal	Date of death
		years			*mm. Hg*	*per cent in 2 hours*	*mgm. per cent*	*cc. per minute*		*cc. per minute*		
144–740	M	50	January 18, 1932	Bismuth poisoning and pyelonephritis	130/75	Trace	217.0	1.4*	3	2	1.4	January 28, 1932
143–846	F	39	November 30, 1931	Arteriosclerosis	180/140	80	7.8	68.0	91	147	99.0	
125–080	F	34	May 13, 1932	Arteriosclerosis	130/85	43	11.1	31.6*	59	157	106.0	
151–642	M	76	March 21, 1933	Hypertrophied prostate	140/80	85	17.6	37.8	50	68	46	
			April 14, 1933	Hypertrophied prostate			16.5	42.6	57	68	46	
151–583	M	65	March 21, 1933	Hypertrophied prostate	120/90	40	57.2	12.1	16	21	14	
			April 5, 1933	Hypertrophied prostate			32.3	27.3	36	44	30	
146–177	M	59	April 14, 1932	Pernicious anemia	115/55		10.8	44.8*	83	98	66	
150–874	F	38	February 14, 1933	Cirrhosis of liver and jaundice	110/70		14.5	39.4*	73	57	39	
141–512	M	50	March 15, 1933	Subacute endocarditis	160/90	15	30.6	24.3	32	24	16	
141–891	F	19	August 26, 1931	Streptococcic septicemia and acute interstitial nephritis	105/60	Trace	88.7	2.5*	5	3	2	September 8, 1931

* Standard clearances.

standard urea clearance, however, may have a greater numerical value than the creatinine clearance determined at the same time, since the concentration ratio is multiplied by the square root of urine volume in the former and by the volume in the latter.

A direct comparison of the two clearance tests is shown in Figure 2 in which the results of each test are plotted as percentage of average normal.

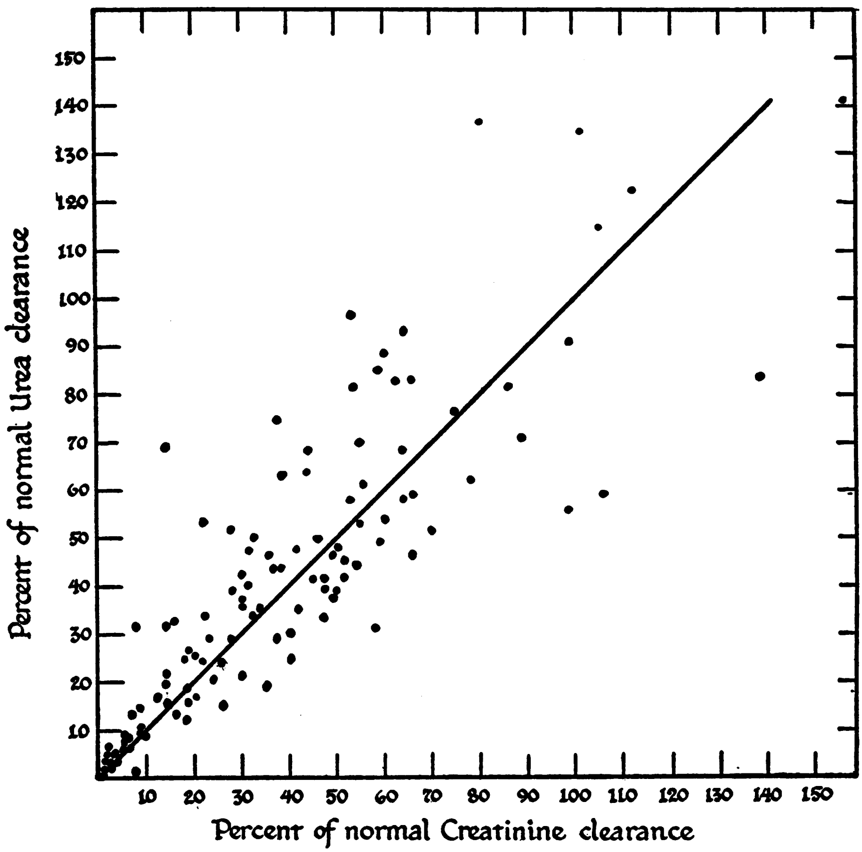

FIG. 2. COMPARISON OF CREATININE AND UREA CLEARANCE TESTS IN PATIENTS WITH BRIGHT'S DISEASE AND CERTAIN OTHER CONDITIONS

Points above the line indicate instances in which the urea clearance showed less reduction than creatinine; those below, instances in which the percentage reduction in urea clearance was greater. In patients with creatinine clearances below 10 per cent of average normal, there is not much difference in the degree of reduction of the two tests. In 82 creatinine clearances between 10 and 80 per cent of average normal, the urea clearance was reduced to a greater degree in 32, while in 50 it was not reduced to the same extent. These differences are of questionable significance when the wide range of normal variation in both tests is remembered. The most that can be said in favor of the creatinine test is that it may indicate a greater decrease in function more frequently than the urea clearance, but not with enough regularity to make up for the greater technical difficulty of the test. Nor have we been able to find any group of patients or any pathological condition in which the results of one test are consistently different from those of the other.

Since the creatinine test is more laborious and expensive, involving the ingestion of creatinine and the analysis of two blood samples, we do not believe it has any advantage in the routine estimation of the degree of impairment of kidney function in the clinic. If it can be satisfactorily shown that the creatinine clearance does approximate the volume of glomerular filtrate, then a comparison of the two tests, run simultaneously, will permit a much more intimate analysis of the parts played by variations in the volume of filtrate and degree of back diffusion in health and disease (19).

CONCLUSIONS

The creatinine and urea clearance tests have been compared in normal persons and in patients with Bright's disease. The mean creatinine clearance in 130 observations of 59 normal subjects was 148 cc. per minute. The variability of the two tests from the mean normal was approximately the same in our hands.

In patients with Bright's disease the creatinine and urea clearance tests are generally equally reduced in relation to the average normal. We were unable to demonstrate any practical advantage in the creatinine test to compensate for its greater technical difficulty.

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