JCI The Journal of Clinical Investigation

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J Clin Invest. 1932;11(5):1053-1064. https://doi.org/10.1172/JCI100458.

Research Article

STUDIES OF UREA EXCRETION. VII

THE EFFECTS OF POSTURE AND EXERCISE ON UREA EXCRETION

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(Received for publication May 31, 1932)

The studies reported in this paper were undertaken primarily to ascertain whether, in determining the blood urea clearance [1] as a measure of renal function, the previously utilized precaution of keeping the subject at rest in a recumbent position is necessary, and whether the mild exercise and change of posture associated with walking about has sufficient effect on renal activity to alter the clearance values obtained. Observations in the two conditions have been made on three normal men and nineteen nephritic subjects with varying grades of renal impairment. The effect of change of posture from lying in bed to sitting in a chair has also been studied. Furthermore, in three subjects with normal renal function, the effect was studied of exercise of the maximum severity which could be maintained for the 2-hour period.

There is evidence that renal function in many details is affected by mere change in posture. Edel (5) in 1901 observed that change from the recumbent to the standing position decreased markedly the volume output of urine, and in subjects with cyclic albuminuria increased the protein excretion. Subsequent authors (6, 9, 15, 17, 22) have confirmed this observation, and have found that the excretion rate, not only of water, but of most of the other normal urinary constituents, is diminished by the change from recumbent to standing posture. Thus White, Rosen, Fischer and Wood (22) found that the average effect in three normal men of changing from lying to standing posture was to diminish the hourly excretions to the following proportions of the outputs in the recumbent position: urine volume to 30 per cent, chlorides to 45 per cent, phosphorus to 67 per cent, sulfur to 71 per cent, urea to 61 per cent, and creatinine to 91 per cent. Cordero and Friedman (4) found that change from recumbent to upright position caused an average decrease of 10 to 13 per cent in the proportion of injected phenolsulfonephthalein excreted in 2 hours by normal subjects.

[1] The terms, "standard blood urea clearance" and "maximum blood urea clearance," used in expressing the urea excreting efficiency of the kidneys, have been defined in the second paper of this series (12).

As possible causes of such effects, Erlanger and Hooker (6) and White, Rosen, Fischer, and Wood (22) observed that the change from recumbent to upright position caused in 30 to 60 minutes a concentration of the blood by seepage of 10 to 11 per cent of the total plasma fluid into the leg tissues, and also that there was a decrease of 10 to 15 millimeters in pulse pressure. That the urine flow is diminished because increased osmotic pressure of the more concentrated plasma proteins retards glomerular filtration and favors tubular reabsorption of water, was believed by Ni and Rehberg (15), while Erlanger and Hooker (6) were inclined to see the chief retarding factor in the decreased pulse pressure and the number of functioning glomeruli.

Whether the urea clearance is affected depends upon whether the relationship between the outputs of urea and water is that allowed for in calculating the clearance. When the volume is below the augmentation limit of about 2 cc. per minute, the calculation of the clearance allows for change of urea excretion rate in proportion to the square root of the urine volume, while with higher volumes urea excretion rate, estimated as the "maximum clearance" (11), is assumed to be independent of urine volume. If standing up does not retard the urea output more than accords with the above allowances for urine volume effect, the value of the clearance will not be affected.

In regard to this question the only data available appear to be observations made by Addis and Drury (1) and MacKay (10) on the effects of vigorous exercise. Addis and Drury found that in a normal subject the maximum blood urea clearance during an hour of continuous running was decreased to 70 per cent of the value observed during rest. MacKay found that during a 2-hour tennis match the standard clearance of a normal man was lowered to about half its usual resting value.

In previous studies by Möller, McIntosh, and Van Slyke (12, 13) administration of 15 grams of urea before the observation period was found to have no significant influence on the clearances of either normal or nephritic subjects resting in bed. Professor G. A. Harrison of St. Bartholomew's Hospital in London has personally communicated to the writers some observations of blood urea clearances during successive hourly periods in several subjects who were up and about. In some cases 15 grams of urea were given before the day's series of observations, while on other days the same subjects were observed without urea administration. It appeared from Professor Harrison's preliminary observations that urea administration to subjects who were up and about might exert a stabilizing effect on their clearance. Professor Harrison did not wish to pursue the question farther. We have accordingly included in the present studies observations in which urea was given and withheld on alternate experimental days.

METHODS

The *standard blood urea clearance*, $C_s = \frac{U}{B}\sqrt{V_c}$, (11, 12) was calculated in all instances in which the volume of urine, corrected for surface area (11) was below the augmentation limit of 2 cc. per minute. When the corrected volume was above this limit the *maximum blood urea clearance*, $\left(C_m = \frac{UV_c}{B} \right)$, was used. In the above formulae, U represents the urine urea concentration, B the blood urea concentration, and V_c the urine volume in cubic centimeters per minute, corrected for body size as described by McIntosh, Möller, and Van Slyke (11). On the charts and in the tables the clearance has been recorded in percentages of the normal mean standard clearance of 54 cc. per minute or of the normal mean maximum clearance of 75 cc. per minute.

The blood and urine urea concentrations were determined by the gasometric urease method (19).

All blood urea clearance tests were performed in the morning. Each patient received at 7 a.m. an ordinary breakfast, unrestricted except for coffee, which was uniformly omitted. Urine was voided at 8:30 a.m. and the specimen was discarded. The urines voided during the two 1-hour periods 8:30–9:30 and 9:30–10:30 were then collected separately. At about 9:30 blood was drawn for urea determination.

Whenever feasible, observations were carried out while the subjects were, on alternate days, in bed and walking about, or in bed and sitting up. Similar studies were made after urea ingestion, 15 grams of urea by mouth being given on the mornings of these tests.

One patient (No. 19), normal except for a slight albuminuria, exercised vigorously by walking up and down the stairs of the hospital on the day of the test. Two normal individuals exercised by playing squash-racquets during the 2 hours of the tests.

Clinical details other than the blood urea clearance will not be given, because they do not appear of significance to these conclusions. The subjects represented in Figure 1 were separable with regard to renal condition as follows: Nos. 1, 2, 3, 4, 5, 6, 7, and 10, were in the terminal stage of hemorrhagic Bright's disease, as defined in a previous paper (21). Nos. 9, 12, 16, 17 and 18 were in the active chronic stage of the same disease. Nos. 11, and 20 were degenerative, and 13 was sclerotic. Nos. 19, 21, 22, and 23 were normal young adults, except that 19 had an occasional slight albuminuria.

RESULTS

The urea clearance values are shown in Figure 1. In Tables 1 and 2 the data in detail are given for the observations on one normal subject and on one nephritic, Subject 6. The latter case was selected for presentation in detail because the subject, more than any other in our series,

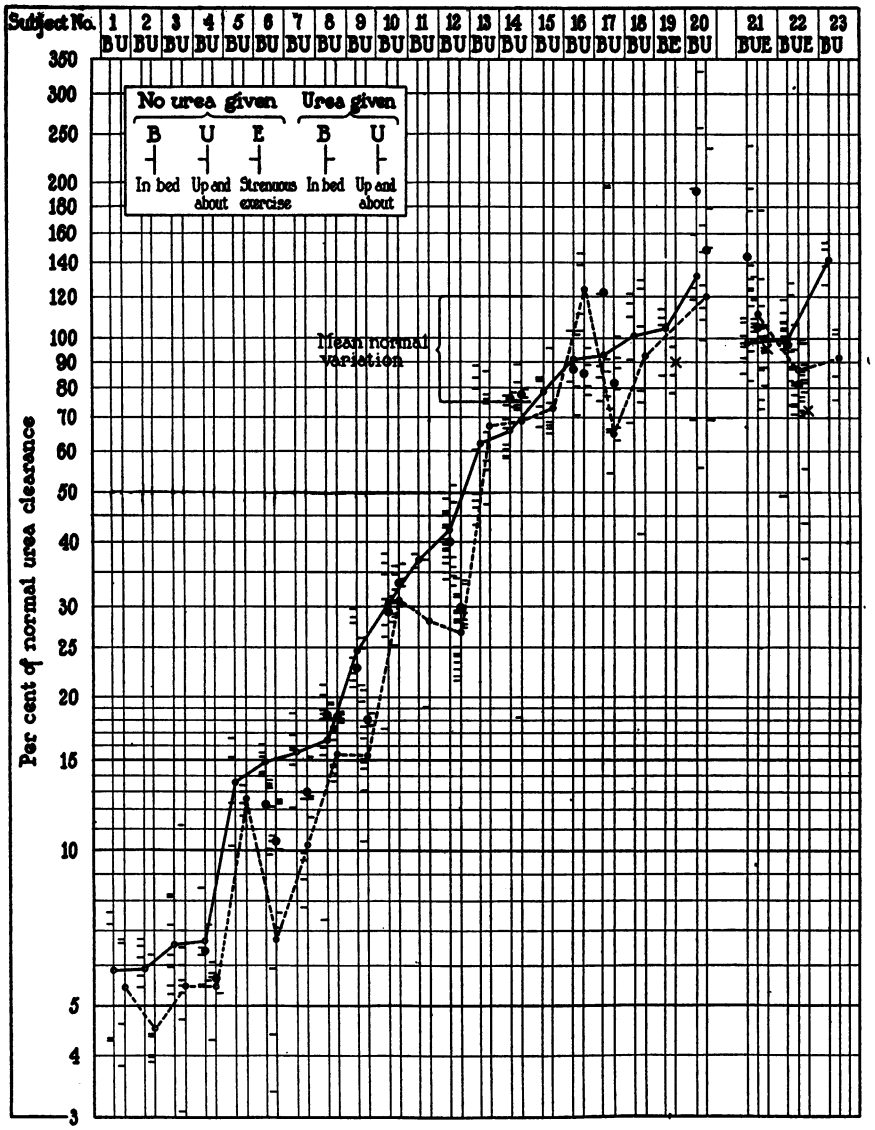

FIG. 1

Solid line connects average clearance values taken while subjects were in bed. Dashed line connects average clearance values taken while subjects were up and about. Hollow circle indicates average of all clearances on a subject, solid circle indicates average of clearances taken after administration of urea. × mark indicates average of clearances taken during hard exercise. Short horizontal lines indicate individual clearance values.

TABLE 1

Observations on A.H., terminal hemorrhagic nephritic, showing maximal effect on urea excretion caused by change from bed rest to moderate activity
Case No. 6: Hospital No. 7525

Conditions of observation		Date	V_{cor}	U	B	$\frac{U}{B}$	Blood urea clearance $\frac{U\sqrt{V}}{B}$ or $\frac{UV}{B}$
		1930–31	*cc. urine per minute*	*mgms. urea N per 100 cc. urine*	*mgms. urea N per 100 cc. blood*	*Concentration ratio*	*per cent of normal*
No urea given	In bed	November 25	0.560	436	42.6	10.2	14.2
		"	1.12	350	42.6	8.2	16.1
		November 28	0.608	431	44.2	9.8	14.1
		"	0.832	407	44.2	9.2	15.5
		December 9	0.592	404	41.0	9.9	14.1
		"	0.896	357	41.0	8.7	15.3
		Average	0.77	398	42.6	9.3	14.9
	Up and about	November 26	0.144	202	42.1	4.8	3.4
		"	0.464	405	42.1	9.6	12.2
		November 29	0.256	274	43.5	6.3	5.9
		"	0.400	387	43.5	8.9	10.4
		December 10	0.126	272	41.0	6.6	4.4
		"	0.320	417	41.0	10.2	10.7
		Average	0.29	326	42.2	7.7	7.8
15 grams urea by mouth before each test	In bed	December 16	1.47	332	55.1	6.0	13.5
		"	1.12	359	55.1	6.5	12.8
		December 18	1.50	444	72.8	6.1	13.8
		"	1.95	381	72.8	5.2	13.5
		January 13	0.895	471	82.6	5.7	10.0
		"	0.943	451	82.6	5.5	9.8
		Average	1.31	406	70.2	5.8	12.2
	Up and about	December 17	0.416	534	63.2	5.5	10.1
		"	0.704	507	63.2	6.7	12.5
		December 19	0.880	526	72.2	6.8	12.6
		"	0.768	556	72.2	6.8	12.5
		January 14	0.480	545	92.1	4.1	7.6
		"	0.416	546	92.1	3.8	7.1
		Average	0.611	536	75.8	7.2	10.4

shows the depressing effect on urea excretion as the result of changing from bed rest to walking about.

The effect of mild physical activity on the blood urea clearance

In normal subjects, and in nephritic patients with relatively slight functional impairment (over 50 per cent of normal clearance) (Subjects 13 to

23), being up and about caused no significant change in the urea clearance from the values observed when the subjects were in bed before and during the excretory periods. In some cases the average clearance obtained when the subjects were up and about was lower, in others higher, than when in bed. As shown by the data of Table 2, given in full for a normal

TABLE 2

Observations on A.A., Normal subject, No. 22

Conditions of observation		Date	V_{cor}	U	B	$\frac{U}{B}$	Blood urea clearance $\frac{U\sqrt{V}}{B}$ or $\frac{UV}{B}$
		1931	*cc. urine per minute*	*mgms. urea N per 100 cc. urine*	*mgms. urea N per 100 cc. blood*	*Concentration ratio*	*per cent of normal*
No urea given	In bed	January 6	2.61	533	15.6		119
		"	4.09	306	15.6		107
		January 13	1.23	871	18.3	48	98
		"	2.30	289	18.3		(48)*
		January 23	1.22	879	16.7	52	107
		"	1.53	722	16.7	43	99
		February 10	1.52	572	13.7	42	95
		"	2.72	425	13.7		112
		February 12	1.58	747	16.7	45	104
		"	1.85	687	16.7	41	104
		Average	2.07	603	16.2	45	105
	Up and about	January 7	0.979	752	15.8	48	87
		"	1.03	681	15.8	43	81
		January 14	0.710	1148	18.9	61	95
		"	0.896	1148	18.9	61	106
		January 22	1.23	837	22.3	38	77
		"	1.20	775	22.3	35	71
		January 30	0.957	853	15.7	54	106
		"	0.833	761	15.7	49	100
		February 3	0.458	964	16.5	59	74
		"	0.537	896	16.5	55	74
		Average	0.880	882	17.8	50	84
	Vigorous exercise	January 8	0.576	950	16.3	58	82
		"	0.945	878	16.3	54	97
		January 15	0.803	920	19.6	47	78
		"	0.831	957	19.6	49	83
		January 31	0.437	1101	15.5	71	87
		"	0.453	1098	15.5	71	88
		March 28	0.265	1044	18.1	58	56
		"	0.365	1155	18.1	64	71
		March 29	0.349	557	16.4	34	37
		"	0.409	603	16.4	37	44
		Average	0.544	926	17.2	54	72

TABLE 2 (*continued*)

Conditions of observation		Date	V_{cor}	U	B	$\frac{U}{B}$	Blood urea clearance $\frac{U\sqrt{V}}{B}$ or $\frac{UV}{B}$
		1931	*cc. urine per minute*	*mgms. urea N per 100 cc. urine*	*mgms. urea N per 100 cc. blood*	*Concentration ratio*	*per cent of normal*
15 grams urea by mouth before each test	In bed	January 20	1.76	956	26.9	36	87
		"	2.14	821	26.9		87
		February 5	2.63	946	27.2		122
		"	2.95	885	27.2		128
		February 13	1.41	1165	34.7	40	74
		"	1.55	1236	34.7	44	82
		February 14	1.39	1164	30.3	54	101
		"	1.85	1153	30.3	52	96
		Average	2.04	1041	29.8	45	97
	Up and about	January 9	1.21	1259	30.4	41	84
		"	0.871	1359	30.4	44	77
		January 10	1.50	1444	33.7	43	97
		"	1.23	1418	33.7	42	87
		January 21	1.78	904	29.7	30	75
		"	1.19	1036	29.7	35	71
		February 4	2.03	944	28.0		91
		"	1.87	798	28.0	28	72
		Average	1.46	1145	30.5	37	82

* Omitted from average.

subject, the most marked renal effect of the change in posture and activity is in the urine volume, much less being excreted while the subject is up and about than when in bed. This phenomenon was uniformly noted both in the subjects with normal renal function and in those with diminished function. The urea concentration in the smaller volume of urine was increased sufficiently, however, to prevent the clearance figures from varying, except in one or two isolated observations, markedly outside the range of clearances observed during bed rest in this group of subjects (Nos. 13 to 23).

In nephritic subjects with less than 50 per cent of normal clearance (Subjects 1 to 12 inclusive) being up and about uniformly depressed the average clearance below that observed during bed rest, except in one patient (No. 10) where there was no change. In three-fourths of the cases the effect was relatively slight and not sufficient to influence the diagnostic import of the clearances, but in cases 6, 9, and 12 being up and about lowered the mean clearance to 60 per cent or less of that observed during bed rest. It is evident therefore that in nephritics with marked renal impairment clearance determinations should continue to be made under standard conditions of rest.

During approximately half of another series of clearance tests each subject sat in a chair. The other clearances of the series were taken with the subjects in bed. The results are shown in Figure 2. They indicate no demonstrable effect of this change of posture on the clearance.

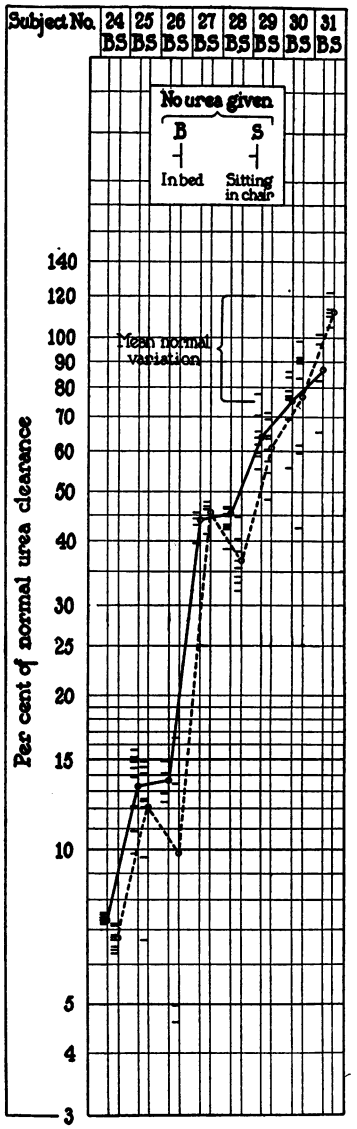

FIG. 2

Solid line connects average clearance values taken while subjects were in bed. Dashed line connects average clearance values taken while subjects were sitting. Short horizontal lines indicate individual clearance values.

The effect of severe exertion on urea excretion in subjects with normal renal function

Severe exertion was tested in three subjects, prolonged stair climbing in Subject 19, and squash-racquets playing in Nos. 21 and 22. The results with Subject 22 are given in detail in Table 2. The severe exercise diminished the average clearance somewhat more than did the mild exercise of merely being up and walking about. The effect of the severe exercise on urea excretion was not great, however, except in two clearances in Subject 22, which were performed after he had exercised nearly to exhaustion, and were found reduced to 35 and 44 per cent of normal. Nearly all of the clearances taken during severe exercise lay within the range normally encountered in subjects resting in bed, the slightly depressing effect of the exercise being apparent only statistically. Presumably severe exercise would depress more markedly the renal function in advanced nephritis.

The effect of urea administration on the renal reaction to physical activity

The data in Figure 1 reveal no effect of urea administration on the clearances, either when the subjects were resting in bed or were up and about. In this respect the results confirm those of previous studies by Möller, McIntosh, and Van Slyke (12, 13).

The effect of exercise on urine volume

As illustrated by the data in Tables 1 and 2, the urine volume in both normal and nephritic subjects was observed to be markedly lower while a subject was up and about than when he was in bed. The relative oliguria was probably due to the change to upright posture, which is known to diminish urine volume (6, 9, 15, 17, 22), rather than to the mild muscular exertion.

In the very severe exercise taken by Subjects 19, 21, and 22, diminution of urine volume is still more marked. It is probable that some dehydration of the blood by sweating occurred, and perhaps also some diversion of blood flow from the kidneys to the heavily working muscles.

Variations of urine concentration

In a normal subject, blood urea being constant, the urea concentration in the urine is greater when the volume of urine excreted per minute is less. When, with constant blood urea content, the urine volume is less than the "augmentation limit" of about 2 cc. per minute, the urea concentration in the urine ordinarily varies inversely as the square root of the volume: if the volume is reduced to 1/4 the concentration is multiplied by 2 (3, 12). Such a relationship is approximated by the data in Table 3 from a normal subject, and is not markedly disturbed by exercise, even when severe. (The three sets of data taken with "no urea given" can be

compared together, while the two sets taken after urea administration form another group comparable among themselves. because of approximate constancy of the blood urea content.) Möller, McIntosh, and Van Slyke (12) found a similar behavior in nephritics of all grades of severity when the subjects were tested during rest in bed. The concentrations of urea in the urine compared with the concentrations in the blood were much smaller in advanced nephritis than in normal subjects, but the variation with urine volume in a given subject was of the same nature.

In nephritic subjects Nos. 6, 9, 12, however, who show marked fall in blood urea clearance caused by leaving bed and walking about, this inverse relationship between urine volume and concentration fails to hold. In No. 6 (Table 1), who shows, of the subjects reported in this paper, the most depression of clearance caused by leaving bed and walking about, there is in the first two sets of data, taken without urea administration, no inverse relationship at all. The urine volume, in the observations made when this subject was up and about averages only 40 per cent as great as the volume when he was in bed, but the urea concentration in the smaller volume, when the patient was up, averages actually somewhat less than in the larger volumes excreted in bed. It is this failure, partial or complete, to increase normally the urea concentration in the smaller volumes of urine passed while up and about, that causes the clearance to be markedly depressed by the latter condition in three of the nineteen nephritics studied. The depression, although evident only in nephritic cases with less than 50 per cent of normal clearance, was not at all directly related to the severity of renal impairment. In some of the most advanced cases being up and about depressed the clearance but little.

SUMMARY

In normal subjects, or in nephritics with more than 50 per cent of normal renal function measured by the blood urea clearance, the clearance has not been found to be essentially different, whether the subjects were kept in bed during the 2-hour observation periods or were walking about. Urine volume was uniformly less while the subjects were up and about, but the effect in depressing urea excretion was about that allowed for in the formulae for calculating the standard and maximum clearances, so that the values of the latter were not markedly affected.

In three of the twelve nephritics observed with less than 50 per cent of normal renal function, measured by the blood urea clearance observed with the subjects in bed, rising and walking about depressed the clearance markedly, the mean values observed being 44, 60, and 67 per cent respectively of those observed in the same patients during bed rest.

Severe exercise taken by three subjects with normal renal function depressed the clearance somewhat, as found by Addis and Drury (1) and MacKay (10), but in only three out of twenty-two clearances determined

during heavy exertion were the values definitely abnormal, i.e., below 70 per cent of the mean normal level.

Administration of 15 grams of urea before the observation periods did not significantly affect the results.

It appears that in normal subjects and in nephritics with more than 50 per cent of average normal clearance, the clearance values can be determined without loss of accuracy while the subjects are up and about. In nephritic patients with less than 50 per cent of normal clearance values, however, it is essential to keep the subject at rest in a recumbent position during the 2-hour excretion period, if the results are to be compared with those heretofore obtained by the clearance test.

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