DETERMINATION OF THE QUANTITY OF SECRETING TISSUE IN THE LIVING KIDNEY.

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In the past the function of the diseased kidney was studied in the hope that by this means some measure of the amount of the kidney tissue which still remained active might be obtained. This was the point of main clinical interest and this aim was always kept in view, though the technical means for its accomplishment had not been perfected.

But in recent years the issue has been confused by the work of Schlayer (1). His failure to find a constant relation between the amount of renal tissue and the rate of excretion of various urinary constituents and foreign substances led him to the conclusion that there was no quantitative relation between anatomy and function and that the size of the kidney could not be determined from its mode of action. He accordingly turned from the quantitative aspects of the subject and attempted to show that by functional studies it was possible to distinguish, if not the amount, at least the kind of renal damage produced by various forms of disease. But even if his claims had been confirmed, they could have had little practical significance, since the microscopic examination of urinary sediments furnishes a simpler method by which such qualitative judgments may be made with a considerable degree of accuracy.

At this time Ambard was formulating his laws of urea excretion (2) as a mathematical expression which he believed included all the essential factors concerned in the activity of the kidney. But the action of the living kidney cannot be circumscribed within the bounds of a mathematical formula. There are important factors which cannot be measured and the formula is defective in the erro-

neous manipulation to which the values are subjected, as well as in its inclusion of one factor, the urinary concentration, which has no appreciable effect on function (3). In spite of these deficiencies Ambard's work represented a considerable advance, in that for the first time the rate of excretion, which previously had been employed as in itself the measure of function, was qualified by the accompanying statement of the concentration of the excretory product in the blood during the period over which the rate was measured. It is because of this fact that the formula has apparently been of some use in clinical work.

Up to within the last year or two Ambard's work attracted little notice outside of France, and attention was turned to the determination of the degree of accumulation of excretory products in the blood as a means of determining the quantitative deficiency of the diseased kidney. This work has been continued up to the present, although in the meantime the measurement of the rate of excretion of phenolsulfonephthalein has provided an easily applicable method whereby gross anatomical defects may be detected. This test owes its success to the fact that in reality it gives more than either a rate or a blood concentration alone. Though only the rate is measured, yet the diffusion of the dye into the blood stream is usually so uniform that the blood concentration tends to become a constant, and is eliminated as a factor influencing the rate of excretion. In effect it is the ratio between the amount of phenolsulfonephthalein in the urine and in the blood which is obtained.

But the phenolsulfonephthalein test only partially attains to measurement of the amount of the secreting tissue in the kidney. No such claim was, indeed, advanced for it. On the contrary, it was demonstrated that even the sudden removal of half the renal tissue of the body was not attended by any great change in the rate of excretion (4). It is only where disease has reduced the amount of effective tissue to a much greater degree than this, that a noteworthy alteration in output is found.

The history of the development of methods of measuring the function of the kidney, which we have thus briefly reviewed, was a guide in the planning of the experiments reported in this paper. They were carried out some years ago, before most of the observations (5) which

seem to have cleared the ground for a further attempt at the solution of the problem had been made. But from the experiments of others it already seemed clear that, except under special conditions, the rate of excretion of urinary constituents was too greatly influenced by non-anatomical factors to be in itself of general value, and we had grounds for the belief that, except in the most extreme instance of disorganization of the structure of the kidney, the concentration of excretory products in the blood would not alone be a measure of the quantity of kidney tissue (6). But we had found that in the case of urea there was a loose relation between the rate and the concentration in the blood, in the sense that the higher the level of blood urea concentration the greater in general was the rate of urea excretion (7). In further empirical observations on the effect on kidney function of removal of part of the kidney tissue, we had noted that the anatomical defect had a manifest influence on function only when the remaining renal structure was subjected to a demand for increased activity in urea excretion induced by the injection of preformed urea (8). Therefore an attempt was made to approximate more closely the conditions met with in disease by a comparison of the degree of anatomical defect resulting from the action of uranium on the kidney and the degree to which the function of urea excretion was disturbed, under conditions involving strain on the damaged kidney.

A disturbance in urea excretion might reveal itself in one or in all of a number of ways. The rate might be diminished, or it might remain the same but be accompanied by an increase in water excretion with a resulting decrease in the urea concentration of the urine. Again the rate and the concentration of urea in the urine might be maintained, but the blood urea concentration might increase. Finally, there might be alterations in the ratio between the urinary and blood urea concentrations or in the ratio between the rate and the blood concentration. It was largely in order to obtain evidence as to which of these manifestations of functional derangement showed the closest correlation with the anatomical findings that the work was undertaken.

Since all these aspects of the function of urea excretion are expressed numerically, there was no difficulty in arranging the results in order of magnitude, but this, of course, was not possible in the anatomical

classification. There are considerable difficulties in the way of attempts to separate kidney lesions according to the amount of damage. These arise partly from want of knowledge as to which are the more essential cellular structures as regards function, and partly from the grossness of the methods employed in their differentiation. It must be admitted that chemical or physical alterations might occur in some important part of the urea-secreting cell which would not be revealed by present methods, and, further, that alterations in less essential components might give rise to an exaggerated idea of anatomical disorganization. The conditions of the experiment were selected with a view to minimize these difficulties as much as possible. Uranium was chosen partly because it produces easily demonstrable lesions varying, according to the amount administered and the susceptibility of the animal, from necrosis to fatty and granular degeneration, but mainly because, except in large doses, it appreciably injures only the proximal convoluted tubule. This is the only part of the kidney tissue in which urea can be demonstrated to exist in high concentration (9). The presence of relatively large amounts of urea in these cells, and the finding that the quantity increases with increase in urea excretion (10) seem strong evidence that they are concerned with the concentration of urea from the blood. The hypothesis of reabsorption from the glomerular secretion, though tenable for urinary constituents such as chlorides, can scarcely be entertained for urea when the consequences of such a mechanism are borne in mind. We had reason, then, to believe that the part of the kidney in which the lesions occurred was the part essential in the function of urea excretion, and that the strict localization of the lesion in this variety of kidney cell facilitated judgment as to the quantity of damage inflicted. A wide variation in the degree and extent of the lesion in different animals was insured by the administration of amounts of uranium varying from those which produced scarcely perceptible damage up to those which induced an almost total necrosis of the terminal part of the proximal convoluted tubules. In each case the same time was allowed to elapse between the injection and the anatomical fixation. This period was of 77 hours' duration, a time which suffices for the full development of the degenerative lesions produced by uranium.

Under these favorable conditions it was possible to separate the cases into three groups, of severe, moderate, and slight lesions.

Anatomical Classification.

As soon as the experiment described below was completed, the animal was killed and sections from both kidneys were fixed in Orth's fluid. Paraffin sections cut from the kidney in such a way as to show the junction of the cortex and medulla were stained with hematoxylin and eosin and by Van Gieson's method.

The preliminary placing of the material in fixing fluid was done by two of us, and then brought to the third for further treatment. In this way the last had no idea of the dose of uranium given, or of the result of the functional test. After a comparison of the sections three groups were made, corresponding to slight, moderate, and severe lesions.

The lesions observed in the kidneys were typical of acute uranium nephritis. In all, the injury was localized in the terminal division of the proximal convoluted tubule. In the severe cases it consisted of an almost total necrosis of the epithelial cells, while in those which were slightly affected granular and fatty changes only were present.

The detailed description of the sections of the twenty-four animals is not given. A typical example of each is described. Class I included the kidneys in which no definite nuclear changes (necrosis) could be found, but only protoplasmic changes such as cloudy swelling and fatty degeneration; Class II showed slight but definite evidence of actual necrosis with degenerative changes in the nucleus; while Class III showed almost complete necrosis of the terminal division of the proximal convoluted tubule.

Rabbits 1 to 6 were in Class I (slight lesions).

Rabbits 7 to 13 were in Class II (moderate lesions).

Rabbits 14 to 24 were in Class III (severe lesions).

The sequence in which the rabbits are arranged within these groups is not intended to indicate any grade of slight, moderate, or severe lesion, for it was not considered wise to attempt further subdivisions.

Typical Examples of Classes I, II, and III.

Class I. Rabbit 1.—The glomeruli and upper divisions of the convoluted tubules are normal. The lower terminal divisions of the convoluted tubules, however, are slightly involved, though the majority are intact with well stained nuclei. The protoplasm of the cells is distinctly swollen and granular, so that it stains more deeply with the eosin than that of the normal upper divisions. A few tubules show beginning nuclear changes, such as karyorrhexis and pyknosis. A moderate number of hyaline casts lie in the collecting tubules.

Class II. Rabbit 7.—The glomeruli and upper parts of the proximal convoluted tubules are normal. The terminal divisions of the latter show a desquamation of the epithelial cells and a few are necrotic. Many of the tubules in this region, however, are almost normal, except for a granular degeneration of the protoplasm. There are a large number of hyaline casts in the normal ascending limbs of Henle's loop and the collecting tubules.

Class III. Rabbit 16.—The glomeruli are normal. The veins of the cortex show a moderate dilatation. The proximal convoluted tubule in the vicinity of the glomerulus is apparently normal, as the nuclei are intact and there are no degenerative changes in the protoplasm. In the lower layer of the cortex and the outer stripe of the outer zone of the medulla there is extensive necrosis of the proximal convoluted tubule. The epithelium is entirely destroyed and the lumen of the tubule filled with granular detritus. The ascending limb of the loop of Henle and the collecting tubules are normal, except that both contain many hyaline and granular casts.

Functional Classification.

The conditions under which the functional results were obtained were as follows: No food or water was given for 17 hours previous to the commencement of each experiment. Blood was then drawn from an ear vein, the bladder was emptied by catheter, and immediately afterwards preformed urea was given by stomach tube. Thereafter the rabbit was catheterized and bled each hour for 3 hours and again

at the end of the 5th. The urine specimens were acidified, diluted to a given volume, and the urea content was determined by Marshall's urease method with the modifications described elsewhere (11). The urease method was also used for the measurement of the blood urea

TABLE I.

Rabbit No.	Body weight.	Dose of uranium.	Amount of urea administered.	Concentration of urea administered.
	gm.	*mg.*	*gm.*	*gm. per cent*
4	2,200	0.25	5	20
5	1,720	0.25	5	20
6	1,550	0.25	5	20
12	2,580	0.25	5	20
1	2,525	0.5	5	20
8	2,475	0.5	5	20
2	1,700	0.5	1.25	1
3	2,510	0.5	1.25	1
10	2,010	0.5	5	20
17	1,880	0.5	5	20
14	1,800	1.0	5	20
7	1,940	1.0	5	20
9	3,050	1.0	1.25	1
11	2,200	1.0	1.25	5
13	2,350	1.0	1.25	5
19	2,300	2.5	2.5	10
20	2,175	2.5	2.5	10
22	2,600	2.5	2.5	10
23	2,700	2.5	5	20
24	3,275	2.5	5	20
15	2,750	5.0	5	20
16	2,240	5.0	5	20
18	2,040	5.0	5	20
21	2,300	5.0	5	20

concentration, using a technique similar to that described by Van Slyke and Cullen (11).

After an interval of at least 4 days a subcutaneous injection of uranium acetate was given. The doses of uranium, the weight of the animals, and the amount of urea administered are detailed in Table I.

Exactly 72 hours after the uranium had been administered, and again following a period of 17 hours during which no food or water was given, the experiment was repeated, care being taken to keep the conditions the same as in the previous test.

At the end of the second experiment the rabbit was killed and the kidneys were removed, cut in thin slices, and placed in fixing solution.

Thus both before and after the administration of the uranium four collections of urine and five samples of blood were obtained. Since the length of time over which the urine collections were made, was known, each experiment gave four consecutive rates of water and urea excretion and from them the concentrations of urea in the urine could be calculated. From the curve of the blood urea concentrations observed at the beginning and end of each collection of urine, the average blood urea concentration during each of the four periods could be determined. By dividing the urea concentration in the urine and the rate of urea excretion by the average blood concentration, the number of times by which concentration and amount of urea in the urine exceeded the concentration and the amount of urea in 100 cc. of blood was also found for each period.

As we have stated above, we believe that the relation between function and structure can only be determined under strain. In these experiments the strain was induced through the increase in blood urea concentration following the administration of urea. This increase was not fully developed until the second period of the experiment. For this reason, and also because there is considerably more error in the calculation of the average blood concentration for the first, than for the subsequent periods, we have discarded the data for the first period, and have taken the sums or the averages of the last three periods in order to obtain a single figure to represent function before and after uranium. These could then be compared and the effect of the uranium on function shown by expressing the result obtained after as a percentage of the result obtained before uranium. The exact details of these procedures can be best illustrated by giving one of the protocols in full.

Protocol of Rabbit 12.

Apr. 15, 1915, 3 p.m. The rabbit was brought to the laboratory and kept in a small cage without food or water.

Apr. 16, 8.30 a.m. 5 cc. of blood were taken from an ear vein. 8.45 a.m. The bladder was emptied by catheter. Immediately afterward 5 gm. of urea dissolved in 25 cc. of water were given through a stomach tube. The times at which urine and blood were collected, the amounts of urea found in them, and the ratios between the urine and blood urea are noted below.

Before Uranium.

Time of catheterization.	Rate of water excretion per hr.	Rate of urea excretion per hr.	Concentration of urea in urine per 100 cc.	Time of bleeding.	Concentration of urea in blood per 100 cc.	Calculated concentration of urea in blood per 100 cc. at middle of period.	Ratio: $\frac{\text{Urea in 1 hr.'s urine}}{\text{Urea in 100 cc. of blood}}$	Ratio: $\frac{\text{Concentration of urea in urine}}{\text{Concentration of urea in blood}}$
a.m.	*cc.*	*mg.*	*gm.*	*a.m.*	*mg.*	*mg.*		
Period 1.								
8.45– 9.45	12.0	285	2.37	8.30	42	96	$\frac{285}{96} = 2.97$	$\frac{2370}{96} = 24.7$
Period 2.								
9.45–10.45	12.8	417	3.25	10.15	204	204	$\frac{417}{204} = 2.04$	$\frac{3250}{204} = 15.9$
Period 3.								
10.45–11.45	17.5	537	3.07	11.40	221	216	$\frac{537}{216} = 2.49$	$\frac{3070}{216} = 14.2$
a.m.—p.m.				*p.m.*				
Period 4.								
11.45– 1.45	20.2	447	2.21	1.40	240	230	$\frac{447}{230} = 1.95$	$\frac{2210}{230} = 9.6$

After completion of the control experiment the rabbit was returned to the animal room.

Apr. 21, 9 a.m. 0.25 mg. of uranium acetate were injected subcutaneously.

Apr. 23, 3 p.m. The rabbit was brought to the laboratory and kept in a small cage without food or water.

Apr. 24, 8.30 a.m. 5 cc. of blood were taken from an ear vein. 8.50 a.m. The bladder was emptied by catheter. Immediately afterward 5 gm. of urea dissolved in 25 cc. of water were given through a stomach tube. The times at which urine and blood were collected, the amounts of urea found in them, and the ratios between the urine and blood urea are noted below.

After 0.25 Mg. of Uranium Acetate.

Time of catheterization.	Rate of water excretion per hr.	Rate of urea excretion per hr.	Concentration of urea in urine per 100 cc.	Time of bleeding.	Concentration of urea in blood per 100 cc.	Calculated concentration of urea in blood per 100 cc. at middle of period.	Ratio: $\frac{\text{Urea in 1 hr.'s urine}}{\text{Urea in 100 cc. of blood}}$	Ratio: $\frac{\text{Concentration of urea in urine}}{\text{Concentration of urea in blood}}$
a.m.	*cc.*	*mg.*	*gm.*	*a.m.*	*mg.*	*mg.*		
Period 1.								
8.50– 9.50	13.8	82	0.59	8.30	49	95	$\frac{82}{95} = 0.86$	$\frac{590}{95} = 6.2$
Period 2.								
9.50–10.50	14.5	138	0.95	10.20	186	186	$\frac{138}{186} = 0.74$	$\frac{950}{186} = 5.1$
Period 3.								
10.50–11.50	16.7	276	1.65	11.45	222	215	$\frac{276}{215} = 1.28$	$\frac{1650}{215} = 7.7$
a.m.—p.m.				*p.m.*				
Period 4.								
11.50– 1.50	15.9	291	1.83	1.45	222	222	$\frac{291}{222} = 1.31$	$\frac{1830}{222} = 8.3$

Immediately after completion of the experiment the rabbit was killed and the kidneys were removed, sliced, and placed in fixing solution.

The results obtained during the last three periods of each experiment were combined in order to obtain single figures for each aspect of function before and after uranium. It will be noted that in the tabulations above the rates of water and of urea excretion are given as volumes and mg. per hour, but Period 4 was of 2 hrs.' duration, and we have taken the sum of the total excretion of Periods 2, 3, and 4 as representing the rate of water and urea excretion. The blood urea concentration taken was, of course, the one which was obtained before the administration of urea. The concentration of urea in the urine and both ratios are represented by the averages for Periods 2, 3, and 4.

The figures are given below. From them was calculated the percentage of change induced by the uranium.

	Before uranium.	After uranium.	Percentage of function after uranium to function before uranium.
			per cent
Rate of water excretion (sum of last three periods)	71 cc.	63 cc.	89
Rate of urea excretion (sum of last three periods)	1.85 gm.	1.00 gm.	54
Concentration of urea in urine (average of last three periods)	2.84 " per cent.	1.48 " per cent.	52
Concentration of urea in blood (before giving urea)	0.042 " " "	0.049 " " "	117
Ratio: $\frac{\text{Urea in 1 hr.'s urine}}{\text{Urea in 100 cc. of blood}}$ (average of last three periods)	2.16	1.11	50
" $\frac{\text{Concentration of urea in urine}}{\text{Concentration of urea in blood}}$ (average of last three periods)	13.2	7.0	53

The results thus obtained on each animal were arranged in order of their percentage relationships, and arbitrary divisions were made to correspond with the anatomical divisions into slight, moderate, and severe lesions. The cases may be classified as follows: those in which the function after uranium was 66 per cent or more of the measurement made in the control experiment, as slight functional derangement; those in which the after result was between 33 and 66 per cent of the original, as moderate defects, and those in which the function was decreased until it was less than 33 per cent of that found in the control experiment, as instances of severe impairment of function. With the rate of water excretion and the blood urea concentration there was in some cases considerably more than 100 per

TABLE II.

Measurement by which the functional classification was made.	No. of disagreements with anatomical classification.	Proportional minimal correction required for agreement with anatomical classification.
Ratio: $\frac{\text{Urea in 1 hr.'s urine}}{\text{Urea in 100 cc. of blood}}$	2	22
" $\frac{\text{Concentration of urea in urine}}{\text{Concentration of urea in blood}}$	6	77
Rate of urea excretion	6	104
Concentration of urea in urine	7	135
Rate of water excretion	11	150
Concentration of urea in blood	13	258

TABLE III.

Ratio: $\frac{\textit{Urea in 1 Hr.'s Urine}}{\textit{Urea in 100 Cc. of Blood}}$.

Rabbit No.	Ratio before uranium.	Ratio after uranium.	Percentage of ratio after uranium to ratio before uranium.	Functional class.	Anatomical class.	Minimum correction.
			per cent			
3	1.54	1.55	101	I	I	
4	2.03	1.75	86	I	I	
5	2.42	1.93	79	I	I	
1	1.74	1.33	77	I	I	
6	1.99	1.36	69	I	I	
2	1.63	1.12	69	I	I	
9	1.89	1.23	65	II	II	
11	1.74	0.90	52	II	II	
12	2.16	1.11	50	II	II	
7	2.27	1.14	50	II	II	
8	1.66	0.62	38	II	II	
13	1.64	0.50	**30**	**III**	II	3
17	1.09	0.19	17	III	III	
10	1.29	0.17	**14**	**III**	II	19
22	1.79	0.20	11	III	III	
14	2.45	0.23	10	III	III	
24	1.63	0.09	5	III	III	
15	1.82	0.08	4	III	III	
23	2.04	0.07	3	III	III	
19	1.51	0.01	1	III	III	
20	1.45	0.00	0	III	III	
21	1.93	0.00	0	III	III	
18	1.86	0.00	0	III	III	
16	0.83	0.00	0	III	III	
Total						22

cent of variation between the before and after results, but proportionally the same grouping was made by dividing the total range into thirds.

It was found that the classification made according to the ratio between the urea content of the urine and of the blood disagreed with the anatomical classification in two instances, those made by the rate

TABLE IV.

$$Ratio: \frac{Concentration\ of\ Urea\ in\ Urine}{Concentration\ of\ Urea\ in\ Blood}.$$

Rabbit No.	Ratio before uranium.	Ratio after uranium.	Percentage of ratio after uranium to ratio before uranium.	Functional class.	Anatomical class.	Minimum correction.
			per cent			
4	11.5	11.4	99	I	I	
5	11.2	10.3	92	I	I	
2	4.8	3.4	71	I	I	
3	11.6	6.9	58	II	I	8
6	12.0	6.9	57	II	I	9
12	13.2	7.0	53	II	II	
9	15.9	7.0	44	II	II	
11	19.3	7.8	40	II	II	
1	17.6	6.6	38	II	I	28
7	15.9	5.3	34	II	II	
8	13.7	4.4	32	III	II	1
17	9.5	3.1	32	III	III	
13	20.4	5.6	27	III	II	6
23	11.3	2.4	21	III	III	
24	17.1	2.9	17	III	III	
22	21.4	3.4	16	III	III	
14	16.2	2.1	13	III	III	
15	16.6	1.8	11	III	III	
10	27.2	2.3	8	III	II	25
19	14.4	0.6	4	III	III	
20	15.2	0.0	0	III	III	
21	15.6	0.0	0	III	III	
18	17.7	0.0	0	III	III	
16	12.4	0.0	0	III	III	
Total						77

of urea excretion and by the ratio between the concentration of urea in the urine and in the blood were both different from the anatomical in six cases, and that made by the concentration of urea in the urine in seven instances. No certain correlation between function and structure was apparent when the measure of function was either the rate of water excretion or the concentration of urea in the blood, for in both there were almost as many disagreements as agreements.

TABLE V.

Rate of Urea Excretion.

Rabbit No.	Rate before uranium.	Rate after uranium.	Percentage of rate after uranium to rate before uranium.	Functional class.	Anatomical class.	Minimum correction.
	gm.	*gm.*	*per cent*			
11	0.63	0.67	**106**	I	II	40
1	1.30	1.26	97	I	I	
3	0.86	0.78	91	I	I	
4	1.67	1.52	91	I	I	
7	2.10	1.76	**84**	I	II	18
5	2.48	1.89	76	I	I	
2	1.01	0.68	67	I	I	
9	1.12	0.66	59	II	II	
12	1.85	1.00	54	II	II	
6	1.65	0.84	**51**	II	I	15
13	0.70	0.36	51	II	II	
8	1.61	0.79	49	II	II	
17	0.22	0.10	**45**	II	III	12
14	1.75	0.59	**34**	II	III	1
22	1.49	0.26	17	III	III	
10	0.68	0.10	**15**	III	II	18
24	1.78	0.14	8	III	III	
15	1.95	0.15	7	III	III	
23	1.19	0.05	5	III	III	
19	1.20	0.01	1	III	III	
20	1.26	0.00	0	III	III	
21	2.21	0.00	0	III	III	
18	2.17	0.00	0	III	III	
16	1.13	0.00	0	I I	III	
Total						104

A more accurate measurement of the relative efficiency of these six aspects of function in measuring the degree of anatomical damage was obtained by summing the minimum numerical values of the disagreements. If, for instance, the function was 64 per cent in the case of an animal included in the group of slight anatomical lesions, this would place it in the group of moderate functional defect and would constitute a disagreement. But if it had been 66 per cent it would

TABLE VI.

Concentration of Urea in Urine.

Rabbit No.	Concentration per 100 cc. before uranium.	Concentration per 100 cc. after uranium.	Percentage of concentration after uranium to concentration before uranium.	Functional class.	Anatomical class.	Minimum correction.
	gm.	*gm.*	*per cent*			
4	2.15	2.40	111	I	I	
5	3.02	2.59	86	I	I	
11	1.75	1.44	82	I	II	16
17	0.94	0.76	81	I	III	48
2	0.76	0.58	76	I	I	
6	3.37	2.20	65	II	I	1
7	3.73	2.03	54	II	II	
12	2.84	1.48	52	II	II	
3	1.68	0.83	49	II	I	17
1	4.15	2.05	49	II	I	17
14	2.86	1.30	45	II	III	12
13	2.14	0.94	44	II	II	
8	3.29	1.26	38	II	II	
9	2.25	0.83	37	II	II	
24	4.15	1.11	27	III	III	
23	3.33	0.87	26	III	III	
22	4.51	1.03	23	III	III	
15	4.10	0.73	18	III	III	
10	3.45	0.30	9	III	II	24
19	2.76	0.22	8	III	III	
20	3.93	0.00	0	III	III	
21	3.98	0.00	0	III	III	
18	4.68	0.00	0	III	III	
16	3.80	0.00	0	III	III	
Total						135

have been classed as a slight defect, so the minimum value of such a disagreement would be only 2. On the other hand, if the function had been 44 per cent the least correction required to make it agree with the anatomical arrangement would have been 22. The relative efficiency of the functional measurements thus determined is given in Table II and the details are given in Tables III to VIII.

TABLE VII.

Rate of Water Excretion.

Rabbit No.	Volume before uranium.	Volume after uranium.	Percentage of volume after uranium to volume before uranium.	Functional class.	Anatomical class.	Minimum correction.
	cc.	*cc.*	*per cent*			
3	57	99	174	I	I	
1	32	56	172	I	I	
10	19	31	165	I	II	49
7	56	84	151	I	II	35
11	37	46	125	I	II	9
8	47	57	121	I	II	5
9	60	72	119	I	II	3
13	32	36	112	II	II	
12	71	63	89	II	II	
4	71	62	87	II	I	29
2	93	81	87	II	I	29
5	85	72	85	II	I	31
6	47	37	79	II	I	37
22	32	24	76	II	III	18
14	59	44	74	II	III	16
17	26	13	50	III	III	
15	44	19	42	III	III	
24	40	13	33	III	III	
23	36	6	17	III	III	
19	47	2	4	III	III	
20	32	0	0	III	III	
21	56	0	0	III	III	
18	44	0	0	III	III	
16	28	0	0	III	III	

Total..... 261 in a range of 174
150 " " " " 100

The ratio between the urea content of the urine and of the blood under the strain induced by the administration of large amounts of urea is clearly the most accurate method of determining the amount of active urea-secreting tissue left after the administration of uranium. The theoretical considerations concerned in the use of this ratio have been recently considered in detail (12), and still more recently evidence

TABLE VIII.

Concentration of Urea in Blood.

Rabbit No.	Concentration per 100 cc. before uranium.	Concentration per 100 cc. after uranium.	Percentage of concentration after uranium to concentration before uranium.	Functional class.	Anatomical class.	Minimum correction.
	mg.	*mg.*	*per cent*			
5	91	37	41	I	I	
4	43	31	72	I	I	
9	77	62	**81**		II	200
6	100	96	96	I	I	
2	77	89	115	I	I	
12	42	49	**117**	I	II	164
3	53	63	119	I	I	
10	41	64	**156**	I	II	125
1	52	89	171	I	I	
22	68	140	**206**	I	III	315
13	38	85	**223**	I	II	58
7	49	115	**234**	I	II	47
23	68	168	**247**	I	III	274
24	70	180	**257**	I	III	264
11	37	97	**262**	I	II	19
8	41	132	322	II	II	
20	68	238	**350**	II	III	171
16	63	250	**397**	II	III	124
21	86	384	**446**	II	III	75
17	41	202	**494**	II	III	27
19	42	224	534	III	III	
18	43	233	542	III	III	
15	47	278	592	III	III	
14	50	381	761	III	III	

Total..... 1863 in a range of 720
258 " " " " 100

drawn from a large mass of data on normal rabbits has been presented which indicates that at high blood urea concentrations the size of the kidney ceases to be a potential and becomes an active factor in determining the magnitude of the ratio (13).

CONCLUSIONS.

1. Under the strain induced by the administration of urea, it is possible to demonstrate the relation between the degree of anatomical damage in the kidney and the degree of defect in the urea-excreting capacity induced by uranium.

2. The closest correlation between structure and function was obtained when the ratio between the urea content of the urine and of the blood was used as the measure of function.

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