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The depressor substance of dog's urine; its disappearance in experimental acute nephritis.

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The urine of a normal dog when injected intravenously into another dog in doses of three cubic centimeters causes an immediate fall in blood pressure varying from 25 to 96 mm. of Hg. This effect, constant for normal urine, is not always obtained when the urine from a chromate or uranium nephritis of the third to fifth day is used. It is still obtained, however, in arsenic and cantharidin nephritis of the same periods. This difference suggests that in the tubular lesions of chromate and uranium nephritis, which are characterized by extensive epithelial destruction, some substance normally eliminated is retained while in the glomerular nephritis caused by arsenic and cantharidin poisoning this retention does not occur. The elimination of the depressor substance would appear therefore to be a function of the tubular epithelium.

In animals with experimental nephritis of the tubular type the disappearance of the depressor substance from the urine is frequently associated with a lowering of the blood pressure which would appear to indicate that the retained depressor substance has a definite effect on the general blood pressure. This observation is not based however on blood pressure determinations on the same animal before and after the development of nephritis but by contrasting the pressure in animals with tubular nephritis with that of normal animals and those with glomerular nephritis.

The nature of the depressor substance has not been determined.

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Observations on the metabolism of a subject of diabetes.

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The subject of the observations was a patient in the service of Dr. Warren Coleman in Bellevue Hospital. Different known

diets were used and the urine was analyzed over a period of more than three months. A portion of the results of the last part of the period is given in the accompanying table. The unusual features of these results will be briefly discussed.

Between twenty and eighty grams of *total* β-oxybutyric acid (the acetone and diacetic acid being calculated as β-oxybutyric acid) were excreted each day for at least eighty days without any signs of impending coma. For more than two months with this severe acidosis the subject showed practically complete carbohydrate intolerance. As shown in the table the diet was then changed to 255 grams of oatmeal. On this diet the acidosis and the glycosuria decreased very much, the former ultimately disappearing. This comparatively sudden transition from a condition of severe to one of mild diabetes is very striking and appears to confirm the good results obtained by von Noorden and others with his so-called "oat cure."

The dependence of β-oxybutyric acid production upon the amount of fat in the food was very clearly shown throughout the observations. The amount of total β-oxybutyric acid excreted varied in general with the amount of fat eaten, which is not usually the case. Note the effect of the addition of butter to the oatmeal diet. The amount of food-fat appears to have determined, in this instance, the amount of fat burned.

An increase in the amount of fat in the food which caused an increased acidosis appeared to result also in a damage to the carbohydrate tolerance; with the increase of acidosis there was a very marked decrease in the amount of sugar burned. This phenomenon is just the reverse of that so often observed, *i. e.*, the decrease of acidosis with an increased burning of sugar, and again emphasizes the close inter-dependence between the metabolism of carbohydrate and fat.

The observations were terminated by the death of the patient. The immediate cause of death was not definitely established but was probably due to the phthisis which complicated the diabetes. There was no sign of coma and in view of the absence of acidosis and of the great improvement in carbohydrate tolerance we can scarcely believe that the diabetes was immediately responsible. The blood obtained at autopsy contained only traces of β-oxybutyric acid, the whole blood containing about 0.3 gram. There was no

suppression of urine, over 500 c.c. being passed in the last five hours.

The urine of the last two days is of interest; there was no acetone and no increase in glycosuria, but a very great increase in ammonia and in total nitrogen indicating a marked ante-mortem increase in protein katabolism.

Sugar was determined by titration with Fehling's or Pavy's solutions; and β-oxybutyric acid and its derivatives by the writer's method.

	Food.		Urine.			
	NH.	Fat.	N.	NH_3—N.	Sugar.	Total β-oxybutyric acid.
Average for 5 days.....	256	164	19.0	4.6	328	19.0
Average for 2 days.....	180	187	19.0		293	24.7
255 gm. oatmeal.....	165	18				
	"	"	7.0	1.8	92	1.7
	"	"	7.1	1.5	94	1.6
	"	"	5.8	1.1	72	0.9
Same, + 50 gm..	"	60	5.1	1.2	85	5.1
	"	"	6.6	2.3	119	11.3
	"	"	6.0	2.65	119	10.3
	"	"	5.5	2.0	108	4.9
Same, washed butter....	"	"	4.6	1.8	64	1.4
	"	"	5.6	0.9	48	0.7
	"	53	6.2	0.8	34	0.6
Same, regular butter.....	"	60	5.6		5	0.0
	"	"	6.4		4	0.4
	"	"	5.9	0.36	17	0.0
	"	"	6.7	0.83	8	0.0
Toast, butter, cane sugar,	170	59	13.4	1.75	16	0.0
eggs.....	less	less	32.2	3.32	8	0.0

Died at 1 P. M. next day.