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THE INFLUENCE OF PROTEIN INTAKE ON THE UREA CLEARANCE IN NORMAL MAN

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Cope (1) has reported that a change in protein content of the diet from 75 grams to 40 grams per day is accompanied by a lowering of the urea clearance in nephritics, who had approximately normal urea clearances during the control period. No doubt Cope's investigations, like our own, were stimulated in part by the observations of Jolliffe and Smith (2) that in dogs the urea clearance may be raised by over 100 per cent by change from a low protein to a high protein diet. Since the effect of diet in Cope's experiments appears to be much less marked than is the case in the dog, it was felt that the problem merited further investigation in normal man to avoid the possibility of overlooking a functional response that might be depressed in a structurally diseased kidney. Consequently we have repeated these experiments upon subjects without renal, cardiac or vascular diseases and with no recent febrile reaction (3). As a further modification of Cope's experiments the protein intake has been varied from 9 grams to 280 grams per day, and in most instances the rate of urine excretion has been above the augmentation limit (2 cc. per minute).

The subjects were volunteers selected from the wards of the Third (New York University) Medical Division of Bellevue Hospital. Urea clearances were performed in the morning without breakfast, with the patient recumbent in bed. During the previous night and up to two hours before the discard preceding the first urine collection period, the subject was given 3,000 to 4,000 cc. of water to insure high rates of urine flow. An effort was made to avoid collection of urine in the ascending phase or at the peak of diuresis. All discards and urine specimens were collected by catheterization to insure complete emptying of the bladder. Blood was drawn from the median basilic vein at the beginning, middle and end of each experiment. When the three blood urea values, as separately determined, checked within three per cent, they were averaged, and when they did not, values interpolated to the middle of each period were used. Urea in plasma and in urine were determined in duplicate by the gasometric

¹ Graduate Students in the Department of Medicine.

TABLE I

Data of urea clearances

		Daia of urea clearan	ces			
	Daily protein intake	Date	V Urine volume	P Plasma urea	UV P(SA) clearance	
M. O., age 40, surface area 1.7 sq. m.	grams 100	November 7, 1933	cc. per minute 3.59 5.00	mgm. per cent 18.9 19.0	cc. per sq. m. per minute 38.9 57.0	
		November 9, 1933	8.31 3.56 17.29 16.50 15.20 11.35	19.0 18.99 21.15 21.39 21.05 20.07	58.0 44.1 47.8 40.4 49.1 44.5	
	Averag	re			47.5	
	9	November 15, 1933 November 17, 1933	12.07 13.68 13.07 12.50 12.00 11.46 11.16 11.80	5.93 6.22 6.15 6.10 6.95 6.52 6.51 6.50	34.6 38.9 39.1 36.6 36.4 37.4 32.8 35.3	
	Averag	re			36.3	
	280	November 23, 1933	19.00 15.70 15.75 14.80	37.89 37.69 37.05 37.55	53.0 34.8 47.2 50.0	
		November 25, 1933 November 28, 1933	15.70 16.00 13.40 13.27 18.25 17.15 14.90	34.10 33.61 33.30 32.96 41.30 39.80 38.70 37.90	44.8 51.9 43.2 46.1 48.2 49.5 43.6 45.3	
	Averag		14.72	37.90	46.4	
P. M., age 48 years, surface area 1.84 sq. m.	100	December 6, 1933 December 8, 1933	4.28 4.28 5.48 7.71 4.52 5.12 3.82 2.60	23.90 23.50 23.38 23.28 25.86 25.80 .25.65 25.50	54.6 56.8 55.1 61.5 57.4 59.4 50.1 42.9	
	Averag	je			54.8	

method of Van Slyke (4). Heparin was used as an anticoagulant. All patients were attended by a special nurse and the diets were prepared by a trained dietician attached to the teaching unit of New York University Medical Service.

The control urea clearances were determined while patients were receiving the usual ward diet containing an average of 100 grams of protein

TABLE I (continued)

		TABLE I (continued	()			
	Daily protein intake	Date	V Urine volume	P Plasma urea	UV P(SA) clearance	
P. M. (continued)	grams 9	December 13, 1933	cc. per minute 3.73 4.64 4.23	mgm. per cent 9.05 8.62 8.60	cc. per sq. m per minute 43.6 54.2 47.7	
		December 15, 1933	3.07 4.86 3.20 3.10 3.30	8.50 9.15 9.15 9.15 9.15	38.2 48.3 46.9 44.3 42.5	
	Averag	ge			45.	
	280	December 20, 1933	2.75 3.70 4.60	41.37 40.84 40.32	48.0 55.3 56.3 56.1	
		December 22, 1933	4.63 6.04 4.80 5.08 3.43	39.83 38.60 38.94 38.45 38.05	59.6 62.3 57.4 55.2	
J. G.,† age 37 years, surface area 1.66 sq. m.	Averag	re			56.	
	9	December 16, 1933	6.41 4.23 3.37 3.50	8.42 8.42 8.42 8.42	31.7 32.5 28.6 30.4	
	Averag	re			30.	
	280	December 22, 1933	11.35 10.45 7.36 3.06	47.35 46.70 46.30 45.90	33.2 40.3 38.6 30.1	
	Averag	ge			35.	
	100	December 29, 1933	12.65 12.35 10.90 9.18	24.05 24.30 23.75 23.35	34.2 38.5 36.7 34.3	
	Averag	re i			35.	

per day. Eight clearances were determined on two different days. Following the last control observation the patient was given a diet containing 9 grams of protein per day. On the sixth day four clearances were determined, and on the eighth day, four more. The same procedure was followed.

TABLE I (continued)

		IABLET	(commune	,			
	Daily protein intake	Date		V Urine volume	P Plasma urea	UV P(SA) clearance	
	grams			cc. per minute	mgm. per cent	cc. per sq. m. per minute	
M. C., age 40 years,	100	January	1, 1934	4.67	18.70	28.5	
surface area 2.08	100	Junuary	-,	5.50	18.05	44.1	
sq. m.		į		5.13	17.95	36.4	
-4,				5.20	17.90	35.0	
		February	2, 1934	23.05	26.90	42.2	
			-,	20.95	26.35	39.6	
		•		21.20	26.20	41.4	
				20.60	26.00	42.1	
	Average					38.6	
	9	February	7, 1934	6.77	8.54	24.5	
		_		6.10	8.83	24.8	
	1			6.54	9.01	31.5	
		1		4.80	9.26	23.6	
	i	February	9, 1934	5.63	6.57	25.4	
	1			4.95	6.57	23.6	
	l			4.08	6.57	21.1	
				4.00	6.57	22.0	
	Averag	ge				24.6	
	280	February	14, 1934	4.52	38.40	44.8	
				6.73	38.40	45.4	
				2.85	38.40	30.5	
				2.64	38.40	34.9	
		February	16, 1934	5.80	41.18	29.7	
				2.45	39.95	25.6	
				2.69	39.78	33.1	
		1		5.35	39.43	46.7	
		February	21, 1934	6.57	39.50	33.1	
				3.17	39.50	34.3	
	1			3.15	39.50	33.1	
		l.,	00 4004	2.62	39.50	32.4	
	l	February	28, 1934	2.73	36.61	31.9	
	1			4.77	35.90	43.9	
				7.73	35.63	45.4	
	1	Man-L	E 1024	6.87	35.23	36.2 21.9*	
	1	March	5, 1934	1.73	40.40	25.7*	
	1			1.55	40.40 40.40	27.4*	
				1.80 1.74	40.40	27.1*	
	Averag	-! ge !				36.3	

lowed on the high protein diet which contained 280 grams of protein. The protein in this diet was composed principally of meat, cheese and milk products, meat constituting about one-third. On one subject (M. C.) clearances were determined on a high protein diet over a period of twenty-five days. A total of 124 urea clearances were determined on five subjects, and with five exceptions the urine flow was above 2 cc. per minute. The results of these observations are given in Table I.

The greatest reduction in clearance observed on the low protein diet was 36 per cent below the control, and the average reduction was 23 per cent. We have no doubt that this change is significant and reflects an

TABLE I (continued)

							
	Daily protein intake	Date		V Urine volume	P Plasma urea	P(S clear	
	grams			cc. per minute	mgm.	cc. per per m	sq. m.
J. J., age 45 years,	100	February	26, 1934	5.42	19.70	35.1	
surface area 1.68	l			2.93	19.50	38.6	
sq. m.				2.30	19.30	36.1	
•				2.64	19.20	43.3	
		March	2, 1934	3.27	17.70	34.8	
				2.85	17.70	38.0	
	l	1		2.086	17.70	30.8	
				1.76	17.70	22.4*	:
	Average						35.2
	9	March	7, 1934	11.00	5.76	28.9	
	_	March	7, 1701	8.14	5.10	31.3	
				5.91	5.18	29.0	
				3.68	5.28	28.9	
	ł	March	9, 1934	12.10	7.47	26.2	
	Į		.,	10.42	7.43	24.1	
				10.10	6.91	26.0	
				8.00	6.47	28.1	
	Average						27.8
	280	March	14, 1934	2.75	44.40	39.8	
			11, 1701	3.23	43.10	47.5	
	l			2.36	42.10	40.0	
				1.92	40.80	41.3	
		March	16, 1934	2.53	46.42	40.0	
			·	2.45	45.98	44.2	
	1			2.42	45.08	38.5	
				2.53	44.22	43.1	
	Average						41.4

^{*} Calculated as "Standard" urea clearance but not included in average.

[†] Note different order in which diets were given.

altered activity of the kidney in the excretion of urea. Increasing the protein intake above normal, however, did not result in a significant increase in clearance. In the one subject on whom protracted observations were made, the average urea clearance after 25 days on the high protein diet was slightly less than on the control diet.

Our observations on normal man confirm Cope's observations on nephritics with approximately normal urea clearances: the urea clearance is not significantly raised by a high protein diet, although it is significantly lowered by a low protein diet. Our observations show further that the lowering of the urea clearance is of the same order of magnitude, whether the clearances are determined above or below the augmentation limit. No explanation can be advanced for the fact that renal activity in man is so much less susceptible to dietary influence than is the case in the dog; it may be pointed out, however, that Jolliffe and Smith fed much larger quantities of protein (15 grams per kilogram of body weight) than our subjects consumed (4 grams per kilogram of body weight) and that in the experiments on the dog all the protein was supplied as meat whereas in man about one-third of the total protein intake is the most that can be conveniently ingested in this form.

SUMMARY

Observations on the urea clearance at urine flows above the augmentation limit in normal men subsisting on diets containing 9 or 280 grams of protein per day show a reduction in clearance at the lower protein level, but no change in clearance at the higher protein level as compared with a control period when the protein intake was 100 grams per day. These results are in agreement with Cope's observations on nephritics with approximately normal urea clearances, which observations were made, for the most part, when the urine flow was below the augmentation limit.

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