XI. A NOTE ON THE EFFECT OF PURGATION ON THE CREATININE CONTENT OF URINE.

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ANDERSON and BOSWORTH [1916] found that the administration of inositol to man, in doses of about 0.5 g. per kilogram of body weight, produced an increased excretion of creatinine, both immediately after the initial dose and during the period succeeding the administration of this substance. They offer no explanation of this increase. (It is regrettable that they employed a diet containing meat as it has been demonstrated that the amount of creatinine excreted has no definite ratio to the amount of flesh ingested [Burns and Orr, 1916].) From their results two points bearing on this subject may be noted:

(a) Inositol is only to a slight extent absorbed by man and has no appreciable effect (except creatinine increase) on metabolism.

(b) The ingestion of inositol was invariably followed by diarrhoea.

Burns and Orr [1914], in studying the effect of copious ingestion of water on the nitrogen metabolism of man, came to the conclusion that the ingestion of water in large amounts either had no appreciable effect on the creatinine excretion or caused (one experiment) a temporary increase. Most of their subjects of experiment had, on the first day of increased water ingestion, rather loose stools. In one instance, the administration of three litres of water at one time caused such severe diarrhoea that the experiment had to be abandoned. The results of this experiment are appended (Table I), from which it will be seen that the creatinine excretion rose from 1339 mg. to 1385 mg. per day.

Table I.

Effect of diarrhoea induced by an excessive intake of water.

Total N.	Creatinine	Creatine	Notes
gm.	mg.		
12.8	1339	Nil	
13.6	1339	"	
13.1	1385	"	3 litres of water extra

The following experiments were designed to show how far the purging effect of inositol might be answerable for the creatinine increase.

Two subjects, B. and W., were employed. They had been often on experimental diets and could, therefore, be relied on to adhere strictly to the routine laid down. The diets prescribed (Table II) were creatine-creatinine-free. Urine was collected in 24 hour periods, made up to a volume of 2000 cc.,

and analysed immediately. After a suitable pre-period the subjects took three teaspoonfuls of Rochelle salts (or in Exp. 5 sodium bicarbonate and in Exp. 6 acid sodium phosphate) in warm water at 11 a.m. and 2 p.m. on one day. The collection of urine was continued for a day or two thereafter.

Results. Detailed results are appended in tabular form (Tables III, IV and V).

Nitrogen. The amount of nitrogen excreted by the kidneys varied but slightly. On the day after the purge the amount was somewhat less than on the preceding days, due probably to a retention of nitrogen succeeding the loss of nitrogen by the bowel on the day before.

Creatinine. In the first four experiments the creatinine output was increased on the day of the purge. In Exps. 1 and 2 (Table III) this increase

Table II.

Diets used during experiments.

<i>Expt. 1.</i>	Breakfast:	Tea—two cups with milk and sugar
		Bread—one slice brown and one white, butter
		Fruit
	Lunch:	Four slices bread and cheese
		250 cc. milk, 50 cc. water (hot)
		Essence of coffee
	Tea:	As breakfast
	Supper:	Porridge and milk (250 cc.)
<i>Expt. 2.</i>	Higher nitrogen intake	
	Same as for <i>Expt. 1</i> with the following exceptions:	
	Breakfast: Cocoa instead of tea and one egg added	
	Dinner and Supper: 300 cc. milk instead of 250 (no added water)	
<i>Expt. 3.</i>	Higher calorie intake	Bread 650 g.
		Potatoes 300
		Rice 200
		Fruit 100
		Margarine 50
		Jelly 50
		Porridge and milk, two eggs, chocolate (measured)
		Tea and cocoa (measured)
<i>Water Expt. As Expt. 1, i.e.</i>		Protein 110 g.
		Carbohydrate 325
		Fat 67

Table III.

Effect of Rochelle salts per os on urinary creatinine.

<i>Expt. 1.</i>	Subject B.	Day	Reaction	Total N. (g.)	Creatinine (mg.)	Notes
		1	Neutral	12.5	1680	
		2	Neutral	12.8	1675	
		3	Neutral	12.7	1680	
		4	Alkaline	12.7	1690	Rochelle salts in warm water
		5	Slightly alkaline	11.9	1810	
<i>Expt. 2.</i>	Subject B.	1	Neutral	15.1	1680	
		2	Alkaline	15.1	1700	Rochelle salts in warm water
		3	Alkaline	12.9	1780	
		4	Neutral	14.98	1690	
		5	Neutral	14.7	1700	
<i>Expt. 3.</i>	Subject W.	1	Acid	12.96	1152	
		2	Acid	10.83	1142	
		3	Alkaline	10.33	1362	Rochelle salts in warm water
		4	Acid	9.83	1100	

was followed by a still further increase. In Exp. 3 the creatinine excretion on the day following the administration of Rochelle salts was slightly sub-normal. After NaH_2PO_4 a decreased creatinine elimination was observed (Exp. 5, Table V).

Table IV.

		Effect of NaHCO_3 per os on urinary creatinine.					
Expt. 4.	Subject W.	Day	Reaction	Total N. (g.)	Creatinine (mg.)	Creatine	Notes
		1	Neutral	10.4	1640	Nil	
		2	Neutral	10.4	1640	„	
		3	Acid	10.5	1680	„	
		4	Alkaline	10.6	1640	„	8 g. NaHCO_3 (no purging effect)
		5	Alkaline	10.89	1634	„	
		6	Acid	10.89	1640	„	

Table V.

Effect of NaH_2PO_4 per os on urinary creatinine.						
Expt. 5.	Subject W.					
	Day	Reaction	Total N. (g.)	Creatinine (mg.)	Creatine	Notes
	6	Acid	10.89	1640	Nil	16 g. NaH_2PO_4
	7	"	12.18	1630	"	
	8	"	11.4	1550	"	
	9	"	11.01	1620	"	

To summarise; diarrhoea induced by:

1. excessive water ingestion,
2. irritation of intestinal wall by an inert substance (inositol—Anderson and Bosworth),
3. inrush of fluid into the intestine by exosmosis from the tissues (Rochelle salts),

is accompanied by an increase in the creatinine content of the urine.

This alteration in the creatinine output might at first sight seem to be associated with an alteration in the H^+ concentration of the urine. Underhill [1916, 1] has reported a series of experiments on rabbits and dogs in which he demonstrates a causal connection between acidosis¹ and creatinuria, and indisputably proves that relief of the acidosis by the administration of alkali leads to a decrease or even to a cessation of the elimination of creatine. The apparent connection between creatine and creatinine is apt to cause one to take for granted that on a creatine-fixed diet the appearance of creatine in the urine is accompanied by a fall in the amount of creatinine excreted—a totally gratuitous assumption. Underhill [1916, 2] in a second paper proves that while the administration of alkali prevents the elimination of creatine in the earlier period of a starvation acidosis, it does not materially affect the creatinine output. In Exp. 4, W. took 8 g. of NaHCO_3 on one day. No diarrhoea resulted and there was no appreciable alteration in the creatinine output. Acid sodium phosphate in a dose of 16 g. reduced the creatinine content of the urine but did not cause the appearance of creatine.

¹ Acidosis is in this paper used in the clinical sense of the term.

Two reasons may be put forward as explanation of this increased creatinine excretion after diarrhoea:

(a) Increased tone of the visceral musculature.

The evidence of the connection of tone of striped muscle with the creatine content of muscle and with the creatinine content of urine seems conclusive [Pekelharing, 1911; Pekelharing and Harhink, 1910; Pekelharing and van Hoogenhuyze, 1916, 1, 2; Cathcart, Henderson and Paton, 1918; Riesser, 1916; Stenvers, 1917].

No evidence has however been brought forward to show that visceral muscle, under sustained contraction, leads to the elimination of increased amounts of creatinine. Further, the increased peristalsis of diarrhoea does not necessarily indicate increased tone of the visceral musculature. It has been proved that muscular work, apart from sustained contraction, does not cause an increased creatinine excretion.

(b) The sensation of well-being experienced after a purge leads one to the conclusion that the organism, having been freed from by-products and residues, is in better working order, and, as a whole, improved in tone. The experiment in which sodium biphosphate was given cannot in fairness be brought in evidence against this, as the acidosis produced would cause a decreased creatinine elimination [Underhill, 1916, 1].

SUMMARY.

Purgation by Rochelle salts or copious water ingestion leads to a slight increase in the amount of creatinine eliminated.

Administration of an alkali which does not induce purgation causes no appreciable alteration in the creatinine output.

The exhibition of an acid purgative (NaH_2PO_4) leads to a slight decrease in the creatinine content of urine (acidosis phenomenon).

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