XC. THE EFFECT ON THE BLOOD-SUGAR AND BLOOD-PHOSPHATE OF INGESTED CREATINE.

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THE variations in the level of the inorganic phosphate of the blood after the ingestion of glucose and the different responses obtained in the normal and in the diabetic organism are now well established [Harrop and Benedict, 1924 and others]. The reverse of this, namely, the effect of ingested phosphate on the blood-sugar has been investigated by Elias and Weiss [1922], Magenta and Biasotti [1924] and by Friedländer and Rosenthal [1926], but the results are not in sufficiently good agreement for any definite conclusion to be drawn. The fact that creatine is now known to be associated with phosphorus in the metabolic processes of muscle [Eggleton and Eggleton, 1928; Fiske and Subbarow, 1929] suggested the possibility that some light might be thrown on the metabolism of creatine and carbohydrate by comparing the action of administered creatine on the blood-sugar and blood-phosphate in normal and diabetic patients.

Some experiments on this subject with normal animals have already been reported. Hill and Mattison [1929] have shown that in dogs, doses of creatine as small as 0.025 g. per kg. given by mouth produce a fall in the blood-sugar provided its initial value is not very low, whilst Brown and Imrie [1931] obtained a fall in the phosphate excretion in the urine after giving creatine to anaesthetised cats. These latter results were not, however, confirmed by Fasold and Loeschke [1932], who examined the effect of creatine on the phosphate excretion of adults and children. They came to the conclusion that in neither was there any change in phosphate excretion and that the changes observed by Brown and Imrie were probably due to the large volume of water given with the creatine.

Method.

The experiments described here were carried out between the hours of 9 a.m. and 1 p.m. on patients who had fasted since the preceding evening. In the case of the diabetic patients no insulin had been given for 15 hours. A sample of blood was taken at the beginning of the experiment from the arm and oxalated to 2 mg. per cc. The patient then drank 2-5 g. creatine in 100 cc. water, and further samples of blood were taken up to 3-4 hours after the beginning of the experiment.

Glucose was determined on the whole blood by MacLean's method [1919]. The plasma was then separated, and the inorganic phosphate and total creatinine (creatine *plus* preformed creatinine) were determined in it by the methods of Fiske and Subbarow [1925] and of Folin and Wu [1919] respectively.

Results.

The results of the blood analyses are collected in Table I, in which the inorganic phosphate is expressed as mg. of phosphorus per 100 cc. The preformed creatinine was determined in several experiments and was found to be constant.

Table I.

Normals						Diabetics					
Exp.	Time after creatine min.	Dose g.	Blood-sugar mg./100 cc.	Plasma-inorganic P mg./100 cc.	Plasma-total creatinine mg./100 cc.	Exp.	Time after creatine min.	Dose g.	Blood-sugar mg./100 cc.	Plasma-inorganic P mg./100 cc.	Plasma-total creatinine mg./100 cc.
1	0	2.0	90	4.00	2.15	11	0	3.0	216	3.92	2.20
	60		104	3.52	4.85		60		291	3.95	4.10
	140		104	3.69	3.84		120		286	4.02	4.16
	185		137	4.06	3.65		180		299	4.00	3.60
2	0	3.0	102	3.92	2.31	12	0	2.0	171	3.29	4.60
	65		125	3.84	4.16		60		181	3.21	4.80
	130		117	4.14	3.68		145		156	—	—
	200		106	3.81	3.14		13		254	3.28	1.86
4	0	3.0	111	3.53	2.23	13	60	3.0	227	3.08	6.80
	60		92	3.33	6.50		120		179	3.10	4.78
	140		104	3.43	4.13		160		177	3.10	4.23
5	0	3.0	106	4.38	2.27	14	0	3.0	450	3.82	2.23
	60		106	4.13	5.20		75		440	2.80	5.20
	140		97	4.56	4.13		165		480	2.75	5.78
6	0	4.0	129	4.54	1.90	15	0	4.0	450	3.70	2.15
	60		125	3.92	4.30		55		441	3.70	6.10
	120		122	3.88	8.05		175		457	3.54	6.25
	180		113	3.62	6.10		16		180	3.50	2.00
7	0	4.0	115	4.22	2.30	16	0	4.0	180	3.10	7.75
	100		120	3.83	6.30		60		180	3.10	7.75
	155		109	4.03	6.50		120		162	2.90	6.70
	225		117	3.98	4.75		180		138	3.11	5.50
8	0	4.0	106	3.90	3.10	17	0	5.0	296	3.82	2.85
	60		109	3.24	6.90		60		291	3.70	5.30
	115		92	3.24	6.10		120		286	3.55	9.25
	200		102	3.28	6.75		180		274	3.38	—
9	0	5.0	102	3.79	2.45	18	0	5.0	378	3.78	3.05
	60		100	3.76	8.00		60		390	3.44	8.30
	120		77	3.57	8.35		120		363	3.28	8.50
	180		69	3.62	7.00		175		383	3.36	8.00

	Normals mg./100 cc.	Diabetics mg./100 cc.
Average change in blood-sugar during 1st hr.	+2	+6
2nd hr.	-6	-9
3rd hr.	+4	-1
Average change in plasma-inorganic phosphate during 1st hr.	-0.34	-0.29

An approximate estimate of the rise in the plasma-creatinine (expressed as creatinine) can be obtained by subtracting 1.5 from the figures in the total creatinine column, *e.g.* in Exp. 1, the rise was from 0.65 to 3.35 and in Exp. 9 from 0.95 to 6.85.

Blood-sugar. It will be seen that the blood-sugar varied very considerably during the course of an experiment, the variations being larger in the case of the diabetics than in the case of the normals. There is no evidence, however, of a tendency for it to rise or fall after creatine in either type of patient, and the averages for both show practically no change.

Plasma-inorganic phosphate. With the exception of one experiment there is a fall in the inorganic phosphate in every case although in three experiments the drop is less than 5 %. It can therefore be said that in thirteen experiments out of fifteen a definite, though in no case very large, drop was obtained (Exp. 12 is not considered, as the drop during the second hour is not known). Further, in

five out of six experiments in which the plasma-creatine reached its maximum at the end of the first hour, the phosphate started to return to normal during the second, and out of the nine experiments in which the creatine continued to rise during the second hour, in eight of them the phosphate continued to drop.

While there is a marked tendency for the phosphate and creatine to vary together, a rise in the plasma-creatine being accompanied by a fall in the phosphate, the fall in the phosphate is not proportional to the rise in the creatine, as is seen by comparing Exps. 9 and 17, where there is a small phosphate drop, with Exps. 1 and 4, where it is large.

Comparing the normals with the diabetics no definite differences are to be seen.

Although the changes obtained are small it is considered that the good agreement of the results eliminates the possibility that they are chance effects, and the conclusion is drawn that a small drop in the plasma-inorganic phosphate follows the ingestion of creatine, but it is by no means constant in amount and is probably influenced by some unknown factor.

SUMMARY.

1. The blood-sugar and plasma-inorganic phosphate have been estimated before and after the ingestion of creatine by normal and diabetic patients.
2. After creatine the blood-sugar shows no decided change in either direction.
3. The inorganic phosphate tends to fall as the creatine content of the plasma rises.
4. Normals and diabetics react essentially in the same way.
5. The phosphate fall does not vary quantitatively with the rise in the plasma-creatine.

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