

THE OUTPUT OF ORGANIC PHOSPHORUS IN URINE

By G. C. MATHISON, M.B., B.S. (MELB.), *Sharpey Scholar*.

From the Physiological Laboratory, University College, London

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The existence of organic phosphorus compounds in normal urine has often been asserted and as often denied. In a previous paper (1) I have shown their undoubted existence. The present investigation deals with the quantity of organic P_2O_5 excreted in the urine of healthy persons on an ordinary diet. The results obtained by many previous workers are unreliable owing to the employment of unsuitable methods. Ehrstrom (2), Gumlich (3), Keller (4), Le Clerc and Cook (5), and older workers such as Lépine (6) and Zuelzer (7) attempted to determine organic P_2O_5 by methods entailing titration of urine with uranium acetate. This method gives a value greater than inorganic, indeed sometimes greater than total P_2O_5 , so that it is valueless for the determination of organic P_2O_5 .

Le Clerc and Cook (5), whose dictum is quoted with approval by F. G. Benedict (8), state that there is insufficient evidence of the existence of organic phosphorus, despite the fact that in twenty-four hours' urine from a dog they obtained a difference of 0.093 gram P_2O_5 between total and inorganic, in rabbits a difference of 0.055 gram. Even though one agree with these workers that the method they employ is not sufficiently exact to afford evidence of the existence of organic phosphorus, one cannot agree that it is sufficiently exact to afford evidence against such existence.

Oertel (9) was the first to use a sound method of estimating organic phosphorus. He precipitated phosphates by means of calcium chloride, and determined organic P_2O_5 in the filtrate. This was evaporated to dryness, fused with KOH and KNO_3 , precipitated with ammonium molybdate, dissolved in ammonia, re-precipitated with magnesia mixture, incinerated and estimated as pyrophosphate. The process is thus very lengthy and involves several manipulations.

Oertel obtained values for the output of organic P_2O_5 in twenty-four hours ranging from 0.12 gram (5 per cent. of total P_2O_5) to 0.03 gram, (1.5 per cent. of total P_2O_5). He considers 0.05 gram to be the usual

quantity. Mandel and Oertel (10), employing the same method, found in the twenty-four hours' urine of three individuals an average of 0.024 gram organic P_2O_5 , equal to about 2 per cent. of the total.

Bornstein (11) made some observations on the output of inorganic and organic P_2O_5 on an ordinary diet and on plasmon. He estimated organic P_2O_5 in the filtrate after barium chloride, by a method somewhat similar to that of Oertel. His results are here summarised:—

	Nitrogen	Total P_2O_5	Organic P_2O_5	Percentage of P_2O_5 as Organic
Average of 14 days ...	14.0	2.09	0.058	2.8
Highest values ...	14.2	1.82	0.16	8.8

Bornstein himself considers that there is some mistake in the highest values, and rejects them in his average.

Bock (12) used methods entailing uranium acetate titration, but also in some cases estimated total P_2O_5 by Neumann's method, and inorganic P_2O_5 with calcium chloride or barium chloride. In rabbits he found as much as 0.29 gram of organic P_2O_5 , equal to 11 per cent. of total, in twenty-four hours' urine, in cats from 0.04 gram, 2.5 per cent., up to 0.20 gram, 11 per cent.

The present observations were carried out on the urines of healthy individuals on an every day diet during January, February and March. All these persons followed sedentary occupations. The estimations were carried out by the methods described in a previous paper (1).

Samples of urine from different individuals gave the following values:—

TABLE I—INORGANIC AND ORGANIC PHOSPHORUS

Grams P_2O_5 in 100 c.c. urine						
	Total P_2O_5	Inorganic P_2O_5	Organic P_2O_5		Percentage of P_2O_5 as Organic	
			By difference	In filtrate		
S. ...	0.092	0.086	0.006	0.004	5.5	
K. ...	{ 0.124 0.121	0.117	0.005	0.005	4.0	
P. ...	{ 0.148 0.145	{ 0.145 0.138	{ 0.003 0.007	— 0.007	5.0	
M. ...	{ 0.098 0.099	0.090	0.008	0.010	9.0	

Since these results were considerably higher than those usually cited, further observations were made on the daily output of different individuals, usually over a period of several consecutive days.

TABLE II—OUTPUT OF ORGANIC P_2O_5 IN 24 HOURS

Subject	Day	Quantity	Grams P_2O_5		Organic P_2O_5	Percentage P_2O_5 Organic	$\frac{N}{P_2O_5}$ ratio
			Total Nitrogen	Total P_2O_5			
M. aet. 25	I	1320	—	3.00	0.303	10.1	—
„	II	1030	—	2.30	0.155	6.7	—
„	III	1000	—	2.43	0.180	7.5	—
„	IV	1240	—	2.75	0.148	5.4	—
„	V	1070	—	2.45	0.225	9.0	—
	Average	—	—	2.58	0.202	7.7	—
M. aet. 25	I	1200	16.44	2.41	0.168	7.0	6.8
„	II	1140	12.77	1.90	0.114	6.0	6.8
„	III	1200	15.28	2.45	0.120	4.9	6.2
„	IV	1050	14.59	2.05	0.121	6.2	7.1
„	V	1500	15.90	2.05	0.180	7.8	6.9
„	VI	1050	13.46	2.31	0.140	6.0	6.5
	Average	—	14.74	2.19	0.140	6.3	6.7
L. aet. 27	I	1100	10.18	2.10	0.104	5.0	4.9
„	II	1230	9.76	1.90	0.041	2.1	5.1
„	III	1400	11.02	2.41	0.063	2.5	4.6
	Average	—	10.32	2.13	0.068	3.2	4.9
D. aet. 40	I	1850	16.63	2.84	0.27	9.5	5.9
„	II	1150	14.78	2.61	0.01	0.4	5.6
„	III	2050	16.43	2.77	0.15	5.5	5.9
	Average	—	15.94	2.59	0.14	5.1	5.8
P. aet. 30	I	1700	13.71	2.32	0.223	10.0	5.9

(Organic P_2O_5 averaged 0.15 gram per diem, equal to 6.2 per cent. of total P_2O_5 .)

The highest output was 0.3 gram, the lowest 0.04 gram.

It will be noticed that the N : P_2O_5 ratio was fairly constant in any one individual, but that it varied greatly in different individuals.

The values obtained for organic phosphorus are considerably higher than those cited by most other workers, even by those who employed accurate methods. This difference must be ascribed in the latter cases to individual variations in output.

THE EFFECT OF INGESTION OF GLYCEROPHOSPHORIC ACID

Although the subject was not on a rigid diet, it was thought worth while to try the effect of adding a large amount of organic phosphorus, in the form of glycerophosphoric acid, to the diet. For several days an approximately similar diet was adhered to, except that on one day glycerophosphoric acid was added. Two series of observations were made on the same subject.

TABLE III—EFFECT OF INGESTION OF GLYCEROPHOSPHORIC ACID

(i) Glycerophosphoric acid (Merck) containing 1.44 grams Organic P_2O_5 , 0.075 grams Inorganic P_2O_5 added to diet early on sixth day.

Subject	Day	Nitrogen	Total P_2O_5	Organic P_2O_5	P_2O_5 as Organic	$\frac{N}{P_2O_5}$
M. act. 25	I-IV (average)	14.99	2.24	0.146	6.4	6.5
"	V	13.46	2.07	0.140	6.0	6.5
"	VI*	13.6	2.76	0.165	6.0	4.8
"	VII	13.77	2.29	0.162	7.0	6.0

(ii) Sodium Glycerophosphate, containing 2.4 grams Organic P_2O_5 and 0.125 grams Inorganic P_2O_5 added to diet on second day.

"	I	14.2	2.47	0.168	6.8	5.7
"	II*	10.44	3.73	0.113	3.0	2.8
"	III	10.55	0.16	0.174	8.0	4.9
"	IV	14.63	2.74	0.150	5.3	5.3

The increase of organic P_2O_5 is well within normal variations—no significance attaches to it. The same might be said of the increase of total P_2O_5 , but for the marked alteration in the $N : P_2O_5$ ratio. It is obvious that a great part of the ingested glycerophosphate has been excreted as inorganic phosphate; it is probable that a considerable portion was not absorbed and would be found in the faeces.

The experiments of Bergmann (13) are of some interest in this connection. He injected into a dog subcutaneously several grams of organic P_2O_5 in the form of glycerophosphoric acid. He found a marked increase in the inorganic P_2O_5 , none in the organic. He used titration methods which would only show large changes. The increase in inorganic P_2O_5 was so great, however, as to leave no doubt that the glycerophosphoric acid had been decomposed here without intervention of alimentary processes. It has been asserted that many organic phosphorus compounds are absorbed as such. To test the probability of this assertion, I have subjected sodium glycerophosphate solutions to the action of active preparations of pepsin, of trypsin, and of fresh pancreatic juice, both with and without enterokinase.¹ The solutions were incubated for weeks at 39° C. Inorganic phosphates were estimated at the beginning and at intervals during the experiment. In no case was any increase in the inorganic phosphates found; the glycerophosphate remained unchanged.

1. The juice was obtained from dogs after injection of secretin. It was used without enterokinase because some authors have asserted that enterokinase destroys the lipase present.

It is probable, therefore, that the ingested glycerophosphate in the experiments detailed above was absorbed unchanged. As the glycerophosphate used was synthetic it does not follow that natural glycerophosphoric acid is unaffected by digestive processes.

THE EFFECT OF EXERCISE

This was investigated on two occasions. The urine was collected over four or five days, an approximately regular diet being taken during this period. On the second day a sharp twenty mile walk was taken, on the other days no exercise beyond leisurely walking a couple of miles. The walk was followed on both occasions by slight stiffness, but beyond this no fatigue was felt.

TABLE IV—EFFECT OF EXERCISE

Subject	Day	Quantity	Nitrogen	Total P ₂ O ₅	Organic P ₂ O ₅	Percentage P ₂ O ₅ as Organic	$\frac{N}{P_2O_5}$
M. aet. 25	I	1440	15.10	2.769	0.181	6.5	5.5
"	II*	1550	15.23	2.81	0.168	5.9	5.4
"	III	1200	13.96	2.58	0.114	4.4	5.1
"	IV	1320	16.01	2.93	0.146	5.0	5.4
"	V	1510	14.30	2.71	0.110	4.1	5.3
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"	I	1360	13.09	2.18	0.163	7.4	6.0
"	II*	1710	14.01	2.44	0.171	7.0	5.7
"	III	1450	15.48	2.70	0.120	4.7	5.7
"	IV	1250	13.94	2.67	0.134	5.0	5.2

*Twenty mile walk during first half of this day.

These figures do not show any increase of organic P₂O₅ after exercise. The diet was not sufficiently rigid to enable any deductions to be drawn from the nitrogen and total P₂O₅ figures.

No statement can as yet be made as to the origin of the organic phosphorus of urine. As far as can be gathered from the present results and from a long series of observations, on which Dr. Aders Plimmer is at present engaged, the quantity of organic P₂O₅ is not affected by food. It is thought that some indication of its origin may be given by investigation of pathological conditions in which gross changes in lymphoid or nervous tissues are present.

SUMMARY

1. Organic phosphorus compounds are normally present in the urine. Contrary statements are due to the employment of incorrect methods.

2. In young adults on an ordinary diet the organic P_2O_5 was usually more than 0.1 gram per day. Occasionally it fell below this, and in one case it reached 0.3 gram.

3. The percentage of the total P_2O_5 present in organic combination varies considerably from day to day. In the cases examined it averaged 6 per cent. of the total.

4. The addition of a large quantity of organic phosphorus in the form of glycerophosphoric acid to the diet had no distinct effect on the output of organic P_2O_5 , while it increased the total P_2O_5 output. Glycerophosphoric acid was not broken down by gastric or pancreatic digestion *in vitro*, so it was probably absorbed unchanged.

5. In the observations made, vigorous exercise was not followed by increased output of organic P_2O_5 .

6. The N : P_2O_5 ratio was fairly constant in any one individual on a fairly regular diet. It differed greatly in different individuals, and also in the same individual when the diet was irregular.

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