

# A CONTRIBUTION TO THE KNOWLEDGE OF THE EXCRETION OF ORGANIC PHOSPHORUS IN THE URINE IN CERTAIN PATHOLOGICAL CON- DITIONS.

By DOUGLAS SYMMERS.

*From the Strecker Memorial Laboratory of the New York City (Charity) Hospital.*

UNTIL very recent years it was thought that the excretion in the urine of phosphorus, in organic combination, is so insignificant in quantity as to be negligible both in health and in disease. Recent investigations, however, have revealed organic compounds of phosphorus in considerable quantities in the urine. This fact, taken in connection with the contradictory statements concerning nuclein metabolism as a whole, more especially in diseased conditions, is deemed sufficient to render a more careful and definite study of the subject desirable.

Some of the older observations were based mainly upon the assumption that the total phosphorus output in the urine was practically equivalent to the output of the inorganic salts, and that the occurrence of organic compounds could be ignored without detracting in any degree from the value of the final determination. On the other hand, there have been occasional attempts to define the real significance of organic phosphorus. For example<sup>(1)</sup>, Lépine, Eymonnet, and Aubert, in a number of single observations, found that in certain lesions the amount of organic phosphorus in relation to nitrogen and the inorganic phosphates was increased, *e.g.*, in hysteria, hystero-epilepsy, apoplexy, and delirium tremens. In a number of other lesions, *e.g.* meningitis, they found a diminution of organic phosphorus to nitrogen, with or without relative increase in the phosphoric acid. Similar observations have been made by Zülzer<sup>(2)</sup>. But such facts are too few, too isolated and indefinite, and have attracted but little attention, probably because, until recent years, so very little was known of the normal output of organic phosphorus in the urine.

Lately, however, Horst Oertel<sup>(3)</sup> has shown that a normal individual, living on an ordinary mixed diet, excretes in the urine in twenty-four hours about 2 grms. of total phosphorus, expressed in terms of  $P_2O_5$ , and that, of this quantity, about 0.05 gm. exists in organic

combination, probably largely as glycono-phosphoric acid (<sup>4</sup>), and also, perhaps, in the form of the more highly phosphorised substances, such as the lecithins. While this amount of organic phosphorus may be taken as the average output, considerable variations may occur; the largest output under normal conditions having been found not to exceed 0.12 gm. in twenty-four hours. Under normal conditions, then, the organic phosphorus represents from 2.5 per cent. to about 4 per cent of the total quantity of phosphorus excreted in the urine. The fact has also been established that the relation of the total nitrogen excretion to that of organic phosphorus varies between 0.1 per cent. and 0.5 per cent. As a rule, individuals with higher nitrogen figures show larger figures for organic phosphorus, but an absolute parallelism does not occur.

In considering the source of organic phosphorus, several possibilities have to be considered. It may be that it is derived from food, or that it is a product of metabolism, or that both factors are concerned in its production, as is exemplified in the formation of uric acid and of the xanthin bases, which are both endogenous and exogenous in origin. Important work bearing directly on this question has been done by Keller (<sup>5</sup>), who studied the question of the excretion of phosphorus in the urine of infants. Keller found the absolute figures proportionately smaller in infants than in adults, but relatively larger in proportion to weight and nitrogen excretion. There was the same lack of absolute parallelism between nitrogen and organic phosphorus.

Formerly the output of organic phosphorus in the urine was thought to depend directly upon the disintegration of nervous structures. But in the light of the observations by Oertel, and by Keller, this must be regarded as fallacious, mainly because of the variations that have been found to exist even under normal conditions. Still further confirmation arises from the variations that have been found in certain pathological conditions, as outlined below.

The investigation of the influence of food on the excretion of organic phosphorus made by Keller revealed the fact that the quantity of phosphorised organic compounds in the food has practically no relation to their excretion in the urine. Loewy has shown that, while nucleins are absorbed with their phosphorus in organic combination, no influence is exerted on the excretion of organic phosphorus in the urine. Confirmatory evidence is offered by Gumlich (<sup>6</sup>), and by Mandel and Oertel (<sup>7</sup>). The two last observers have demonstrated that a diet absolutely phosphorus free, such as rice, and one rich in organic phosphorised compounds, such as calf's brain, shad roe and meat, while exerting a decided influence on the excretion of nitrogen, leave the excretion of organic phosphorus untouched. This is strikingly shown in their tables, of which an example is given on the opposite page (Table I.).

It may, then, be regarded as certain that the exogenous factor is

entirely foreign to the question of the excretion of organic phosphorus in the urine. Finally, it has been shown that active muscular exercise is also without effect.

TABLE I.

Diet.	Day.	Quantity.	Total N.	Total $P_2O_5$ .	Organic $P_2O_5$ .	N : Total $P_2O_5$ .	N : Organic $P_2O_5$ .	Percentage. Total $P_2O_5$ as Organic.
Rice. . .	1	1360 c.c.	7.97	1.59	0.015	100 : 20	100 : 0.185	0.9
	2	1680 „	7.94	1.07	0.016	100 : 13.5	100 : 0.203	1.50
	3	1820 „	7.79	0.94	0.016	100 : 12.1	100 : 0.209	1.70
	4	1060 „	5.90	0.60	0.011	100 : 10.2	100 : 0.183	1.80
Shad roe .	5	960 „	13.84	1.32	0.019	100 : 9.5	100 : 0.138	1.43
	6	830 „	16.66	1.26	0.016	100 : 7.5	100 : 0.0987	1.30
	7	970 „	18.65	1.18	0.010	100 : 6.3	100 : 0.0560	0.87
	8	850 „	18.11	1.06	0.014	100 : 5.8	100 : 0.0779	1.33

Pursuing still further the study of the source of organic phosphorus one must consider, first, its existence in the urine in pathological conditions; and, second, experimental evidence. As far as either is concerned, there is practically nothing in the literature, with the exception of one experiment by Keller, who, having starved himself for four days, found that the excretion of organic phosphorus showed, at first, no departure from the normal; it was then followed by a rather sudden rise from 0.01 grm. to 0.05 grm. This, of course, suggested that an increased excretion of organic phosphorus may originate in tissue disintegration depending upon starvation, *a fortiori*, since it is known that in starvation the lymphoid elements are the first to suffer. Further than this, nothing is really known of the source of this substance.

The observations that follow represent the results obtained from a number of analyses of pathological urines, and were made with the purpose of determining, as far as possible—(1) the influence on the excretion of organic phosphorus of diseases in which the lymphatic system is extensively concerned, inasmuch as it is known that this system is rich in nuclein; (2) the influence of nervous diseases; (3) the influence of increased tissue destruction; (4) the influence of conditions attended at once by lessened oxidation and by increased decomposition.

This paper does not attempt to treat the subject exhaustively, but because of the importance of the subject, and in order to obtain the co-operation of others working along similar lines, it seems advisable to put the present observations on record. The results of experi-

mental work and of further pathological investigation, tending to elucidate the question of the source of organic phosphorus, will be announced at a later date.

In making the various determinations the following methods were employed:—

The total nitrogen by the Kjeldahl method.<sup>1</sup> The inorganic phosphates by titration with uranium nitrate, and the total phosphates by titration with the same substance after fusing with sodium hydrate and potassium nitrate, the difference representing the amount of phosphorus in the organic state. Uric acid by the Hopkins-Folin method.

1. In studying the influences of diseases in which the lymphatic system is involved, advantage was taken of a typical case of lymphatic leukæmia occurring in the service of Drs. N. B. Potter and T. C. Janeway at the New York City Hospital.

The patient was a longshoreman, æt. 59, and single. He was admitted with a temperature of 103° F., which lasted, however, a few hours only. Physical examination revealed, among other things, great enlargement of the cervical, supra- and infra-clavicular, axillary and inguinal lymphatic glands, and presumptive evidence of involvement of the intrathoracic glands. The visible mucous membranes were blanched, and the skin of the entire body was dusky green or greenish yellow in colour. The spleen was palpable almost as low as the level of the umbilicus. The liver was likewise greatly enlarged, and its left lobe could be differentiated from the spleen only with difficulty. The feet and ankles were œdematous, and evidence of the existence of fluid in the abdomen was easily discoverable. An examination of the blood at the time of admission revealed 72,500 leucocytes, a differential count of which exhibited a preponderance of lymphocytes, especially of the large variety. The red cells numbered 1,536,000. Poikilocytosis was apparent, but no nucleated red cells were detected in the course of numerous examinations, until after the lapse of several days. After ten days in the hospital, during which period the patient's temperature was normal, except as noted upon admission, there occurred suddenly and without definable reason a chill lasting half an hour, followed by elevation of temperature to 105° F. After this the white cells were found to number 568,000, and the stained specimen contained numbers of nucleated red cells. Except for such periods as the one just described, the patient felt quite well, although slightly weak. There were no digestive disturbances, so that absorption was probably good.

The table of results (Table II.) bearing upon the examination of the urine from this patient, while it largely explains itself, contains a number of points that merit emphasis. It will be observed that the daily output of total phosphates exhibits considerable variations in the absolute figures, ranging from 0.77 gm. to 3.56 grms., as contrasted with the normal output of 2 grms. The percentage of organic phos-

<sup>1</sup> In the beginning of this study it was not possible to make the total nitrogen determination by the Kjeldahl method, but in order to obtain some information concerning the nitrogen metabolism, urea was determined by the sodium hypobromite method. Because of the comparative uncertainty of this method, however, the figures so obtained were not used to establish ratios, but remain merely as absolute values. Later, when it became practicable to employ the Kjeldahl apparatus, the total nitrogen excretion was determined in every instance, and the urea determinations were continued in a few cases for a short time as a means of comparison.

phorus in the total excretion is seen to be almost always high, varying from 2 per cent. to 89 per cent. This would seem to indicate periods of phosphorus retention followed by an exaggerated output, the whole pursuing a somewhat rhythmical course. In the light of observation that, under normal conditions, a small part of the total phosphorus output exists in organic combination, and because of the discovery in the patient whose case is now under consideration and in other pathological conditions, of both a relative and absolute increase in the excretion of organic phosphorus, often reaching limits heretofore unsuspected, it is difficult to reconcile with the results of this investigation one of the statements occurring in the report of a study of nuclein metabolism in lymphatic leukæmia recently made by Henderson and Edwards<sup>(8)</sup>. These workers state, rather indefinitely, that "in order to discover whether there might not be an elimination of phosphorus in organic combination, a number of determinations were made of the total amount after evaporation of a sample of urine and ignition with sodium hydroxide and potassium nitrate. The results, however, agreed entirely with those obtained by the titration method"! The figures representing the excretion of inorganic phosphates, in the cases now under consideration, taken alone, would hardly indicate the true index of phosphorus metabolism, since, in many instances, they do not represent any decided variation from the normal, but in reality the total output is seen to be much greater when the inorganic and organic compounds are considered together. Lack of consideration of this very point has, I believe, contributed in great measure to the confusion that now obtains concerning nuclein metabolism, for the output of total phosphates and of inorganic phosphates has been regarded as practically identical, so that, as already stated, the determination of the latter has been regarded as equivalent to the determination of the former. From this it appears that no phosphorus determination is in any degree accurate which fails to define both the inorganic and organic compounds excreted. The latter point is illustrated in almost every determination contained in the following tables, where the percentage of organic phosphorus in the total output is almost always far above the normal.

Returning to the consideration of the table, it is worthy of note that the ratio between the total excretion of nitrogen and the total output of phosphorus is sometimes high and at other times within normal limits. On the other hand, the ratio between the total nitrogen excretion and the output of organic phosphorus is practically always very high, the normal ratio varying between 100:0.0560 and 100:0.479, as contrasted with the variations set forth in Table II.

2. In nervous lesions of the degenerative type a number of determinations have been made, and the results incorporated in Table III. It is seen that the excretion of organic phosphorus in

TABLE II.—*Lymphatic Leukemia. Male, et. 59.*

Date.	Total Quantity.	Specific Gravity.	Total Nitrogen.	Urea.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Total Nitrogen : Total $P_2O_5$ .	Total Nitrogen : Organic $P_2O_5$ .	Percentage Organic $P_2O_5$ in Total $P_2O_5$ .	Leucocytes.	Remarks.
1904. May 28	C.c. 1075	1018	Grms. ...	Grms. 19.30	Grms. ...	Grms. 2.78	Grms. 1.56	Grms. 1.22	...	..	41.0	64,600	Typical chronic course. Cells moderately large; uniform in size.
" 29	1200	1015	...	16.80	0.40	1.39	0.86	0.53	...	...	37.0	...	
" 30	1360	1013	...	19.40	0.50	1.03	0.68	0.35	...	..	33.0	...	
" 31	860	1015	...	10.30	...	0.77	0.34	0.43	...	...	56.0	...	
June 13	1800	1020	...	11.00	0.65	1.65	0.93	0.72	...	...	43.0	June 7	Peculiar degenerative forms in shape of large blotches.
" 14	2580	1013	...	12.90	0.35	1.80	0.72	1.08	...	...	60.0	434,000	
" 15	2510	1016	...	15.00	0.33	1.45	0.95	0.50	...	...	30.0	...	
" 16	1950	1015	...	19.50	0.37	1.09	0.11	0.98	...	...	89.0	...	
" 17	1610	1018	...	20.90	0.44	1.12	0.83	0.29	...	...	25.0	...	Progressive anemia, becoming pronounced toward end of June with the appearance of nucleated red cells, and a red count of—1,136,000.
" 18	2200	1015	...	26.50	0.20	1.36	0.88	0.48	...	...	35.0	296,000	
" 19	2125	1015	...	25.50	0.64	2.88	0.97	1.91	...	...	66.0	...	
" 20	1400	1020	...	19.60	0.57	1.12	0.50	0.60	...	...	53.0	...	
" 21	1720	1020	12.16	27.52	0.58	1.65	1.03	0.62	100 : 13	100 : 5.0	37.0	...	
" 22	2030	1020	13.90	30.45	0.50	1.14	0.81	0.33	100 : 8	100 : 2.3	28.0	...	
" 23	1600	1018	13.40	25.60	0.58	2.24	1.00	1.24	100 : 16	100 : 9.2	55.0	...	
" 24	2000	1018	14.28	34.00	0.71	2.40	1.28	1.12	100 : 16.5	100 : 7.2	46.0	302,000	

25	1740	1020	13.00	29.60	0.65	1.70	1.07	0.63	100.13	100:4.8	37.0	...
26	1950	1016	12.30	29.20	0.54	1.75	1.36	0.39	100.14	100:3.1	22.0	...
27	1960	1017	12.55	29.40	0.29	2.54	2.15	0.39	100.20	100:3.1	15.0	...
28	2100	1020	14.70	33.60	0.98	3.36	1.97	1.39	100.22	100:9.4	41.0	...
29	1910	1015	12.03	30.50	0.35	2.27	1.22	1.05	100.19	100:8.7	46.0	...
30	1950	1016	15.56	29.25	0.51	2.73	2.14	0.59	100.17	100:3.7	21.0	...
July 1	2000	1016	14.56	32.00	0.71	2.92	2.32	0.60	100.20	100:4.0	20.0	...
2	1800	1017	13.35	...	0.58	3.56	1.98	1.58	100.26	100:11.8	44.0	...
3	1910	1018	13.10	...	0.64	2.61	1.91	0.70	100.19.9	100:5.3	26.0	...
4	1680	1015	11.00	...	0.59	2.15	2.01	0.14	100.19	100:1.2	06.5	...
5	2125	1015	15.31	...	0.69	2.75	2.45	0.30	100.17.8	100:1.9	10.0	...
6	1750	1015	12.74	...	0.65	2.24	1.92	0.32	100.17.5	100:2.5	14.0	...
7	1500	1015	11.13	...	0.53	1.93	1.89	0.04	100.17	100:0.35	02.0	...
8	1465	1015	9.81	...	0.73	2.07	1.69	0.38	100.21	100:3.8	18.0	376,000
9	2115	1015	15.06	...	0.70	2.53	2.23	0.30	100.16	100:1.9	11.0	...
10	1850	1015	13.00	...	0.55	1.59	1.48	0.11	100.12	100:0.80	06.9	...
11	1600	1015	10.30	...	0.55	2.11	1.85	0.26	100.20	100:2.0	12.0	...
12	1860	1015	11.45	...	0.76	2.83	2.23	0.60	100.24	100:5.0	21.0	...
13	1900	1017	8.50	...	0.75	1.86	1.52	0.34	100.21.8	100:4.0	18.0	...
14	1800	1015	12.00	...	0.76	1.94	1.80	0.14	100.16	100:1.1	07.0	...

TABLE III.—*Nervous Lesions.*TABES. MALE, *et. 51.*

Date.	Total Quantity.	Specific Gravity.	Urea.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Per-centage Organic $P_2O_5$ in Total $P_2O_5$ .	Remarks.
1904. May 21.	C.c. 1830	1012	Grms. 21.90	Grm. ...	Grms. 3.14	Grms. 1.09	Grms. 2.05	64.0	...
" 23.	" 1250	1016	16.25	"	1.32	0.87	0.45	34.0	...
June 11.	" 2280	1012	18.24	0.51	1.27	0.82	0.45	35.0	...
" 13.	" 2500	1009	6.15	0.28	1.60	1.30	0.30	18.0	...
" 17.	" 2340	1010	22.20	0.042	1.31	0.93	0.38	29.0	...

TABES. MALE, *et. 50.*

Date.	Total Quantity.	Specific Gravity.	Urea.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Per-centage Organic $P_2O_5$ in Total $P_2O_5$ .	Remarks.
May 24.	" 2130	1012	17.04	"	3.80	3.50	0.30	8.0	...
June 11.	" 1800	1017	14.40	0.15	1.44	1.18	0.26	18.0	...
" 12.	" 1120	1021	5.60	0.36	2.54	20.6	1.47	38.0	...
" 15.	" 1900	1015	22.80	0.07	2.31	1.82	0.49	21.0	...
" 19.	" 1700	1016	18.70	0.38	3.33	2.43	0.90	27.0	...
" 26.	" 1220	1020	19.50	0.39	3.05	2.56	0.49	16.0	...



CEREBELLAR ATAXIA. MALE, *et.* 40.

May 22.	.	.	.	3170	1010	25.30	...	4.50	2.09	2.41	53.0	...
" 28.	.	.	.	1250	1025	25.00	...	3.92	1.61	2.31	58.0	...
June 10.	.	.	.	1790	1017	18.90	...	3.58	2.39	1.19	33.0	...
" 11.	.	.	.	1910	1017	28.60	0.24	3.24	2.59	0.65	20.0	...
" 12.	.	.	.	2900	1012	14.50	0.32	2.32	1.39	1.00	48.0	...
" 15.	.	.	.	3000	1010	18.00	0.45	2.16	1.62	0.54	25.0	...

AMYOTROPHIC BULBAR PALSY. MALE, *et.* 55.

May 20.	.	.	.	1280	1012	...	...	1.92	0.76	1.12	58.0	...
" 23.	.	.	.	1360	1010	12.80	...	1.68	0.84	0.84	50.0	...

TABLES. MALE, *et.* 54.

May 30.	.	.	.	1450	1012	8.70	...	3.21	0.50	2.70	84.0	June 30. Total nitrogen = 5.65 grms. Total nitrogen to total $P_2O_5$ = 100 : 7. Total nitrogen to organic $P_2O_5$ = 100 : 1.
June 13.	.	.	.	900	1014	9.00	0.23	0.95	0.79	0.16	17.0	July 2. Total nitrogen = 4.88 grms. Total nitrogen to total $P_2O_5$ = 100 : 37. Total nitrogen to organic $P_2O_5$ = 100 : 7.
" 16.	.	.	.	1800	1010	9.00	0.017	1.08	0.18	0.90	83.0	
" 30.	.	.	.	730	1010	6.57	0.027	0.45	0.39	0.06	13.0	
July 2.	.	.	.	2550	1010	...	0.047	1.83	1.47	0.36	19.0	

TABLE IV.

## DIABETES MELLITUS. FEMALE, æt. 40.

Date.	Total Quantity.	Specific Gravity.	Total Nitrogen.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Total Nitrogen to Organic $P_2O_5$ .	Per-centage Organic $P_2O_5$ in Total $P_2O_5$ .	Remarks.
1904. July 4	C.c. 2350	1023	Grms. 8.34	Grms. 0.17	Grms. 4.13	Grms. 2.11	Grms. 2.02	100 : 49	100 : 24	Marked obstructive (?) jaundice. Syphilis twenty years ago. No aceto-acetic acid ; moderate amount acetone in distillate ; urine contained bile in large quantities, except specimen examined July 9, which was comparatively free.
" 5	1500	1025	5.29	0.045	1.50	1.29	0.21	100 : 28	100 : 18	
" 6	1780	1025	6.72	0.090	2.34	1.35	0.99	100 : 34	100 : 14	
" 9	2000	1025	7.84	0.11	2.20	1.44	0.76	100 : 28	100 : 9	

## ETHER NARCOSIS. FEMALE, æt. 19.

July 5	1100	1015	7.23	0.50	1.93	1.82	0.11	100 : 26	100 : 1.5	Patient on restricted diet.
" 11	1640	1013	10.56	0.57	3.14	2.95	0.19	100 : 29	100 : 1.7	" mixed diet.
" 13	750	1021	8.29	0.52	3.97	3.52	0.45	100 : 47	100 : 6.2	June 12. Laparotomy for double pyosalpinx. 125 grms. ether administered in one and a half hours by Dr. J. B. Talmage, jun.

TABLE IV.—*continued*.ENTERIC FEVER. MALE, *æt.* 26.

Date.	Total Quantity.	Specific Gravity.	Urea.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Per-centage Organic $P_2O_5$ in Total $P_2O_5$ .	Remarks.
1904. June 11.	C.c. 1580	1015	Grms. 23.70	Grms. 1.20	Grms. 3.31	Grms. 2.08	Grms. 1.23	37.0	June 11. Temperature, 105° F.
" 16.	"	1008	14.50	0.41	1.44	0.41	1.03	71.0	June 28. Total nitrogen = 18.30 grms. Total nitrogen to total $P_2O_5$ = 100 : 7.3. Total nitrogen to organic $P_2O_5$ = 100 : 2.6.
" 23.	1930	1013	21.20	0.51	1.73	1.34	0.39	22.0	July 10. Total nitrogen = 10.33 grms. Total nitrogen to total $P_2O_5$ = 100 : 11. Total nitrogen to organic $P_2O_5$ = 100 : 0.6.
" 25.	1670	1015	21.70	0.53	2.87	1.60	1.27	44.0	June 28. Convalescence established. Light diet.
" 28.	1875	1019	37.50	0.44	1.34	0.86	0.48	35.0	
" 30.	1050	1022	17.85	0.57	1.78	1.57	0.21	11.0	
July 10.	1640	1013	...	0.49	1.21	1.14	0.07	6.0	

ANKYLOSTOMIASIS. MALE, *æt.* 28.

Date.	Total Quantity.	Specific Gravity.	Urea.	Uric Acid.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Per-centage Organic $P_2O_5$ in Total $P_2O_5$ .	Remarks.
June 17.	690	1020	13.80	0.13	0.71	0.62	0.09	12.0	Moderate degree of anemia. History of vomiting of a year's duration. Pronounced loss of weight.
" 19.	650	1015	12.40	0.31	0.58	0.46	0.12	20.0	
" 21.	640	1018	10.80	0.26	0.62	0.47	0.15	23.0	

TABLE V.—*Pulmonary Tuberculosis (Ten Cases).*

Date.	Sex.	Age.	Total Quantity.	Specific Gravity.	Urea.	Total $P_2O_5$ .	Inorganic $P_2O_5$ .	Organic $P_2O_5$ .	Per-centage Organic in Total $P_2O_5$ .	Remarks.
1904. May 17	Male.	22	C.c. 570	1025	Grms. 26.80	Grms. 1.53	Grms. 1.18	Grms. 0.35	22.00	Moderate loss of weight.
" 19	"	38	1000	1019	9.80	1.70	1.20	0.50	28.00	Moderate loss of weight; signs at affected apex indefinite; tubercle bacilli abundant in sputum.
" 27	"	"	700	1018	...	1.09	0.85	0.24	22.00	
" 19	"	34	4260	1004	12.70	2.13	1.27	0.85	39.00	Wasting rapid and marked; spleen and liver enlarged. Great thirst; frequent elevation of temperature to 103° F. or 104° F. Moderate wasting.
" 22	"	30	1500	1015	21.00	1.65	1.23	0.42	25.00	" "
" 22	"	30	1560	1007	14.40	1.09	0.093	0.99	80.00	Tuberculous osteitis of knee.
" 26	"	33	1000	1018	24.00	2.76	2.50	0.26	9.40	
" 28	"	25	1250	1018	15.10	1.03	0.68	0.35	33.00	Marked wasting; diarrhoea; no vomiting.
" 19	"	28	680	1012	...	0.98	0.78	0.20	20.00	Marked loss of weight.
June 16	"	60	1500	1010	16.50	1.74	1.35	0.39	23.00	Uric acid = 0.43 grm.; severe secondary anaemia.
" 23	Female.	29	550	1024	20.00	2.03	1.81	0.22	10.00	Patient passed through attack of croupous pneumonia between June 22 and 30,—highest temperature being 103°-8 F. on June 23. Persistence of mild degree of fever after crisis. Later, tubercle bacilli found in sputum. Uric acid = 0.55 grm., 0.24 grm., and 0.15 grm. respectively.
" 28	"	"	950	1014	16.15	2.35	1.99	0.36	15.00	
" 30	"	"	900	1020	14.40	2.43	2.05	0.38	15.00	

this class of patients is subject to the same wide variation as in the case of the patient with lymphatic leukæmia, the percentage of organic phosphorus in the total output ranging from the extreme normal (?) limit of 8 per cent. in one case to 84 per cent. in another. While no case has been followed from day to day for any length of time, the records already obtained show that there are periods during which such patients conform to the same rhythm of apparent retention and exaggerated excretion. The patient represented in the table as cerebellar ataxia is remarkable in that, on one occasion, he excreted in twenty-four hours 3170 c.c. of urine, containing 2.41 grms. of phosphorus in organic combination, followed a few days later by 1250 c.c. of urine containing 2.31 grms.

3. and 4. In pulmonary tuberculosis (Table V.) and in conditions attended by lessened oxidation and increased decomposition, as in diabetes mellitus (Table IV.), ether narcosis, etc., a few observations have been made, but they cannot be regarded as sufficiently extensive to warrant definite deductions or detailed comment, and, for this reason, are incorporated with the results obtained in several miscellaneous cases, likewise deemed insufficiently investigated.

#### CONCLUSIONS.

1. That an appreciable and important amount of  $P_2O_5$  in organic combination is excreted in the urine in various pathological conditions, so that frequently 25 or 50 per cent., and, in occasional instances, almost all the  $P_2O_5$  appears in the organic state. Therefore, *the determination of the inorganic  $P_2O_5$  cannot be regarded as a true index of phosphorus metabolism.*

2. That the excretion of organic  $P_2O_5$  is to an extent rhythmical, periods of excessive excretion alternating with what may be either retention or diminished production, so that in cases in which an average output is to be established, frequent determinations must be made.

3. That the excretion of organic  $P_2O_5$  is pronounced in lymphatic leukæmia, where there is a marked change in ratios of nitrogen to organic  $P_2O_5$  as well as an absolute increase in the percentage of organic  $P_2O_5$  in the total  $P_2O_5$ , *while the ratio of nitrogen to total  $P_2O_5$  and to the inorganic  $P_2O_5$  shows little if any departure from the normal.*

4. In nervous diseases of the degenerative type the absolute amounts of organic  $P_2O_5$ , as well as their percentage in the total  $P_2O_5$ , are increased, sometimes to an enormous extent. It seems impossible that such amounts could be derived directly from the destruction of nervous tissues. In this connection the question of trophic influence assumes importance.

5. It seems unlikely that the increased excretion of  $P_2O_5$  could be derived, as has been suggested, from bone. We have confirmation

of this statement in the fact that in diseases in which bony structures are directly and extensively involved, *e.g.* osteomalacia, the output of  $P_2O_5$  has not been found increased. The foregoing observations, however, do lend weight to the assumption that the increased phosphorus output depends upon general metabolic causes, probably in the waste of organic phosphorised endogenous compounds. The abnormal increase of the organic  $P_2O_5$ , as shown especially in the ratio and percentage of organic  $P_2O_5$  in the total  $P_2O_5$ , may be explained in two ways—either it is an increase in the production of phosphorised endogenous metabolic compounds, or an expression of lessened oxidation, with the inorganic phosphates as the end product.

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