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ORGANIC AND INORGANIC PHOSPHORUS COMPOUNDS

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Concerning the behaviour in the body of certain organic and inorganic phosphorus compounds (1)

BY

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Phosphorus was discovered in 1669 by Brandt of Hamburg amongst the products formed by the distillation of the residue obtained by the evaporation of urine. It was not, however, until a century later that Gahn showed that it was a constituent of bones. Shortly after this, phosphorus and its compounds began to attract the attention of physicians and physiologists and to become of therapeutic interest. In the first instance, probably on account of its attractive physico-chemical properties, great virtues, in many cases as unwarranted as mystical, were attributed to it. In modern therapeutics, however, while the activity of the element itself and the physiological importance of certain of its combinations remain firmly established, yet nevertheless exact studies concerning the assimilation of different phosphorus compounds in the human body are few. Oddly enough, this seems especially true of the human child, a subject a priori most likely to give interesting results in this connection on account of the relationship of phosphorus to growth metabolism. The universal presence of phosphorus in the tissues and tissue elements of the organism and in its natural food, as also the difficulty of separating the phosphorus chemically from certain proteids without entirely destroying them, makes it almost certain that phosphorus has an essential importance for the life of the cell and for the biochemical processes going on within it.

Phosphorus (2), as we take it, exists in one or other of two forms

⁽¹⁾ A paper read at the International Congress of Medicine at Lisbon, 1906.

⁽²⁾ The term phosphorus throughout this paper refers to phosphorus in combination and not to the element.

which may be termed inorganic and organic. The inorganic phosphorus compounds, of which the official calcium phosphate $Ca_3(PO_4)_2$ may serve as a type, contain their phosphorus directly attached to a metallic ion. The phosphoric acid in these compounds can be demonstrated chemically by means of molybdic acid. Substances of this class have long been given as medicinal agents and have earned upon clinical grounds a reputation of exerting a nervine tonic action and of acting as adjuvants to growth, especially of bone, which latter substance consists largely of calcium phosphate.

The other form in which we meet with phosphorus dietetically and therapeutically is in so-called organic combination. These organic compounds of phosphorus are, from a chemical standpoint, in many instances very complex and may be regarded as being built up on the type of phosphoric acid, by the replacement of its hydrogen atoms by complex organic radicles, which latter have also in certain instances their hydrogen atoms likewise replaced by other organic radicles. The most notable instance of such a substance is lecithin which may be regarded as derived from phosphoric acid and glycerine, first of all by the esterification of one of the hydroxyl groups of the latter and the subsequent replacement of the two remaining hydroxyls of the glycerine by two stearyl radicles, and the combination of the resulting di-stearo-glycerophosphoric acid with the base cholin. This substance lecithin and its congeners cephaline and protagon form essential constituents of the nervous system and are so immediately concerned in its functional activity as to give rise to the dictum that without phosphorus there can be no thought.

To pass from the nervous system to the other tissue cells we find organic phosphorus compounds present as nucleins and nucleo-albumins, especially in such organs as the muscles, the thymus gland, the thyroid gland, the liver, the kidneys, and the spleen. The phosphoric acid rest as it exists in these organic combinations cannot be demonstrated by the molybdic acid reaction and must, moreover, be regarded as being directly attached not to a metallic ion but to an organic radicle. Our ordinary food contains phosphorus in both organic and inorganic form; recently, however, a number of substances which may be regarded as partly foods and partly medicines, consisting of more or less complicated organic phosphorus compounds, have found extensive therapeutic use and seem to be gradually replacing the older inorganic phosphates.

The history of this subject is of sufficient interest to justify us in

entering into it somewhat in detail. As early as 1875 Brücke (1) drew attention to the nutritional importance of egg yelk (lecithin). Some 20 years later this subject was taken up by DANILEWSKY (2), whose researches may be regarded as forming essentially the foundation of the modern therapeutic use of lecithin. According to this observer lecithin even in the most minute doses exerted an extraordinarily favourable influence upon nutrition. Its effect in this regard must belong to the class of action known as catalytic, or similar to that of a ferment. The experiments, however, made on animals by Sorono were not entirely confirmatory of the work of Danilewsky. According to Sorono (3) lecithin was not absorbed as such but was split up by the action of a ferment in the digestive tract. After lecithin attention was next directed to the glycero-phosphates, mainly because phosphorus was contained in lecithin in the form of a glycero-phosphate and it was thought that by the supply of a glycero-phosphate to the organism its lecithin loss could be covered. Bulow (4) and PASQUALES (5) showed that the glycero-phosphates of the food as those from the organism itself were decomposed in the body and excreted in the urine as phosphoric acid. Pasquales after feeding with glycero-phosphoric acid demonstrated considerable quantities of this substance in the blood and expressed the view that its action was due to the nascent phosphoric acid developed from it. The observations of ROBIN (6) upon the excretion of phosphorus compounds in neurasthenia and the experiments of Sanson (7) (who showed that the phosphorus balance could be increased by the administration of the glycero-phosphates) led to the extensive use of these substances as nervine tonics and stimulants.

The next class of organic phosphorus compounds to receive attention on account of their possible therapeutic value were those substances in which the phosphorus was in combination with proteids. Numerous bodies of this class have been investigated, the chief one being perhaps casein. Most observers seem agreed that the phosphorus of these compounds is absorbed practically in its entirety. The results with nuclein,

⁽I) BRÜCKE: Vorlesungen über Physiologie, 1875.

⁽²⁾ Comptes rendus de l'Académie des Sciences, Dec. 30th, 1895, and July 20th, 1896.

⁽³⁾ Archives Italiennes de Biologie, 1897, vol. XXVII., p. 349.

⁽⁴⁾ Pflügers Archiv, 1894, vol. VII.

⁽⁵⁾ Annales de Chimie et de Pharmacie, 1884, vol. XX.

⁽⁶⁾ ROBIN : Bulletin de l'Académie de Médecine, 1894.

⁽⁷⁾ Comptes rendus de la Société de Biologie, 1896.

however, seem contradictory (1); some workers finding that the administration of this substance in the food causes a retention of phosphorus and nitrogen in the body in the same proportion as these elements existed in the introduced nuclein, others (2) that nuclein and its derivatives stimulate proteid katabolism, causing an increase in the excretion of P_2 O_5 at the cost of the organic phosphorus compounds in the body. Before leaving the history of this question I should mention the work of ILJIN (3) upon the beneficial influence of organic phosphorus upon the assimilation and retention of nitrogen. This effect of organic phosphorus compounds may now be regarded as established.

Almost simultaneously with the researches above described upon the therapeutic value of organic phosphorus considerable work was being done from a more purely physiologico-chemical standpoint in order to elucidate the question of phosphorus metabolism and to what extent, if at all, the body was capable of building up from simple inorganic phosphates those complicated organic phosphorus compounds which admittedly performed so important a rôle in essential bio-chemical processes. It is not germane to the present work to enter into these researches in detail and I shall merely enumerate the views, mainly three, which have, so to speak, crystallised out from them. HAMMARSTEN (4) regards phosphorus and nitrogen excretion and retention as having a fixed quantitative relationship approximately as 1 is to 8. Other later workers have failed to corroborate this and the view now held is that these two substances can be retained in, or excreted by, the body quite independently of each other. RÖHMANN (5) and his pupils maintain that the organism cannot utilise inorganic phosphates for the purpose of building up complicated organic phosphorus compounds. Ehrström (6) from his exhaustive researches concludes that this dictum cannot be regarded as established and that the behaviour of the inorganic phosphates when administered in the food is at present not clearly known.

⁽¹⁾ Lowi: Sitzungberichte der Gesellschaft zur Beförderung der Naturwissenschaft, Marburg, 1900. JACOB und BERGELL: Zeitschrift für Klinische Medicin, vol. XXXV., 1898. VIDE KELLER: Die Verwendung der organischen Phosphor-Verbindungen, Zeitschrift für Physikalische und Diätetische Therapie, vol. IV., p. 669.

⁽²⁾ MALCOLM and MILROY: Journal of Physiology, 1899.

⁽³⁾ WRATSCH, 1901, No. 22, p. 1132.

⁽⁴⁾ Vide Buchmann: Zeitschrift für Physikalische und Diätetische Therapie, vol. VIII.

⁽⁵⁾ RÖHMANN: Berliner Klinische Wochenschrift, 1898.

⁽⁶⁾ Skandinavisches Archiv für Physiologie, vol. XIV.

A subject nearly allied to the above question, and one forming the most essential subject matter of this paper-viz., the relative value as sources of phosphorus to the organism, and as influencing the assimilation of nitrogen, of phosphorus in organic and inorganic combination has not received much attention at the hands of pharmacologists. Vos-GIEN and CEROLINE (1), working on animals, found that inorganic phosphates were absorbed from the alimentary canal and influenced nutrition at least to the same extent as the glycero-phosphates. The only comparative experiment made on the human subject of which we are aware is that of Keller (2). This observer made a complete phosphorus metabolism experiment in two children, aged a few months, one sickly and one healthy. The only nourishment in the case of the sick child was human milk and the only nourishment in the case of the healthy child was cow's milk. To each child's milk KELLER added for an equal period an equal quantity of sodium phosphate and found in the case of both children that during the sodium phosphate period more phosphorus was retained in the body than could be accounted for by the organic phosphorus of the food. From his researches Keller infers that at least one half of the phosphorus retained in the body was derived from the sodium phosphate. Some comparative experiments which he intended to carry out on the same children, and in which both an organic phosphorus compound and sodium phosphate were to be added for equal periods of time to the respective milks, unfortunately broke down, so therefore no control was really established and no comparison between the action of an organic and an inorganic phosphorus compound is obtainable from these observations. Moreover, the experiments as such are not convincing, one of the children at least being in a condition of "phosphorus hunger," i.e., having a large negative phosphorus balance at the time the sodium phosphate was added to the milk. This experimental error is, indeed, pointed out by KELLER himself who, having these observations of his own and the others quoted by us before him, sums up the question of the relative value of organic and inorganic phosphorus in the following words: "The main question remains unanswered-viz., whether organic phosphorus so far as concerns its assimilation by and retention in the body achieves more than the ordinary phosphates."

⁽¹⁾ Comptes rendus de la Société de Biologie, 1899, p. 770.

⁽²⁾ KELLER: Archiv für Kinderheilkunde, 1900, vol. XXIX, p. 54.

Having in view this state of the subject the observations which follow were planned, their object being to help in the elucidation of the following questions. (1) Whether in the healthy human child it is possible by increasing the phosphorus of the diet to increase the amount of phosphorus retained in the body; (2) to compare the value as sources of phosphorus to the body of an inorganic and organic phosphorus compound; and (3) to observe the effect of an inorganic and an organic phosphorus compound upon proteid assimilation.

The organic phosphorus compound used for these experiments was a compound of glycero-phosphoric acid and pure casein, a substance known as Sanatogen (1). This substance was chosen as containing two varieties of organic phosphorus, viz., that contained in the glycerophosphoric acid and that contained in the casein; when giving this substance we were at once administering a proteid phosphorus compound in a state of purity and sodium glycero-phosphate or what may be regarded as an organic phosphorus lecithin rest. This compound is further quite free from inorganic phosphorus and hence in using it we were quite sure that the extra phosphorus supplied in the diet was all of the organic variety. Another reason which influenced us in choosing Sanatogen as our type of an organic phosphorus compound was the recognised clinical value of this substance in cases of mal-nutrition, which value heretofore has been attributed entirely to the proteid moiety of the substance. The literature upon this subject is so ample that space does not allow individual mention of it. It was probably for similar reasons that Keller worked with the same substance, regarding it as a typical example of an organic phosphorus compound.

Sanatogen in our hands gave upon analysis 13.14 per cent. of nitrogen and 1.32 per cent. of phosphorus; figures closely approximating to those given by König (2).

The substance chosen as a type of an inorganic phosphorus compound was the calcium phosphate of the B.P., which contains 20 per cent. of Phosphorus. The inorganic phosphorus compound used by Keller was phosphate of sodium.

The subjects of these researches were two children, a boy aged two years, and a girl, aged two years and ten months; they will subsequently be referred to as A and B. They were quite healthy, well fed and

⁽¹⁾ König: Die menschlichen Nahrungs und Genussmittel, 4th edition, vol. II, p. 222.

⁽²⁾ Loc. cit., vol. II., p. 539.

looked after before they became the subjects of these observations. This fact is to be noted, as in neither child was there any question of "phosphorus hunger." They were kept under observation for some time before the actual experiment began and their life was uniformly regulated and supervised by a lady trained in the conduct of metabolic experiments. The total nitrogen and phosphorus was estimated in all ingesta and egesta and in no case were so-called average figures taken: No attempt was made to discriminate between organic and inorganic phosphorus in the food or ejecta, nor for the same reason were the bases K, Na, Ca, or Mg estimated. The experimental periods were arranged, the urine and fæces correspondingly were separated and collected, and the diet arrangements were conducted in an exactly similar manner to that described in former metabolic experiments (1). The methods of chemical analysis were also identical with those used in the former experiments. We have again to thank the Aylesbury Dairy Company for supplying us with pasteurised milk in large quantities from the same churn and with preservative free butter of uniform composition.

In the case of each child the nitrogen metabolism table is given along with the phosphorus one. The work of previous observers quoted by König had adequately demonstrated the complete and rapid absorption of the proteid moiety of the sodium glycero-phosphate of casein and any prolonged discussion of this subject is unnecessary; nevertheless, the influence of an organic phosphorus compound upon the assimilation of the total proteid of the diet has never been studied in the case of the human child and is obviously of interest. It is for the purpose of demonstrating this influence that the nitrogen metabolism of both children is given in full. Table I shows the percentage composition of the foods consumed.

TABLE I.

		Fo	Nitrogen per cent.	Phosphorus per cent.			
Meat (I)					 	3.22	0.15
Meat (11)		***			 	3.09	0.12
Meat (III)					 	3.02	0.10
Bread					 	1.35	0.08
Milk					 	0.56	0.10
Butter					 	0.10	
Apple comp	ote				 	0.07	0.03
Sanatogen					 	13.14	1.32
Calcium Pho	sphat	te (Ca.	(PO,)	.)	 		20.00

⁽¹⁾ I should like to express my indebtedness to my friend, Dr. Otto Rosenheim, for much help in this research.

For the sake of clearness we shall treat each child separately.

OBSERVATION 1: Child A .- The child was a boy, aged two years, and weighed at the beginning of the experiment 11.683 kilogrammes. He remained in good health during the experiment and took the following food daily: meat, 30 grammes; Milk, 500 cubic centimetres; butter, 20 grammes; bread, 175 grammes; apple compote, 50 grammes; water, 100 cubic centimetres; and toffee, 10 grammes. It occasionally happened that he did not consume the whole of this food; his leavings of each article were weighed and deducted from the above amount and in constructing the nitrogen and phosphorus diurnal tables a corresponding allowance was made by calculation. The child's nitrogenous metabolism was under observation for 11 days; of these, two were devoted to the fore period in which the child had the above diet only. The next six days composed the organic phosphorus period in which in addition to the above diet 20 grammes of Sanatogen (1) were consumed per diem. The remaining three days formed the so-called after period but were also utilised for the purpose of investigating the influence of an inorganic phosphorus compound, viz., Ca₃(PO₄)₂, upon nitrogenous metabolism; the diet thus differing during this period from that during the fore period in that to it was added per diem one gramme of calcium phosphate. In the case of this child the phosphorus metabolism during this last period was not worked out. Table II. gives the results of this observation.

Referring to Table II., we purpose classifying our remarks under the following headings:—

Nitrogenous metabolism.—During the fore period the daily quantity of nitrogen taken in the food was 5.95 grammes; of this quantity 0.98 gramme was not assimilated, being lost with the fæces, corresponding to 16.47 per cent. From this it follows that the assimilation of nitrogen during the fore period amounted to 83.53 per cent. From our earlier observations upon nitrogenous assimilation in children we should regard this as being an average figure. The daily amount of nitrogen excreted with the urine was 2.21 grammes, and if we subtract this from the total amount assimilated, we obtain the figure 2.75 grammes, which represents the nitrogen balance or that amount of nitrogen actually retained

⁽¹⁾ Sanatogen was given in two doses of about two teaspoonfuls each.

TABLE II.

Body weight in kilogrammes.			9.11	9.11	1	1	9.11	9.11	11.7	8.11	11.8	6.11	+300	+ 50	6.11	6.11	6.11	1	1
LISM	noi	Phosphorus assimilation %		1	1	73.91	1	1	1	1	1	1	1	78.76	1	1	1	1	1
PHOSPHORUS METABOLISM		Balanc umerg ni	1	1	0.76	0.38	1	L	1	1	1	1	2.93	0.49	1	1	-	1	1
INS MI	horus in	Food.	99.0	0.71	1.39	69.0	0.97	0.97	0.97	96.0	96.0	96.0	5.79	96.0	1	1	1	1	1
PHOR	Grms. of Phosphorus in	Fæces.	0.26	0.10	0.36	0.18	0.15	0.13	0.33	0 24	91.0	0.22	1.23	0.20	1	1	1	T	1
PHOS	Grms.	Urine.	0.24	0.03	0.27	0.13	0.24	0.19	0.00	0.41	0.33	0.37	1.63	0.27	1	1	T	1	1
	uo	Nitroge assimilati %	1	1	1	83.53	1	1	1	1	1	1	70.19	1	I	1	1	1	84.77
M.	Balance		1	1	5.51	2.75	1	1	1	1	1	1	24.49	4.08	1	1	1	4.46	1.48
METABOLISM		negortiN boot semmerg)	5.72	6.19	16.11	5.95	8.82	8.82	8.82	8.79	8.79	8.79	52.83	8.80	5.57	5.57	6.13	17.27	5.76
META		Nitrogen (grammes).	1.5	0.47	1.97	86.0	29.0	0.62	1.25	0.83	0.54	0.81	4.72	0.78	1.31	09.0	0.72	2.63	0.88
	FÆCES	Dry (grammes).	17.5	8.5	26.0	13.0	12.0	11.0	20.5	14.0	9.0	13.5	80.0	13.3	12.2	10.0	12.0	34.2	11.4
NITROGEN		JaioM (genmerg).	71.5	42.5	0.411	57.0	43.5	43.0	76.5	50.0	33.0	48.5	294.5	49.1	42.8	36.0	41.0	8.611	39.9
Z	NE.	Nitrogen (grammers).		0.53	4.43	2.21	3.94	2.31	1.12	5.58	4.59	80.9	23.62	3.93	2.94	3.48	3.76	10.18	1
	URINE	Quantity (C. C.)	217	30	247	123	204	132	64	270	206	257	1133	188	192	194	230	919	1
-	Day of Experiment.			7	2 days	ı day	3	4	5	9	7	00	6 days	1 day	6	IO	11	3 days	I day
	7715	To so set		:	:					die die	THE REAL PROPERTY.	78 T	:	:	la se	:	7 19	:	-
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op.				1	1	:			perio	1			:	:		:		:	-
	PERIOD.			:	:	:			phorus				:	:		:		:	:
				rore period	Total	Average			Organic phosphorus period	1		100	Totai	Average		After period		Total	Average
I			1 5	1	To	Av			0	,			To	Av		Aff		To	Av

in the body. The body-weight during the fore period remained constant.

If we adopt precisely the same reasoning and referring to the same table turn our attention to the figures of the organic phosphorus or Sanatogen period we find that the percentage of nitrogen assimilated increased to 91.07 per cent., or to the extent of nearly 10 per cent., and that the nitrogen balance also increased from 2.75 grammes to 4.08 grammes, and that also the body-weight underwent an average augmentation of 50 grammes per diem. Adopting for the third time the same reasoning and applying it to the after period in which the child's diet was the same as that consumed during the fore period except that he received 0.2 gramme of phosphorus per diem in the form of calcium phosphate, we find that the nitrogen assimilation went back to 84.77 per cent., and the nitrogen balance to 1.48 grammes, or approximately to the amounts obtaining during the fore period. Before drawing the conclusions from this observation we will consider the phosphorus metabolism results.

Phosphorus metabolism.—The daily amount of phosphorus in the food during the fore period was 0.69 gramme. Of this 0.18 gramme was lost, being voided with the fæces; consequently 0.51 gramme was assimilated, amounting to 73.91 per cent. of the total phosphorus in the food. Of the 0.51 gramme assimilated, 0.13 gramme was excreted in the urine; thus 0.38 gramme was retained in the body and constituted the phosphorus balance.

If we adopt this method of calculation and apply it to the second or organic phosphorus period, we find that the phosphorus in the food has been increased to the extent of 0.27 gramme per diem by the addition of 20 grammes of Sanatogen to the diet. The total amount of phosphorus consumed per diem during this period thus amounts to 0.96 gramme. The phosphorus contained in the fæces corresponding to this period has increased to 0.20 gramme, or to the extent of two centigrammes. The amount of phosphorus assimilated has also increased to 78.76 per cent. Of the 0.76 gramme of phosphorus daily assimilated during this period 0.27 gramme was excreted daily in the urine, thus leaving 0.49 gramme as the phosphorus balance. We can before leaving them look at these figures in another light. From them it appears that by increasing the phosphorus in the diet to the extent of 0.27 gramme

we only increase the phosphorus in the fæces to the extent of 0.02 gramme. In other words, 93 per cent, of the phosphorus added to the diet in the form of Sanatogen was assimilated. The analytical figures given above justify the following conclusions from the observations made on child A:—

- 1. NITROGENOUS METABOLISM.—The addition of an organic phosphorus compound was followed by a very considerable increase in the assimilation of the proteid constituents of the diet. The addition to the diet of an inorganic phosphorus compound calcium phosphate, had no favourable influence upon the amount of the proteid food assimilated.
- 2. Phosphorus metabolism.—The analytical figures obtained in this connection confirmed the results of earlier observers in that they show that phosphorus metabolism runs a course quite independently of nitrogenous metabolism and that no fixed proportion exists between the retention or excretion of these two elements. The figures further show that by the administration of an organic phosphorus compound, such as Sanatogen, we can increase both the amount of phosphorus retained in the body, and also the proportion of the phosphorus of the diet assimilated; in other words, that this substance is both a source of phosphorus to the body and also exerts a favourable influence upon the assimilation of the other phosphorus constituents of the diet.

OBSERVATION 2: Child B .- The subject of this observation was a healthy girl, aged two years and ten months and weighing 13.4 kilogrammes. She remained in good health during the experiment. The observation was carried on concurrently with that on child A and under similar conditions. The diet for this child was the same as for child A except that instead of 175 grammes of bread per diem, 200 grammes were given. The diet was well taken. In the case of this child the period of observation was much longer as both the phosphorus and nitrogen metabolism were observed for 12 days. These days were divided into a fore period of three days, an organic phosphorus or Sanatogen period of six days, and an inorganic phosphorus period of three days, which latter period served also, as far as the nitrogenous metabolism was concerned, as an after period. In the case of this child we were able to observe and compare the action of an organic and an inorganic phosphorus compound, not only as in child A upon the nitrogenous metabolism, but also upon the phosphorus metabolism itself.

TABLE III.

Body Weight in kilogrammes.			13.4	1	13.45	0.05	0.017	13.45	13.45	13.60	13.55	13.65	13.80	0.36	90.0	13.8	13.8	13.9	0.10	0.033
LISM	uo sn.	Balance in grammes. Phosphorus assimilation %		1	1	79.45	1	1	1	1	1	1	1	1	87.93	1	1	1	1	72.41
PHOSPHORUS METABOLISM				1	1	0.81	0.27	1	1	1	1	1	1	2.65	0.44	1	ļ	1	1	0.35
US MI	norus in	Food.	0.73	0.73	0.73	2.19	0.73	0.99	0.99	66.0	96.0	86.0	86.0	5.91	66.0	0.87	0.87	0.87	2.61	0.87
PHOR	of Phosphorus in	Fæces.	0.11	0.22	0.11	0.44	0.15	0.22	0.09	1	0.20	1	0.20	0.71	0.12	0.15	0.35	0.21	0.71	0.24
PHOS	Grms.	Urine.	0.32	0.31	0.31	0.94	0.31	0.23	0.31	0.57	0.57	0.36	0.51	2.55	0.43	0.27	0.36	0.22	0.85	0.28
	uo	Nitrogen assimilation %		1	1	1	88.51	1	1	1	1	1	1	1	95.06	1	1	1	1	96.98
M.	Balance.		1	1	1	1	2.56	1	1	1	1	1	1	22.27	3.72	1	1	1	7.27	2.45
METABOLISM	3-3	Nitrogen food (grammes)	6.53	6.53	6.53	19.59	6.53	9.16	9.16	9.16	9.13	9.13	9.13	54.87	9.14	5.80	5.80	5.80	17.40	5.8
IETAI		Nitrogen (grammes).	0.52	1.23	0.51	2.26	0.75	0.99	0.70	1	1.3	1	1.37	4.36	0.72	0.57	1.00	0.70	2.27	92.0
	FÆCES	Dry (grammes).	10.0	21.5	8.0	40.0	13.3	15.6	11.5	1	20.5	1	16.5	64.1	10.7	13.0	16.5	12.5	42.0	14.0
NITROGEN		faioM (semmerg)	30.5	72.5	30.0	126.0	42.0	58.0	0'09	1	67.5	1	62.5	248.0	41.3	34.0	61.5	35.5	131.0	43.7
Z	NE.	Nitrogen (grammes).	3.72	3.49	2.47	89.6	3.22	2.32	2.91	6.04	6.53	4.25	6.17	28.24	4.70	2.42	3.22	2.22	7.86	2.62
	URINE.	Quantity (C. C.)	342	208	255	805	268.3	192	203	331	328	205	325	1584	247	204	271	138	613	204
ι,	Day of Experiment.			2	3	3 days	ı day	4	5	9	7	8	6	6 days	ı day	10	11	12	3 days	ı day
		of george				:	:	100			:		0.00	:	:				:	:
						:	:			-				:	:		:		:	:
DD.				or I would be					Period						:		Period		-	:
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	a, The Hope			poin		:	:			Dhoe	1 103			:	:		1 Phos			:
-		Fore Period		Total	Average		Organic Phosphorus Period					Total	Average		Calcium Phosphate Period		Total	Average		

Table III. gives the figures obtained in this observation. In reviewing them we shall not enter into such detail as in the former instance, but shall treat them in the same order.

Nitrogenous Metabolism.—In the fore period the proportion of the nitrogenous food assimilated was 88.51 per cent. During this period an average increase of weight of approximately 20 grammes per diem took place. If we now turn our attention to the Sanatogen period we find that not only is the amount of nitrogen retained in the body increased, but that the administration of this form of phosphorus was followed by an increase in the percentage of the nitrogenous food assimilated. In the third period, in which the organic phosphorus corresponding approximately to the Sanatogen was replaced by calcium phosphate, the nitrogen balance fell to practically the fore period level and the percentage of nitrogenous food assimilated fell slightly below its fore period level. Hence the conclusions which we can draw concerning the influence of an organic and an inorganic phosphorus compound upon nitrogenous metabolism are the same in this child as in child A.

PHOSPHORUS METABOLISM.—During the fore period, which lasted for three days, the average amount of phosphorus in the food was 0.73 gramme per diem; of this 0.15 gramme was lost, being voided with the fæces, and consequently 0.58 gramme was assimilated or approximately 79 per cent of the total phosphorus ingested. During the organic phosphorus period the phosphorus in the food was increased to 0.99 gramme per diem, 0.26 gramme of this being derived from the 20 grammes of Sanatogen given. Of this 0.99 gramme only 0.12 gramme appeared in the fæces. The daily amount assimilated was therefore 0.87 gramme, or approximately 88 per cent of the total phosphorus ingested. From these figures it can be inferred that the whole of the phosphorus added to the diet in the form of sodium glycero-phosphate of casein was absorbed and that this substance also exerted a favourable influence upon the assimilation of the other phosphorus constituents of the food. The three days following the Sanatogen period were occupied by watching the effect upon the child's phosphorus metabolism of the addition of one gramme of calcium phosphate per diem to the diet. By this means the total phosphorus of the food was increased as compared with the fore period from 0.73 gramme to 0.87 gramme per diem. Of this 0.87 gramme 0.24 gramme was lost, being excreted in the fæces; in other words, during the inorganic phosphate period with a less total amount of phosphorus in the food than during the organic phosphorus period, nearly double the amount of phosphorus appeared in the fæces. The result of this was that only 72.4 per cent of the total phosphorus of the food was assimilated during this period, or 15 per cent below the organic phosphorus period and 7 per cent below the fore period.

The most striking result of the observation of the phosphorus metabolism of child B is the almost complete assimilation of the phosphorus of an organic phosphorus compound and the almost complete non-assimilation of the phosphorus of an inorganic phosphorus compound. This result clearly confirms the work of Röhmann and his pupils, and militates against that of Ehrström and Keller.

General Conclusions.—I. In the healthy child the addition of an organic phosphorus compound to the diet is followed by an increase in the amount of phosphorus assimilated by and retained in the body.

2. The addition of an organic phosphorus compound to the diet of children increases the amount of the nitrogen of the food assimilated.

3. The addition of calcium phosphate to the food did not increase the amount of phosphorus assimilated or retained by the child, nor did this compound exert any favourable influence upon the assimilation of the nitrogen of the food.

4. The phosphorus contained in the sodium glycero-phosphate of casein (Sanatogen) is practically entirely assimilated by the body.

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