PHOSPHATES,

Their Chemical Composition and Uses

IN THE

Different Tissues of the Body.

BY

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PREFACE.

In this pamphlet I have tried to show the importance of certain inorganic materials in the food, and the part they play in the tissues. If my views are as correct as I believe them to be, a new field is opened up to the profession for the investigation of the cause of organic diseases, hitherto but little understood, and possibly also for the successful treatment of many of these diseases.

The conclusions arrived at as to the dual composition of the capillaries, and the important part tribasic phosphate plays in their nutrition, are the result of experiments undertaken to ascertain the use of phosphoric acid in food. I had no theory on the subject, so that the conclusions have arisen from, and grown with, my investigations. I have not worked to try and prove a case, but have simply kept a record of a series of experiments, which I subseqently tried to interpret. As I wished to curtail the present pamphlet as far as practicable, I have omitted an account of the methods of analysis employed, but I have not adopted any plan until I had satisfied myself by standard experiments of its accuracy.

I have avoided, as much as possible, technicalities; but in order to make myself intelligible have been obliged to resort occasionally to their use. My object is to bring my views, not only before the profession, but before the public also, so that the truth, or error, of my ideas may be fairly tested. In matters of chemistry I have used the old notation in preference to the new, because the majority of workers in the present generation understand the old better than the new.

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PHOSPHATES,

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For some time past, phosphorus, in some way or other, has been known to play an important part in animal and vegetable life. Its general existence in plants in the form of phosphates, and in nervous matter in that or some other form, has been long known, as well as the fact that as tricalcic phosphate it enters largely into the composition of bone; but the exact part that phosphorus plays in the animal economy, and the condition in which it exists in the different tissues of animals, has not, to my knowledge, been made a subject of special investigation.

It shall be my endeavour briefly to point out what I believe to be the combinations of phosphorus in the animal system, and to indicate the use of these combinations.

The properties of phosphorus are too well-known to need more than a passing notice; it is a colourless waxy-looking solid, which does not naturally exist in an elementary state, owing to its great affinity for oxygen. Even at ordinary temperatures the combination of phosphorus and oxygen to form phosphoric acid quickly takes place. The oxides of phosphorus are four:—

Sub-oxide	P_2O.
Oxide (Hypophosphorous Acid)	PO.
Phosphorous Acid	PO_3.
Phosphoric Acid	PO_5.

The most important of these different oxides of phosphorus is phosphoric acid, as it is in this form phosphorus is generally met with in the mineral, vegetable, and animal kingdoms; and it is only as a phosphate that I have met with phosphorus in the tissues. The different kinds of food, both animal and vegetable, that are the carriers of phosphorus-compounds to the human system, all contain their phosphorus as phosphates, and as phosphates only. The reduction of phosphoric acid to lower oxides, and to its elementary state, is a matter of difficulty, and can only take place under conditions which do not exist in the human body. As phosphoric acid, in combination with certain bases (a phosphate), all phosphorus finds its way naturally into the human body, and as a phosphate it does its work in life. The combinations between the acid and base may be, and are altered for their different uses in the tissues, but as a phosphate phosphorus is taken in the food, as a phosphate it does its work, and as a phosphate it is eliminated.

There are some peculiarites respecting the behaviour of phosphoric acid with bases, which have an important bearing on the state in which the phosphates exist in the different animal tissues. Phosphoric acid combines with water, and with bases in certain multiple proportions. There are three hydrates of phosphoric acid. In each of these water plays the part of a base, and any portion of the base water may be replaced by the equivalent quantity of some other base. With water phosphoric acid forms three different aqueous salts, analagous to the three kinds of salts it forms with other bases; these last are—1st, one equivalent of base to one of acid (monobasic); 2nd, two equivalents of base to one of acid (dibasic); 3rd, three equivalents of base to one of acid (tribasic).

It is to this class that the phosphates in tissues belong. Bone phosphate may be taken as affording a good illustration of this class of salt, as it is composed mainly of a tricalcic phosphate, a compound in which one equivalent of phosphoric acid enters into combination with three equivalents of lime ($_3$Ca.O, PO_5). In the formation of a tribasic phosphate, the combination between the acid and base need not be confined to one particular base, but a series of salts can be produced in almost endless variety, for the three equivalents of base may be built up of two, three, four, or more different bases, provided that three equivalents of basic matter be presented to one of acid, so that in this way we may obtain such salts as the following:—Starting with tricalcic phosphate ($_3$Ca.O, PO_5) as typical of this class of salt, for two equivalents of lime may be substituted one equivalent each of magnesia and soda, so as to obtain a salt with the formula CaO, Mg.O, Na.O, PO_5. There are here three equivalents of base to one of acid, just as in the tricalic compound. I have obtained with a salt of magnesia, added to different phosphates in solution, several varieties of an insoluble tribasic phosphate, with varying quantities of each different base, but always in such proportions as that three equivalents of base exist to one of acid.

These peculiar combinations of phosphoric acid and bases are of great importance in the nourishment of animal tissues, and their existence can be clearly made out; there is probability of their existence also in the vegetable kingdom; but as vegetable ash for the most part contains a large assortment of acids and bases, it is not an easy matter to define the exact state in which the salts exist. In the analysis of vegetable ash, or rather in the synthesis of the analysis, the saddle may be put upon the wrong horse; but this is not likely to happen in the examination of the ash or residue of animal tissue; for in this last the number of acids and bases is much more limited, and their synthesis is consequently rendered more easy.

The different animal tissues here named have yielded the following quantities of phosphoric acid:—

	Tissue.	*Phosphoric Acid per cent.*
	Pig Skin	·147.
	Kidney of Pig	·244.
	Brain of Pig	·589.
	Lung of Pig	·392.
	Brain of Sheep	·752.
	Lung of Sheep	·443.
	Heart of Sheep (muscular fibre)	·398.
	Liver of Sheep	·437.
	Kidney of Sheep	·282.
	Aorta of Pig (outer coat)	·167.
	Aorta of Pig (inner coat)	·512.
	Aorta of Ox (middle coat)	·192.
	Aorta of Ox (inner coat)	·384.
	Aorta of Ox (inner and middle coat)	·281.
No. 1.	Human Brain (cerebrum)	·728.
	Human Brain (cerebellum)	·723,
	Human Lung	·280.
	Human Kidney	·327.
No. 2.	Human Brain (cerebrum)	·597.
	Human Brain (cerebellum)	·482.
	Human Kidney	·244.
	Human Spleen	·244.

The human tissues in No. 1 were from a healthy adult, killed by an accident, those in No. 2 were from a man who died of disease. All the tissues were examined in the fresh state, and in each case 100 grammes of fresh tissue were taken. The tissue was well charred, but not reduced to ash, and the phosphoric acid washed out with hydrochloric acid, and then precipitated and weighed.

In different kinds of food, &c., I found—

	Phosphoric Acid per cent.
Bread	·282.
Beer	·076.
Rice (raw)	·115.
Lemon Juice	·032.
Apple (American)	·025.
Milk	·141.
Grape Juice (foreign white)..	·032.
Wine (Madeira)	·064.
Cod Liver Oil..	·010.
Potato (raw)	·141.
Meat (raw beef)	·343.
Diabetic Bran Biscuit	·758.
Cheese (American)	1·140.
Onion	·080.
Hops	1·028.
Malt	.450.
Liebig's *Extractum Carnis*	6·455.
Coffee..	·501.
Cocoa	·990.
Tea	·951.
Pea (dried split)	·874.
Egg	·182.

A table of this kind shows the general presence of phosphoric acid in food, but is of only partial use for forming an estimate of the comparative value of food as a phosphate bearer, as the condition in which the phosphoric acid exists, whether soluble or insoluble, is not shown, and some of the foods mentioned, such as tea and coffee, are not eaten in their entirety, but have only a portion of their phosphates extracted by water before use. Good and well-made tea yields up about a third of its phosphates to water. The substances which have a chemical reputation as condensed and nourishing foods, show, however, a large percentage of phosphoric acid. Liebig's *extractum carnis* heads the list; next comes cheese, a strong and nutritious food; and close to it is the pea, the nourishing properties of which were amply tested in the Franco-German war, in the far-famed pea-sausage.

In what state does phosphoric acid exist in food and in tissue? I have never detected free phosphoric acid in food, but have always found it in combination with a base. In the tissues, where I have always found it as a phosphate, the only indications I have ever had of the existence of free phosphoric acid have been in the brain of an ox, and here the indications were not conclusive. There is a remarkable similarity between the inorganic matter taken in food, and that found in the excreta. I have compiled a table from the diet list of the army, showing the analysis of the food consumed by a soldier daily on full diet, and given two analyses of the urine passed by an adult in 24 hours. One of these is taken from Parkes' work, the other was made by myself. I have omitted from the tables urea and sulphuric acid.

TABLE SHOWING LIME, &c., CONSUMED BY A SOLDIER IN HOSPITAL ON FULL DIET :—

Article of Food and quantity.	*Lime in Grammes.*	*Magnesia in Grammes.*	*Potash in Grammes.*	*Phosphoric Acid in Grammes.*
Meat, 12oz., containing	·123	·120	·756	1·194
Bread, 18oz. ditto	·111	·235	·784	1·847
Potatoes, 16oz. ditto	·164	·298	1·720	·656
Milk, 6oz. ditto	·160	·046	·044	·270
Vegetables, 4oz. ditto	·135	·045	·462	·124
Total ..	·693	·744	3·766	4·091

TWO ANALYSES OF URINE PASSED IN 24 HOURS :—

A.—Analysis by Parkes. Urine passed in 24 hours. 1501c.c., containing—

Lime	·314	grammes.
Magnesia	·345	ditto.
Potash	3·012	ditto,
Soda	14·947	ditto.
Phosphoric Acid	3·164	ditto.
Chlorine	8·210	ditto.
Solids	61·14	ditto.

B.—Analysis by Anderson. Urine passed in 24 hours. 1496c.c., containing—

Lime	·495	grammes.
Magnesia	1·674	ditto.
Potash	1·020	ditto.
Soda	4·830	ditto.
Phosphoric Acid	1.728	ditto.
Chlorine	6·300	ditto.
Solids	45·000	ditto.

There is altogether a larger quantity of saline matter in *A* than in *B*, but the relative quantity of bases and phosphoric acid shows great similarity. This relative proportion of acid and base is still more marked if we remove in each case the equivalent quantity of soda to combine with the chlorine to form chloride of sodium. I am inclined to look upon Parkes's analysis as showing saline ingredients in excess of what is ordinarily passed by an adult who only takes the necessary amount of food to supply the daily waste of the tissues. A soldier taking two or three pints of beer a day would increase the quantity of saline matter found in the urine, and a considerable portion of this would find its way directly into the urine through the kidneys, without having taken any part in the nourishment of the tissues. A reference to the amount of phosphoric acid, as shown in Table 5 in the appendix, proves this, for in this table food is clearly seen to influence the quantity of phosphoric acid passed in the urine, as the quantity of phosphoric acid passed by the soldier on milk diet alone, was much in excess of that passed by any of the others. In estimating the quantity of phosphates daily voided, I have not taken into consideration the quantity in *fæces*, because although phosphates exist there, they are in an insoluble form and have never taken any part in the vital process: they simply exist as unabsorbed and unassimilated matter. (Phosphates, I believe, exist in the bile as an exception to this—but the quantity eliminated in this manner is small.) Looking at the urine as the channel for the elimination of used-up tissue, and assuming that phosphates in some form or other exist as a necessary part of the inorganic part of food, and that we have evidence of their utility in the system by their presence in the great eliminator of waste tissue, the urine, we ought to be able to obtain evidence of their existence in the tissues. The table given on a former page, and in the appendix, shows the existence of phosphoric acid in all the tissues there named, but does not show the condition in which it exists. The following analyses show that in the brain and lung of man phosphoric acid exists in combination with bases.

Analysis of Human Brain.

	Per cent.
Lime	·185
Magnesia	·082
Potash..	·197
Soda	·187
Phosphoric Acid..	·728

Analysis of Human Lung.

	Per cent.
Lime	·152
Magnesia	·224
Potash	·060
Soda	·094
Phosphoric Acid..	·280

In both these there is evidence of the same relative proportions of acid and base, and in every other analysis of tissue that

I have made I find the same relative proportions existing, although the absolute quantities vary. Why is there this general distribution of phosphoric acid and bases in all the organs? and what is there in common between them all, in which a phosphate may be expected to play an essential part? What are the physical and chemical properties of a phosphate, and in what way can they aid in supporting life?

In bone we have a clear answer to these questions. Tricalcic phosphate adds stability and strength to the osseous structure. The same properties that exist in a tricalcic phosphate exist also in tribasic phosphates as found in the tissues, but in this last compound there is a much greater affinity for water. These insoluble compounds of phosphoric acid have, in many respects, a great resemblance to each other. They all separate from their solutions under suitable conditions, as amorphous compounds, so that a precipitate of tribasic or tissue phosphate, looks very much like a precipitate of tricalcic phosphate.

If the investigation as to the use of phosphates in the tissue be carried out, it will, I believe, be found to depend entirely upon its presence in the capillaries. Blood vessels are composed of an organic or membranous portion, and an inorganic portion. The inorganic portion is composed mainly, if not entirely, of a tribasic phosphate, which I propose to call tissue phosphate. These two materials, the organic and inorganic, are so blended together as to form a homogeneous whole, in which the mineral, or inorganic portion, is not apparent; its existence can only be demonstrated by analysis. It is impossible for analytical purposes to separate the capillaries from the surrounding tissues, but the larger blood vessels can be examined, and in these I have found all the same indications of phosphoric acid and bases as in the different organs. The inner portion of the aorta, which is the vessel that I have examined, contains larger quantities of phosphates than the middle and outer coats, and it is this inner coat which enters mainly into the composition of the capillaries. If it were possible to isolate and examine separately the capillaries, a tissue phosphate would probably be found in much larger quantities than in the larger vessels.

The aorta of the pig contains—

	Per cent.
Lime	·028
Magnesia	·026
Potash	·121
Soda	·130
Phosphoric Acid	·160
Chlorine	·080

There is no trace of Sulphates.

The inner sheath showed—

	Per cent.
Phosphoric Acid	·512

The aorta of ox (inner portion) showed—

	Per cent.
Lime	·056
Magnesia	·093
Potash	·231
Soda	·223
Phosphoric Acid	·384
Chlorine	·180

No trace of Sulphates.

Aorta of ox (fibrous membrane) showed—

	Per cent.
Lime	·020
Magnesia	·036
Phosphoric Acid	·192

Potash and Soda not determined.

Aorta of ox (inner and middle portion together) showed—

	Per cent.
Phosphoric Acid	·281

The analogy between the inorganic part of the different kinds of food, the inorganic part of tissue, and the inorganic part of the aorta, is very marked. These all bear a close resemblance to the inorganic matter of urine, although in this last I cannot clearly show the presence of a tribasic phosphate. The different materials which form a tribasic phosphate are nevertheless present in the urine; but as these compounds are insoluble, some change in their composition has probably taken place, so as to facilitate their elimination as soluble compounds.

For some years past phosphorus has been known to exist in cerebral matter. My conviction is that it exists as phosphoric acid in combination with a base, and in no other form. If cerebral matter be boiled for a short time, or even macerated in distilled water, and the solution be examined for phosphoric acid, the presence of this acid is shown in considerable quantities. The quantitative examination of brain matter for phosphoric acid cannot be made without the aid of heat to get rid of the organic matter, owing to the difficulties that attend its filtration in the presence of organic matter. Does this alter in any way the condition of the phosphorus? I am confident that it does not, if the experiment be carefully conducted. In the examination of the inorganic constituents of plant and animal tissue, especially for the detection of phosphates, care should be taken not to carry the incineration to any length; the material should only be charred sufficiently to carbonize the mass. If heat be continued for any length of time, so as to produce a white ash, a portion of the phosphoric acid is volatilised, and a part reduced to phosphorus by the oxidation of the carbon in the tissue, at the expense of the phosphoric acid. The carbon seizes hold of the oxygen of phosphoric acid to form carbonic acid, and the phosphorus volatilises, and is treated as free phosphorus in the determination. Besides this, long-continued heat produces other changes, and may even volatilise some portions of the bases. It is only in this way that I can explain the discrepancies that exist between the results of my investigations and such results as have up to the present time been received as representing the composition of the inorganic constituents of tissue. In Watts' Dictionary of Chemistry (the best and most compendious work published on this science in the English language) appears the following:—"In 100 parts of fresh brain, Breed found 0.027 parts of ash" (article nervous tissue), and then follows the per centage composition of the ash. If the whole of the inorganic constituents of the brain only amount to 0.027 parts per cent., there cannot possibly be ·728 parts per cent. of phosphoric acid. I should be inclined to regard the paragraph quoted as a misprint, but that I find the same discrepancies between my experiments, and those of others, to exist in many instances. I am led to the conclusion that the analysis of any organic compound for the determination of its mineral constituents should not be conducted by reducing the organic compound to ash, and that this method has led to great errors.

A precipitate can be readily made by using certain salts of phosphoric acid and the proper bases, which, on ignition, bears a close analogy to the phosphate found in tissues. A theoretical compound phosphate, consisting of Ca.O., Mg.O, Na.O, PO_5, would show a per centage composition of—

Lime	17·28
Magnesia	19·80
Soda	19·12
Phosphoric Acid	43·80

For comparison I have placed this by the side of two precipitates made in my laboratory and analysed, and the analysis of the inorganic constituents of human lung, human brain, and the arteries of ox and pig—

No. 1.—Theoretical Tribasic Compound Phosphate, (CaO, Mg.O, Na.O, PO_5).

Lime ..	17·28
Magnesia	19·80
Soda ..	19.12
Phosphoric Acid	43·80
	100·00

No. 2.—Tribasic Compound Phosphate, prepared in Laboratory.

Lime ..	31·70
Magnesia	18·10
Soda ..	10·34
Phosphoric Acid	39·86
	100·00

No. 3.—Tribasic Compound Phosphate, prepared in Laboratory.

Lime ..	9·88
Magnesia	17·85
Soda ..	24·87
Iron ..	2·00
Water ..	3·61
Phosphoric Acid	41·79
	100·00

No. 4.—Phosphate from Lung.

Lime ..	18·76
Magnesia	27·65
Potash	7·40
Soda ..	11·60
Phosphoric Acid	34·56
Loss ..	00·04
	100·00

No. 5.—Phosphate from Aorta of Pig.

Lime ..	5·13
Magnesia	4·77
Potash	22·20
Soda ..	23·85
Phosphoric Acid	29·35
Chlorine	14·70
	100·00

No. 6.—Phosphate from Aorta of Ox.

Lime	4·80
Magnesia	7·96
Potash	19·79
Soda	19·10
Phosphoric Acid	32·93
Chlorine	15·42
	100·00

No. 7.—Phosphate from Brain of Man.

Lime	13·41
Magnesia	5·94
Potash	14·30
Soda	13·56
Phosphoric Acid	52·79
Chlorine	0·00
	100·00

In comparing analyses of compound tribasic phosphate, it is impossible, or next to impossible to get exactly the same results by analysis, as the combined quantity of base may be indifferently supplied by various bases, each with its own combining equivalent, in different quantities, but always in such proportions as united to form a tribasic compound. The preponderance of any one base over another will necessarily alter the per centage composition of the tribasic compound, the alteration being dependent on the difference of the combining equivalent of the base. Bearing in mind this cause of discrepancy, and making due allowance for it, these analyses show precisely the same results. The acid and base bear these proportions to each other—

	No. 1.	*No. 2.*	*No. 3.*	*No. 4.*	*No. 5.*	*No. 6.*	*No. 7.*
Base ..	56·20	60·14	58·21	65·44	55·95	51·65	47·21
Acid ..	43·80	39·86	41·79	34·56	29·35	32·93	52·79
Chlorine	..	..	..	..	14·70	15·42	..
	100·00	100·00	100·00	100·00	100·00	100·00	100·00

Nos. 1, 2, and 3, are counterparts of each other. Nos. 5 and 6 both contain chlorine. Making allowance for the chlorine as a diluting material in giving the per centage composition, and allowing also for the abstraction of that portion of the base with which it is in combination, Nos. 5 and 6 will show as nearly as possible the same per centage composition as the others. With these corrections, Nos. 5 and 6 will read—

No. 5.

Base	59·40
Acid	40·60
	100·00

And *No. 6.*

Base	45·69
Acid	54·31
	100·00

All these analyses show the existence of tribasic phosphate. The presence of the chlorine I consider to be accidental, and dependent upon the method of formation of the tribasic phosphate in tissues, for, in all probability, common salt helps in the formation of this compound, and some of the chlorine remains in the tissues. Water of combination enters largely into the composition of tribasic phosphate, as found in the tissues, and carries with it in solution salts, which remain in the tissues. In the finer capillaries there is less indication of these impurities than in the coarser large blood vessels, for in the brain I have failed to detect chlorine. In bone we get evidence of the same kind of impurity, in the presence more particularly of magnesia, although this base has nothing to do with true bone phosphate; yet from the absence in any quantity of water of combination, bone phosphate is less likely to carry impurities than tissue phosphate.

Do all the phosphates found in the tissues as compound phosphate take part only in the formation of blood vessels and capillaries, or do they enter as well into the formation of the tissue of the different organs? Is cerebral matter composed of phosphorus, or any compound of phosphorus in any way except such as is dependent upon its capillary development. On this point I cannot offer conclusive evidence, but all the evidence I possess tends to show that there is no phosphorus in any organ or tissue, except such as exists in the capillaries in the form of tissue phosphate, excepting, of course, tricalcic phosphate in the osseous structure. Liebig, in his Organic Chemistry of Physiology and Pathology, makes this statement at page 78 of that work: "All the tissues, with the exception of cellular tissue and membrane, contain phosphoric acid and sulphur." Why are these two tissues in particular void of phosphoric acid? I do not accept the statement that they are absolutely void of phosphoric acid, but nearly so; and why? Because they are very scantily supplied with blood vessels. There is no capillary system to need a large supply of tissue phosphate.

The relative per centage proportion of tissue phosphate in the organs and blood vessels analysed may appear, at first sight, to favour the supposition that phosphoric acid plays some other part in the different organs, to that which I assign it. Phosphates, it may be urged, exist in larger quantities in the brain than in the aorta. This is true; but I am unable to separate the capillaries of the brain, and show their per centage composition. If I could I should expect to be able to show that they contained a far larger proportionate quantity of inorganic material than the larger blood vessels. I infer the existence of certain conditions from collateral evidence.

In the lungs, liver, kidney, spleen, and muscles of animals, I have found quantities of phosphoric acid, varying from ·25 per cent. to ·45 per cent. In the brain of the ox I have found as much as ·81 per cent of phosphoric acid. Is this increased quantity of phosphoric acid due to increased vascularity, and dependent entirely upon difference in the capillary arrangement; or does phosphoric acid enter into the structure of the brain substance itself? Either way, the same relations between acid and base exist, so that the whole of the phosphoric acid exists as a tribasic compound, or tissue phosphate. It would be a strange coincidence if we could find tissue and organs possessing such different properties and such different functions as the brain, liver, kidneys, lungs, and skin, and yet showing the same relative arrangement of their inorganic materials, unless their inorganic composition depended upon something common to them all. Is it possible, considering the properties of phosphorus, especially with regard to its ready oxidation, that free phosphorus could exist for many minutes in an oxidising furnace such as the human body? Whence could it be obtained? There is no chemical action that could take place in the human body which would produce it. It does not exist in food. No elementary bodies are abstracted and separated from their compounds by any process going on in the human body, either of solution, digestion, assimilation, nutrition, or secretion; but rather compounds are produced by oxidation, such as carbonic acid from hydrocarbons, and urea from protein compounds. The chemical actions taking place in the human body are referable entirely to oxidation, and not to deoxidation. The human body is an oxidising open furnace, and not a closed retort. No food contains phosphorus, but all foods contain phosphoric acid, with the exception of the hydrocarbons, and these have their special function as heat generators, and not as tissue formers. The termination of the capillaries in brain is unlike that of any other organ, and the vascularity of nervous tissue is excessive. These causes alone are sufficient to account for the increased quantity of phosphate in the brain.

If there be any truth in this doctrine of the dual formation of the capillaries, it should agree with the evidences of pathology, and clinical observation ought to be able to confirm the existence of an inorganic material in the capillaries, by the symptoms which mark the absence of the materials necessary to its formation. The symptoms of some diseases confirm, in a remarkable manner, the existence of this inorganic strengthening material (tribasic or tissue phosphate) in the capillaries.

All organic diseases are dependent upon innutrition: this may depend upon local or general causes; in the majority of cases, although the symptoms may in the first instance be localised, the cause is in the system. In phthisis, cancer, and leprosy, although our attention may be directed to a particular locality, as the seat of disease, there is doubtless some systemic cause producing the disease.

In many cases there is hereditary predisposition to certain organic diseases, but even in these there is generally some exciting cause which lights up the mischief. In phthisis, exposure to cold, privation, or bad ventilation, are some of the exciting causes. These act by depressing the system, lowering the vital powers, producing loss of appetite, and thus preparing the way for innutrition of the tissues. The first tissues to suffer are the capillaries; these from the want of the saline ingredients necessary to their healthy maintenance, lose tone and stability, and cease to act in transmitting the blood to the neighbouring tissues; a capillary block takes place, and this leads to death of the part from innutrition. In cases where the progress of the disease is slow, nature attempts to remedy the want of strength in the capillaries, by supplying material (fibrous tissue) ill-adapted for the purpose. This produces thickening and imperfect action of the capillaries; or the capillaries become so weak and lax as to allow of exudation of blood through their walls.

By adopting this theory of capillary innutrition as the immediate cause of many organic diseases, all the phenomena of these diseases admit of ready and complete explanation. Scurvy is a disease which is universally admitted to depend upon a deficiency of some material in food necessary for the healthy condition of the blood. I maintain that the material, the deficiency of which is the cause of scurvy, is tribasic phosphate, and that all the phenomena of scurvy arise from a weakened and relaxed state of the capillaries, caused by an absence or insufficient supply of tribasic phosphate or its component parts in the food.

By referring to Table 6 in the appendix, it will be seen that a soldier on full diet consumes about 4 grammes of phosphoric acid, together with a proportionate quantity of bases for the formation of tissue or tribasic phosphate. An adult, on the average, passes about 2½ grammes of phosphoric acid daily in his urine. All the phosphoric acid found in the food does not take part in the formation of tissue phosphate, as a portion is insoluble and cannot, therefore, take part in nutrition. This portion is found in the *fæces*, and amounts to about one gramme per diem. The quantity of available phosphoric acid on this diet is thus reduced to three grammes, to supply a waste of 2½ grammes; but this is not all the waste. My analyses were made on uncooked food, and as the effect of cooking food, more particularly boiling it, is to deprive it of a portion of its phosphates, a still further reduction must be made. If the water that potatoes have been boiled in be examined for phosphates, very perceptible quantities of phosphoric acid will be found, as also in the water that meat has been boiled in. On such a diet as that given there appears to be no more than enough phosphoric acid to furnish the requisite amount of tissue phosphate for daily use. The diet comprises a fair amount of nutritious food, so that it may be held that on ordinary diet a sufficiency, and no more, of inorganic material is taken to furnish the system with its proper quantity of inorganic material for capillary and bone nourishment. Any circumstances which either lessen the quantities of phosphates, or render them insoluble, and thus prevent their absorption, will consequently produce conditions dependent upon loss or absence of tissue phosphate.

In scurvy these conditions exist. This disease, although not confined to seamen, more generally appears among that class of men than any other, because they are more likely to be placed under conditions favourable to its development. What are these conditions? First and foremost the use of salt meat, together with the absence of vegetables and fruit. Not that salt meat takes any active part in producing scurvy; but it is deficient in certain nourishing materials possessed by fresh meat, and it is the absence of these that produces the disease. The effect of salting meat is to deprive it of a very large quantity of its phosphates; the phosphates so abstracted are of necessity those which are the most soluble and consequently the most easily assimilated—that is, the most nourishing and best tissue phosphate formers. A sample of good fresh beef which I analysed showed ·353 parts per cent. of phosphoric acid. A sample of good salt navy beef from H.M.S. *Hector*, which had been in brine for some three or four months, showed only ·147 per cent. of phosphoric acid, so that the effect of salting beef is to deprive it of nearly two-thirds of its total phosphates, and these the best and most nutritious. Fresh meat is a good antiscorbutic, because the phosphates it contains are in a readily soluble form For the same reason the potato acts well; but in addition the potato and most fruits and vegetables contain malic, citric, or other acids, which act as solvents of the phosphates. But in any outbreak of scurvy these articles of food are wanting, and the sailor is reduced to rations of junk and hard biscuit, helped down with rum or other spirit. His junk has had nearly all the available phosphates soaked out. True, his biscuit contains phosphates in considerable quantities, but in a condition of little use against scurvy, as the phosphates in flour are in an insoluble state as compared with the phosphates of fresh meat and potato. If he gets tea, this helps him, but only slightly, for although tea and coffee contain phosphates in large quantities they are only taken sparingly. His rum is quite free from phosphates; in short, all his food is deficient in phosphates, or contains them in an insoluble form.

Under these circumstances, what is done to ward off an outbreak of scurvy? Lime juice is used. What is the composition of lime juice? and why is it an antiscorbutic? Lime juice contains a small quantity of phosphates, one hundred parts of fresh lemon juice containing ·082 parts of phosphoric acid. This is evidently too small a quantity to bear any active or essential part in tissue nourishment. It is not its phosphates, but it possesses two substances which play a very important part as antiscorbutics. These are citric acid and potash. The action of citric acid is remarkable It is a complete and perfect solvent of phosphates; even tricalcic phosphate is completely dissolved by it. I have tried all the mineral acids, tartaric and acetic acid also, and find that as a solvent no acid is equal to citric acid. It does not decompose the salts of phosphoric acid, as hydrochloric and sulphuric acids do, by entering into combination with their bases, but acts solely as a solvent. A simple experiment will show this:—Dissolve some phosphate of lime, or other insoluble phosphate, in water with hydrochloric or sulphuric acid, then add ammonia gradually until a precipitate begins to form; this will occur while the liquid is still acid. Instead of a mineral acid use citric acid to another portion of an insoluble phosphate, and when dissolved add ammonia. No precipitate appears until the liquid has been rendered strongly alkaline, and then only slowly and gradually. Citric acid also prevents the formation of insoluble phosphates of iron and magnesia, and the consequent loss of phosphoric acid required for the formation of tissue phosphates. In all my experiments for estimating phosphoric acid, I have made use of citric acid to prevent the formation of uncertain and irregular precipitates of phosphoric acid, and with the best results. Neither alumina, iron, or magnesia, is precipitated in an ammoniacal solution as a simple phosphate if citric acid be present in sufficient quantities. The potash in lime juice is useful, as supplying one of the bases necessary for the formation of tribasic phosphate, and for this reason, as well as because it contains a small quantity of phosphates, lime juice is more useful as an antiscorbutic than citric acid alone; but the principal efficacy of lime juice is in the citric acid, dependent on its solvent powers on phosphates.

In scurvy we are able to connect cause and effect. We see that certain symptoms set in under certain conditions. In organic diseases cause and effect are not so clearly defined, nor so easily recognised; but a study of the phenomena which occur in scurvy and in organic diseases, or, at least, in a large proportion of them, will show many points of similitude between them. I am to a certain extent obliged to depend upon analogy to prove my case, for were I to depend upon proof by actual analyses of different organs in disease, I should have to gather my data from *post-mortem* examinations, and as in private practice opportunities of this kind seldom occur, I might spend a lifetime without being able to advance my views. Having shown that in ordinary food phosphates exist to a considerable extent, that phosphates exist also in all the organs of the body and in the blood vessels, and that an absence in the food of soluble phosphates, or of phosphates capable of being made readily soluble, produce scurvy, let me now point out what are the symptoms of scurvy, and how far these symptoms show a weakened capillary condition dependent upon loss of the inorganic or mineral materials necessary for their support.

The symptoms of scurvy, as described by Dr. Aitken in his "Science and Practice of Medicine," are "change of colour of the skin, particularly of the face and eyelids, the skin round the orbit may be puffed up into a bruise-coloured swelling, pains in the limbs, weariness, and depression of spirits. The countenance appears pale and yellow and bloated, the gums become soft, spongy, and hang over the teeth in fleshy masses, very much discoloured, and easily excited to bleed. All parts suffer from pressure in scurvy, the merest rub causes an ecchymosis, the slightest blow produces an extensive bruise. A small eruption, like flea-bites of a purple hue, appears on the skin, the muscles in parts become hard and painful, and in a day or two the skin over the pained part becomes first yellow and then purple." Dr. Aitken continues his description, going more minutely into an account of the extravasations, and finishes up this part of his description with this sentence: "The source of these extravasations would seem to be the softened capillary vessels permitting the leakage of altered blood." All my experiments tend to prove that this softening is dependent upon the loss of tissue phosphate, the inorganic constituent of capillaries.

In many cases of organic disease we get this hemorrhagic tendency,—for instance, in phthisis and cancer; in others, as in leprosy, there is also evidence of faulty nutrition, as shown by ulceration of the skin, in all cases such faulty nutrition arising in the capillaries. In the conditions known as atheroma and ossification of arteries there is still further evidence of the truth of my views respecting the existence of a mineral matter in the blood-vessels: in the former condition there are patches of soft matter deposited in the coats of the arteries, producing a condition of things likely to lead to rupture, and doubtless arising from a deficiency of mineral matter; whilst in ossification of arteries we get the arteries converted into mere bony tubes. In this last condition, from some perversion of nutrition, tricalcic phosphate takes the place of the healthy mineral constituent of arteries (tribasic or tissue phosphate). In examining the aorta of animals killed for food, presumably, therefore, in health, I have frequently found plates of real bony matter embedded in the aorta, and always lying close to the epithelial surface. The attention of the profession has been lately drawn to a thickened condition of the kidney capillaries in some forms of kidney disease. I have a strong conviction that this thickening is dependent on an insufficient supply of tribasic phosphate to the capillaries, and a consequent weakening of these vessels, thus leading to an attempt of nature to strengthen the weakened capillaries by such material as is at hand, namely fibrine; this material being supplied in such quantities as to cause thickening, and consequent total or partial obliteration.

Evidence, chemical, microscopical, and clinical, favours the idea that organic diseases commence in the capillaries; the exciting cause may depend upon deficiency of some material necessary for healthy nutrition, or upon some local cause; but in either case a knowledge of what is actually happening in the nutrition of the organs must materially increase the probabilities of recovery. If the innutrition of the capillaries is dependent upon non-assimilation of mineral constituents, which in health are obtained from the food, we may, by supplying the mineral matter in an easily digested and easily assimilated form, check the progress of the disease by keeping up the capillary nutrition.

The difference in the inorganic composition of the tissues in health and disease is a field open to profitable investigation, and one that I have had only limited opportunities of studying in connection with morbid pathology; but I lately had a case which bears out very clearly my views regarding the deficiency of phosphates in cases of organic disease.

The case was of a soldier who died in military hospital in Coventry. He had been in hospital some three or four months, when I saw him with Dr. Murray, in charge of the troops here. He was then pallid, with feeble, quick pulse, enlarged liver, and repeated hemorrhages from the nose. The blood corpuscles under the microscope looked small and shrivelled, with irregular outline, not nummular-shaped. The *post-mortem* examination showed a very large, mottled, and soft liver. One kidney was greatly hypertrophied, with its capsule thickened and hardened; the other was of natural size, and the capsule apparently healthy. The brain was soft, more particularly the cerebellum. The brain and one kidney (that apparently healthy) were the only organs I had an opportunity of examining chemically, and both these showed a great deficiency of phosphates. The analysis was only partial as regards the total bases; but the quantity of phosphoric acid was carefully determined :—

PER CENT. IN CEREBRUM.

Lime	·053
Magnesia	·114
Phosphoric Acid	·597

Soda and Potash not determined.

PER CENT. IN CEREBELLUM.

Lime	·058
Magnesia	·257
Phosphoric Acid	·482

Soda and Potash not determined.

PER CENT. IN KIDNEY.

Magnesia	·064
Phosphoric Acid	·244

In all these three determinations there is a very marked deficiency of phosphoric acid, as compared with the corresponding tissues of a man in health.

Phosphorus, and some of its compounds, have been for some time used in medicine; but there is no preparation, either in the British Pharmacopœa, or amongst the medicines in general use, which is capable of forming a tribasic phosphate, such as that found in the tissues.

The Pharmacopœal preparations are phosphorus and phosphoric acid; in addition to these, phosphates simple and compound, amongst the latter Parrish's solution, and various hypophosphites are in general use, although not described in the Pharmacopœa.

As regards the use of phosphorus, I cannot see the advantage, or utility, of prescribing free phosphorus. If it is only of use as a phosphate, why necessitate its oxidation in the system? This process can be far better carried on outside than inside the body; even when oxidised and converted into phosphoric acid it is left to chance to find the proper bases with which to unite to form the true phosphatic constituent of the tissues (tribasic phosphate). This last objection applies also to phosphoric acid.

The hypophosphites contain bases which may be useful in the formation of tissue phosphate; but the acid is not the acid that enters into capillary formation; nor is it with certainty converted into phosphoric acid. All the hypophosphites, or, at least, those prescribed in medicine, are soluble, and hypophosphorous acid does not possess the property of forming compound salts, in the way that phosphoric acid does. The hypophosphites may be in certain cases useful in furnishing bases instrumental in the formation of tissue phosphate; but in order to do this must part from the acid, which is useless except as a carrier of the base.

The phosphates in such a combination as that of Parrish's serve as a useful medicine in many cases. Parrish's compound syrup of phosphates contains, amongst other phosphates, phosphate of lime in a state readily available for bone formation, and for this reason is a very valuable medicine for children, in whom bone formation and development is a matter of great importance, but it is not well adapted for the formation of tissue phosphate.

All these preparations of phosphorus have been largely used in medicine without producing any of the marked effects on the capillaries, which, I believe, a proper combination of acid and bases may be made to produce, for the reason that in the different forms and proportions hitherto prescribed they are not capable of forming the material which in many cases of disease is the one compound we ought to produce, viz., a compound tribasic or tissue phosphate.

In looking at the composition of the tissues, as regards the comparatively small quantity of inorganic material entering into their structure, it may appear that the quantity of inorganic material is too small to play such an important part as my arguments suggest. A more attentive consideration will show that the quantity of inorganic matter is large enough to play a very important part in capillary nutrition. The brain contains in 100 parts of fresh cerebral matter ·728 parts of phosphoric acid, and ·651 parts of bases; in all, 1·379 parts of mineral matter. Eighty per cent. of cerebral matter is water, so that the remaining 20 per cent. of solids contains the whole of the mineral matter; in other words, the solids of cerebral matter contain 6·89 per cent. of mineral matter. I maintain that all this mineral matter enters into the composition of the capillaries; and as the capillaries form only a part of the solids, the quantity of inorganic matter is by no means unimportant. What the relative quantity of capillary and cerebral solids is, must, of course, be mere matter of conjecture; but assume that the capillaries are one-half of the solids, we shall then have 13·78 per cent. of inorganic matter in the capillaries of the brain. This is a quantity quite sufficient to bear an important part in the integrity of the whole.

As regards the application of this doctrine of inorganic capillary composition to the treatment of disease I have but little to say, as the idea is too new to have given me time to test any plan of treatment based on this doctrine, and I prefer that evidence on this head should come from other sources.

In organic disease other causes may be at work to originate and spread disease, besides capillary innutrition; but the evidence I have been able to collect leads me to believe that in many cases the disease begins in the capillaries, and that by keeping up capillary nutrition it may be arrested or cured. If the assimilative power be destroyed, or be inert, no appropriation of material necessary for the support of tissues can take place; but if the assimilative power be merely weakened and lowered for the time, we may, by presenting the necessary material in an easily digested and easily assimilated form, help the weakened tissue to recover. In the treatment of disease, the physician orders food in the most digestible and most easily assimilated form; but attention has hitherto been directed principally to giving organic food, while the importance of inorganic materials has been overlooked. The ordinary diet of an invalid contains some of the necessary inorganic salts, but not in sufficient quantity to keep up a proper supply, and where there is a tendency to inefficient supply from the character of the disease the quantity of inorganic material is far too small to aid in repairing injury.

In offering this short essay on my investigations to the public and the profession, I am only at present able to give the results of laboratory experiments, and may be met with the remark that obtaining certain results in the laboratory and in the human body are different things, that in the human body we have extra forces at work. True; but there is no antagonism in nature. Chemistry and physiology go hand in hand, and any action in inorganic chemistry which can be produced in the laboratory, can also, under similar conditions, be produced in the body during life. The practice of medicine is, to a great extent, empirical. We find out by accident or chance that certain drugs produce certain effects, and having ascertained this, we turn our knowledge to account, without troubling ourselves much about the reason why.

Chemistry, as a science, is yet in its infancy, and organic chemistry is a difficult branch of the study; but the lessons of inorganic chemistry are more easily learnt, as this contribution to the inorganic chemistry of the tissues, which I now offer testifies.

APPENDIX.

(No. 1.)

Phosphoric Acid in different kinds of Food.

	Phosphoric Acid per cent.
Bread	·282
Beer	·076
Rice (raw)	·115
Lemon Juice (fresh)	·032
Raw Apple	·025
Milk	·141
Grape Juice	·032
Wine (Madeira from Wood)	·064
Cod Liver Oil	·010
Potato (raw), No. 1.	·141
,, ,, No. 2.	·128
Raw Meat (beef)	·353
Salt Beef from H.M.S. *Hector*	·147
Flour	·330
Diabetic Bean Biscuit	·758
Cheese (American)	1·140
Onion	·080
Salt Beef, in soak for one month	·257
Brine from which beef was taken (in 100 c.c.) ..	·707
Hops	1·028
Malt	·450
Liebig's *extractum carnis*	6·455
Coffee with Chicory	·514
Coffee in Berry	·501
Cocoa (Nibs)	·990
Tea	·951
Pea (dried split)	·874
Egg—Albumen and Yolk together	·182

APPENDIX.

(No. 2.)

Phosphoric Acid in Tissues.—In all cases the fresh undried tissue was examined.

	Phosphoric Acid per cent.
Pig Skin	·147
Kidney of Pig	·244
Brain of Pig	·589
Lung of Pig	·352
Brain of Sheep	·752
Lung of Sheep	·443
Heart of Sheep (muscular fibre)	·398
Liver of Sheep	·437
Kidney of Sheep	·282
Aorta of Pig	·167
Aorta of Pig (inner lining)	·512
Aorta of Ox (fibrous middle coat)	·192
Aorta of Ox (inner tube)	·384
Aorta of Ox (inner and middle coat)	·281
Human Brain (healthy adult) cerebrum ..	·728
Human Brain " " cerebellum ..	·723
Human Lung " "	·280
Human Kidney " "	·327
*Human Brain (death from disease) cerebrum ..	·597
Human Brain " " cerebellum ..	·482
Human Kidney " "	·244
Human Spleen " "	·244

* The cerebellum in this case showed well marked softening.

APPENDIX.

(No. 3.)

Analysis of Inorganic Residue from Human Tissues.

ONE HUNDRED PARTS OF FRESH TISSUE CONTAIN, IN LUNG.

Lime	·152
Magnesia	·224
Potash	·060
Soda	·094
Phosphoric Acid	·280

HUMAN BRAIN—CEREBRUM.

Lime	·185
Magnesia	·082
Potash	·197
Soda	·187
Phosphoric Acid	·728

CEREBELLUM.

Lime	·050
Phosphoric Acid	·723

Other Bases not determined.

KIDNEY.

Lime	·045
Phosphoric Acid	·327

Other Bases not determined.

The Brain (cerebrum) showed neutral action with litmus, when boiled with distilled water. Distinct evidence of Phosphates in considerable quantities is given on examining water in which brain has been boiled. Brain substance is sometimes acid in action, but more often neutral.

N.B.—These tissues were from an adult, apparently in sound health, who was accidentally killed.

APPENDIX.

(No. 4.)

Analysis of Inorganic Residue from Human Tissues continued from No. 3. One hundred parts contained—

Brain.

(Cerebrum)	Lime	·053
	Magnesia	·114
	Phosphoric Acid	·597

Soda and Potash not determined.

(Cerebellum)	Lime	·058
	Magnesia	·257
	Phosphoric Acid	·482

Soda and Potash not determined.

Kidney.

Magnesia	·064
Phosphoric Acid	·244

Other Bases not determined.

These tissues were from a soldier who died in military hospital from disease of supra renal capsule of one kidney, and enlarged, mottled, and degenerated liver. There was well marked softening *(post-mortem)* of the substance of the cerebellum. The quantity of phosphates shows a marked deficiency as compared with the quantities given on the previous page, the one set being taken from a man killed while in health, the other from a man who died from disease.

APPENDIX (No. 5).—Table showing Phosphoric Acid taken in Food by Four Soldiers, on Different Diets; and Phosphoric Acid passed in Urine in Twenty-four Hours.

	Diet.	Phosphoric Acid in Food.	Urine in 24 hours.	Containing Phosphoric Acid in grammes.
No. 1.	Milk, consisting of 8 pints of New Milk only ..	6·407 grammes.	1450 c.c.	2·508
No. 2.	Chop, consisting of—			
	Meat, 8 oz.	·878 ,,		
	Bread, 18oz.	1·130 ,,		
	Potatoes, 8oz.	·542 ,,		
	Milk, 6oz.	·263 ,,	1400 c.c.	1·52
	Vegetables, 4oz...	·100 ,,		
	Total ..	2·913 ,,		
No. 3.	Half, consisting of—			
	Meat, 8oz.	·878 grammes.		
	Bread, 16oz.	1·004 ,,		
	Potatoes, 8oz.	·542 ,,		
	Milk, 6oz.	·263 ,,	500 c.c.	1·67
	Vegetables, 4oz...	·100 ,,		
	Total ..	2·787 ,,		
No. 4.	Varied, consisting of			
	Meat, 12oz.	1·307 grammes.		
	Bread, 18oz.	1·130 ,,		
	Potatoes, 16oz.	1·084 ,,		
	Milk, 6oz.	·263 ,,	670 c.c.	1·29
	Vegetables, 4oz...	·100 ,,		
	Total	3·884 ,,		

APPENDIX. (No. 6.)

Table showing the Quantities of Lime, Magnesia, Soda, Potash, and Phosphoric Acid, consumed by a Soldier in Military Hospital, on Full Diet.

Article of Food and quantity.	Lime in Grammes.	Magnesia in Grammes.	Potash in Grammes.	Soda in Grammes.	Phosphoric Acid in Grammes.
Meat, 12oz.	·123	·120	·756	·717	1·194
Bread, 18oz,	·111	·235	·784	·210	1·847
Potatoes, 16oz.	·164	·298	1·720	·180	·656
Milk, 6oz.	·160	·046	·044	·190	·270
Vegetables, 4oz.	·135	·045	·462	·084	·124
Total	·693	·747	3·766	1·381	4·091

Urine passed by an Adult in Health, on Ordinary Diet, during Twenty-four Hours, showed—

Lime in Grammes.	Magnesia.	Potash.	Soda.	Phosphoric Acid,
·495	1·674	1·020	4·830	1·728

APPENDIX. (No. 7.)

Table showing Analogy between Tricalcic Phosphate, Tribasic Phosphate, and Phosphate in Aorta, Brain, and Lung.

	Bone Phosphate.	Tribasic Phosphate. CaO, MgO, NaO, PO_5	Tribasic Phosphate made in Laboratory, No. 1.	Tribasic Phosphate made in Laboratory, No. 2.	Phosphate from Aorta of Ox.	Phosphate from Human Brain.	Phosphate from Human Lung
Lime	54·19	18·66	31·70	27·07	6·77	13·42	18·76
Magnesia	00·00	13·34	18·10	9·17	11·25	5·95	27·65
Potash	00·00	00·00	00·00	00·00	27·97	14·24	·741
Soda	00·00	20·66	10·34	15·93	7·42	13·60	11·62
Phosphoric Acid	45·81	47·34	39·86	47·83	46·59	52·79	34·56
	100·00	100·00	100·00	100·00	100·00	100·00	100·00

Of the two samples of Tribasic Phosphate made in Laboratory, No. 1 was precipitated from an alkaline solution, and shows, therefore, an excess of base; No. 2 was obtained from an acid solution. In the Phosphate from Lung, the tissue examined contained blood, which was analysed with the lung substance. As blood contains alkalies, this would account for the excess of base shown. Making allowance for these causes of apparent discrepancy, it will be seen that these analyses show the same chemical combination.