INFLUENCE OF PHOSPHATE OF SODA

ON THE

EXCRETION OF URIC ACID

AND SOME OF THE CONDITIONS WHICH PREVENT
ITS ACTION.

BY

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IN a Thesis for the Degree of M.D. (John Bale and Sons, 1888¹), p. 14, I have drawn attention to the fact that phosphate of soda is a well-known solvent of uric acid and that it increases the excretion of this substance; but further investigation has shown me that while the above statement is practically true for the pure neutral phosphate ($\text{Na}_2\text{H}_2\text{PO}_4$), it does not necessarily apply to all specimens of phosphate sold as Sodii Phosphas, B. P.

After writing the above Thesis I was led by my results with the phosphate to recommend its use in a case of gout, the notes of which have been published in 'St. Bartholomew's Hospital Reports' for 1888, p. 217.

But I found to my surprise that it not only did no good in this case but actually precipitated an attack of gout;

¹ And 'British Medical Journal,' July 7th, 1888.

several specimens of the salt from different sources having the same effect.

And examination of the urine showed that it caused no plus excretion of uric acid, but on the contrary retention, the retention coinciding with the attacks of gout which were obviously due to it.

I then tried these various specimens of phosphate on myself, and as they gave results which were very different from those I had previously obtained with phosphate of soda, I concluded that there must be some chemical difference between the various specimens. I therefore got them analysed, and I now give some of the results obtained in Messrs. Savory and Moore's laboratory by Mr. J. E. Saul, F.I.C.

Proportion of sulphate occurring in disodic phosphate. The contamination is calculated as dry disodic sulphate, and the percentage is taken on the anhydrous phosphate :

- No. 1. (Recrystallized) 1·2 per cent.
- No. 2. (Recrystallized) 1·9 per cent.
- No. 3. (Recrystallized) 2·8 per cent.¹
- No. 4. (Commercial) 6·8 per cent.

From this it will be seen that all the specimens contained as an impurity a certain small percentage of sulphate, varying from 6·8 in the commercial to 1·2 in a specimen of the recrystallized salt. One specimen not given in Mr. Saul's Table contained even less than 1·2 per cent., and by great good fortune I had obtained and used some of this in my first experiments with phosphate of soda.

Having found in this way that the contamination with sulphate was probably of great importance with reference to the action of the phosphate on uric acid, I asked Messrs. Savory and Moore to try and obtain for me an absolutely

¹ No. 3 in Mr. Saul's Table was the salt first used in the case of gout at St. Bartholomew's.

pure phosphate of soda. They found, however, that re-crystallization even many times repeated did not suffice to remove all trace of sulphate from the commercial phosphate, and they therefore prepared for me a pure phosphate by the careful combination of sodium hydrate and phosphoric acid.

FIG. 1.

Having in this way obtained a pure salt, I proceeded to experiment on myself with it, and I found that, with a few exceptions, the causes of which I shall go into further on, it might be relied on to cause a plus excretion of uric acid, and I have given in Fig. 1 the results obtained by taking one drachm of the pure salt three times a day for five days.

It will there be seen that the uric acid is only slightly above the urea on the first day, but rises higher above it on the second and third, and remains above it as long as the salt is taken; and this is the same result as I had

previously obtained with phosphate of soda and mentioned in my Thesis. The rise of urea and part of the rise of acidity on the second and third days are due to meat and wine taken on the second day ; part of the rise of acidity is due to the phosphoric acid, or acid phosphate of soda, and is constantly seen when the phosphate is taken (see previous reference to Thesis).

FIG. 2.

I then proceeded to combine the pure phosphate with a known amount of sulphate, viz. ten grains of sulphate to each drachm of phosphate, corresponding roughly to about 15 per cent. of sulphate, and I have given in Fig. 2, the results obtained with this mixture of phosphate and sulphate, and also with the sulphate taken alone. It will be seen that the uric acid is below the urea every day in this observation, and that the phosphate when combined with the sulphate did not cause a plus excretion of uric acid.

Moreover, a reference to my notes shows that on these days when the mixed salts were taken, there were very marked pricking and shooting pains in the joints and muscles, so that the clinical signs of uric acid retention were present.

I have said in the paper on gout in 'St. Bartholomew's Hospital Reports,' previously referred to, p. 224, that the bad results obtained were due to the impurity of sulphate in the specimen of phosphate used ; but I think that it is now possible to go further and to say that while the pure neutral phosphate of soda (Na_2HPO_4) is a good solvent of uric acid and causes a plus excretion of that substance ; yet if the phosphate meets with any acid when in solution, such acid may by combining with part of its alkali reduce some of it to the condition of an acid phosphate and destroy its power of producing a plus excretion of uric acid.

And in accordance with this I have found that there is no plus excretion of uric acid with the pure phosphate when a little dilute phosphoric acid has been added to its solution, and, on the other hand, when a little bicarbonate of soda has been added the plus excretion is very marked.

I have also found that some specimens of the pure phosphate act better and more certainly than others, and that those specimens act best which contain most of the pure Na_2HPO_4 , while other specimens, apparently in the process of crystallization, get mixed with a certain amount of acid phosphate (NaH_2PO_4) and cause little or no plus excretion of uric acid.

I have been told by Mr. Saul that when a solution of Na_2HPO_4 having an alkaline reaction is set aside to crystallize it may come to have an acid reaction during the process, and I think that then possibly some of the phosphate may be crystallized as NaH_2PO_4 rather than as Na_2HPO_4 , and when any specimen contains much of NaH_2PO_4 it fails to act well on the uric acid. When the phosphate is mixed with sulphate it has a harsh bitter taste in the mouth, and is very liable to cause some intestinal pain and irritation, with some relaxation of the bowels : the pure Na_2HPO_4 has a bland and pleasant taste, and has but little tendency to affect the intestines.

The point to be attended to in practice then is to obtain a pure neutral phosphate of soda (Na_2HPO_4) which is not only free from sulphate, but free from any considerable

admixture with the acid phosphate (NaH_2PO_4) ; and it should not be given along with acids, but rather with the addition of a little bicarbonate of soda, such as ten grains of the latter to one drachm of phosphate.

If we can obtain such a salt we have a substance which is pleasant to take, and has, so far as I know, no bad effects either on the intestines or the kidneys ; and yet, if the ingestion and formation of acids can be kept within moderate limits, it insures a free daily excretion of uric acid so long as it is taken. Since it causes such free excretion of uric acid it is almost certain to be useful in diseases which take origin in the retention and accumulation of uric acid, and about its action in some of these I shall now say a few words.

It is not likely to be very useful in acute gout because high and rising acidity is so marked a factor, indeed, the actual cause of this disease, and high acidity may, as we have seen, overcome and prevent the solvent action of phosphate of soda on uric acid.

This is an important point, for it shows up in marked contrast the action of phosphate of soda and salicylate of soda ; acids may overpower the phosphate, while the influence of the salicylate is, as I have pointed out in 'Med.-Chir. Trans.,' vol. lxxi, p. 131, actually assisted and increased by a high and rising acidity ; and in my experience salicylate of soda is very useful in acute gout, while the phosphate is of much more doubtful value.

In mental depression, however, in so far as this condition is dependent on uric acid ('Practitioner,' November, 1888), I believe that the phosphate may be able to turn the tables on the salicylate, for mental depression generally coincides with a low and falling acidity, that is, with a plus excretion of uric acid under alkali. This condition favours, as we have seen, the complete excretive action of the phosphate, and further, this salt while providing for the free excretion of uric acid slightly raises the acidity and produces feelings of brightness and well-being.

In my own experience there is no drug which causes

such steady and continuous feelings of mental brightness and well-being as the pure phosphate of soda. To obtain this result I have not found it necessary to go beyond the dose of one drachm of the salt to be taken in a tumbler of hot water every night at bed time, and I have been able to continue this for weeks and months without any bad effect. So far as my experience goes the same result can be obtained in others. The same will hold, also, good for the uric acid headache, which presents all the conditions of mental depression only in greater intensity ('Med.-Chir. Trans.,' vol. lxx, and 'St. Bartholomew's Hospital Reports,' vol. xxiii).

With regard to headache phosphate of soda has one effect in common with salicylate, viz. that the plus excretion of uric acid occurring under either of them is not accompanied by any headache, or by any feelings of mental depression as it is when it occurs under the influence of an alkali alone; and this fact is, I think, a sufficient answer to anyone who would be inclined to ask, Why give the phosphate of soda to increase the excretion of uric acid rather than the bicarbonate of soda?

By all means let those who do not suffer from headache, and who do not fear a little mental depression, take the bicarbonate if they prefer it; but the phosphate is no foreign substance to be kept out and avoided, it is, on the contrary, a natural constituent of the tissues and fluids of the body, and probably one of the natural solvents of uric acid in the system (See 'Med.-Chir. Trans.,' vol. lxxi, p. 288).

There are other conditions connected with uric acid in which my experience with the phosphate is not sufficient to allow of my saying much at present, beyond the general statement of its probable utility.

My object, however, in this paper is to point out again that phosphate of soda is useful in some uric acid diseases, and now more especially that it may be used with advantage in some cases where the powerful action of salicylate of soda is not absolutely necessary.

The salicylate is a powerful excretant of uric acid, and its chief importance depends on the fact that acids increase rather than diminish its activity; on the other hand, it has undoubted toxic properties which are more or less manifest in every case where large doses are given; it often, even in ordinary doses, causes gastric irritation and nausea; and it is not free from the suspicion of causing albuminuria, delirium, and other troubles.

The phosphate is a less powerful excretant of uric acid, and the mineral acids or their salts may more or less interfere with its action; but when its power is sufficient it has the advantages of being a natural constituent of the tissues and fluids of the body, of having no toxic properties, and of causing little or no irritation in the stomach or intestines; and last, but not least, its taste is bland and by no means unpleasant.

Note.—The present price of the pure phosphate as made by the combination of sodium hydrate and phosphoric acid, is relatively high (viz. 6*d.* per oz., or in quantities of 50 lbs., 4*s.* per lb., or of 112 lbs., 3*s.* per lb.), but no doubt this would soon be reduced if it were used to any large extent.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. i, p. 131.)