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(13)

# ON THE SOLVENT TREATMENT OF URINARY CALCULI;

## AN EXPERIMENTAL AND CLINICAL INQUIRY.

BY

WILLIAM ROBERTS, M.D.,

PHYSICIAN TO THE MANCHESTER ROYAL INFIRMARY.

COMMUNICATED BY

HENRY BENCE JONES, M.D.

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The possibility of dissolving urinary concretions, or any class of them, within the living passages, is a question of practical interest for the treatment of renal, and, in a less degree, of vesical calculi.

A solvent treatment of these affections cannot, at the present day, be said to have a standing-place in therapeutics. Vesical calculi are made over to the surgeon as soon as they are discovered, to be dealt with by mechanical means, and scarcely any purpose of dealing radically with renal calculi can be said to exist. The opinion expressed by Marcet in 1819 is still the belief of the profession, namely, that "no reasonable expectation can be entertained that calculi lodged in the urinary organs, and already too large to be discharged by the natural passages, can be actually dissolved by any mode of internal treatment. The only benefit which we may with any confidence expect from medicine in this disease is either to prevent the increase of calculi already formed, or, what is still more important, to guard the constitution of those who are subject to the disorder against the prevalence of the particular diathesis from which it arises."[1]

More recent writers on the subject (Civiale, Rees, Heller) express themselves as doubtfully about solvent remedies; and the small doses which they recommend, indicate very clearly, that the most they expect from their operation is to facilitate the spontaneous expulsion of the concretions, to prevent their further growth, and to palliate their symptoms.

Nevertheless, the past history of the subject contains some convincing proofs that calculi have been dissolved within the bladder by means of alkaline substances; and it appeared worthy of inquiry whether a more exact re-examination of the question might not reveal the causes of the discrepant results obtained in past times, and indicate, with some approach to certainty, what may be rationally expected from a solvent treatment, the cases in which it is applicable, and the precise mode of carrying it out effectually.

With this view, numerous experiments and observations were made by the author at intervals extending over several years; and the results obtained seem to demand a considerable modification of the prevailing opinion. They do not by any means indicate the general possibility of substituting a solvent for a mechanical treatment of vesical calculi, but they suggest an essential improvement in the treatment of renal concretions; they also indicate that uric acid and cystin, under certain circumstances, are capable of solution in the bladder by means of medicines administered by the mouth, at a rate which admits of practical application, and that in certain picked cases a solvent treatment deserves to

[1] Marcet, 'On Calculous Disorders,' p. 143.

be resolutely tried before having recourse to the more dangerous methods of lithotomy and lithotrity.

It may be stated at the outset that the inquiry has not led to the discovery of any new solvent for the stone, but rather to a better application of a treatment which has long been known in principle, but which has forfeited the confidence of the profession by the faulty manner in which it has been carried out, and its employment in cases where it was sure to fail.

For the present purpose urinary concretions may be considered as consisting of *uric acid, oxalate of lime,* and the *earthy phosphates.* Of the rarer varieties, cystin and the urates fall into the same category with uric acid, and carbonate of lime into the same category with the phosphates.

The first part of this paper is devoted to experiments and observations relating to the solvent treatment of uric acid, by alkalizing the urine, through the internal administration of medicines. The second part is devoted to experiments relating to the solvent treatment of uric acid by injections into the bladder, and to experiments on the solvent treatment of oxalate-of-lime and phosphatic concretions.

With regard to uric acid the inquiry is tolerably complete in the directions taken. Oxalate of lime gave results which did not promise any useful application. Sir B. Brodie's method of dissolving phosphatic calculi by injecting acid solutions into the bladder was imitated in one experiment with results highly favorable to further trial in the same direction.

## PART I.

### OBSERVATIONS AND EXPERIMENTS RELATING TO THE SOLVENT TREATMENT OF URIC-ACID CALCULI, BY ALKALIZING THE URINE, THROUGH THE INTERNAL ADMINISTRATION OF MEDICINES.

The idea of imparting solvent properties to the urine by means of medicines taken internally is of very ancient date, and a multitude of substances have attained, at different times, a temporary reputation as solvents for the stone. But there is no reason to believe that any of them possess real virtues except those which are capable of rendering the urine alkaline.

It has now been known for many years that the fixed alkalies, in the caustic state, or as carbonates, citrates, acetates, or tartrates, when administered by the mouth, appear in the urine as carbonates, and thus render the urine alkaline.

It has also been asserted, and on the other hand has been denied, that the alkaline carbonates exercise a solvent action on uric acid.

This power of alkalizing the urine at will, has been hitherto very imperfectly studied in its application to the solvent treatment of urinary calculi. We have no information as to the degree of alkalescence which can be communicated to the urine by given doses of any salt, nor as to the relative alkalizing power of different salts. We are also ignorant of the relative solvent power on uric acid of carbonate of potash and carbonate of soda; we do not know the best strength of solution to employ, nor the effect of quantity of the solution on the results obtained, nor the absolute rate of dissolution attainable. Only the rudest notions prevail of the actual effect of alkalized urine on calculi in the bladder, and of the collateral circumstances which favour or impede its operation.

An extended inquiry was found necessary to elucidate all these points, including a long series of experiments in the laboratory, numerous observations on healthy persons, and clinical observations on patients suffering from renal or vesical calculi.

These experiments and observations are detailed in the following pages in the above order. An experimental basis is first established, so far as is practicable, then the clinical facts are added, and finally the rules for conducting the solvent treatment[1] are enunciated.

Tentative experiments soon showed that solutions of the carbonate of potash and carbonate of soda did exercise a solvent action on uric acid, but only within certain limits of strength.

The questions which first presented themselves for decision were:—the relative solvent powers on uric acid of carbonate of potash and carbonate of soda, the relative effects of solutions of different strength, and of varying quantities of solutions of the same strength, also the absolute rate at which dissolution proceeded under conditions which might be more or less closely imitated within the body of a patient.

Answers to these questions were sought by placing sections of uric-acid calculi, weighing about 100 grains, in ten-ounce phials, and causing currents of the different solutions to pass over them at a regulated rate. The plan adopted was to immerse the phials in a water bath, kept constantly at the temperature of the body. Each phial was connected on the one side by means of india-rubber tubing with a reservoir of the solution to be tried. On the other side an exit-tube was provided, which was fitted at its extremity to a piece of glass tube drawn to a fine point. The bore of this tube at the point regulated the rate of flow. The flow of the solution over the stone was maintained, in a large number of experiments, at the rate of six pints in the twenty-four

[1] Whenever the term "solvent treatment" is used in the first part of this paper it signifies exclusively the method of treating uric-acid calculi by alkalizing the urine by the administration of medicines by the mouth.

hours; in some experiments it was increased to eight, ten, and fifteen pints; in others diminished to three pints or less. The experiments were contrived so as to imitate, in as close a manner as possible, the gentle but incessant flow of the urine along the ureters.

### Section I.—*Comparison of solutions of carb. potash and solutions of carb. soda.*

The potash salt was found sensibly to excel the soda salt as a solvent for uric acid. When the granular carbonate of potash of the shops was compared with the dried carbonate of soda, the advantage lay with the former when equal weights were employed, and still more when corresponding atoms were compared. Solutions of these two salts yielded the following results:

| | |
|---|---|
| A solution of *carbonate of potash* containing 30 grains to the pint dissolved daily (mean of twelve day-experiments[1]) | 11·9 per cent. |
| A solution of *carbonate of soda* containing 30 grains to the pint dissolved daily (mean of eight day-experiments) | 10·3 „ |
| A solution of *carbonate of potash* containing 60 grains to the pint dissolved daily | 20·2 „ |
| A solution of *carbonate of soda* containing 60 grains to the pint dissolved daily | 14·3 „ |

Carbonate of potash possessed a further advantage over carbonate of soda in its *wider range* of solvent power with the stronger solutions. This point will be better understood after the effects of solutions of different strength have been considered in the following section.[2]

1 By day-experiments are meant experiments continued for twenty-four hours.

2 Some experiments were also made with carbonate of lithia, which has been vaunted in recent times as a solvent for uric acid. Its power was found much inferior to that of the carbonates of potash and soda. Its reputation seems to have been gained through its comparative insolubility. Only weak solutions of it *could* be employed, and then were com-

Section II.—*Comparison of solutions of different strength.*

The strength of the solution was found to affect its solvent capacity more than any other condition. The greatest solvent power was found to lie in solutions containing from forty to sixty grains of carbonate to the imperial pint. With stronger solutions than these the fragments became covered over with a white crust of alkaline bi-urate, which seriously interfered with the solvent action.

A solution of carbonate of soda containing 120 *grains to the pint* caused the production of a stiff coating of bi-urate, resembling white paint, which altogether prevented any dissolution taking place. The fragment, after undergoing the effect of such a solution for twenty-four hours, had not lost any weight; and when the white coating had been scraped off with the nail the loss of weight was only three quarters of a grain.

A solution of carbonate of potash containing 120 *grains to the pint* also produced a crust of bi-urate, but of a much looser texture. The fragment had lost weight to the extent of 3 or 4 per cent. in the twenty-four hours, and when the crust was scraped off the loss amounted to from 6 to 11 per cent.

With solutions containing 160 *and* 240 *grains to the pint* there was no loss of weight with potash or soda; the fragments were invested with a thin tough coating of white bi-urate, which put a stop to all solvent action.[1]

With solutions of carbonate of potash containing 80 *grains to the pint* the fragment was found covered with a loose detachable crust of bi-urate, like a layer of whitewash, which chipped off readily in large flakes or scales when touched

pared with solutions of potash and soda which were much too strong for effective dissolution. The lithia experiments will be found recorded in the second part of this paper.

[1] For the analysis and further particulars of the white coating of bi-urate, see an extract of a paper by the author in the 'Transactions of the British Association for the Advancement of Science' for 1861; also in 'Beale's Archives' for 1862.

with the nail. Two experiments, each of twenty-four hours' duration, made with a solution of this strength, showed a mean dissolution of 9·8 per cent. when the fragments were weighed without detaching the loose crusts. After detaching the crusts the loss of weight amounted to 13 per cent.

With a solution of carbonate of potash of 60 *grains to the pint* the fragment was usually dissolved clean, without a trace of bi-urate crust; but in some experiments detached scales of bi-urate were found on the spots where the stone had rested in the phial. Dissolution went forward with great rapidity with solutions of this strength, and the production of the loose crusts did not appear to interfere sensibly therewith. Seven day-experiments with this solution dissolved the fragments at a mean daily rate of 20·2 per cent. of their weight.

Solutions of carbonate of soda of the same strength (60 grains to the pint) showed a complete and more adherent crust of bi-urate than the corresponding potash solution. The mean loss of weight in two day-experiments, after detaching the crust, amounted to 14·3 per cent.

Weaker solutions than 60 grains to the pint dissolved the fragments without the formation of bi-urate crusts, or only with traces of such; the red surface of uric acid remained clean and appeared water-worn. The dissolving powers declined gradually as still weaker solutions were used.

Solutions of carbonate of potash gave the following results:

| | | Per cent. |
|---|---|---|
| 40 *grains to the pint* | (daily flow, six pints—mean of three experiments) dissolved in twenty-four hours ........................................ | 15·6 |
| 30 " " | (daily flow, six pints—mean of three experiments) dissolved in twenty-four hours ........................................ | 11·9 |
| 20 " " | (daily flow, six pints—mean of three experiments) dissolved in twenty-four hours ........................................ | 11·0 |
| 10 " " | (daily flow, six pints—mean of three experiments) dissolved in twenty-four hours ........................................ | 6·5 |

| | | Per cent. |
|---|---|---|
| 5 *grains to the pint* | (daily flow, eight pints—mean of two experiments) dissolved in twenty-four hours | 6·0 |
| 2½ " " | (daily flow, eight pints—mean of two experiments) dissolved in twenty-four hours | 2·8 |
| 1 " " | (daily flow, eight pints—mean of two experiments) dissolved in twenty-four hours | 1·2 |

The effect of dilution was further tried in a second set of experiments, in which the flow of the solution was reduced to between one and two pints per day. The results stand as follows, with solutions of carbonate of potash:

| | | Per cent. |
|---|---|---|
| 40 *grains to the pint* | (mean of four experiments) dissolved in twenty-four hours | 17·1 |
| 20 " " | dissolved in twenty-four hours | 7·0 |
| 10 " " | " " | 5·0 |
| 7 " " | " " | 6·6 |
| 6 " " | " " | 5·8 |
| 5 " " | " " | 3·7 |
| 4 " " | " " | 2·9 |
| 3 " " | " " | 1·3 |
| 2 " " | " " | 0·7 |
| 1 " " | " " | 1·0 |

From the two sets of experiments we gather that solutions containing less than 3 grains to the pint exercise only a feeble solvent action on uric acid. The Manchester pipe-water was found to possess a solvent power not greatly inferior to this. In an experiment extending over seven days, the pipe-water, flowing at the rate of nine pints a day, at blood heat, dissolved 5 grains from a fragment of uric acid weighing 112 grains, or at the rate of ·6 per cent. in twenty-four hours.

Solutions containing from 4 to 10 grains to the pint had a sensibly greater effect. The daily rate of dissolution with solutions of this strength ranged from about 3 to about 6 per cent. of the weight of the fragment.

Solutions of 20 grains to the pint and upward, as high as

60 grains to the pint, displayed a still more powerful action. They dissolved the fragments at daily rates varying from 7 per cent. to more than 20 per cent.

### Section III.—*Comparison of the effects of varying quantities of solutions of constant strength.*

The natural flow of urine in healthy persons varies from two to three pints a day, but by copious water-drinking the quantity may be readily increased to six or ten pints a day. It was, at the outset of the inquiry, thought that the quantity of the solvent permitted to flow over the stone would greatly influence the rate of dissolution, but when the point was tested experimentally the effect of quantity, between the limits necessarily imposed by the capacity of the kidneys to eliminate aqueous fluids, proved to be comparatively unimportant.

In order to obtain comparable results, different quantities of a solution of constant strength were passed over the same stone on successive days.[1]

A solution of carbonate of soda containing 30 grains to the pint gave the following results:

| | Per cent. |
|---|---|
| With a daily flow of 15 *pints* the loss of weight was (mean of four experiments) | 10·9 |
| With a daily flow of 8 *pints* the loss of weight was (mean of four experiments) | 10·2 |
| With a daily flow of 5 *pints* the loss of weight was (mean of two experiments) | 9·8 |

A solution of carbonate of potash containing 30 grains to the pint gave the following results:

[1] Absolutely exact comparative results are necessarily impossible in experiments of this kind. Uric-acid stones differ considerably among themselves in density of structure, and the fragments vary in form, weight, and surface, so that some offer considerably greater facilities for solution than others. The experiments were, however, repeated a sufficient number of times to cover discrepancies from these sources. The general conclusions may be confidently relied on.

| | Per cent. |
|---|---|
| With a daily flow of 15 *pints* the loss of weight was (mean of four experiments) ...... | 13·0 |
| With a daily flow of 8 *pints* the loss of weight was (mean of two experiments) .. ...... | 15·0 |
| With a daily flow of 6 *pints* the loss of weight was (mean of four experiments) ...... | 10·2 |
| With a daily flow of 4 *pints* the loss of weight was (mean of two experiments) ...... | 9·5 |

A solution of carbonate of potash containing 60 grains to the pint yielded the following results :

| | Per cent. |
|---|---|
| With a daily flow of 14 *pints* the loss of weight was (mean of two experiments) ...... | 19·0 |
| With a daily flow of 6 *pints* the loss of weight was (mean of two experiments) ...... | 21·4 |

A number of other experiments, which it is needless here to reproduce, pointed to the same deduction, namely, *that with solutions of constant strength a flow of eight to fifteen pints a day scarcely dissolved more than a flow of three to six pints a day.*

The inquiry, so far, has led us to the following conclusions :

*a.* Carbonate of potash is a better solvent for uric acid than carbonate of soda.

*b.* The maximum solvent power of the alkaline carbonates on uric acid lies in solutions containing from 40 to 60 grains to the pint.

*c.* That within the limits prescribed the effect of quantity of the solution is unimportant.

## SECTION IV.—*Absolute rate of dissolution of uric-acid calculi in solutions of the alkaline carbonates.*

With regard to the absolute rate of dissolution, the experiments above detailed opened out an inviting prospect. The solutions of maximum solvent power dissolved from 10 to 20 per cent. of the weight of the stones in the course of twenty-four hours. If results approaching these, or one half, or even one quarter, could be obtained within the living body, a little consideration will show that such an impression could be made on the concretion in a few weeks, as would either entirely dissolve it, or reduce its dimensions to a point which would enable it to escape by spontaneous expulsion.

The next points to be ascertained were—the best way of alkalizing the urine so as to impart to it an alkalescence corresponding to that of solutions of carbonate of potash in water of maximum solvent power; also to examine the actual effect of alkalized urine passed over uric-acid calculi in a phial at blood heat.

### SECTION V.—*The most convenient way of alkalizing the urine, the degree of alkalescence which can be communicated to it, and the doses required to produce the desired effect.*

The urine may be rendered alkaline by a variety of substances; but the best adapted for the purpose are the alkaline bicarbonates, acetates, and citrates. These salts have very little taste, they do not disturb the stomach and bowels, and they may be administered for weeks and months without deleterious effects. All of them appear in the urine as carbonates of their respective bases.

After a large number of comparative trials the acetate and citrate of potash were found to offer advantages superior to any of the others. They form draughts which are nearly tasteless; being neutral salts, they do not saturate the free acids of the stomach, and thereby interfere with digestion; they are also extremely soluble.

The degree of alkalescence communicated to the urine by these salts depends on the quantity and dilution of the dose.

To maintain a persistent alkalescence of the urine by acetate or citrate of potash, required, in an adult, six or eight drachms to be given daily, in divided doses. When administered in these large doses about two thirds of the potash reappeared in the urine as free carbonate.

When the acetate or citrate of potash, in the dose of 40 grains dissolved in 5 ounces of water, was administered every two hours, it communicated to the urine an alkalescence, equivalent to that of a solution of carbonate of potash containing from 20 to 80 grains to the pint.[1] This corresponds sufficiently closely with the maximum solvent power of that salt as already ascertained. (See Section II.)

It is, of course, quite impossible to maintain the urine at a constant degree of alkalescence, however short may be the intervals at which the medicine is administered. The activity of the kidneys oscillates from hour to hour; at one time the urine is secreted abundantly and highly dilute, and then the degree of alkalescence falls; at another time it is secreted more scantily and in more concentrated form, and then the degree of alkalescence rises. When, however, the dose is exhibited with regularity, at intervals of two or three hours, the oscillations rarely pass the limits above indicated, namely, an equivalent to 20 to 80 grains of carbonate of potash to the pint; and, as a rule, the alkalescence ranges between 35 and 60 grains of carbonate to the pint.

The *tartrates* were found unsuitable, from their bitter taste, and their tendency, unless greatly diluted, to act on the bowels.

The *common phosphate of soda* and the *basic phosphate of soda* were found to possess very inferior alkalizing powers. The former, even in the quantity of 640 grains daily, in divided doses, only produced a total daily alkalescence equal to 34 grains of carbonate of potash; and the subphosphate, in the same quantity, only a total alkalescence equal to 48 grains of carbonate of potash per day; whereas the same quantity of citrate produced a total daily alkalescence of more than 300 grains of carbonate of potash.

[1] The degree of alkalescence of the urine was estimated by volumetrical analysis with a standard solution of dilute sulphuric acid. Whenever carbonate of potash is referred to in this paper as a standard of alkalescence, the granular carbonate of potash of the shops is signified. This preparation contains, according to Phillips, 16 per cent. of water, and its combining equivalent is reckoned as 82·5.

*Borax* proved objectionable on account of its unpleasant effects on the stomach and its feeble alkalizing powers. With 320 grains of borax a day, which was difficultly borne by the stomach, the total alkalescence produced in twenty-four hours was only equal to 14 grains of carbonate of potash.

These observations on the phosphates of soda and borax were made on eight different individuals, and extended in each case over several successive days.[1]

### SECTION VI.—*The effect of alkalized urine on uric-acid calculi.*

Having ascertained the method of alkalizing the urine to a degree corresponding with the maximum solvent power of solutions of carbonate of potash in water, an experiment was now performed imitating still more closely actual clinical experience. This consisted in subjecting uric-acid calculi to the operation of alkalized urine in a phial at the temperature of the body.

Some practical difficulties were encountered in performing this experiment. It was found impossible to maintain a constant current over the stone, on account of the clogging of the tubes; and a simpler method had to be adopted. This was to transfer the alkalized urine, immediately it had been voided, into a ten-ounce phial containing a uric-acid calculus. The phial and its contents were kept in a water bath at blood heat. Each time the bladder was emptied the old urine was thrown away and replaced by the fresh urine.

But even when thus simplified, certain precautions were found essential to the successful performance of the experiment. And as these precautions depend on a circumstance of great importance to the efficient carrying out of the solvent treatment in practice, a few explanations are here necessary.

It is well known that fresh urine has a tendency to become quickly ammoniacal when exposed to the contact of stale or decomposed urine; this is especially the case when

[1] In the second part of this paper will be found some observations on the solvent power on uric acid of watery solutions of these salts.

the urine is re-warmed in the air. Alkalized urine exhibits this tendency more strongly than acid urine. In my earlier trials this tendency came into play, and caused some embarrassment; eventually it led to a valuable practical deduction, as may be seen from the following observation.

Alkalized urine from a person taking bicarbonate of potash was placed in a phial with a fragment of uric acid, and maintained at blood heat. The urine was changed, according to the frequency of micturition, every two or three hours. At the end of twenty-four hours the fragment was found to have an offensive smell, and to be covered in great part with whitish patches. It had diminished in weight from 78 to 76 grains. The experiment was continued for thirty-six hours longer, and the fragment re-examined. It was now covered with a complete white crust; it was very offensive and ammoniacal to the smell; its loss of weight was almost inappreciable until after the white crust had been scraped off. The phial in which the experiment was performed was also encrusted with a whitish substance of similar character. The crust on the fragment and the deposit on the sides of the phial were found on examination to be composed of a mixture of triple phosphate and amorphous phosphate of lime; in other words, of "fusible matter" or "secondary" calculous deposit.

In a second experiment, performed similarly, the phosphatic crust was estimated to be a tenth of a line thick; the fragment entirely ceased to lose weight after the second day.

From these experiments the important deduction was drawn—*that in an ammoniacal urine the solvent power of alkalized urine is completely nullified by the deposition of the mixed phosphates on the surface of the concretion.*

In subsequent experiments the following simple expedient was adopted, which obviated this difficulty. At each change of urine the fragment was dipped into cold water, so as to remove all traces of the previous urine; the phial, in like manner, was thoroughly cleansed at each remove. By this means the fragment and phial were kept perfectly sweet and free from the contamination of decomposing urine.

Performed in this manner, the experiment succeeded perfectly; not a particle of phosphate was deposited, the surface of the fragment remained clean and red, and dissolution went on uninterruptedly.

In two such experiments, each of twelve hours' duration, a section of uric-acid calculus weighing 180 grains lost weight to the extent of 6 grains in one and 6½ in the other, or at the rate of 12½ grains in the twenty-four hours. As absolute values, these numbers are necessarily too low. At each change of urine a certain time was lost, and the urine-solvent was thereby allowed to cool to a certain degree; a further temporary lowering of the temperature was occasioned by the washing of the fragment and phial in cold water.

The following tables exhibit the condition of the urine during the performance of these two experiments—showing its varying quantity, specific gravity, and alkalescence, at each micturition.

The individual whose urine was employed was fully under the influence of citrate of potash in the dose of 40 grains, administered every two hours, in 5 ounces of water.

First Experiment.—The immersion of the fragment commenced at 9.40 a.m., and terminated at 9.40 p.m. The urine used was secreted between 7.30 a.m. and 8.8 p.m.; it was transparent throughout. The fragment weighed before the experiment 180½ grains; after the experiment 174 grains. Breakfast at 8.40 a.m.; dinner at 1 p.m.; tea at 5 p.m.

| Time during which the urine was secreted. | Quantity of the urine. | Sp. gravity. | Alkalescence per pint in terms of pot. carb. of shops. |
|---|---|---|---|
| 7.30 to 9.36 a.m. | 6 oz. | 1022 | 65·0 grains. |
| 9.36 to 10.50 „ | 15¼ „ | 1008 | 26·9 „ |
| 10.50 to 12.20 p.m. | 8 „ | 1012 | 35·5 „ |
| 12.20 to 2.3 „ | 9 „ | 1013 | 43·6 „ |
| 2.3 to 3.15 „ | 12¼ „ | 1009 | 35·5 „ |
| 3.15 to 4.45 „ | 9 „ | 1013 | 49·8 „ |
| 4.45 to 5.57 „ | 6¾ „ | 1013 | 46·7 „ |
| 5.57 to 6.45 „ | 7 „ | ? | 17·7 „ |
| 6.45 to 8.8 „ | 10¾ „ | 1008 | 20·8 „ |

Second Experiment.—The immersion of the fragment commenced at 9.30 a.m., and terminated at 9.30 p.m. Its weight before the experiment was 174 grains; after the experiment 168 grains. The urine employed was secreted between 7.37 a.m. and 9 p.m.; it was perfectly clear throughout. Breakfast at 7.40; dinner at 1.40; tea at 5 p.m.

| Time during which the urine was secreted. | Quantity. | Sp. gravity. | Alkalescence per pint in terms of carbonate of potash of the shops. |
|---|---|---|---|
| 7.37 to 9.30 a.m. | 3½ oz. | 1025 | 82·2 grains. |
| 9.30 to 10.50 ,, | 12 ,, | 1008 | 30·4 ,, |
| 10.50 to 1.30 p.m. | 9¾ ,, | 1015 | 58·4 ,, |
| 1.30 to 4.20 ,, | 9¼ ,, | 1013 | 48·0 ,, |
| 4.20 to 5.55 ,, | 5½ ,, | 1018 | 72·0 ,, |
| 5.55 to 7.10 ,, | 10 ,, | 1006 | 26·9 ,, |
| 7.10 to 9.0 ,, | 5 ,, | 1016 | 59·9 ,, |

The urine of patients taking full doses of acetate or citrate of potash is generally clear, as in the above experiments, and shows no tendency to precipitate even on standing. But this is not invariably the case; it is sometimes turbid from deposition of the amorphous phosphate of lime. Two conditions seem especially to favour this deposition, namely, the febrile state and the digestion of a heavy meal. The amorphous phosphate is not infrequently deposited after a meal in healthy persons who are not taking any alkalizing medicines; the circumstance is therefore not to be regarded as an unnatural or hazardous one.[1]

The amorphous phosphate of lime differs essentially from the "mixed phosphates" or "fusible matter" thrown down in an ammoniacal urine. The former is a loose flocculent substance, which shows no tendency to aggregate into concretions; the latter, on the other hand, is partly crystalline, and speedily encrusts any object brought into contact with it. The establishment of this distinction disposes of one objection which has been urged against the use of alkaline solvents.

[1] See a paper by the author "On the Daily Changes of the Urine," in the 'Edinburgh Med. Journ.' for March and April, 1860.

The inquiry has now brought us to the following additional conclusions:

*d.* Urine can be readily alkalized to a mean degree corresponding with the maximum solvent power of a solution of carbonate of potash in water.

*e.* Urine so alkalized, maintained at the temperature of the body, in contact with a uric-acid calculus, was found, on actual trial, to dissolve the concretion at the rate of 12 or 13 grains in the twenty-four hours.

*f.* The oscillations in the degree of alkalescence of the urine did not appear to exercise any unfavorable influence on its solvent power.

*g.* The fragment experimented on showed no tendency to contract a coating of bi-urate or of earthy phosphate.

It now remains to bring forward illustrations of the application of the solvent treatment in actual practice; to distinguish the cases in which the treatment is applicable from those in which it is inapplicable; to lay down directions for carrying it out effectually; and, finally, to examine some of the objections which have been urged against its employment.

## SECTION VII.—*Illustrations of the application of the solvent treatment in practice.*

A.—*Cases of renal calculi and gravel.*

One of the first rational attempts to treat renal gravel of uric acid by the alkaline carbonates was made by the celebrated Mascagni on his own person. He gives the following account of his case in the 'Memoirs of the Italian Society' for 1804:

"I had been subject for several years to pains in the lumbar regions, and I voided from time to time gravelly concretions of a yellow-ochre and brick-red colour. Knowing that gaseous alkaline fluids had been used in such cases, I took some on several occasions with benefit. I imagined I could get greater effects with carbonate of potash.

"In the months of August and September, 1799, having been obliged to lead a sedentary life, I was cruelly attacked with pains in the kidneys, and I voided a considerable number of small concretions, some of which were large enough to be regarded as veritable calculi. They were reddish and crystalline, they were deposited at the bottom of the vessel each time I made water, and I could see their glistening facets through the transparent urine. I was also subject to an excess of acid in the stomach, which was perceived in the mouth. I examined my urine and found in it a free acid, which, as well as the concretions, I recognised as consisting of uric acid.

" Having thus assured myself of the nature of the concretions I was voiding, I resolved to make use of the carbonate of potash and to observe the result. I took the first day about a drachm, one half in the morning fasting, and the other half in the evening. I dined at one o'clock in the afternoon. This salt, dissolved in ten ounces of water, had very little taste, it caused no disturbance of the stomach or bowels; but as soon as I swallowed it, it occasioned a considerable disengagement of carbonic acid gas, which was felt in the mouth and discharged by the anus.

" The second day I took two drachms, and the third day three drachms; and I continued this dose, dissolved in twenty ounces of water, for ten days. Before using the carbonate my urine was very acid, and intensely reddened blue litmus paper. On the second day the paper changed colour very little, and none at all on the third day. The acid of my urine was therefore saturated. At this time the renal pains diminished, and I voided no more gravel with the urine. Afterwards the pains ceased entirely, the urine became less loaded, and *I recognised the potash in excess.*

" I ceased to use the carbonate of potash, and for months I voided no concretions. Being subsequently attacked by the same symptoms, I had recourse to the same remedy, and had the same good results. I have repeated this medico-chemical experiment every time I have felt the same inconvenience, and always with success. Two years have now elapsed since I voided any concretions, though I no longer make use of the potash."[1]

Cases resembling this might be readily multiplied; but their evidence in favour of dissolution having positively occurred, falls short, from the nature of the circumstances, of rigorous demonstration. I will only add to it one which occurred in my own practice.

In July, 1860, a stout middle-aged gentleman brought me eleven small concretions, varying in size from a large pin's head to a pea. He had voided these with the urine a few days previously; they were composed of nearly pure uric acid. He stated that three years before, he was attacked with severe renal colic, which subsided on the third day with the discharge of a small calculus by the urethra. From this period to the time of my seeing him attacks of renal colic, terminating in the discharge of small brownish concretions, recurred with great regularity at intervals of three or four months.

The urine was found to be acid and high coloured; the general health was somewhat impaired by his periodical sufferings.

In projecting the plan of treatment it was considered that the patient had in all probability a number of similar concretions still lodged in the kidneys. The dissolution of these was the first object; the next was to prevent their future formation. Seeing the small size of the concretions, it was thought that, by keeping up a persistently alkaline state of the urine for a week or two, complete dissolution of them would be effected. With this view, citrate of potash, in two-scruple doses, dissolved in half a pint of water, was administered every three hours for the space of a fortnight. Afterwards the patient took a drachm of the same salt in a tumbler of water, night and morning, for a period of three months. As no recurrence of the renal pains took place, nor the discharge of any concretions, the medicine was then discontinued; but the patient was instructed to take every

[1] Magendie, 'De la gravelle,' p. 85.

night before going to bed a tumbler and a half of simple water, a practice which he has continued up to the present time (October, 1864). There has been no return of the symptoms.

B.—*Cases of vesical calculi.*

A considerable number of examples of the successful treatment of vesical calculi by alkaline solvents lie buried in the forgotten publications which appeared in this country about the middle of the last century, when the remedy of Miss Stephens made so great a noise.[1] Some fifteen or twenty cases were also collected by Chevallier and Petit when the question was resuscitated in France thirty years ago.

Most of these reports are vitiated by the absence of information as to the nature of the stone and the condition of the urine. At the former epoch (1740) urinary calculi were all supposed to be of one nature, and that an unknown one. At the latter epoch the chemical composition of urinary calculi was, indeed, known, but some of the most important points in their development were misunderstood; urinary chemistry was still in its infancy; and the same absurd pretension of universal efficacy was put forth on behalf of alkaline substances which swamped their reputation in 1740.

One of the best illustrations from the earlier records is supplied by Dr. James Jurin, who was himself the sufferer. He states that he was subject for many years to red gravel. At Christmas, 1740, he voided a small stone, after suffering four days from nephritic colic. In January and February following he perceived unmistakeable signs of stone in the bladder. These he describes at great length and with remarkable clearness.

In March he began to take lixivium of soap or soap-ley (a strong solution of caustic potash), in gradually increasing quantities until he reached the amount of an ounce or an ounce and a quarter daily. He took for a single dose one or two teaspoonfuls of the ley, diluted with three quarters of a pint of water. The soap-ley which he employed was

[1] Ploucquet gives a list of more than forty papers and pamphlets published on the subject about 1740.

"one-fifth part heavier than river water" (*i.e.* its specific gravity was 1200, which is about three times as strong as the liquor potassæ of the London Pharmacopœia).

He continued this treatment for five months. On July 10th he voided a small smooth stone, of the size of an oat and of a reddish colour. On the 27th of the same month he voided a second stone. On August 6th he voided a third stone, and about the beginning of September a fourth. All his symptoms now disappeared, and he discontinued the medicine; but in December he had a return of the vesical symptoms; he also noticed that his urine again furred the chamber-pot, and that he voided a little red gravel, as he had previously done. He went back to the soap-ley, and in the course of a week parted with a small, rough, reddish stone. From this time he continued perfectly easy. He still took a couple of teaspoonfuls of the lixivium each day, and this he found sufficient to keep the urine from furring the utensil.

The concretions in this case were undoubtedly uric acid, as may be learnt, not only from their red colour, but also from an experiment which Dr. Jurin has recorded. He states that they dissolved entirely in the alkaline ley and in lime water.[1]

Of the cases recorded in France I shall only cite one. In Chevallier's essay on 'Solvents for the Stone,'[2] ten cases of the successful use of bicarbonate of soda are described. Dr. Charles Petit[3] has contributed some half-a-dozen additional cases illustrating the effects of Vichy waters (which contain 44 grains of bicarbonate of soda to the pint). The following is one of the latter.

[1] The record of this case may be found bound up with Rutty's 'Observations on Joanna Stephen's Medicine for the Stone,' Lond., 1742. Another good case is related by Whytt, in his 'Essay on Lime-water,' p. 5, Edin., 1752; and a third, in which the successful result is vouched for by a post-mortem examination made seventeen years afterwards, is recorded in the 'Philos. Trans.' for 1757, by Dr. Pringle.

[2] Translated by Edwin Lee in the 'Med. Gazette,' vol. xx, p. 542.

[3] Dr. Ch. Petit, 'Du mode d'action des Eaux Minérales de Vichy,' Paris, 1850.

M. de L—, æt. 51, was sounded by Leroy d'Etiolles, who found a stone in the bladder. This he believed not to be large, and to be suitable for crushing. The patient, however, went to Vichy, and drank, the first day, seven or eight glasses of the waters. The next day he took fifteen, and the urine, which was previously very acid, became strongly and constantly alkaline. In a few days he took twenty-two and twenty-four glasses. The symptoms, which were before severe, now subsided more and more; and after seventeen days of treatment he voided a smooth uric-acid concretion, which bore evident traces of dissolution. From this moment he continued wholly free from symptoms, and was able to take violent equestrian exercise without the least inconvenience.[1]

Before proceeding to relate my own experience, it may not be amiss to examine shortly into the reasons why the solvent treatment, in spite of a large mass of evidence in its favour, failed to maintain itself, and fell into universal neglect, both after 1740 and more recently after 1840. This question is now not difficult to answer. At both epochs the advocates of solvents claimed to be able to deal successfully with urinary calculi of every kind. It was alleged that alkaline remedies, either by solution or disintegration, could destroy them all, sooner or later. Dr. Petit, indeed, admitted that mulberry and bone-earth calculi were only very slowly acted on; but with regard to the mixed phosphates, he insisted, on the faith of some ill-contrived experiments, that they were easily soluble in the alkaline bicarbonates. The capital fact, announced in a previous page, was then unknown—that in ammoniacal urine the alkaline carbonates are absolutely powerless to dissolve any stone, or even to prevent its increase, in consequence of the continual precipitation of fresh phosphatic deposit on its surface.

The indiscriminate use of the alkaline treatment could only result in disappointment; failures multiplied more rapidly than successes. Some of the individuals whose cases

[1] Ch. Petit, loc. cit., p. 272.

were reported as cures by the Parliamentary commission appointed to examine the effects of Miss Stephens's remedy (soap and calcined egg-shells), were found, when their bodies were opened after death, to contain large stones in their bladders. Civiale and others published cases in which patients had passed from bad to worse under the alkaline treatment, and had at length been reduced to a point at which operative procedures were no longer available. The facts which told against the efficacy of solvents were, from their very nature, more incontestable than those which told in their favour. When a patient had taken the solvent for an adequate period, and yet a stone was afterwards extracted from his bladder by operation, or was found there after death, that was a kind of fact which could not be evaded by any sophistry; whereas explanations were not so difficult to find for the disappearance of the symptoms and signs of a vesical calculus under a course of alkalies, without admitting that dissolution of it had taken place. In the absence of any key to explain the direct contradiction of the evidence on the two sides, opinions settled, as was natural, on the side of the more palpable facts. The reported cures were explained away: either (it was said) the sounding was fallacious, and there never was a stone in the bladder; or, if concretions came away under the use of the medicine, these never had been any larger—their coming away was a mere coincidence, and not a consequence of the treatment.

Nor was the indiscriminate use of the remedy the only cause of its disgrace. We must also take account of the imperfect manner in which the treatment was carried out, and the absence of any reliable data whereon to form an opinion as to the rate or speed at which dissolution could take place in the body. In the earlier epoch alkaline substances were given in the form of soap, calcined egg-shells, lime water, or solutions of caustic potash—all of them nauseous, apt to derange the stomach, and difficult to administer in sufficient doses to prove efficacious. In the second epoch Vichy waters were chiefly relied on. These contain soda, which, as we have seen, is an inferior solvent to potash, and the great dilution of the remedy in the Vichy waters must have seriously impaired its power.

I now proceed to give an account of my own experience. It was gathered before some important points were properly understood, which later inquiries have made clear to me. My first case was one of uric-acid calculus, and in every way suitable for the solvent treatment; but owing to my want of better knowledge at that time the treatment was carried out very imperfectly, and was not persevered in sufficiently long to effect complete dissolution. In my second case the stone was composed of alternate layers of uric acid and oxalate of lime. The latter substance completely resisted the solvent, while the former was partly worn away. The specimen, from the peculiarity of its structure, offers an interesting and irrefragable proof of the solvent power of alkalized urine on uric-acid concretions. The third patient proved to have a mulberry or oxalate-of-lime calculus. When afterwards extracted by operation it showed not the slightest trace of dissolution.

Case 1.—David F—, æt. 4, a well-grown healthy child, was admitted into the Manchester Royal Infirmary, December 1st, 1858, under the care of Mr. Southam. The patient's mother stated that distinct symptoms of stone (pulling the prepuce, dancing and screaming with micturition) had appeared three years before, and had continued, with interruptions, ever since. On sounding, a stone was detected; the symptoms were quiescent on admission.

By the courtesy of Mr. Southam the case was made over to me for the purpose of trying the effects of solvents. The urine was freely acid, of an amber colour, perfectly natural, except that it contained a few pus-corpuscles. Frequent examination failed to detect any crystalline deposit in the urine, except after long standing, when it let fall some crystals of uric acid. The bladder was not irritable. The condition of the urine indicated that the calculus was composed either of uric acid or of oxalate of lime or of alternating layers of these two substances, but which of the three kinds there was no evidence to decide.[1] The acid reaction of the urine precluded the idea of any phosphatic concretion.

On December 17th, 20 grains of the tartrate of potash-and-soda (Rochelle salt), dissolved in four ounces of water, were ordered to be taken every two hours. The urine next day was alkaline; its specific gravity varied from 1007 to 1015. The same doses, at the same intervals, were administered regularly without change or interruption for a period of three weeks. The urine, which was frequently examined during this period, amounted generally to three or four pints a day. It was perfectly sweet when voided, and always more or less alkaline; the specific gravity ranged from 1006 to 1016, the night urine being always denser than that of the day.

On January 7th, 1859, the tartrate was increased to 30 grains, dissolved in five ounces of water, every two hours. On January 12th the same dose was directed to be taken in six ounces of water. This treatment was continued until January 28th. On that day the boy was sounded by Mr. Southam, and the stone detected. We thought it unadvisable to persist longer with the treatment; two days after, the patient was cut by Mr. Southam, and two small stones were extracted by the lateral operation. The boy made an excellent recovery.

The condition of the urine in the last three weeks was as follows:—The quantity varied from five to six pints daily; its specific gravity ranged from 1004 to 1007, sometimes it rose to 1011. It was invariably alkaline, but very feebly so. It was always sweet when voided, and quite free from any signs of ammoniacal decomposition.

The two calculi weighed together 22 grains; they were composed of pure uric acid. Their surfaces were devoid of the granular or minutely tuberculated appearance usual on uric-acid calculi, but perfectly smooth and polished, like river

[1] Strictly speaking, the stone might also have been cystin, but the great rarity of this calculus, and the still greater rarity of such a calculus existing without any cystin deposit in the urine, rendered this possibility a very remote one. So far as regards the solvent treatment, cystin falls into the same category with uric acid. (See Appendix to Part I of this paper.)

pebbles, with a finely veined structure. Not a particle of phosphatic deposit existed on their surfaces.

The additional experience which I now possess enables me to see that the treatment in this case was not carried out in an effective manner. I was then under the impression that the *volume* or *quantity* of alkalized urine which flowed over the stone was of great importance, and that the rate of dissolution would be proportionate to the rate of flow. Subsequent experiments have shown that this is not so, and that the *degree* of alkalescence is of much greater consequence. The large quantity of liquid in which the salt was dissolved diluted the urine unduly and greatly reduced its solvent power.

It is evident also that the dose of salt exhibited was too small. Rochelle salt, on account of its large quantity of crystallization-water, has less alkalizing power, by more than one third, than an equal weight of the citrate of potash; so that the 20-grain dose which the lad took in the first three weeks corresponded only to about 13 grains of the citrate, and the 30-grain dose administered in the second three weeks corresponded only to about 20 grains of the citrate.

Notwithstanding these drawbacks, it is not possible but that a considerable amount of dissolution had taken place. The urine was kept constantly, though feebly, alkaline for six weeks; there was no carbonate of ammonia developed in it, and no traces of phosphatic deposit on the stones. These are conditions in which, as the experiments already detailed inform us, uric acid cannot do otherwise than dissolve. The two calculi, when extracted, weighed only 22 grains, and yet one or both of them must have existed in the bladder for period of three years. It is scarcely conceivable that in so long a time they had not attained a greater magnitude than this. And it seems not too much to suppose that had the treatment, imperfect though it was, been persevered in for another week or fortnight, the size of the concretions would have been sufficiently reduced to permit their escape spontaneously by the urethra.

The absence of granulations on the surface of the calculi, with their polished, water-worn appearance, would have been highly indicative of solvent action had there been but one stone n the bladder; but the presence of two robs this character of its distinctiveness, inasmuch as a similar effect might have been produced by their mutual attrition.

Case 2.—J. C—, æt. 12, a healthy boy, was an inmate of the children's hospital in this town, under the care of Dr. Borchardt and Mr. Smart, who kindly permitted me to direct the treatment.

Symptoms of stone in the bladder had existed for a long time, and on sounding no difficulty was experienced in detecting a calculus. The urine was always found acid; it contained a moderate quantity of pus, and deposited crystals of uric acid freely on standing. No oxalate-of-lime crystals were detected at any time, nor, of course, any triple phosphate. The urine, in fine, was natural, except that it contained pus, and had an inordinate tendency to deposit uric acid. The bladder was somewhat irritable.

The stone was conjectured to be uric acid, but it might be composed of oxalate of lime or of a mixture of these two substances, which, indeed, it proved to be.

On the 19th of September, 1860, the lad was directed to take 20 grains of acetate of potash in two ounces of water every three hours. The urine was speedily rendered alkaline. The medicine was continued in the same doses with great regularity and without change for a period of thirty-four days. No particular alteration in the general state of the patient took place during this time. The appetite and sleep continued good, and the vesical symptoms were not more troublesome than usual. Frequent micturition was the chief inconvenience complained of. In the last ten days of the treatment a few crystals of triple phosphate were found in the urine after standing a while, but the secretion was perfectly sweet when voided, and no slimy mucus came away with it.

The stone being still found on sounding, after thirty-four days of treatment, operation was decided on, and the stone was successfully extracted by Mr. Smart on the 24th of October. The patient recovered without a bad symptom.

The calculus measured one inch and three eighths in length, and an inch in breadth; it weighed 180 grains, and its form was a flattened oval.

It was found on examination to be composed of alternating layers of uric acid and oxalate of lime, and its surface presented a most peculiar appearance, which I shall endeavour to describe with the aid of the annexed illustration (Plate IV).

The outermost layer consists of yellow uric acid (figs. 1, 2, 3, *u*, *u*, *u*), and over the larger circumference of the stone it has a thickness in its deepest part of about a line and a half; but on the flattened surface this layer is dissolved away, and the subjacent layer of oxalate of lime crops through it to a considerable extent. On one side the patch of exposed oxalate (fig. 1, *o*) is as large as a sixpence, and presents the ordinary tuberculated surface and dark-brown colour of a mulberry calculus. On the opposite side two islets of oxalate are uncovered, each about the size of a large split pea (fig. 2, *o*, *o*). These are separated from each other by an intervening isthmus of uric acid.

Surrounding these exposed patches of oxalate of lime on the flattened surfaces are found the remains of a thinner, lighter-coloured, more superficial and incomplete layer, also composed of oxalate of lime. The irregular patches of this incomplete stratum occupy a higher level than the surrounding surface of uric acid (figs. 1 and 2, *o′ o′ o′*); and here and there little elevations of uric acid can be seen, surmounted with a shield of oxalate of lime (figs. 1 and 2, *e*). These elevations are partially undermined; the uric acid has been attacked by the solvent, and the protecting shield of oxalate of lime was in the process of being thrown off by the gradual melting of its support.[1]

[1] To compare small things with great, these capped elevations resembled both in appearance and their mode of origin the "glacier tables" of the Alps. Forbes, in describing them, says, "These consist of masses of rock lying on their flat sides, and supported above the general level of the glacier by an icy pedestal. This recalls our attention to a most important

The general surface of uric acid has a characteristic water-worn appearance, which is well represented in figs. 1 and 2. There are no minute mammillations such as usually beset the surface of uric-acid concretions; but the surface is undulating, and the hollows and intervening ridges are perfectly smooth. This undulation of the surface is evidently due to a want of uniformity in the composition of the stratum—the hollows corresponding to the spots where the uric acid is purest, and the ridges to the spots where it is mingled with a larger proportion of oxalate of lime.

The specimen is a remarkable one; it furnishes the clearest evidence yet adduced of the solvent action of alkalized urine or uric-acid calculi within the bladder.

No trace of phosphatic deposit existed on any portion of the stone.

Complete solution of the calculus was impossible in this case. A concretion composed of a uniform mixture of uric acid and oxalate of lime was found to be attacked with considerable facility by a solution of carbonate of potash in the phial; and the present specimen shows that thin and incomplete layers of oxalate of lime may be undermined and disintegrated by alkalized urine; but if the stratum of oxalate be complete and entirely invest the stone, it puts necessarily an absolute bar to further solvent action. This was the case in the instance before us. The partially uncovered layer of oxalate of lime surrounded the entire stone, and as soon as the dissolution of the superincumbent layer of uric acid had been completed no further diminution of size could have taken place.

The solvent treatment was inefficiently carried out in this

circumstance of glacier economy—that there is a perpetual waste at its surface. The action of the stone (mass of rock) is very evident; if the thickness of it be considerable, it forms a pretty complete shelter against the direct action of the sun's rays as well as against the contact of warm rains and wind." ('Tour of Mont Blanc,' p. xxiv.) In this comparison the uric acid corresponds to the ice, the oxalate of lime shields to the superincumbent mass of rock, and the alkaline solvent to the sun's rays and the warm rains and wind.

case. The dose of the acetate should have been nearly double. This would, probably, have more than doubled its solvent effect. The alkalescence of urine produced in a boy of twelve by twenty grains every three hours is only feeble, and does not approach the highest solvent power capable of being communicated to the urine.

Case 3.—Albert B—, æt. 6, was admitted into the Manchester Infirmary, under my care, on January 27th, 1862. On sounding, a calculus was found in the bladder. The patient was in good general health, and the vesical symptoms were quiescent.

The urine was repeatedly examined shortly after his admission; it was acid, clear, free from pus, blood, and albumen; it deposited uric acid freely on standing. No oxalate of lime or other unnatural ingredient was found in it.

From the absence of oxalate of lime and cystin, the calculus was conjectured—erroneously, as it turned out—to be composed of uric acid. A phosphatic stone was, of course, incompatible with a persistently acid state of the urine.

The patient was directed to take twenty grains of citrate of potash in six ounces of water every two hours. Three days subsequently, the dose was increased to twenty-five grains every two hours, in the same quantity of water. This quantity was administered regularly during the day, and moderately so during the night. The treatment was continued without change for a period of two months. The dose was then raised to thirty grains, every two hours, in eight ounces of water, and continued for a month longer, so that the entire period of treatment extended over three months.

The boy's health and spirits were excellent during this interval, and the vesical symptoms remained quiescent.

I am indebted to my former pupil, Dr. Gwyther, who was then my clinical clerk, for a most laborious and exact account of the state of the urine. The secretion was invariably alkaline. The degree of alkalescence was determined on eighty different occasions. The average of whole numbers was 35 grains of carbonate of potash to the pint; sometimes it fell as low as 8 or 10 grains to the pint; sometimes it rose to 70, 90, and on one occasion to 120 grains to the pint. The average density of the urine was 1012, and the range extended from 1003 to 1022. The daily quantity, measured on three successive days, averaged 84 ounces.

Towards the latter period of treatment some pus-globules appeared in the urine; but the secretion was always sweet when voided, and quite free from any ammoniacal odour.

On the 7th of May the boy was sounded, and the stone easily detected. He was then transferred to the care of Mr. Southam, who extracted the stone by the lateral operation. With the exception of some degree of fever for a couple of days, the recovery was uninterrupted.

The stone was a typical specimen of the mulberry calculus. Its surface was exceedingly rough, and covered all over with spiny tubercles. Not a trace of phosphatic deposit existed on any part, and not the slightest evidence of solution could be detected. The stone was spherical in shape, and about as large as a good-sized marble. When sawn across, a nucleus composed of uric acid was displayed. Around this were some additional layers of the same substance. The crust of oxalate of lime was about a line and a quarter thick.

The solvent treatment was carried out in this case with undoubted efficiency for the space of three months. The only defects which my later experiments enable me to point out are the unnecessarily large amount of liquid taken, and the unnecessarily frequent repetition of the dose. If half the quantity of liquid had been administered an equal effect might have been produced with the same dose of the salt, repeated every third instead of every second hour.

These three observations permit a deduction of great importance to be drawn from them, namely, *that a continuously alkaline state of the urine does not determine any precipitation of the earthy phosphates, so long as the urine is free from ammoniacal decomposition.*

## SECTION VIII.—*Discrimination of the cases in which the solvent treatment is, and is not, applicable.*

The first and most general limitation is—

*The solvent treatment is inapplicable to all cases in which the urine is alkaline.*

The loss of the acid reaction of the urine in calculous cases is due, in an overwhelming majority of cases, to ammoniacal decomposition of the urine in consequence of vesical catarrh.[1] This state of the urine determines the precipitation of a phosphatic crust on the surface of the stone, and withdraws it completely from the influence of alkaline solvents.

If the urine preserve its natural acidity the case may be regarded, *prima facie,* as suitable to the solvent treatment; but there are still numerous limitations which reduce the cases really suitable to a much narrower compass.

(*a*) In the first place, *all those cases are excluded in which it is known or strongly suspected that the stone is composed of oxalate of lime.* This is sometimes ascertained from the patient having previously voided concretions of oxalate of lime; sometimes the character of the urine indicates the nature of the stone. If it deposit on cooling an abundant sediment of octahedra or dumb-bells, the stone may be inferred, with great certainty, to be composed wholly or in part of oxalate of lime.

(*b*) When the examination of the urine and the previous history of the patient give *no indication of the nature of the stone* we are left in doubt (supposing the urine to be acid) whether it is composed of oxalate of lime, or uric acid, or of alternating layers of these two substances. There are no data at hand for an opinion as to the probabilities here involved. Different countries, and even different districts of the same country, show considerable diversities in the rela-

[1] The only exceptions are those very rare instances of calculi consisting of bone-earth or carbonate of lime. In these cases the urine is alkaline without being necessarily ammoniacal.

tive proportion of uric-acid and mulberry calculi. Calculi situated in the kidneys also differ essentially in regard to this point from vesical calculi. The former are generally composed of a single substance, and in about five sixths of the cases this is uric acid. The latter, if they have sojourned any considerable time in the bladder, are very frequently composed of two or more substances arranged in alternate layers. And here in reality lies the chief difficulty of the solvent treatment as applied to vesical calculi.

In cases of *renal calculi* the patient should evidently have the benefit of the doubt. No other treatment than that by alkaline solvents is open to the choice of the practitioner, and if the calculi should turn out to be composed of oxalate of lime the alkaline treatment will not aggravate, if it do not ameliorate, the state of the patient.

In cases of *vesical calculi* the question stands differently. The solvent treatment here comes into competition with the mechanical methods of lithotomy and lithotrity, which long experience has stamped with success. And this is not all, for it comes into competition in the very cases (small stones of uric acid or cystin with a healthy state of the urine) in which these methods attain their highest safety. It is no longer a question of the mere possibility of removing a calculus by means of solvents, but of doing it with less risk than by lithotomy or lithotrity.

Future experience alone can decide whether it is better in cases of this class (where the nature of the stone is quite uncertain) to consign them at once to the operating-table or to give a preliminary trial to the solvent treatment. It would appear from the cases reported in the preceding section that patients who have undergone such a trial may be afterwards transferred to the surgeon with undiminished chances of a successful operation. Probably the most advantageous course to follow, if the stone be a small one, would be to try the solvent treatment for a limited period—for six weeks or two months—and, if unsuccessful at the end of that time, to proceed without further delay to operation.

(*c*) *When the stone is known to be a large one* the solvent treatment should not be attempted. The existence of a large stone in the bladder is itself an ever-present source of danger, and the larger it is, the greater the probability that it contains one or more layers of oxalate of lime which will resist the solvent. The length of time which a stone above the weight of an ounce would require for dissolution, also detracts greatly from the advantages of the solvent treatment, as compared with the swift though more hazardous method of lithotomy.

(*d*) The cases of vesical calculi *which are especially suitable to the solvent treatment are those in which it is known or strongly inferred that the concretion consists of uric acid and has not yet attained any great size.*

It sometimes happens than an individual voids spontaneously, from time to time, small calculi of uric acid, and that afterwards he becomes the subject of vesical calculus. Some one of the concretions, being perhaps larger than its predecessors, is unable, after its descent into the bladder, to pass out along the urethra as previous ones have done. After a season of rest the bladder begins to resent the presence of the foreign body, and symptoms of stone in the bladder awaken the patient to a knowledge of his situation. In such a case a dissolution of twenty or thirty grains from the surface of the stone would reduce its size sufficiently to enable it to traverse the urethra. This is what occurred in all probability in the person of Dr. Jurin, as related in a previous part of this paper. I am not unaware that in the case supposed, lithotrity, in the hands of a practised operator, who could in two or three sittings pulverize the stone effectually, subjects the patient to a minimum of risk, yet it is clearly a far greater risk than the use of acetate or citrate of potash for two or three weeks.

(*e*) It is probable that the solvent treatment, judiciously carried out, will form a useful *adjunct to lithotrity.* It is, however, essential to its employment than no vesical catarrh with ammoniacal decomposition of the urine, ensue after the operation. If the urine maintain its acidity after the stone is crushed, and if the fragments discharged prove to be uric acid, then the solvent treatment might be expected to act advantageously by obviating the inconvenience and danger of repeated sittings.

To sum up in the affirmative—the solvent treatment is only applicable in those cases of vesical calculi in which *the urine is acid, the stone not large, its composition known to be uric acid* (*or cystin*), *or strongly suspected to be such.*

## Section IX.—*Rules for carrying out the solvent treatment.*

(*a*) The action of alkalized urine is essentially slow; quick solution, by any manner of applying it, is impossible. To make up for this defect its operation must be *continuous and incessant.* To rest content with alkalizing the urine for a few hours each day, is not only to reduce the solvent effect to an insignificant quantity, but sometimes, at least, to nullify it altogether. I have known urine, kept continuously alkaline by acetate of potash for several successive days, recover its acidity and deposit uric acid within a few hours of the latest dose. So that it is possible, with an insufficient maintenance of the alkalescence of the urine, that the dissolution effected during one part of the day may be nullified by fresh deposition of uric acid during another part of the day. It is also of the utmost importance not only to keep the urine continuously alkaline, but to *keep it alkaline to a certain degree.* The experiments described in the second section of this paper prove that solutions with an alkalescence below three grains of carbonate of potash to the pint, have scarcely a greater effect on uric acid than common water. A feebly alkalized urine acts so slowly that, in cases of vesical calculi, the delay incurred, counterbalances the safety of the treatment as compared with mechanical means, and robs it of the preference which it might otherwise deserve.

To secure a continuous alkalescence, the dose must be repeated at short intervals during the day, and, as far as possible, during the night. An interval of two or three hours between each dose is sufficiently short to ensure an adequate constancy of effect, and is not burdensome in practice.

During the waking hours perfect regularity can be easily maintained. A dose should be taken the last thing before retiring to rest. This will probably necessitate the emptying of the bladder once at least in the course of the night, and furnish an opportunity to take another dose, which will carry the patient to the time of waking. Indeed, patients with vesical calculi are rarely able (quite apart from the effect of medicine) to pass the night without awaking once or more to relieve the bladder.

(*b*) The most convenient salts for alkalizing the urine are the citrate, acetate, and bicarbonate of potash. The percentage of base in each is almost the same, so that they may be given in equal doses. The acetate and citrate of potash seem, on the whole, to deserve the preference. The citrate, as found in the shops, is generally impure, and contains a good deal of insoluble matter. It is better to make a solution of fixed strength from the crystallized bicarbonate of potash and crystallized citric acid. The following prescription yields a solution containing a drachm of the citrate in each fluid ounce:

℞ Potass. bicarb., ʒxij;
Acidi citrici, ʒviij + gr. xxiv;
Aquæ ad ℥xij. Solve.

A fluid ounce of this solution mixed with three or four ounces of water, makes a draught which has scarcely any taste, and which even children take without any difficulty.

For an adult, the dose should not be less than 40 or 60 grains, and for children not less than 20 to 30 grains, every third hour, dissolved in three or four ounces of water. If the dose be given in less water than this, the patient is apt to be a little thirsty and to drink capriciously in the course of the day, thereby introducing an unnecessary irregularity into the flow of the urine and an excessive oscillation in the degree of alkalescence.

(*c*) It is essential that the freshly voided urine should be frequently examined during the progress of the treatment. If at any time it show signs of ammoniacal decomposition the treatment should be given up. The advent of this state is recognised by the offensive ammoniacal smell of the secretion, the increase of pus and flaky matter in it, and the speedy gelatinization of the pus into a viscid mass. As long as the urine continues *sweet when voided* no fear need be entertained of the deposition of the mixed phosphates on the surface of the stone.[1]

SECTION X.—*An examination of some of the objections which have been urged against the principle of the solvent treatment.*

(*a*) The most plausible objection against the alkaline treatment is the alleged danger of the precipitation of the phosphates on the surface of the stone. The facts advanced in the preceding pages dispose of this objection completely. If there be ammoniacal decomposition of the urine, the phosphates are deposited whether alkaline medicines be given or not, and the concretion goes on increasing; but if the urine be alkaline solely from fixed alkali not a particle of phosphatic deposit takes place.[2]

(*b*) It has been said that the natural reaction of the urine is acid, and, therefore, that rendering it alkaline introduces an unnatural state, which cannot fail to act deleteriously on the general health. In a state of fasting the natural healthy urine is doubtless always acid, but the researches of Dr. Bence Jones, fully confirmed by my own, show that the urine is normally alkaline (from fixed alkali) for several

[1] Means might be easily suggested for restoring the urine to its natural state after it has become ammoniacal from vesical catarrh, with a view to the resumption of the solvent treatment; but it is pretty evident, at least in the present position of the question, that a solvent treatment so complicated could not compete with the mechanical methods.

[2] A want of knowledge of the essential difference of properties between urine alkaline from fixed alkali and urine alkaline from carbonate of ammonia, runs like a thread of error through all the elaborate argument of Civiale, in his chapter on the dissolution of the stone in the interior of the body. (See chap. iv of his work 'Du traitement médical de la Pierre.')

hours daily, after meals, in many, if not in all, healthy persons. So that the maintenance of an alkaline reaction of the urine by fixed alkali is by no means so unnatural a state as some have supposed.

(*c*) Alkaline substances, it is urged, impair digestion. This objection was valid against the ruder methods of alkalizing the urine formerly employed. But the acetates and citrates have no such effect. The introduction of these salts, in recent times, for the treatment of articular rheumatism, has afforded an immense field for watching their effects. Indeed, the solvent treatment here recommended is identical with the prevailing mode of treating rheumatism, except that the dose is administered in a somewhat more dilute form. In the last eight years I have employed the bicarbonate, the acetate, and citrate of potash, both in private and public practice, in quantities of four, six, and eight drachms in the twenty-four hours, in a very large number of cases. The majority were cases of articular rheumatism, the remainder embraced a variety of slighter and more severe disorders—skin diseases, emphysema, diabetes, acute Bright's disease, &c. The urine was kept continuously alkaline for periods varying from a fortnight to three months, and in no instance were deleterious effects observed. In a patient with emphysema of the lungs the urine was kept uninterruptedly alkaline for fourteen weeks, with marked improvement of the general health and steady increase of weight. In short, the acetate and citrate of potash have appeared to me about as harmless as so much sugar.

## Appendix to Part I.

### *Experiments having reference to the solvent treatment of cystin calculi.*

Cystin is soluble both in the carbonates of the fixed alkalies, and in mineral acids. It may therefore be attacked, when existing as a calculus in the bladder, either by alkalizing the urine, as in the solvent treatment of uric acid, or by injecting acid solutions into the bladder.

Two experiments were performed with a view of testing the solubility of cystin calculi in a solution of carbonate of potash containing 40 grains to the pint.

A section of a pure cystin calculus, weighing 97 grains, was employed. In the first experiment two pints of the solution were passed over the fragment, at blood heat, in the course of twelve hours. The loss of weight, at the end of that time, amounted to 9½ grains.

In the second experiment, similarly performed, but with a flow of three pints, the loss of weight, in twelve hours, was 10½ grains.

These experiments yield a rate of solution of about 20 per cent. in twenty-four hours. Cystin may, therefore, be regarded as being even more favorable to the application of the alkaline solvent treatment than uric acid.

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## PART II.

### SECTION I.—*Experiments on the solvent treatment of uric-acid calculi by injections into the bladder.*

It has been conceived that considerable advantage would be gained in cases of vesical calculi if the solvent were directly injected into the bladder by means of a double-current catheter, instead of being made to pass by the more circuitous route of the circulation and the secreting tissue of the kidneys.

The advantages which the injection method seemed to offer were—

(*a*) A much greater mass of the solvent could be passed over the surface of the stone in a given time.

(*b*) The solvent could be used in a more concentrated form.

(*c*) Certain substances could be used as solvents which are not capable of reaching the stone through the medium of the circulation.

(*d*) The inconvenience of a long course of medicines in large doses would be avoided.

The following experiments, however, show pretty conclusively that with respect to uric acid these advantages are illusory.

The mode of proceeding adopted was, to place a section of a uric-acid stone in a ten-ounce phial, and to pass over it at blood heat a current of the solvent to be tried, as large as the capacity of the urethra might be supposed to permit.[1] The current was kept up for two or three hours continuously.

At first, saturated solutions of bicarbonate of potash and the common phosphate of soda were employed, but they failed to make the least impression on the stone. Afterwards solutions containing 240 grains to the pint were used, with a like result. I was not then aware that the maximum solvent power of these, and kindred salts, on uric acid, lay in much weaker solutions. After attaining to this knowledge I employed a solution of *carbonate of potash* containing 50 grains to the pint, which represents the maximum solvent power of that salt on uric acid.

Two experiments, each of three hours' duration, yielded the following results:

| | |
|---|---|
| Hourly rate of flow of the solution . . | 42 pints. |
| Weight of the fragment of uric acid . . | 57 grains. |
| Hourly dissolution . . . . | 2 ,, |

This result, insignificant as it is, could probably not be approached in the living bladder, on account of the mechanical difficulties to be overcome.

Four experiments with *carbonate of lithia* yielded still smaller results.

[1] The method of treating vesical calculi by injections was proposed so long ago as 1744 by the Rev. Dr. Stephen Hales, who invented the double-current catheter for the purpose; it was further investigated by Langrish in a large number of experiments on bitches. 'Physical Experiments on Brutes,' by Browne Langrish, London, 1746.

A solution of 10 grains to the pint, with an hourly flow of thirty pints, dissolved less than a grain per hour.

A solution of 20 grains to the pint, with an hourly flow of twenty-six pints, dissolved one grain and a quarter per hour.

Solutions of the following substances were also tried in a similar manner, namely, *borax, borax with liquor sodæ, double borate of potash and soda, common phosphate of soda, basic phosphate of soda,* and *potash soap,* but their solvent effects never reached beyond a loss of weight (on a fragment of uric acid weighing about 100 grains) of one or two grains in the hour.

*Lime water,* in a continuous current, at the rate of thirty pints an hour, dissolved a fragment weighing 86 grains, at the speed of one and a half grain each hour.

Seeing the very small results thus obtained, I proceeded to try the caustic alkalies, which are the most powerful known solvents for uric acid.

Sixty minims of the *liquor potassæ* of the London Pharmacopœia (sp. gr. 1063) were added to each pint of water. A solution so made was perceptibly acrid in the mouth. Fifty-six pints of this solution dissolved in an hour two grains from a fragment weighing 100 grains.

Twenty pints of a solution containing 120 minims of liquor potassæ to the pint dissolved also two grains per hour.

Twenty-four pints of a solution containing 240 minims to the pint dissolved nearly three grains per hour.

*Liquor sodæ* (sp. gr. 1056), in the proportion of 120 minims to the pint, dissolved two grains per hour with an hourly current of twenty pints.

A solution of the same, containing 240 minims to the pint, with an hourly current of thirty-four pints, dissolved two and three quarter grains per hour.

The stronger solutions of the caustic alkalies had so great a pungency in the month, that it seemed impossible that they could be safely used as injections into the bladder.

The general conclusion from all the foregoing experiments is, that under the most favorable conditions, and with the most effective solvents capable of being borne by the living bladder, no greater dissolution than one or two grains per hour can be accomplished in the case of uric-acid concretions. In actual practice the conditions would necessarily be much less favorable than in an experiment performed in the laboratory. A little consideration is sufficient to show that these results hold out no prospect of any useful practical application.

### Section II.—*Experiments on the solvent treatment of oxalate-of-lime calculi.*

It has been asserted by Chevallier[1] and Ch. Petit[2] that the alkaline carbonates produce slow solution of oxalate-of-lime concretions. This assertion is based on experiments made by immersing mulberry calculi in the warm springs of Vichy. The enormous quantity of the solvent flowing over the calculi, under these circumstances, involves, however, a condition which is unattainable in the living body, and no practical inference can therefore be drawn from such observations.

I found that a flow of six or eight pints per twenty-four hours of a solution of *carbonate of potash* containing 40 grains to the pint had no perceptible effect on a calculus of oxalate of lime.

In the case of Albert B—, reported in the first part of this paper, alkalized urine flowed over a mulberry calculus for a period of three months, without producing the least sign of solution.

Better effects, it was conceived, might be obtained by a solution of *dilute nitric acid* (which is the best solvent of oxalate of lime), employed in a manner so as to imitate injections into the bladder.

A solution, containing 120 minims of concentrated nitric acid to the pint, was prepared; it was found to possess an

[1] 'Med. Gaz.,' vol. xx, p. 581.

[2] 'Mode d'action des Eaux minérales de Vichy,' p. 199.

acridity probably a good deal beyond what the living bladder could withstand; and yet twenty-four pints of this solution, passed in the course of an hour, at blood heat, over a mulberry calculus weighing fifty-three grains, only dissolved half a grain. The excessive hardness of oxalate-of-lime calculi accounts for this extreme slowness of solution.

There is little difficulty in concluding from these experiments that oxalate-of-lime concretions are practically unassailable by solvents applied in any known method.

### Section III.—*Experiments on the solvent treatment of the mixed phosphates or fusible calculus.*

The observations of Chevallier and Petit on the effects of immersing phosphatic calculi in the Vichy springs led them to believe that rapid disintegration of these concretions would take place in solutions of the alkaline carbonates. The conditions of these experiments, however, bear no analogy to the actual circumstances of a phosphatic calculus in the bladder. Such a calculus is bathed in an ammoniacal urine, and the calculous matter continues to be deposited just as before, notwithstanding the addition of a fixed alkaline carbonate to the urine. An observation recorded in the first part of this paper, Section VI, places this matter beyond doubt.

Some direct experiments on the effect of solutions of *carbonate of potash* on phosphatic calculi were also made. Solutions containing 30, 40, and 80 grains to the pint were passed, at blood heat, at the rate of six pints in the twenty-four hours, over a rough, porous, phosphatic stone weighing 371 grains.

In two experiments there was no loss of weight; in three others a few fragments chipped off, and occasioned a diminution of weight amounting to two grains in the twenty-four hours.

The results indicated very clearly that alkalized urine could have no effect in the human bladder in dissolving or disintegrating a calculus composed of the mixed phosphates.

Far more promising results were obtained by dilute nitric acid, used so as to imitate injections. The following experiment is to be regarded merely as rudely tentative.

A solution containing a drachm of the commercial nitric acid per pint was passed, at blood heat, over a phosphatic stone weighing 153 grains, at the rate of thirty-six pints in the hour. The loss of weight which followed amounted to twenty-one grains per hour. A modification of this proceeding was successfully employed, as is well known, by Sir B. Brodie, in actual practice. My colleague Mr. Southam has recently tried the same method, and with complete success. The stone had been repeatedly broken with the lithotrite, but new phosphatic concretions formed in the bladder as fast as the old ones were crushed, and it was found impossible to completely clear the bladder. In this difficulty an injection, containing two drachms of dilute nitric acid to a pint of water, was practised every day or every second day. In the course of a short time the old fragments were entirely dissolved, and the formation of new ones was prevented. The urine ceased to be ammoniacal, and the bladder was speedily cleared. This method seems capable of wider application than is now made of it by surgeons.

The following conclusions may be drawn from the experiments described in Part II:

1. That uric-acid calculi cannot be successfully treated by alkaline solvents used as injections into the bladder.

2. That oxalate-of-lime calculi are practically insusceptible to acid and alkaline solvents.

3. That phosphatic calculi are insusceptible to the action of alkaline solvents, but that they offer an encouraging prospect for the use of acid injections into the bladder.

## DESCRIPTION OF PLATE III.

(See page 117.)

FIG. 1.—Upper flattened surface of the stone.

*u u*. Water-worn layer of uric acid.
*o*. Exposed patch of oxalate of lime.
*o′o′*. An imperfect, more superficial, partly undermined, lighter-coloured layer of oxalate of lime.

FIG. 2.—Lower flattened surface of the stone (the *letters* refer to the same parts as in Fig. 1).

FIG. 3.—Section of the stone vertically through the exposed patches of oxalate of lime.

Fig. 1.

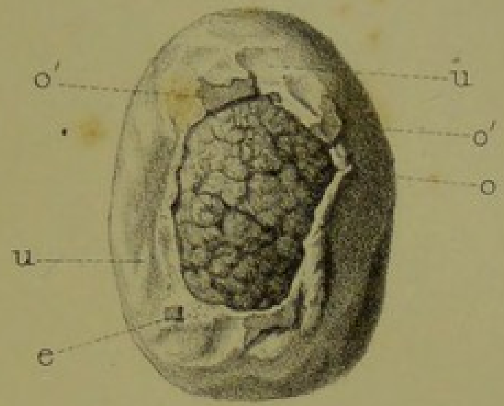



Fig. 2.

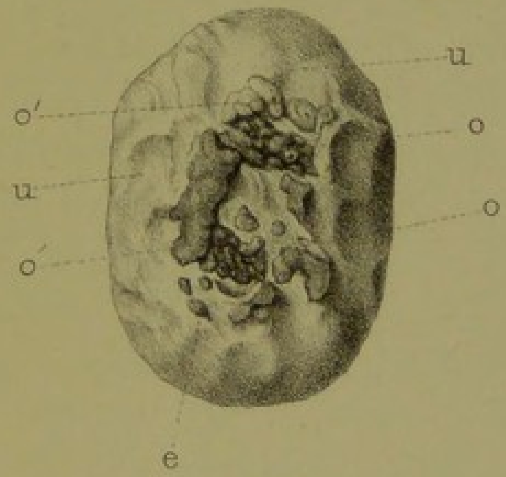
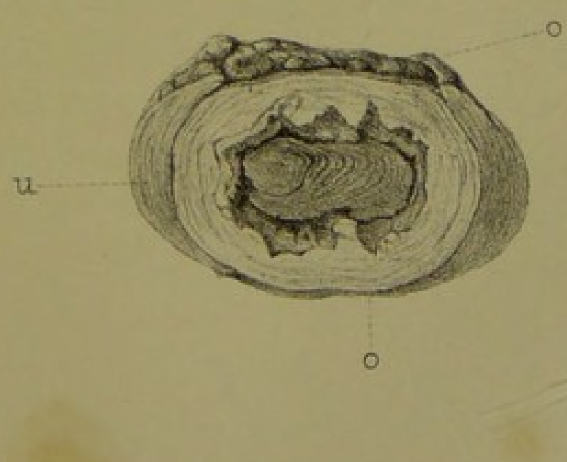



Fig. 3.




C.H. Ford lith.

W. West imp.