II. Researches on the Decomposition and Disintegration of Phosphatic Vesical Calculi, and on the Introduction of Chemical Decomponents into the Living Bladder. By S. Elliott Hoskins, M.D. Communicated by P. M. Roget, M.D., Sec. R.S.

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IN the following account of my humble investigations, I shall confine myself, as much as possible, to the physical phænomena which have fallen under my observation; reserving those of a physiological or pathological character for a sphere more exclusively professional.

Although Fourcroy strongly expressed it as his opinion, that calculi would, sooner or later, be dissolved by the introduction of chemical agents into the living bladder; and, although some eminent writers of the present day are of the same opinion; there are others, no less eminent, who entertain doubts as to the adaptation of any direct chemical means to so desirable an end.

I must here state, that my reason for clinging to the creed of the former rather than to that of the latter, was founded on the increasing list of new agents, which chemistry is daily placing at the disposal of the experimenter. Amongst these I hoped to discover some agent which should be more energetic in its action on calculi, and less obnoxious to the living tissues, than any hitherto proposed.

For several months my efforts were confined to attempts at dissolving uric acid and the urates, knowing that they constitute a predominating variety among calculous concretions: and, although I met with sufficient success to encourage perseverance, reasons not necessary to mention, induced me to abandon these experiments, and to prosecute others on phosphatic calculi. The results of the latter it is now my purpose to detail.

A series of experiments was undertaken with the whole range of acids, vegetable as well as mineral, combined in various ways and in various proportions. There could be no doubt as to the solvent power even of the weakest; but their irritating effect on the tongue, and on the conjunctival membrane, was equally obvious. Not one among them was found calculated to fulfil the two indications I required; a circumstance which tends to corroborate, in a great degree, Dr. Prout's statement,—"that uncombined agents of the alkaline or acid kind are ill-calculated to act as solvents for calculi; and that solvents are to be sought for among a class of harmless and unirritating compounds, the elements of which are so associated as to act at the same time with respect to calculous ingredients, both as alkalies and acids*."

* PROUT on the Stomach and Urinary Diseases, p. 458.

"At present," continues Dr. Prout, "no such class of compounds of a decided character are known, or appear likely to be discovered; yet, as no chemical fact can be stated à priori, we know not what remains in store among the arcana of nature."

The conviction I had acquired of the truth of these observations induced me to abandon all attempts at positive or direct solution, but rather to try the effect of indirect means, namely those of *decomposition* and disintegration; as preliminaries to solution by some bland fluid, or to mechanical removal, by the injection of a continuous stream of liquid through a double current catheter.

It appeared, hitherto, to have been the object, to act on calculi by *single* elective affinity only; that is, to dissolve the base before it was disengaged from its associated acid. This mode having failed to produce agents sufficiently active on the one hand, and mild on the other; it seemed more in accordance with chemical principles, and more likely to effect the desired end, if *complex* affinity could be brought into play.

It frequently happens, that reactions occur under the influence of double decomposition, which are not produced by simple affinity: thus, ammonia alone will not decompose nitrate of lime, though carbonate of ammonia answers the purpose readily. The triteness of this example will, I trust, be excused in favour of the aptitude with which it illustrates my meaning.

For the above purpose an agent is required, the base of which shall be so attractive of the acid of the calculus, as to withdraw it from its allegiance; whilst the acid of the agent unites with the basic ingredients of the calculus, to form with them salts of easy solution.

This view of the subject seems to reveal a class of agents so mild as to come directly under Dr. Prour's category. During their employment, the combined acids are set free only in combining proportions, to be neutralized in their nascent state by the proper base, and removed out of the sphere of action before they have time, as it were, to act upon the animal tissues. Whereas, free acids of sufficient strength to act on the concretion, and in sufficient quantity, cannot be prevented from irritating, in a greater or less degree, the animal membranes with which they happen to be in contact.

The facility with which salts of lead decompose the phosphates, a facility which has led to their employment as tests of the presence of phosphoric acid, pointed them out as agents well-fitted for the present purpose.

Fragments of phosphatic calculi were accordingly immersed in solutions of neutral acetate of lead, of various degrees of concentration, and at different temperatures, but without result; even when the assay, reduced to powder, was placed in these fluids and viewed with the microscope, no chemical action, however slight, was discernible. I was disappointed, but nevertheless induced to try some other combination of the metal.

Dr. Prout mentions, in his valuable work before cited, that fluids containing malic acid possess peculiar powers in arresting the deposition of the phosphates. The same gentleman informed me that the solvent powers of the *Alchemilla arvensis* reside in the malic acid which this plant contains, My own experience has unequivocally

proved to me the efficacy of cider, as an ordinary drink, in cases of phosphatic urinary deposit accompanying rickets, and diseases of the lumbar vertebræ.

From these circumstances I was inclined to believe, that although the acetate had failed, a malate or super-malate of lead would be likely to act as a decomponent of phosphatic concretions. Another reason for selecting malic acid was the solubility of the salts it forms with the bases of these calculi, viz. magnesia, lime, &c. Having no readier means of procuring the malate, I sought to prepare it from cider vinegar, or what is called *cidre-aigre* in contra-distinction to *vin-aigre*, a liquid commonly used as a substitute for wine or malt-vinegar, in the farm-houses and cottages of the Channel Islands.

To this cidre-aigre a watery solution of neutral acetate of lead was added, till precipitation no longer took place. The liquid, on being filtered, was clear, devoid of acidity or acrimony; and, as Dr. Christison states, with respect to acescent wines to which lead has been added, it possessed "a very pleasant sweetness, quite unmingled with metallic astringency*."

The whole of the passage, relating to French wines, from which the above sentence is quoted, seems particularly applicable to the liquid under consideration. In default, however, of any authentic analysis of cider-vinegar, my observations induced me to believe, that the acids it contained were the acetic, malic, and tartaric; but as I was unwilling to interrupt the course of experiments, in order to analyse it, I am unable to determine this point with the necessary accuracy.

Nevertheless, whatever may be its composition, the immersion of fragments of phosphatic calculi in the liquid formed as before stated, was followed by very striking results: rapid chemical action ensued, visible to the naked eye; when viewed by means of a low microscopic power, vehement decomposing action was manifest, the calculous particles becoming surrounded by *areolæ* or *nebulæ* of white sediment, which continued increasing until each fragment was reduced to a pulpy state resembling mortar, perfectly soluble in very dilute nitric acid.

On suspending a fragment of fusible calculus, by means of horse-hair, in a test-glass containing the fluid, it became at once involved in a white cloud, from which a continuous stream of precipitate gravitated to the bottom of the glass. After the lapse of half an hour the calculus was found to have lost weight. This was an important fact, without which it might have been supposed that decomposition of the solution alone had given rise to the precipitate.

Being inclined to doubt the evidence of my senses, rather than arrive at a false conclusion, I repeated the experiment. Another particle of triple phosphate was placed in a fresh quantity of the liquid; at the moment of immersion chemical action commenced, and pursued the same course, until the fragment became a semi-solid mass, readily disintegrated. After a time nothing remained but the shreds of mucus, or other animal matter, which had cemented the earthy ingredients together.

The result of analogous experiments, performed subsequently, warrants me in sta-

ting that the precipitate in the present instance was chiefly phosphate of lead*; it may likewise be fairly inferred, that the other ingredients composing the calculus had formed soluble salts with the malic and acetic acids of the decomponent. For it was manifest that the acids contained in *cidre-aigre* had formed soluble salts with oxide of lead, and that these salts, even when dissolved in such a quantity of fluid as to possess scarcely any taste and no pungency, were capable of decomposing phosphatic calculi. The liquid in this state, however, was objectionable, in a practical as well as a scientific point of view, on account of its colour, odour, and indeterminate strength. It therefore became desirable to attempt the formation of some definite salt, of analogous composition, which, by solution in water, should form a decomposing agent, of a strength which might at all times be depended on; capable also of being varied according to circumstances.

In theory, the nearest approach to an agent of this kind seemed to be a super malate of lead; for, although the neutral malate was known to be insoluble in water, it was deemed possible that, by some modification, its solubility might be increased. This I found to be the case.

Crystals of malate of lead, in fine powder, were diffused in water, and thoroughly decomposed by sulphuretted hydrogen, so as to leave malic acid in solution; this was filtered and boiled to expel the gas. While still hot, fresh crystals of malate of lead were added to the fluid, which was then allowed to cool, and again filtered. On suspending specimens of phosphatic calculi in this liquid (which, though sensibly acid when tested, was perfectly insipid), chemical action took place, but by no means rapidly. This was, nevertheless, one step towards the acquirement of a definite compound.

Recurring to my former conjectures as to the nature of the salts held in solution by the filtered aigre, pure crystals of malate of lead were gradually added to warm dilute acetic acid. This mixture was heated gently for some time, and afforded a better decomponent than the former, but still not so active as the original cider-vinegar compound.

After a long series of experiments to the same effect, which it is unnecessary to detail, I arrived at the following conclusions:—1st, that malic acid, unless concentrated, exerts but little solvent action on phosphatic calculi; 2nd, that a weak solution of super-malate of lead *does* act as a decomponent; 3rd, that a solution of acetomalate, if I may be allowed so to call the liquid last described, is tolerably active; but finally, that none of the preparations of malic acid, already alluded to, are so active as the cider-vinegar solution.

The close resemblance said to exist between genuine malic acid, procured from the Sorbus aucuparia, and the factitious, prepared by the action of dilute nitric acid on sugar, induced me to turn my attention to what, by some chemists, is called saccharic, by others oxal-hydric acid. By slightly varying Berzelius's process‡, so as to avoid the discoloration produced, as he says, by humic acid, a very pure saccharate

^{*} See p. 280. † Five parts of pure acid to 480 of distilled water.

[†] This modification consists in heating the mixture of dilute acid and sugar, until the evolution of red fumes

of lead was prepared. From this, saccharic acid and super-saccharate of lead were obtained by the aid of sulphuretted hydrogen, as described when speaking of the malates of lead. Saccharic acid, however, unless concentrated, exerted no greater influence on phosphatic concretions than malic acid; the neutral saccharate of lead was likewise inert, whereas the supersalt proved so active, and yet so mild, that it seemed better calculated than any agent hitherto tried, to fulfil the prescribed conditions. But as the sulphuretted hydrogen process was tedious and unpleasant, Thenard's statement as to the solubility of the malate in acetic acid was applied to the saccharate of lead: a preparation of this kind seemed the more likely to answer from its similarity to the *cidre-aigre* solution.

An aceto-saccharate was, in the first instance, formed according to Berzelius's directions*; but as this process was likewise somewhat elaborate, I endeavoured to abbreviate it as follows:—Five parts of saccharate of lead, and the same number of minims of strong acetic acid, were added to a fluid ounce of distilled water, which was gently heated for a short time; a small quantity of the lead salt was thereby dissolved, not more than half a grain. This solution, although perfectly tasteless, acted speedily and with energy on any phosphatic fragment of calculus suspended in it. The solution on the most careful evaporation yielded no crystals, but was converted by heat into a viscous syrup, which ultimately became a species of caramel. The liquid, therefore, although available for experimental, was not sufficiently definite for practical purposes. But as Liebic mentions no less than three definite compounds of oxide of lead with saccharic acid, I did not despair of succeeding in the formation of a salt, such, in all respects, as I required. "L'acide saccharique," says Liebic, "est très rémarquable par le grand nombre de combinaisons qu'il forme avec les bases."

It now became my object to form an *acid* saccharate of lead, which was accomplished thus:—a portion of pulverized saccharate of lead was dissolved in a sufficient quantity of cold dilute nitric acid. The solution, after being filtered, and gradually evaporated, yielded a quantity of perfectly transparent, amber-coloured crystals, in the form of regular hexagonal plates or prisms. I have reason to believe that the colour is essential to the salt, for when I endeavoured to purify it by re-solution in dilute nitric acid, although it still formed hexagonal crystals, the salt had lost its activity as a decomponent.

One grain of this salt, which I shall call nitro-saccharate of lead, moistened with

commences, and then instantly removing the spirit-lamp. The fumes continue to be disengaged for some time, and when they have entirely ceased, decomposition by lime, and precipitation by acetate of lead may ensue.

^{* &}quot;Quand on chauffe," says he, "un mélange d'acide acétique et de saccharate calcique dissous, et qu'on ajoute à ce mélange de l'acétate d'oxyde de plomb jusqu' à ce que le précipité commence à ne plus se rédissoudre, le sel écailleux cristallise en plus grande quantité par le refroidissement." These crystalline scales, moistened with acetic acid, and dissolved in water, form a good decomponent.

[†] One acid to nineteen water.

five drops of pure saccharic acid, and dissolved in a fluid ounce of distilled water, formed a bland liquid without any astringency, although it possessed slight acid reaction. It acted with rapidity on various specimens of phosphatic calculi, forming around each, at the moment of immersion, the dense nebula formerly described, from which a white precipitate subsided. Chemically speaking, this was the most active agent yet experimented with, whilst its sensible character was so mild as to be tolerated with perfect impunity by the urethral and conjunctival membranes.

The following experiments, selected from a great number of others, to the same effect, will suffice to show the results of the action of this nitro-saccharate solution on human phosphatic calculi.

Experiment I.—Seven fragments of various sizes and figures, taken indiscriminately from a collection of phosphatic specimens, were placed in distilled water until airbubbles ceased to be disengaged from them: they were found to weigh collectively, after being allowed to drain for a minute or two on bibulous paper, one hundred grains.

These fragments, each suspended by a horse-hair, were placed in ten fluid ounces of the above-mentioned nitro-saccharate solution for twenty-five minutes, during which time the temperature of the fluid was maintained at 98° Fahr. They were then removed and plunged into ten ounces of fresh solution, of the same strength and temperature, for a quarter of an hour. In both cases, copious precipitation took place from each fragment, and accumulated at the bottom of the glasses. The calculi were then removed, drained for a few minutes on filtering paper, and, on being re-weighed, were found to have lost twelve grains *.

The two portions of solution, together amounting to twenty ounces, were then passed through a filter; and the precipitate, after being washed and carefully dried, was found to weigh eleven grains. A small quantity of it, heated alone on charcoal by means of the blowpipe, gave indications of the presence of phosphate of lead. In order, however, to determine the nature of the acid contained in the lead precipitate, another portion of it was dissolved in dilute nitric acid; to this solution was added a drop or two of nitrate of silver, and on being cautiously neutralized by weak liquid ammonia, a yellow precipitate, characteristic of the presence of phosphate of silver, made its appearance.

A third portion of the dried precipitate was mixed with borax, and fused by the blowpipe on charcoal; the bead thus formed was transfixed by a fine needle, and strongly heated in the interior flame; on being broken after cooling, it was found to

- * The greater the extent of surface, the greater, generally speaking, will be the amount of decomposition, so that agents of this kind will, I trust, come with great effect to the aid of lithotrity.
- † I may perhaps be permitted to remark, that in order to render this test determinate, the following precaution is necessary. If the assay be dissolved in *dilute* nitric acid, *weak* liquid ammonia must be used for neutralization, otherwise no yellow precipitate will be formed. On the other hand, if *strong* nitric acid is used for solution, it must be neutralized by strong liquid ammonia. In both cases the ammonia must be added cautiously, for an excess, however small, destroys the yellow colour of the precipitate.

consist of magnetic particles of phosphuret of iron, affording another proof of the presence of phosphoric acid in the precipitate.

With respect to the filtered solution, half of it, amounting to ten ounces, on being cautiously evaporated to dryness, yielded rather more than nine grains of solid residue, which, however, was not analysed. The remaining ten ounces were treated with sulphuretted hydrogen, so as to decompose the *whole* of the salt of lead: it was then filtered, boiled, and tested with oxalate of ammonia, which produced after a time a trifling precipitation of lime: the superaddition of liquid ammonia gave no evidence of the presence of magnesia.

At the commencement of the experiment the solid materials amounted to 120 grains, viz.—

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Seven calculous fragments \dots \dots \dots \dots = 100 \text{ grs.}

Nitro-saccharate of lead in solution \dots \dots \dots \dots = 20

120
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After the operation the following seems to have been the arrangement of the ingredients:—

Supposing the precipitate from the calculi to have consisted entirely of phosphate of lead, the equivalent of acid would, on a rough calculation, have been 2.4; so that, had the assay been inorganic, or definite in composition, the exact amount of decomposed salt might have been estimated. Under existing circumstances rude approximations are sufficient; but I hope to be enabled to illustrate this part of the subject at some future period, by more careful and extended analyses.

The second experiment was conducted by suspending a fragment of fusible calculus, weighing thirty grains, in five ounces of the nitro-saccharate solution for half an hour. At the expiration of this period the fragment had lost eight grains, and the precipitate arising from its decomposition, when carefully dried, weighed rather more. The filtered fluid, treated as in the former experiment, contained a small quantity of lime.

In the course of the present experiment some very curious and interesting phænomena were observed. A copious, dense, white sediment, descended as usual in a stream from the calculus; but, besides this, an ascending current was remarked: it consisted of air bubbles, bearing with them a white stream, similar to, though smaller than that which was seen descending; on arriving at the surface the bubbles escaped, and the white particles they had rendered buoyant, subsided steadily, like sparks from an exploded rocket. This circulation, similar to the ascending and descending

currents produced in liquids by heat, continued until decomposition from saturation of the solution, or other causes had ceased.

The same fragment was afterwards immersed in other solutions of a similar kind, with a view of ascertaining its rate of decomposition:—but after decomposition had been going on steadily for some time, precipitation suddenly ceased. Under the idea that precipitation had ceased in consequence of the solution having become saturated, fresh quantities were tried, but without any renewal of chemical action; although other phosphatic fragments plunged into the same fluid were readily acted on. The cause of cessation, therefore, could only be attributed to some change in the character of the assay; on examination, instead of being white, friable, and homogeneous in texture, it had become fawn-coloured, dense, and striated; and yielded unequivocally, uric acid reaction. This accounted for the abrupt cessation of chemical action, and bore testimony to the effects of the saturnine solution on the phosphatic ingredients; for it was evident that the latter had constituted the outer coating of an uric acid nucleus in the fragment under examination.

The result of experiments with other salts of lead, as well as with those of mercury, baryta, and others, confirm the facts already stated; viz. that almost all supersalts of lead, especially with vegetable acids, act as ready decomponents of the calculi under consideration. Even the acetate, which in its neutral state is inert, becomes active by the superaddition of a minute quantity of its own proper acid: and, in like manner, the addition of a few drops of lactic*, malic, racemic, or formic acids to solutions of their neutral salts, produces a class of active decomposing agents, so effectual, that either of them may be considered to afford secure means for discriminating the phosphatic from other varieties of calculi.

An interesting and perchance important circumstance connected with this part of the subject, relates to the *strength* of the solution, which appears to be in *inverse ratio* to its decomposing power. Thus, a saturated solution of acetate of lead, acidulated pretty strongly with acetic acid, is inactive; whereas, one grain of the salt, with five drops of the acid, dissolved in one fluid ounce of tepid water, produces rapid and steady decomposition.

This fact has been carefully verified by repeated experiments; for instance, the moment a portion of calculus, which had been steadily decomposing in a weak solution, is plunged into a stronger, action abruptly ceases; it is as suddenly re-established when the assay is returned to the weaker solution. This alternation from weak to strong, and the reverse, was often repeated with solutions variously modified, but invariably with the same general result.

On first remarking the above circumstance, I was not aware that Berzelius had previously recorded a somewhat similar fact in relation to the action of weak solu-

^{*} When a fragment of phosphatic calculus is placed in a solution of super-lactate of lead, under the microscope a dense areola at first surrounds it; from this, after a time, radii proceed, until the assay assumes a stellar appearance, of dazzling whiteness.

tions of borate of soda on uric acid; and that, on the authority of Wetzlar, he had stated that uric acid is soluble in weak solutions of carbonate of potash*.

The preceding experiments being apparently conclusive as to the decomposing effect of certain salts of lead on phosphatic calculi, out of the body; the next point to be determined was the effect likely to be produced by the introduction of their solutions into the living bladder. They had been found, on repeated trial, inoffensive to the eye and to the urethra; they are constantly applied to abraded and inflamed surfaces, as well as used internally, with the greatest advantage: and, although some of these salts, by long-continued absorption, are apt to produce a train of specific morbid symptoms, it has been stated by physicians of eminence, that lead acts deleteriously only when imbibed in the shape of a carbonate; that when the acetate appears to produce colica pictonum, it does so from being converted, after its reception into the body, into a carbonate; and furthermore, that this conversion may be avoided by super-acidulation, the salt may then be administered with perfect safety in large and efficient quantities. My observations tend to prove, that this super-acidulation is essential to the due action of the decomposing fluids I propose. Whatever salt of lead may be employed must be moistened with a small quantity of its own proper acid, or a few drops of pure acetic acid, previous to the addition of water. In a chemical as well as therapeutical point of view this is essential:—1st, it secures the perfect solution of the salt and its consequent activity as a decomponent; 2nd, the superaddition of acid secures against the formation of any of the deleterious carbonate.

In order, however, that I might be perfectly satisfied as to the comparatively innocuous qualities of the before-named salts, I undertook a series of experiments with them on sheep; introducing the fluids into the bladder daily, for several weeks consecutively, and having the animals killed at different periods during the investigation. In none of the sheep experimented on, were untoward symptoms excited, either general or local.

It may be objected, that the membrane lining the viscera of graminivorous animals is less susceptible than that which performs the same office in man; but as, on trial, liquids which irritate and inflame the human organs, act in the same way, and with the same rapidity on those of the sheep, I see no reason to believe that the one is less susceptible of such impressions than the other. Experiments of a personal nature, not necessary to particularize, were also resorted to, and contributed to the conviction, that no evil could accrue from the continued introduction of saturnine solutions into the bladder. The following cases not only prove this fact, but

^{* &}quot;Quand la liqueur ne contient qu'un demi pour cent de carbonate alcalin, l'acide urique s'y dissout assez rapidement." Berzelius, Traité de Chimie.

[†] I refrain, for obvious reasons, from entering into particulars as to the general effect of solutions of the salts of lead in various morbid states of the bladder; although I may be allowed perhaps to direct attention to the property these salts possess of coagulating mucus,—a property they do not fail to exercise on the secretion from the living organ, independently of their decomponent effects on the phosphate of lime which that secre-

furthermore that the solutions are freely tolerated by the organ, even when rendered morbidly irritable by the presence of the stone.

The first case to be mentioned is that of a gentleman, seventy years of age, who had long been suffering from vesical affection, accompanied by alkaline urine, phosphatic sediment, and the copious formation of ropy mucus. The catheter, when introduced, was felt to grate over calcareous concretions imbedded in the prostate gland.

In this case, a very dilute solution of nitric acid, one drop to the ounce of water, could only be retained a minute or two, its use being followed by considerable pain, which lasted for several hours; whereas the nitro-saccharate of lead solution, although retained for *fifty* minutes, produced no inconvenience, either at the time or subsequently. It was repeated daily, or every second day, for upwards of a month, and has been again resumed at the patient's request*.

The second case was one in which two calculi existed; the one was crushed successfully. The bladder was extremely irritable; nevertheless, the solution, injected at frequent intervals, for a fortnight or three weeks, produced no greater uneasiness at the time, or irritability afterwards, than an equal quantity of warm water. The fragments voided by this patient were found to consist of a mulberry nucleus with a coating of phosphatic material, readily acted upon by the solution.

The third case was also one of phosphatic calculus in an irritable bladder. The solution of nitro-saccharate was used daily for a week, and retained for half an hour at a time, not only without annoyance, but often with positive comfort. The gentleman, however, not having patience to await its action on the calculus, nothing further was ascertained.

It will be sufficiently evident, from these mere outlines, that the cases themselves were utterly unfavourable for testing the LITHONTRIPTIC powers of the solution: they are, nevertheless, well-fitted to afford evidence of its being neither irritating nor injurious, when introduced with proper restrictions into the bladder.

The establishment of the latter fact, although an important feature in the present communication, is not more so than the results which tend to denote the advantage of using decomponents, rather than solvents. The latter view of the subject reveals a class of mild, but effectual, agents hitherto untried, and points out a principle, the application of which, I trust and anticipate, will lead to the discovery of similar agents for the decomposition of the other varieties of calculi which afflict the human race.

Guernsey, December 1, 1842.

tion often contains. Other matters connected with the mechanical means for introducing the fluid, the action of various decomponents contained in the urine, &c., must be reserved for consideration elsewhere.

* This gentleman is, I understand, much benefited. The instrument is no longer felt to grate over calcareous matter; and he voids the vesical contents more freely.