THE LUMLEIAN LECTURES ON URIC ACID: ITS PHYSIOLOGY AND ITS RELATION TO RENAL CALCULI AND GRAVEL.

Delivered before the Royal College of Physicians.

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LECTURE III.

At the conclusion of my last lecture I spoke of the effects of saccharine food and of different alcoholic beverages on the uric acid excreting function.

To-day, before proceeding to the more purely therapeutic part of our subject, I must devote a few minutes to the discussion of other classes of food in reference to the same function; and, first, with respect to the influence of a nitrogenised, and especially of an animal diet. Observations are not wanting to show the effects of a pure meat diet on the urine. Those of Lehmann are, perhaps, the most satisfactory; they are so valuable that I must now call your attention to the results.

He first determined the daily excretion of the principal constituents of his urine when on an ordinary mixed diet; he then placed himself on a purely animal diet (chiefly eggs) for twelve days; afterwards, for another twelve days, on a purely vegetable diet; and subsequently, for two days on a purely non-nitrogenised diet, which consisted of fat, milk, sugar, and starch. You will see the results in the table, in which I have left the original numbers obtained by Lehmann, in grammes, as the smaller numbers are easier of comparison with each other than would be the case if the results were reduced to grains.

Table Exhibiting the Mean Results of Lehmann's Observations on the Effect of Different Diets on the Excretion of the Urinary Constituents. Expressed in Grammes.

	Total Solids.	Urea.	Uric Acid.	Salts and Extractives.
On a mixed diet	67.82	32.498	1.183	12.746
On an animal diet	87.44	53.198	1.478	7.312
On a vegetable diet	59.24	22.481	1.021	19.168
On a non-nitrogenised diet.....	41.68	15.408	0.735	17.130

The conclusions which particularly interest us at present are that the total solids, as well as the urea, are much increased by animal food, while they are considerably decreased by a vegetable diet, and still more so by one which is non-nitrogenised; whereas the uric acid is not nearly so much affected by the nature of the food, provided that it contains nitrogen. Thus, it is seen that the urea, on an animal diet, was to the uric acid 53.198:1.478; on a vegetable diet, 22.481:1.021; and on a mixed diet, 32.498:1.183. Estimating the amount of uric acid, on a mixed diet, as 1, animal food brought it up to 1.27; a vegetable diet lowered it to 0.863; and a non-nitrogenised diet to 0.63.

Lehmann found that after the use of purely animal food the urine of man closely resembles that of the carnivorous mammals, becoming of a light amber colour; having a strong acid reaction, and containing neither lactic nor hippuric acid.

On the other hand, after a course of vegetable food, the urine becomes of a brownish-red tint, is much less acid, often deposits the earthy phosphates, and always contains alkaline lactates with oxalate of calcium—in fact, the urine closely approaches to that of the herbivorous mammal. It might be added, though Lehmann does not allude to the fact, that, under these circumstances, there is also found hippuric acid in considerable quantities.

As a result of all the experiments made by different observers—both on man and the lower animals—I think we may fairly come to the conclusion that meat, taken in such quantities only as are sufficient to keep up the nutrition of the body, has no tendency to increase the excretion of uric acid; that, when the diet is purely animal, but the quantity small (as is the case with the carnivorous

animals when in confinement), the uric acid, far from being large, becomes exceedingly small in amount, more especially when it is compared with the urea. On the other hand, that the taking of a great quantity of meat—an excess compared with the requirements of the system—tends to increase the uric acid, though, even then, not more than in proportion to the urea. Funke states that uric acid is less affected by food than any other ingredient of the urine; it is, however, influenced by the time of taking it: that is, uric acid is thrown out in larger quantities after a meal than during the hours that an individual is fasting.

These different facts can be advantageously applied in practice in the treatment of gravel and calculus. In such cases, there is certainly no reason why a proper quantity of animal food should not be taken; and the knowledge of this is important, seeing that many patients have been lowered in health by being kept on insufficient diet, with the idea that, by these means, a lessening of the excretion of uric acid would result.

Fatty and Oleaginous Food.—With regard to the influence of such food on the urinary excretion, the experiments of Dr. Böcker seem to be most trustworthy; and from them it would appear that no influence whatever is exerted on the excretion of water, urea, uric acid, or any other constituent of the urine, by taking from about a quarter of an ounce to three ounces of butter daily.

Causes of Gravel and Calculi.—In the course of our experience, most of us have noticed that there are certain individuals who are prone, either to pass an urine thick from urates or containing uric gravel, or to void numerous small calculi; others, again, have no such tendency, and only on rare occasions observe any thickness in their urine. Can we link this condition with any other constitutional peculiarity? I think we can; and that we shall find, on inquiry into the history of those liable to pass gravel and calculi, that they frequently inherit gout. In looking over 1,900 cases of this disease, which I have had extracted from my books, I find it mentioned that, of this number, comparatively few had passed calculi. If, on the other hand, we examine cases of calculus, we shall find that a much greater percentage of these patients are the children or grandchildren of gouty parents.

In the course of my experience, it has frequently occurred to me to see a man suffering from gout, and to find that he has one child who has had attacks of joint-gout; another who is suffering from eczema; and a third who is passing uric gravel or calculi. It is not very uncommon to find articular gout and calculus present in the same person. Sydenham, in his own person, was a good example of this combination; in fact, we may fairly conclude that those who suffer from an abnormal condition of the uric acid function on the inner side of our imaginary partition, mentioned in the first lecture—that is, in the blood or system at large—are also more prone than others to experience the effects of a morbid state of the same function on the outer side, or in the urinary tract; in other words, gouty subjects, or those who inherit that diathesis, are more liable than others to gravel and calculus.

There are, however, many influences which act strongly in determining the morbid action to the urinary tract—influences which will often cause the occurrence of such troubles in those who do not inherit them. We see, for example, that, in England, stone is more common in some counties than in others, and at one time of life more than at another. How can we account for this?

Anything that checks the cutaneous function, such as the cold east winds of spring, felt so acutely in Suffolk and Norfolk, appears to act as an exciting cause, and it is well known that in these counties gravel and calculus are very common. When the action of the skin is checked, there is no increase of urates, but an undue acidity of the urine, which leads to the precipitation of the uric acid. Cold alone is not necessarily a cause, for in Sweden and Norway calculous diseases are very rare. Another cause which, I believe, leads both to an increase of the excreted uric acid and to its deposition in the urinary organs, is portal congestion. Of the exact pathology of this we are at present ignorant, but, in the prophylactic treatment of gravel and calculus, it is important to look to this point; and much good is produced by the frequent use of remedies which tend to relieve such a condition. Hence the value of Carlsbad waters and salts, and of the numerous saline purgative waters which, of late years, have been so much employed. It must always be borne in mind that, in this administration in the diluted form, the water itself becomes an important element in their action upon the system.

Effects of Water on Gravel and Calculus.—I have already told you that water plays an important part in the formation of uric gravel and calculus, and this must be at once evident when we observe that, in different animals, uric acid is thrown out in the solid or liquid

condition according to the relation existing between the solids and water contained in their urine. From this, it follows that the proper exhibition of water in the prophylactic as well as the medicinal treatment of calculous disorders must be a subject of much importance.

Many observations have been made on the effect of increasing and diminishing the quantity of water taken with food or when fasting. In the latter case, especially if the water does not pass off by the intestines, it causes the urine to become pale and copious (the *urina potius* of old writers); but, at the same time, the action of the skin is augmented. It has been asserted that the amount of uric acid is lessened, but it is doubtful whether this is really the case; but any increase in the quantity of the urine helps to keep this principle in solution, and may thus mask its presence.

When the quantity of water taken with food is increased, it appears that certain of the urinary principles are augmented in amount, owing probably to the increased metabolism of the tissues; but, at the same time, it is stated that the uric acid is decreased. Further observations are much required before we can come to any accurate conclusions on this point. That the quantity of water passed by the kidneys in a given time has a great influence upon the physical condition of the urine, is evident. If, for example, a healthy man during one day passes an ordinary quantity of urine, and, during a second day, but half the amount, it is probable that, on the latter occasion, the urine will be turbid and thick from the precipitation of urate of sodium, whilst the first day's urine will remain bright and limpid; and yet the daily elimination of uric acid may be the same on both occasions, and it only requires that an equal quantity of water should be added to the concentrated urine to bring it to the same condition as the more limpid specimen. If a patient continues day by day to pass urine so concentrated that it rapidly becomes thick, perhaps even in the bladder itself, a very slight change in the acidity of the fluid will cause uric acid to be set free and crystallisation to take place, and then uric gravel, in the shape of cayenne pepper deposit, is formed.

If these changes only ensue after the urine has been passed, of course it is of no real consequence; but if they take place while the urine is still within the urinary organs, then either free acid or some urate may become deposited and form gravel, or increase the size of any calculus already existing within the urinary passages. The deposition of uric gravel is of very common occurrence in children; and I know, from clinical experience, that this often depends on the deficient amount of water excreted. I could give many instances of this, but one or two will be sufficient.

1. A little boy, about five and a half years of age, was passing, from day to day, urine which either contained uric acid crystals or gave rise to a copious red sediment almost immediately after it was voided; his health was otherwise good. I had the urine of the twenty-four hours carefully collected, and found that it amounted to sixteen fluid ounces, with a specific gravity of 1031. On simply causing the child to take five fluid ounces of water an hour before breakfast, and the same before his late afternoon meal, the quantity of urine was at once brought up to twenty-four fluid ounces, and the specific gravity reduced to 1017, nor could any uric acid be discovered when the fluid had stood for thirty-eight hours from the time when the last portion was passed. In a few days, the quantity of urine was increased to thirty-seven fluid ounces, and the specific gravity lowered to 1013.

2. A little girl, about eleven years of age, had the same condition of urine as the last, red gravel being constantly present. The total daily quantity of urine was twenty-four fluid ounces, specific gravity 1026. By the administration of water before two of the meals, the quantity was at once increased to forty-five fluid ounces, with specific gravity 1015, and after a few days to about forty-six fluid ounces, specific gravity 1013, the urine remaining free from any red crystals.

These cases, selected from a large number, are sufficient to illustrate the value of water as a therapeutic agent where there is a tendency to the rapid deposition of uric acid from the urine. In many cases, it is only necessary to give simple water, such as is usually supplied for drinking purposes—a fact constantly acted upon by patients suffering from such complaints when they resort to warm mineral springs, such as those of Contrexeville, Vichy, and other places, where, although the mineral constituents of the spring may to some extent influence its action, yet a considerable amount of its therapeutic value is due to the imbibition, at proper times of the day, and under favourable circumstances, of a large amount of water.

The importance of the proper administration of simple water in

these cases as a part of the diet is the greater, seeing that the plan of treatment can be pursued for an indefinite period; whereas the duration of a course of mineral waters is necessarily limited to a few weeks. I believe that, as yet, the medical profession have not laid sufficient stress on the proper administration of water in the treatment of gravel and calculous diseases.

Effects of Alkaline Treatment.—In the treatment of uric gravel and calculus, the different alkalies and their salts play a most important part, and it is very desirable that their special actions, as well as their relative values, should be clearly made out: this I now propose to do.

I may at once bring to your recollection the fact that, if we give any fixed alkali in the state of a carbonate, it is absorbed and passes through the kidneys in an unaltered form; that is, a carbonate, when taken by the mouth, appears as such in the urine, and, therefore, necessarily diminishes the acidity of that fluid, sometimes rendering it neutral or even alkaline, according to the quantity administered; so that, if we give, at frequent intervals throughout the day, a quantity of the alkali equal to the neutralisation of about thirty grains of oxalic acid—the average acidity of the day's urine—we shall, as a rule, keep that fluid in a neutral state.

In considering the equivalents of the different alkaline metals whose salts are employed in medicine, we find that the neutralising power for acids of the different bases must vary considerably. The most practical method of estimating this power is to measure the different alkaline metals, in the form of their carbonates, against each other; when we find that 74 parts of carbonate of lithium equal 84 parts of carbonate of calcium (chalk or its congeners), 106 parts of carbonate of sodium, and as much as 138 parts of carbonate of potassium. This is an important practical fact, and one that must not be lost sight of in the treatment of calculous diseases.

It must, however, be remembered that it is not merely the neutralising power for acids of the above compounds that has to be considered in treating of uric acid disorders; we must also look at the character of the salts which result from the combination of the acid with the metal, for some urates are very much more soluble than others.

In my first lecture, I drew your attention to a table of solubilities of uric acid and several of its salts, drawn up from the results of a very careful set of experiments, the accuracy of which may, I believe, be relied on. This table is still before you.

On looking at it, we at once see that a considerable difference in the solubility of urates is manifested. Two of those given in the table are insoluble, viz., those of lead and iron; that is, no amount of distilled water, at the temperature of the body, could, apparently, dissolve either of them to the slightest extent. This fact is most important, though rather with reference to manifestations of uric acid in the system in the shape of gout, than its injurious effects as exhibited in the form of gravel or calculus.

It is a matter of clinical experience that lead-impregnation powerfully disposes to the production of gout; and I can also assert, as a result of long-continued observation, that iron-salts have a considerable tendency to cause a recurrence of an attack, when administered, as they often are, with a view to overcoming debility.

The difference of solubility in the alkaline urates forms a subject of great interest, for the value of a solvent may often be expressed correctly as the product of its neutralising power plus the solubility of the resulting salt. Let us take, for example, carbonate of sodium. It has been shown that its neutralising power is large compared with carbonate of potassium, 106 parts of the former doing the work of 138 parts of the latter; but, on looking at the table of solubilities, it is seen that the soda-salt has less than half the solubility of the potash-salt. The same remark applies to carbonate of magnesium, as, although it possesses great neutralising power, the resulting salt is very little soluble, and the very sparing solubility of the lime-salt renders its employment as a solvent of uric acid undesirable. Lime-salts, however, have been thus used, as we learn from the composition of the famous quack remedy of Mrs. Stephens, for the purchase of which the sum of £5,000 was granted by the Government in the earlier part of last century.

The other properties of the alkaline salts must also be taken into consideration when they are administered as remedies. On comparing a soda-salt with a corresponding potash-salt, it is found that the latter is more prone to produce diuresis than the former; at the same time, there is good evidence that the alimentary canal and its appendages, especially the liver, are more influenced by soda than by potash. This is what might naturally be expected, seeing that true bile consists essentially of glycocholate and taurocholate of sodium. Magnesia-salts act more or less as purgatives, and lime-

salts as astringents, but all act as neutralisers of acidity, and, to some extent, as solvents of uric acid. Gravel and calculi usually consist of free uric acid, and even the least soluble of the urates, omitting lead and iron, are much more soluble than uric acid itself, which, as we may see from the table, requires as much as eight thousand times its weight of water at 100° Fahr. to dissolve it.

There is one alkali—lithia—which will require some few minutes' consideration, and upon which I propose to bring forward several new observations and experiments; but, before proceeding to discuss its value, I may make some remarks on the different salts of the alkalies, some of which are more eligible for exhibition, especially in the treatment of gravel, than the carbonates.

All of us are probably aware that, if an alkaline citrate is given by the stomach, it is changed, either in the blood or kidneys, into the corresponding carbonate. The same is the case when an acetate or tartrate is administered; in fact, most of the vegetable salts are thus decomposed in the system, carbonates appearing in the urine. The establishment of this point is important, inasmuch as we can, by the use of these valuable salts, introduce into the system, through the mouth, salts which have no alkaline action on the stomach and form, often, an important part of vegetable food, and can still produce the remote alkaline influence where it is wanted; in short, we can often give even an acid salt, grateful and useful to the stomach, and yet have the very opposite effect induced upon the urine.

I will now draw your attention to the salts of lithia, which were first introduced as remedies by myself as far back as 1859. If we look to the atomic weight of the metal lithium, we find it very low, only 7. The number representing the carbonate of lithium is also small—compared with carbonate of potassium it is as 74 to 138; hence the neutralising power for acids possessed by carbonate of lithium is greater than that of carbonate of potassium in the above proportions. Next, if we look at the table of solubilities of the urates, we see that the acid urate of lithium requires only 220 parts of water at the body temperature to dissolve it; the corresponding potash-salt requiring 500 parts, and the soda-salt as much as 1,130 parts, while the magnesia and lime urates take 1,600 and 2,800 parts respectively; so that, with respect both to neutralising power and solubility the lithia-carbonate has a great advantage over the corresponding salts of potash, soda, magnesia, and lime.

I must now allude to a paper in the *Medico-Chirurgical Society's Transactions*, vol. xlviii, 1875, by one of our distinguished Fellows, Dr. William Roberts, of Manchester. The subject of this communication is "The Solvent Treatment of Urinary Calculi." I presume that the author's opinions are not changed since then, as, in the last edition of his work on "Urinary and Renal Diseases," the results set out in the paper are embodied.

Dr. Roberts came to the conclusion that potash-carbonate dissolves uric acid more rapidly than the soda-salt. This he ascertained by placing sections of uric acid calculi in phials, and causing currents of the different solutions, at blood-heat, to pass over them at a regulated rate. He also found that the strength of the solution employed was of much importance, the greatest amount of solvent power being exhibited in solutions containing from forty to sixty grains of the alkaline carbonate to the imperial pint (twenty fluid ounces). Below this strength, the power of the solutions gradually declined, until, with those which contained less than three grains to the pint, the solvent power scarcely exceeded that of water. On the other hand, if the strength was above sixty grains to the pint, the pieces of the calculus became encrusted with the alkaline bi-urates which were then deposited, and thus the further action of the solution was impeded. This was especially noticeable when the strength of the solutions was much above one hundred grains to the pint.

Even without the actual experiment with pieces of uric calculi, I think we could predict that potash would prove a more powerful solvent than soda; for we have only to glance at the table to see that urate of potassium requires, at the body-temperature, only five hundred parts of water to dissolve it, whereas the corresponding soda-salt takes as much as eleven hundred and thirty parts. The soda-salt certainly has an advantage in its greater neutralising power, but not sufficient to make up for the far less solubility of the resulting urate.

In the paper in the *Medico-Chirurgical Transactions*, and in his book, Dr. Roberts has the following foot-note with reference to the action of carbonate of lithium. He says: "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 carbonate of potash and soda. Its reputation seems to have been gained through its comparative insolubility. Only weak solutions of it could be employed," emphasis being particularly laid on

the word "could." I refer to this passage because other authors have evidently been influenced by the statement; for example, Sir Henry Thompson, in his little work on *The Preventive Treatment of Calculous Disease*, almost repeats the above words, when he says: "Dr. Roberts finds carbonate of potash to be the most powerful solvent; better than soda, much better than lithia."

Having myself introduced lithia-salts to the profession as internal remedies, and having used them continuously for twenty-five years, I felt it was my duty to bring forward evidence in support of their value as therapeutic agents, and to ascertain the truth or error of the statement which had been put forward as to their comparative inutility.

For this purpose, I have recently had a series of experiments made, the results of which are seen in the table on the board.

TABLES.

Effects of Solutions of Carbonates of Sodium, Potassium, and Lithium, upon Fragments of Uric Acid Calculi.

Strength: 60 grains to 20 fluid ounces. Temperature, 100° Fahr. Time of action, 12 hours.

In 9 experiments—3 with each carbonate—the solvent powers were as follows.

With Carbonate of Sodium:

21.2—18.1—15.3 per cent.

Mean = 18.2 per cent.

With Carbonate of Potassium:

28.6—27.6—38.3 per cent.

Mean = 30.5 per cent.

With Carbonate of Lithium:

43.8—58.6—47.7 per cent.

Mean = 50.0 per cent.

In 3 experiments. Strength of solutions, 50 grains to 20 fluid ounces. Time, 12 hours. Temperature, 100° Fahr.

With carbonate of sodium.....16.2 per cent.

With carbonate of potassium23.1 per cent.

With carbonate of lithium37.7 per cent.

1 Experiment.

Carbonate of lithium—100 grains to 20 fluid ounces.

Solvent power—70.2 per cent.

2 Experiments, using carbonate of potassium and lithium, 20 grains to the 20 fluid ounces.

With carbonate of potassium.....21.2 per cent.

With carbonate of lithium33.1 per cent.

2 Experiments, using carbonate of potassium and lithium, 10 grains to the 20 fluid ounces.

With carbonate of potassium.....11.2 per cent.

With carbonate of lithium17.5 per cent.

The substance employed was a large uric acid calculus given to me by my friend Mr. Erichsen. It was first cut; to ascertain its internal structure, and to see if this was pretty uniform throughout; then a portion was broken up, and the fragments washed with distilled water, and carefully dried. About equal weights of the calculus were put into three bottles, and solutions of neutral carbonates of sodium, potassium, and lithium were added to them.

The solutions were of the strength of 60 grains to the 20 fluid ounces; the action upon the calculus continued for twelve hours, at the temperature of 100° Fahr., with frequent agitation. Separate quantities of the calculus were taken, here called Nos. 1, 2, and 3. No. 1 was first treated with the lithia solution, then with those of potash and soda; No. 2 was treated first with the potash solution, then with those of soda and lithia; and No. 3 with the three solutions in the order, soda, lithia, and potash.

The quantity of the solution used in each case was the same. The results of these experiments are very striking. Let us first consider the soda numbers; we find that the percentage of solvent power in the three experiments was 21.2, 18.1, and 15.3, the average being 18.2 per cent. The percentage of the potash numbers was 28.6, 27.6, and 35.3, the average being 30.5 per cent. The corresponding lithia numbers were 43.8, 58.6, and 47.7, the average being 50.0 per cent. In all three cases, the difference between the mean and the extremes is not very large; and such differences must always exist when we use an impure substance, such as the fragments of a calculus, which is never composed of a pure chemical salt. We see, then, that, in solutions of the strength mentioned, the value of the lithia-salt over that of potash, and still more over that of soda, is most evident. Other experiments were afterwards made with solutions of different strengths. Thus, in three experiments, the

solutions contained fifty grains to the twenty fluid ounces. Time, twelve hours; temperature, 100° Fahr.; with frequent agitation.

The carbonate of sodium solution dissolved 16.2 per cent.

"	"	potassium	"	"	23.1	"
"	"	lithium	"	"	37.7	"

In another experiment, the sixty-grain lithia solution being used, but the time altered, at first to ten hours at 100° Fahr., then to eight hours at about 60° Fahr., the solvent power was 60.8 per cent.; but, when a solution containing one hundred grains to the twenty fluid ounces was employed, the solvent power was as high as 70.2 per cent.

Lastly, it will be observed that, when the comparison of the solvent power was made between the potash and lithia salts, using twenty and afterwards ten grains to the pint—the quantity used by Dr. Roberts in his lithia experiments—the results were in each case more than 50 per cent. in favour of the carbonate of lithium.

It will be seen from these experiments that so far as soda and potash are concerned the results obtained exactly agree with those of Dr. Roberts; they exemplify the greater solvent power of the latter over the former, a result which might have been clearly anticipated, but, on the other hand, they are totally opposed to his conclusions with respect to lithia. How is this to be explained? On looking at the solubility of urate of lithium, as seen in the table, we find it more than twice that of the potash-salt, or as 220 to 500, and we can scarcely believe that in solutions of the two carbonates the uric acid would be found to be most soluble in the one which contained the alkali which gave the more insoluble urate; this would be absurd—in fact, we should anticipate that the lithia solution would prove as superior to the potash as we have already found the potash to be to the soda solution.

We must look for some means of explanation. Dr. Roberts used the expression "only weak solutions of carbonate of lithia could be employed," italicising the word "could;" and he appears to have used in his four experiments, two of which are given in the *Medico-Chirurgical Society's Transactions*, solutions of the strength of 10 and 20 grains to the 20 ounces, whereas, in case of the potash, he found that a 60-grain solution is the most powerful. Now it will be seen in the table that solutions of carbonate of lithium were employed containing 60 and even as much as 100 grains to the imperial pint; and that, in the case of lithia, as the strength was increased the solvent power also was augmented. I should imagine that Dr. Roberts either used an impure carbonate of lithium or assumed that only one grain was soluble in the fluid ounce, as he used only 10 and 20 grain solutions; whereas as much as 100 grains can be dissolved, at the temperature of the body, in the imperial pint of water. Impurity of the salt and the use of solutions which were far too weak will at once explain the discrepancies and the cause of the erroneous statements with regard to the solvent power of the lithia-salts. No one who has thoroughly investigated the action of these salts, in comparison with those of soda and potash, as internal remedies, can come to any other conclusion than this, viz., that lithia-salts are far more powerful solvents of uric acid than potash-salts, while these latter are more efficacious than those of soda.

We have only to take three small phials, filled with a solution of the three carbonates, of the same strength, and to put into each the same quantity of small uric calculi, the amount being such that the lithia will dissolve them. If we carry these in a warm pocket, after a short time it will be seen that all the calculi have disappeared from the lithia solution, while more than half are left undissolved by the potash, and about four-fifths by the soda solution.

I have been informed by some patients that they have been deterred from using lithia-salts, although they had found them valuable, by having been told that their employment would prove injurious, owing to their caustic effects upon the renal organs. In answer to this objection, I may say that I have found the action of carbonate of lithium to possess less destructive power than the corresponding salts of potash and soda upon animal tissues.

The only effect that I have ever noticed has been that, when the quantity is increased beyond a certain amount, a little tremor of the hands is produced, which passes off at once on the diminution or omission of the dose of the salt. I have known patients, of their own accord, continue the use of lithia-salts for more than ten years, with the effect of entirely preventing the recurrence of the symptoms to remove which they were first prescribed, and without the production of any injurious effect. For myself, I have not the least doubt as to the value of lithia-salts as therapeutic agents, and am convinced that, by their employment, depositions of uric acid in the renal organs can to a large extent be prevented. Free dilution and administration on a fasting stomach are points of much importance,

which should be attended to in the administration of alkaline remedies. I have been much in the habit of using potash with lithia, in the form of the citrate or the carbonate; the former to give neutralising, the latter to increase the solvent power.

In concluding my remarks on the action of alkalies, I may state that I do not myself believe in the value of any injections into the bladder in the treatment of vesical calculus; at the very best, the process must be most tedious; and at the present day, when the surgery of the subject has reached to such great perfection, when a calculus can often be removed completely from the bladder in a few minutes without the use of the knife, I cannot but think that the surgeon is better qualified for the treatment of such cases than the physician.

[To be continued.]

ABSTRACT OF LECTURES ON PHYSIOLOGICAL DISCOVERY.

Delivered at the Royal Institution of Great Britain.

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LECTURE II.—THE CIRCULATION OF THE BLOOD: THE CONTROLLING INFLUENCE OF THE NERVOUS SYSTEM.

As the walls of the heart and the coats of the arteries contain contractile tissue, we might anticipate that they would be more or less governed by the nervous system, thus influencing the rhythmic movements and the distribution of blood. It was also consistent with experience that various emotions acted on these organs; consequently, in the dawn of scientific thought, men referred many of the feelings of the mind to the heart (sacred writers, Aristotle, Plato, Galen, etc.). Many of the old writers accounted for the heart beating strongly under excitement, for flushing and palor, for the existence of pain in certain parts different from the seat of disease, by the use of the word sympathy, which expressed the fact of kindred feeling, but explained nothing. It was not until after the discovery of the circulation that any rational attempt was made to account for such phenomena. Vieussens (1641-1716) supposed that the pallor and flushing of the face under violent emotion were caused by the nerves compressing the carotid arteries in the first case, and the jugular veins in the second. Boerhaave (1668-1738) accounted for the systole and diastole of the ventricle by intermittent compression of the cardiac nerves. De Gorter (1689-1762) supposed that such compressions occurred in the wall of the heart itself. For many years, the doctrine of the *anima* of Stahl (1660-1734) influenced physiological thought, and the beat of the heart was referred, with all such phenomena, to the direct and usually conscious operation of the *anima*. Then arose Robert Whytt, a man whose life and labours have been nearly forgotten, even by physiologists. He was born in Edinburgh in 1714, graduated as M.A. at St. Andrews, studied medicine in Edinburgh and London, graduated as M.D. at Rheims in 1736, became Professor of the Theory of Medicine in Edinburgh in 1747, and died in 1766. In his great work *On the Vital and other Involuntary Motions of Animals*, he modified the opinions of Stahl. Whilst such motions as the action of the heart were caused by the operation of the mind, said Whytt, the mind governed them through the nervous system. In this work, also, there is the first glimmering of the doctrine of reflex actions. Sympathies occur, not by one part being directly connected with the other by means of nerve, blood-vessel, or membrane, but through the intervention of the spinal cord and brain. Whytt was a vigorous experimentalist, and investigated in this way the heart and vessels. He attributed flushing, etc., to an oscillatory motion of the small vessels, excited either by a stimulus directly applied, or by afflux of blood.

In those days, there was much discussion as to the arteries being contractile. Haller (1708-1777) held that they were, and in this he was vigorously supported by Cullen (1712-1790) and Whytt. In their experiments, these observers confounded not unfrequently the movements of the great arteries, due to elastic recoil, with an active muscular contraction; and the relative degree of elasticity and of contractility was not clearly established till John Hunter (1728-1794) made numerous experiments on the subject (see Hunter *On the Blood*, edition of 1794, p. 125).

At the time of Hunter's death (1794), the notions held as to the