

For Dr. Laycock

SOME REMARKS

ON

URIC ACID GRAVEL.



BY



ANDREW MILLER.M.R.C.S.E.

The following remarks on Uric acid gravel deal with the subject only in a very general way. Much has been written which I have had no opportunity of reading and a quotation of which would therefore lead to misapprehension. In referring to experiments I take it for granted that the medical profession are already sufficiently acquainted with the details if not with those who conducted them.

Habits and appearance of patients affected with uric acid gravel.

If patients affected with the gouty diathesis were always found to present the features of this diathesis in either of its two well-marked forms, namely, the

Sanguine and the Bilious, there would be less difficulty than there really is in speaking of the habits and appearance of persons affected with Uric Acid Gravel. In point of fact, however, the gouty diathesis is not always or even generally presented to us in either of its typical varieties, and doubtless the same remarks which apply to the gouty, are more or less applicable to the Strumous diathesis. From intermarriage and other causes, the diatheses get mixed and modified - so that whilst we cannot question the fact in the case of many patients that gout is present, we have no little difficulty in reconciling this with their general appearance, that is so long as we adhere to the common descriptions of the Arthritic diathesis. It is certain, for example, that Strumous affection is met with in gouty families, and thus we are compelled to admit the existence of a strumous arthritic diathesis. Again, whilst some are prone to fatty degeneration especially in the coats of blood vessels, others are as prone to the accumulation

of fat around internal organs. It is also a matter of common observation that whilst some gouty patients are thin and of spare habit, others are, just as remarkably, of full habit.

The Nervous-Arthritic ought indeed to be considered as truly a form of the Arthritic diathesis, as the Sanguinic-Arthritic itself, which is one of the typical forms recognised by authors.

Natural dispositions vary much more perhaps than the shades of diathesis; and that which may be excess in one case, is only moderate indulgence in another, or perhaps abstinence in a third, and thus the habits of those affected with Uric Acid gravel will be found to differ very much.

The whole subject of diathesis has received less attention from medical men than a matter of such grave importance deserves, and thus we are constantly meeting a particular form of disease, in those whom we never

suspected of any such tendency.

While then we may have much variety both as to the habits and appearance of patients, it is well to keep in mind the chief points which characterise the Sanguine and Bilious-Arthritic diatheses respectively.

But, it may be asked, Is uric acid never deposited except by patients in whom gout is developed in some form or another? To this question it would, at present, be difficult if not impossible to give a direct answer. Well then, it may be said, Is half the population gouty? and to this again, we are compelled to return an evasive reply. Perhaps fully half the population may be arthritic to some degree, and the more the subject is enquired into the more possible does it appear that nearly all the urinary deposits are in some way dependant for their formation upon the presence of uric acid in increased quantity.

The connection between

the gouty and Rheumatic diathesis, if indeed the latter should be looked at as a diathesis, is a subject of much interest; but of this we have no clear account at present. Urates are largely deposited during the progress of Rheumatism; and altho the urate most commonly met with is the urate of Ammonia, whilst that which is more characteristic of Gout is the urate of Soda, still the difficulty remains unsettled so far as the deposit is concerned - for why ^{should} the uric acid seize upon the Ammonia in the one case, and upon the Soda in the other.

Our investigation into the morbid changes going on in affected tissues in the two diseases is, of course, beyond the province of this thesis, and therefore we proceed at once to a consideration of uric acid deposits as commonly met with in the uric.

Then I'd
have
helped

Uric Acid Gravel, and the circumstances leading to its deposition.

Urine depositing Uric Acid is often more highly coloured than perfectly healthy urine, altho' its specific gravity be not much altered. As it cools a sediment is gradually deposited and this is invariably crystalline. The crystals vary a good deal in size and also in form, i.e., in a variety of specimens of urine depositing Uric Acid, we find a considerable variety in the crystalline form of the deposit, altho' in each specimen the crystals have much the same shape. What relation the different forms in the Uric Acid may have to the diseased condition under which they are produced is but little known for the composition of the acid is always the same, viz:— $C_{10}H_4N_4O_6$; or according to its rational formula $2HO, C_{10}H_6N_4O_4$. As already stated it has usually a red colour, but this is not invariable, and indeed

pure Uric Acid is quite colourless, altho' it is never so when met with as a urinary deposit. The usually high colour of the sediment is accounted for on the principle that the same condition of body which leads to the excessive production of uric acid, leads also to the development of more colouring matter. Whatever may be its colour and whatever its crystalline form, it never re-dissolves to any perceptible degree on simply heating the urine which has deposited it - even if the urine be boiled "red sand" does not redissolve: altho' the addition of a little aqua potassæ will soon cause it to disappear, because urate of potash is formed, and this is one of the most soluble salts of uric acid at present known.

That uric acid ^{should} not re-dissolve on heating the urine in which it occurs as a sediment is not at all remarkable; for if it is so sparingly soluble as has been asserted, namely,

that "one grain requires 10,000 parts of cold water" (Miller) to dissolve it", we should not expect that heat applied to a small quantity of urine, having a considerable amount of sediment in it, could produce any decided change. But now comes the difficulty—Since Uric Acid is so very difficult of solution, and since it is only in a perfectly dissolved state that it can pass through the capillary membrane of the renal-blood vessels, how is it maintained in solution until it actually becomes a component of the urinary secretion, and how then is it afterwards deposited. Doubtless the animal fluids have a power of dissolving substances which it is difficult to account for upon any ordinary chemical principle; for we know that certain phosphates, for example, are conveyed to the alimentary canal, and yet the channel by which they are conveyed is by no means obvious.

Two theories have been

advanced to account for the easy elimination of the uric acid by the kidneys. According to one view, the uric acid reacts upon the ammonia of the double phosphate of Soda and ammonia present in the urine, forming the super. urate of ammonia and leaving the urine in a state of increased acidity dependent upon free Phosphoric acid; according to another view the double phosphate of Soda & ammonia acts as a vehicle for the uric acid, which would on this view be itself the cause of acidity in the urine, and as the urine cools the phosphate deposits it. Even if the latter explanation were in part correct, still the difficulty arises why is the uric acid not again redissolved on heating the urine which has deposited it, seeing that the body which held it in solution is still present in the fluid. It seems difficult to account for the phenomena observed in connection with the deposit of uric acid gravel, unless we admit that

urates
are
deposited
by uric acid

which is after all so very likely, viz:—
that the same substance may exist in
several distinct conditions, in one
of which it is quite soluble in water,
but in another insoluble or nearly so.
To take this view of the case is indeed
to save ourselves much trouble—for
after all, there may be certain subtle
changes in the urine leading to the
deposit of uric acid just as there are
unaccountable changes in the blood
leading to its coagulation. Still it is
quite certain that very ^{sparingly} soluble substan-
ces are gradually formed in fluids (as
crystalline deposits) which will not re-
dissolve them even under the agency
of heat—these substances must have
existed in a state of solution previous
to their deposition just as is the case
with uric acid. It is easy to under-
stand that uric acid in passing from
a state of solution to a crystalline
form should pass from the soluble to
the insoluble; and this upon the sup-
position even that the uric acid had

not been held in solution by either Ammonia or Phosphates previously to its excretion. The existence of crystals in the circulating blood is at the very best an exceedingly improbable occurrence and one at all events which could not be proved. Upon the whole this last mode of accounting for the deposition of "red-sand" when Uric Acid is formed in excess is consistent with what has been observed in the case of other bodies, and scarcely affected by any objection of a tangible kind. At some period of its history the most insoluble body deposited from fluid must have been in a state of perfect solubility. So long as Uric Acid is still within the blood vessels, and therefore still a component of the blood, it is under the influence of forces which do not tend to favour the assumption of crystalline form, but rather to resist this; for a short time after its escape from the blood it may be affected by the same forces in a minor degree,

major
lyphatic

and thus its crystallization still prevented, but when it has fairly reached the bladder, and is ready to be cast out of the body as that which is prejudicial to the interests of the Economy it ceases any more to be affected by organic forces and thus comes within the sphere of purely physical agencies which favor its aggregation into some form bounded by plain surfaces.

For the most part Uric Acid is not deposited by the urine until after being voided; but in those cases in which there is a well-marked tendency to the formation of calculi probably the nucleus of the stone is formed even as high up as the pelvis of the kidney.

As our knowledge increases it may yet be ascertained that the varying degree of tendency to the accumulation of Uric Acid depends upon the presence of some other body in the urine, which con-

= tributes to accelerate or retard not merely the crystallization of uric acid but even its tendency to aggregate.

Taking into account the chief explanations that have been advanced up to the present time in reference to the excessive formation and deposition of uric acid, it must be confessed that little of a truly satisfactory nature has as yet been made manifest; and perhaps there is no other condition of body which more strongly carries to the mind the conviction that what is called a diathesis is no mere effort of the imagination. Palliate how you may, neutralise the products of the disease, or even for a time, as is possible, change the nature of the products, still no sooner are the various means set aside than the tendency and its results become as manifest as ever. Physicians have indeed given up any attempt to cure Gout, which may be

regarded as that form of the Uric Acid
diathesis most obstinate and intractable.
Even the recently introduced preparations
of Lithia are only palliative; and that
strong remedy Colchicum, which strikes
as it were at the very root of the dis-
ease has only to be used a little
carelessly, and then it becomes more
injurious than useful.

I have not entered
particularly upon the microscopic ap-
pearance of the sediment, because
the crystalline forms have been very
fully examined, and as fully de-
scribed in various works on the
Urine - and are thus perfectly famil-
iar to every one interested in the
subject. What appears to require at-
tention is the very thing the ordinary
Explanation of which is somehow
accepted as satisfactory. The Uric Acid
is described as combining with ammonia
and as entering the Urine in the form
of a urate - being subsequently

14

deposited by the action of some acid present in the urine, which removes the ammonia and thus allows the insoluble uric acid to subside. We have only to accept this explanation and difficulty vanishes. We have only to enquire into its value, and the further the investigation proceeds the more convinced do we become of its unsoundness. How does the urine become so strongly acid? What is the acid which thus seizes upon the ammonia? Is it Phosphoric acid? It cannot be Phosphoric acid, because the amount of free Phosphoric acid is never great; and besides granting even that Phosphoric acid might effect the purpose attributed to it, there is this difficulty in the way, namely, that the same circumstances which cause an increased generation of uric acid do not cause an increased supply of Phosphoric. The amount of phosphates in the urine indeed probably varies but little, and at all events

suffers but little change in the circumstances under consideration.

In view of these things it need not appear strange if the ordinary explanations given of the deposition of uric Acid are held to be at least unsatisfactory. It is not my purpose to call in question the correctness of various observations at present generally received, such for example as, that gastric acidity and the acidity of the urine are vicarious of each other - the urine being most acid when digestion is not going on, and least so after digestion has progressed for some time. All that is contended for is simply this, that the ordinarily accepted explanations of the deposition of uric Acid fail to carry with them the conviction of their own accuracy.

Theory of the origin of uric Acid.

The Nitrogenised tissues of the body having served their purpose in the economy become broken down, and restored to the blood in a fluid form.

Severe muscular exertion even without increase in the quantity of the food causes an increased amount of azotised matter to appear in the urine. From this & other facts we infer that waste of tissue can go on with great rapidity. We do not know positively how long a portion of Albumen remains in the organised state - there being no certain means of ascertaining this - and it is only from the fact before stated, namely, that after severe ^{Exercise} Nitrogen is found in excess in the urinary secretion, that we are led to the conclusion that disintegration is easily and rapidly effected.

It is usually stated by Physiologists that in health the materials of muscular and other tissues are acted upon by the Oxygen in the blood and converted principally into Urea, in which form they appear in normal urine, and although Urea is not the only product of this chemical change, it is on account of its large percentage of Nitrogen, perhaps the most interesting when looked at in connection with this subject. Should any

17

morbid action interfere with this process and check to any serious degree, the transformation of muscular substance into Urea, the result will be the excessive production of another very interesting compound of Nitrogen, known as Uric Acid, and it is to a partial arrest in the normal change of Nitrogenised tissue into Urea that the over-development of Uric Acid in the gouty diathesis is commonly attributed.

But Science, in the state in which we find it, is so inexact that we are familiarly in the habit of speaking of many things as well-ascertained regarding which it would be exceedingly difficult, were we required to do so, to supply positive evidence. This is especially true with regard to the changes which take place in the body, about which we really possess no very certain data, few of our opinions on this subject being based upon actual fact - Causes are judged of from the effects observed to follow them.

The ultimate products of

the oxidation of organic matter are very much the same, whether the oxidation takes place within the body or out of the body - It is in the succession of changes that the difference really lies. The question to be settled is not simply what are the products of the oxidation of dead muscular fibre, or of inanimate albumen, but through what successive changes do living muscular fibre or albumen in any other organised shape pass, under the conflicting agencies of vital force on the one hand and chemical force on the other. Who can say that he knows anything of the first step in the process of disintegration? And if we do not know the first step of transition of what value is a knowledge of the future stages. Still altho' we may fairly suppose that the chemical processes continually going on in the human frame differ considerably from similar ones in the laboratory, few persons of unbiased mind would reject the theories commonly held as to the production of urea, and other highly azotised excreta. For example

it is a generally acknowledged fact, that if Albumen be acted upon by the Permanganate of Potash, Urea & other similar products will be the result - it is equally true that when an individual is subjected to a diet containing a large amount of Albumen, the quantity of Urea passed by the kidneys in such a case is very sensibly increased. Now we know that the Permanganate of Potash is a powerful oxidizing agent, and we know also that oxidation is constantly going on in the body - the processes are alike, the materials are alike, and the results are the same, and thus we are driven to the conclusion that the production of Urea, whether in the living body or in the laboratory is effected in much the same manner.

Chemists tell us that when organic matter is consumed the products differ according to the freedom with which Oxygen has been supplied during the process and this is a fact which admits of no doubt, for example, if Sugar be treated

with Nitric Acid, it yields Oxalic Acid and if strongly heated in the air, becomes resolved into Carbonic Acid and water - the products being generally simple in proportion as the supply of Oxygen is abundant.

It has been asserted that the quantity of Urea passed by the Kidneys is not always increased, but even considerably diminished in some instances by unusual exertion. It is fair to mention this even at the risk of unkinging some portions of generally received theories; perhaps, however, as our knowledge increases, even should this assertion prove correct, it may not be found inconsistent with well established facts. It should be kept in mind that the purpose of a good theory is to account for all the observed phenomena.

It is stated that Uric Acid, when subjected in the laboratory to the action of oxidizing agents, may be converted into Urea, and other more or less harmless products according to the amount

of oxygen supplied. More lately it has been ascertained that if uric acid be given to animals the quantity of urea passed by the kidneys is considerably increased.

With these data before us, it seems scarcely possible to resist the inference that the super-abundance of uric acid, and other products of imperfect oxidation is the result of a deficiency either in the power or in the supply of the oxidising agent, and that if only this oxidation could be increased the presence of uric acid in the urine to any large amount would be entirely prevented.

If this be indeed the true pathology of the case one is naturally led to enquire, How is it that with a knowledge of these facts no treatment has yet been found adequate to arrest the production and excessive deposition of uric acid; for we know that it does still go on, even in persons who are best circumstanced as regards the application of every remedy modern science has contrived for their relief. The answer to

this question, if a right answer could be found, would at once solve the mystery of uric Acid gravel, and set our at present vague conjectures as to the cause of gout on the right track. Gout is a disease not limited to any particular class of patients, indeed it is found perhaps most frequently in those who whatever may be said to their discredit, are at least in a position to give a most favorable opportunity for the trial of any remedy. The sufferings of gouty patients are often attributed to want of self-denial. In the majority of instances this is not the case. Certainly, no class of men have more reason for temperance, if indeed a temperate mode of life would bring them relief, for the pain they endure is well known most intense. Many men, having once suffered from this dreadful complaint and dreading a recurrence of it, have adopted a rigorously temperate diet, but this does not appear to have prevented their old enemy from again attacking

them. This treatment too would have the effect of improving the general health if pushed very far.

Just as with other diseases we find that the excessive indulgence in certain articles of diet has a tendency to increase the morbid action, so in gout, highly azotised food and fermented liquors doubtless aggravate the intensity and increase the frequency of attacks.

Making every allowance, however, for obstinacy and recklessness on the part of patients, we have still to account for a remarkable tendency to the over-development of uric acid in a large proportion of the community and that notwithstanding the various agencies which seem to place the disease at our disposal, but which are no sooner given up, than the results of the morbid action re-appear sometimes in greater force than ever.

Modes of Treatment.

Before leaving this subject it may be as well to mention some of the remedies which have been used from time to time in the treatment of uric acid gravel. First on the list, perhaps, ought to be placed the Bicarbonate of Potash, which from its efficiency as an antacid as well as its cheapness would enable it to be used in all cases. It has scarcely a disagreeable taste, no tendency to render the urine alkaline, (which is certainly the case with the Carbonate of Potash and with Aqua Potassa) it forms a salt with uric acid which is inferior in solubility only to theurate of lithia, and even if it should be given in excessive quantity, on account of its being a bi-carbonate, it is but little likely to prove harmful. It may be worth while to mention here that the risk

which some consider likely to follow upon the over-neutralization of the urine is not considered real by others, and that even if the urine were rendered somewhat alkaline, a deposit of a phosphatic character would not certainly follow: but here again we have to take into account all the circumstances of the case.

The especial advantage of the Salts of Lithia must depend upon the great solubility of theurate of Lithia. It is scarcely necessary perhaps to mention that the salts of Soda exist in the Vichy waters, and that these, upon theoretical grounds, ought to be unsuitable in the treatment of the diathesis now under consideration, whilst in point of fact they are in reality beneficial. Mineral waters are however, in many ways, different in character from mere solutions of mineral salts made artificially. A question of no small importance ought here to be noticed, namely, how

far an alkaline mode of treatment is really beneficial to the patient, for it is to be kept in mind that the presence of alkali in excess tends to the development of acid in excess; and unquestionably patients have been often injured by the persistent use of alkalis in excessive quantity. An intelligent patient is often best able to act as his own physician—he watches his symptoms and can apply the suitable remedy at a time when the most skillful physician might be unable to see the necessity for it. One great principle which is becoming more and more recognised in the present day is that medication should be used only when we are driven to its use, and then the less medication that can be done with the better. This principle has doubtless a very special application to those who have a tendency to the over-secretion of uric acid. They are often, perhaps generally, in what might

be called pretty good health, at all events not far removed from what should be regarded as good health in their particular case. There may be a good deal of suffering, but still were it not for the pain and inconvenience to which they are subjected, they would sleep well, and take their food, and pursue their ordinary avocations as well as the majority of other men. Now in our treatment these things should be borne in mind, and whatever can be effected by the ordinary means, apart from medicine should never be attempted by alkalis, however easy a means they may seem to afford as of putting things right at once.

In reference to the Therapeutic action of Calchicum, several views have been held; at one time it was supposed that under its influence the amount of urea secreted was increased and thus the quantity

of Uric Acid in the blood was diminished. Again, it has been thought that both Urea & Uric Acid are thrown off by the Kidney in increased quantity, and thus the blood is relieved of both these secretions. But others again have more lately entertained the idea that the administration of Colchicum has in some way the effect of diminishing the amount of Uric Acid formed by the tissues, in some way arresting or modifying their transformation.

The action of Benzoic Acid in cases of the Uric Acid diathesis is peculiar, and at first sight might seem to furnish us with a mode of successfully treating the strongly developed tendency to the over-formation of Uric Acid. During the administration of Benzoic Acid, instead of the sparingly soluble Uric Acid we have Hippuric Acid produced and this we know to be freely soluble in water. The Chemical relations

between Benzoic Acid, Hippuric Acid
Uric Acid and Glycosuria are interest-
ing but they are more curious than
useful; indeed we might say they
are as tantalizing as they are re-
markable. We seem to have placed
within our reach, as it were, an
easy mode of dealing with an
otherwise intractable disease, yet
no sooner is the administration of
Benzoic Acid suspended than the
Uric Acid returns to its former condition-
Hippuric Acid is once more re-placed
by Uric Acid and the patient is
nothing the better.

It would be tedious to
enter upon the many other remedies
from various sources which have
been used in cases of Gout, for pro-
bably the Veratrum Viride acts very
much in the same way as Colchicum,
and the Winter Cherry probably owes
any little efficacy which it possesses
to some sedative effect upon the cir-
culation. Any new remedy, if not

in itself positively hurtful, is likely to do the patient good, if in no other way, at least by suggesting the hope of relief if not of cure; and any tonic which would tend to build up the general health, would of course aid in resisting the morbid tendency.

Although, as already stated, it is usually thought that very great prudence as to eating and drinking would enable the patient to ward off impending attacks, it is of equal importance that the system should not be lowered. A man may appear to have a degree of health and vigour which he really does not possess, and it is quite certain that a person who has been accustomed to animal food and stimulating drink cannot change these for a vegetable diet, and absence of stimulants, without suffering a loss of vital energy. If it were really the case as some may have supposed

that the Uric Acid is formed from Nitrogenised food, the less of this the patient could do with the better, but an imperfect knowledge of Chemistry may be easily misapplied in the treatment of disease, and so there is reason to fear it has been in some cases of Gout. It is quite true that an excess of Nitrogenised food causes increase in both the Urea and Uric Acid passed by the kidneys, but it is not true that abstinence in this respect arrests the formation of Uric acid.

In conclusion, the following considerations are submitted as worthy of the attention not only of those carrying on physiological & pathological investigation, but also of those more immediately engaged in the treatment of disease.

1st Even in those passing much Uric Acid the blood is invariably alkaline.

2nd Urea has the composition of a salt but acts as a base; thus a body which according to theory should be neutral is found able to neutralise even Nitric Acid.

3rd Two substances having exactly the same Empirical formula may be the one neutral and the other acid - therefore is it not possible that a substance isomeric with Uric Acid may change into Uric Acid after leaving the kidney, or perhaps immediately after being filtered from the blood. It is certain however that Uric Acid has been detected in the blood, or at least Uric Acid has been obtained from the blood as if it existed there in the free state.

Is it not possible that the solubility of Uric Acid may be due to its state of combination with Urea; and its subsequent deposit may follow upon the tendency to the formation of a crystalline deposit of Uric Acid. Whether the above view be correct or not, it is certain that the Urea after being passed is a body possessed of basic properties just as certainly as that the Uric Acid is possessed of acid properties ~~yes~~

these two bodies of opposite chemical nature
are not in combination.

4th In cases of abundant deposit of uric acid it would be necessary to ascertain the proportion of urea present with reference to the healthy standard for that patient, and the same information would be required for in cases of deposition of urates.

5th The entire amount of agglutinated matter contained in the urine in case of disease would require attention, seeing that, as Dr. Harley has shewed, a large amount of pro-haematin may be present, and yet the colour of the urine appear to be natural.

6th Dr. Harley considers that the Urea is not produced from any one tissue, such as the muscular, but is the product of the disintegration of all the nitrogenised tissues as also of the oxidation of a portion of the food. The fact that Urea has not been detected in any of the tissues proves nothing.