acid which is formed as the result of metabolism, but of this there is no proof, and indeed there are certain facts against this view. At present the *modus operandi* of what is an undoubted fact is quite unknown.

It is obvious that many other forms of oedema are open to explanation in the same way as that given above. In the oedema of chlorosis it is evident that there is a chronic starvation of the tissues, at all events of oxygen; while the constipation which is usually present may possibly enter in some way into the question. It is also possible, in view of the fact that anæmia is frequently accompanied by a pulse of high tension, as shown, independently, by Archibald Garrod and Dickinson, that a renal element may play a subordinate part.

Cachectic dropsy manifestly depends upon starvation of the tissues. To take three typical examples. Dropsy of the ankles occurs at the end of cases of pulmonary tuberculosis, of malignant disease, and of malaria. In tuberculosis the heart is always small and ill-nourished; in malignant disease the blood supply is largely diverted for the growth of a tissue which is physiologically outside the body; in malaria there is a great destruction of corpuscles. In all these cases, therefore, there is ample explanation for starvation of the tissues, and the effect of starvation has already been considered. Oedema of the lungs is a subject of more uncertainty. The lung tissue obtains its nutriment through the bronchial arteries, which are small in comparison with the area they have to supply. Whether the lungs obtain food from the blood of the pulmonary artery it is impossible to say, though such a source seems improbable. Having regard, however, to the fact that in cardiac disease oedema of the lungs is a sign of cardiac failure as much as is oedema of the ankles, we may provisionally regard oedema of the lungs as the result of a failure in nutrition of the lung tissue. The subject, however, is so fraught with difficulties from an experimental point of view that the solution given must not be regarded as more than a possible one.

(To be continued.)

REMARKS ON THE CHEMICAL PATHOLOGY, SYMPTOMS, AND TREATMENT OF URIC ACID GRAVEL.

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EXPERIMENTAL medicine has during the last two decades been especially turned towards bacteriology, and consequently the important branch of pathology embraced in the word "metabolism" has received but scant attention. In spite of this, as regards the question of uric acid formation so much has been done in this direction that it may be said our views are entirely different from what they were a quarter of a century ago, and we are now able to treat patients suffering from uric acid disease on new scientific instead of old empirical principles.

As it would take up too much time to discuss the entire uric acid diathesis, I will merely call attention to that form known under the name of uric acid sand or gravel, and leave the question of its concretions with gout entirely out of the question.

Our first step in an inquiry into the causation of uric acid gravel is as regards the formation of uric acid in the organism. Until quite recently uric acid was regarded as one of the normal products resulting from the breaking down of proteids in the processes of metabolism. Sir William Roberts regarded it in man as a vestigial feature of some ancestral form. Chemists had succeeded by a process of oxidation and hydration in converting uric acid in the test tube through the transitional stages of alloxan, parabanic acid, oxaluric acid, and oxalic acid into the final products of urea and carbonic acid. Physiologists considered that proteids passed through the stage of uric acid in the animal body before being converted into urea by oxidation. If, then, uric acid is under normal circumstances oxidised in the animal body into urea and carbonic acid, one might expect that in diseases

in which oxidation is hindered there would be an increase in the uric acid eliminated into the urine. Contrary to this expectation, Senator, as early as 1868, failed to find any increase in the uric acid in the urine when the respiratory processes were artificially interfered with, and Naunyn and Reiss equally obtained negative results when tissue oxidation was retarded by venesection. Further, pathology shows us that in simple anæmia there is no increased elimination of uric acid.

Bunge explains the failure of the oxidation theory by calling attention to the fact that in birds in whom respiration is most active the bulk of the nitrogen is eliminated as uric acid. While Frerichs, Wöhler, Zabelin, and others had previously shown that when uric acid was given, either by the mouth or intravenously, it appeared in the urine as urea, and no increase of uric acid could be recognised. Haig has lately pointed out that this is probably due to precipitation of uric acid in the organs, and if it is given while the blood is kept alkaline there is really an increased elimination of uric acid in the urine. It thus follows that, experimentally, we have no evidence that uric acid is converted into urea in the organism.

The researches of Horbaczewski, Kossel, etc., have led to the view that uric acid is not derived from the metabolism of the general proteids which yield urea, but from nuclein derived from the nucleo-albumin of the cells. Horbaczewski showed that when splenic pulp is mixed with blood and kept for some time at the temperature of the body it yields xanthin bases; and that when the same process is carried out in the presence of an abundant supply of oxygen instead of xanthin bases uric acid is formed.

The constituent of the spleen which yielded these xanthin bases was found to be nuclein. Other observers, in addition, found that all the tissues of the body that contain nuclein are in like manner capable of yielding uric acid.

Horbaczewski further showed that feeding animals with nuclein, or injecting it subcutaneously, causes an increase in the elimination of uric acid, not only in animals, but also in man. This last statement has been contradicted by Stadthagen in the case of dogs, in whose urine he says he found, if anything, the amount of uric acid decreased, and, on the other hand, the urea markedly increased.

These contradictory statements have likewise been made, as already stated, as regards the effects of feeding with uric acid, and we must leave them for the present for further investigation.

We can now turn to observations made on man to see if we find this nuclein view of uric acid formation supported.

Marès examined the urine as to the quantity of uric acid excreted from time to time, and found that, after a meal, it rose rapidly, so that in two to five hours it had reached double or even three times what it was during fasting; it then slowly fell for the first thirteen hours after food, and then remained constant until fresh food was taken. He found the rise was greatest after animal less after vegetable diet. Urea, on the other hand, does not begin to be increased in quantity until some time after food, and only reaches its maximum nine or more hours after the meal, and then still more gradually falls. It is known that after a large meal, especially of animal food, a great increase of leucocytes takes place in the blood, and at the time that they are being destroyed and their nuclein liberated it appears that there is this increase in the amount of uric acid eliminated in the urine.

As early as in the year 1868 Bartels showed that in leucocythæmia four times the normal amount of uric acid was eliminated with the urine in twenty-four hours. Schultzen, Ebstein, and others have confirmed the statement that the quantity of uric acid is always markedly increased in this disease.

Fleischer and Penzoldt, on comparing the quantity of uric acid passed by a leucocythæmic patient with that of a healthy patient on the same diet, found that while the first was more than double the amount of uric acid eliminated by the healthy man, the quantity of urea excreted was the same in both cases. This fact of the urea remaining the same shows that the nitrogenous matter taken as proteids in the food was equally eliminated in both cases, while the excess of leucocytes in the blood of the one caused an excessive break-

ing down of them in this case and a proportionate excess of uric acid.

Lately von Jaksch found that in pneumonia, when there is an increase of leucocytes in the blood, there is at the same time an increase in the uric acid present.

Moreover, it has been for some time past known that phosphorus and pilocarpin induce a leucocytosis which is also accompanied with an increase of uric acid in the urine. The same thing again holds good for alcohol; both Chittenden and Cameron found that both in animals and man the taking of alcohol caused an increase in the quantity of uric acid in the urine.

If we have these pathological supports to the nuclein view of the uric acid formation, we find we have an equally good physiological one in the case of children. In early life the number of leucocytes to red blood corpuscles is much greater than in adult life, as shown in the following table:

Table showing Number of Red Blood Corpuscles to Leucocytes at various Ages in Males.

Author.	Age.	White.	Red.	Proportion of White to Red Corpuscles 1=
Dupérié	2 months	8,200	4,433,000	541
" " " " " "	2 years	3,900	4,805,000	1,232
Bouchut and Dubrisay...	2½ to 15	6,704	4,269,000	648
Rieder " " " " " "	11 to 15	9,800	—	—
Dupérié " " " " " "	18	3,900	5,704,000	1,463
" " " " " "	26	6,700	6,138,000	916
Bouchut and Dubrisay...	20 to 30	6,113	4,192,687	700
" " " " " "	30 to 58	—	4,080,113	616
Dupérié " " " " " "	69	4,700	4,898,000	1,042
" " " " " "	78	5,400	4,712,000	873

The quantity of uric acid eliminated daily is also relatively larger than in later life, so that clinical experience supports the view that uric acid is a derivative of nuclein.

THE SEAT OF URIC ACID FORMATION.

As regards the organs or organ in which uric acid is formed, we are still very much in the dark. Schröder, who experimented by either extirpating the kidneys or shutting them off from the circulation in hens, found that the uric acid accumulated in all the organs of the body; and that in snakes which survived the operation for some days, this increase in the quantity of uric acid in the organs was still more marked. It thus appears that both in the case of birds and snakes uric acid cannot be said to be formed only in the kidneys. Clinically, in kidney disease, in which elimination of uric acid has been hindered, an increase in the uric acid of the body has been found to follow, so that in all probability the same holds good for man.

Meissner in 1868 pointed out that normally the quantity of uric acid is always higher in the liver than in the blood of birds.

Minkowski, who succeeded in keeping geese alive from six to twenty hours after extirpation of the liver, found that, while in the normal goose from 60 to 70 per cent. of the total nitrogen is eliminated as uric acid, after the liver is extirpated only from 3 to 6 per cent. is passed as uric acid. On the other hand, the ammonia increases after the hepatic extirpation, so that 50 to 60 per cent. of the total nitrogen is in this form, while in healthy geese only 9 to 18 per cent. of the nitrogen appears as ammonia.

From the results obtained in the above-alluded-to experiments, one is led to look upon the liver as the principal seat of uric acid formation. Indeed they might have been regarded as conclusive had not experiments made conjointly by Hahn, Massen, Nencki, and Pawlow led to opposite conclusions. They shut the livers of dogs almost completely off from the general circulation by diverting the portal circulation into the inferior vena cava, and found that, although the dogs passed less urea (the nitrogen being nearly all eliminated in the form of carbamate of ammonia), the uric acid voided was considerably increased.

From this summary of the recent experimental work on the genesis of uric acid, it appears that, although we have made considerable progress in discovering what are the precursors

of uric acid in metabolism, the actual seat of its formation is a point still unrevealed to us.

THE CAUSE OF URIC ACID PRECIPITATION IN URINE.

It has been shown by Sir William Roberts that the uric acid always exists in the urine in the form of quadriurates. According to him, the first step in the precipitation of uric acid is the breaking up of the quadriurates by the action of water into a biurate, and the setting free of a quantity of uric acid, which from being but slightly soluble is precipitated, while the more soluble biurate remains in solution. The next step is that the biurate is acted upon by the monometallic phosphate and thereby converted into the quadriurate, and the phosphate itself being converted into dimetaltic phosphate— $2\text{MHu} + \text{MH}_2\text{PO}_4 = \text{H}_2\text{u}$, $\text{MHu} + \text{M}_2\text{HPO}_4$. This process is continued either until all the urates are precipitated as free uric acid or alkaline fermentation sets in.

If this view be correct, it follows that in urines which do not precipitate uric acid there must be a something which hinders this breaking up of the quadriurates by the action of the water. This something appears to be the sulphates, chlorides, and phosphates, as well as the colouring matter of the urine; the potassium salts appear to act more powerfully in this way than the sodium or ammonium ones, while a fixed alkali entirely prevents the change taking place.

The acidity of healthy urine is now known to be due not to the presence of free acids, but to the acid salts such as acid phosphate of soda (NaH_2PO_4). This is derived from the blood, and it was supposed the basic sodic phosphate (Na_2HPO_4) was converted into the acid by the uric acid, hippuric acid, sulphuric acid, etc., taking themselves part of the soda, or that acid salts more readily diffused through the kidney.

Neither of these explanations was very satisfactory, and Liebermann has now shown that the kidney substance contains an acid-reacting substance (lecithin-albumin) which is capable of converting an alkaline reacting salt (such as Na_2HPO_4) into an acid one, and that even blood serum, or defibrinated blood, when filtered through a layer of lecithin-albumin, is converted into an acid filtrate. An alkaline solution of Na_2HPO_4 , when artificially circulated through a freshly extirpated dog's kidney, yields an acid urine. In the normal formation of urine the bases which combined with the acid lecithin-albumin are in their turn broken down by the carbonic acid formed in the tissues, so as again to set free the acid lecithin-albumin for renewed action. If this view is correct, under ordinary circumstances, a sufficient quantity of alkaline (Na_2HPO_4) salts being present in the blood, the renal cells do not break up the soluble urates in their passage into the urine. When, however, this equilibrium is upset by a diminution of the alkaline salts, the soluble urates being in normal quantity, the renal cells will set free uric acid, which will be precipitated in the urinary tubules; or, if the urates are in excess, the alkaline salts may fail to be in sufficient quantity to keep the urates in a soluble form.

Liebermann found if a saturated solution of uric acid in Na_2HPO_4 be divided into two parts, and one of them diluted with water and the other with Na_2HPO_4 , when they are passed over lecithin-albumin, the latter contains the most uric acid, from less of it having been retained—that is, precipitated. An excess of lecithin-albumin in the kidney, it is thus seen, would lead to an acid urine being excreted; and it looks as if the alkaline urine of herbivora is due to the amount of lecithin-albumin in the kidneys not being sufficient to break up the alkaline salts of their diet.

THE CAUSE OF URIC ACID GRAVEL.

Having discussed the chemistry and physiology of uric acid, it behoves me now to turn to the pathology of the state we know as uric acid gravel.

Under the head of uric acid gravel we place that diseased condition in which uric acid is precipitated in the urine either in the tubules of the kidney, urinary tract, or in the urine immediately after being passed. We have already seen that uric acid under normal conditions is kept in solution in the urine by certain means, and, further, the quantity found in the animal body depends upon certain definite circum-

stances. The appearance of a precipitate of uric acid can arise from two causes:

First, an excessive formation of uric acid whereby the solvent power of the urine is insufficient to keep the increased quantity in solution.

Secondly, a diminution in the quantity of the natural solvents for uric acid in the urine, which leads to its precipitation, although the total quantity may be normal or even less than the normal standard.

As regards the first cause we know that hereditary predisposition plays an equally important part in uric acid gravel deposits as it does in gout. The hereditary cases in which there is a total daily increase of uric acid may be put down, according to our present knowledge of the matter, to some more or less marked form of leucocytosis. In children, in whom uric acid gravel is common, new cells are both rapidly built up and rapidly broken down, and in them the leucocytes of the blood are in a greater proportion than in adults, as has been previously stated.

In the next place, the kind of diet is supposed to have an important influence on uric acid gravel, animal proteids seemingly increasing it more than vegetable. As regards the daily quantity of uric acid passed, A. Herman found on a vegetable diet 0.478 grammes, on a mixed diet from 0.636 to 0.674 grammes, and on an animal diet as much as 0.981 grammes. Marès obtained equally strong results favouring the supposition that animal proteids lead to a larger formation of uric acid than vegetable proteids do. Alcohol, also as already stated, increases the quantity of uric acid formed. The taking of large quantities of water was found by Schöndorff and others to have no influence on the quantity of uric acid eliminated. The former found the following tabulated results in an experiment extending over a month:

Diet.	Uric Acid per Diem.	Total Nitrogen per Diem.
	Grammes.	Grammes.
Ordinary diet	1.184	18.5
" " + 2,000 c.cm. H ₂ O...	0.931	20.4
" " + 4,000 c.cm. H ₂ O...	1.016	20.6
" " + 1,000 c.cm. H ₂ O...	1.143	23.8

Muscular exercise has also an effect on the daily amount of uric acid excreted. Levison found—that in his case being subject to uric acid gravel—horse riding increased the uric acid output in one experiment from 0.6 grammes to 0.981 and 0.955 grammes, and in another to 1.089 grammes. Excessive muscular exercise tends to a leucocytosis, so would explain the increased uric acid elimination. The exercise may not be excessive in the ordinary sense of the word, but horse riding in one not accustomed to it would be classed under the same head.

If we turn to the second cause of uric acid gravel, we find heredity here also probably plays an important part. It has been by many observers noticed that urines that tend to deposit uric acid are often very pale. I have frequently found these pale urines depositing uric acid, although the total quantity is not increased, are to be especially met with in people suffering from the condition we now recognise under the head of neurasthenia, and this is, as you all know, often hereditary.

Diet alone also plays an important part in this form of uric acid precipitate when no excess of uric acid occurs. The mere taking of food poor in salines increases the tendency to gravel, and that even when the daily quantity of uric acid excreted is very small, as, for example, when an almost starving amount of food is being taken. Sir W. Roberts pointed out that uric acid concretions are common among Hindus, who live almost exclusively on rice, a food poor in salines. Hutchinson showed that uric acid gravel is rare among sailors, who eat salt meat and consequently take in a superabundance of salines, while naval officers, who live much the same life but take fresh meat, are by no means immune. Muscular exercise, when carried to excess, has also a tendency to increase the acidity of the urine, and hence the deposit of uric acid by this means.

SYMPTOMS AND DIAGNOSIS OF URIC ACID GRAVEL.

The principal factor in this condition is naturally the presence of free uric acid crystals in the urine either before or immediately after being passed. The recognition of these crystals is often somewhat difficult from a specimen of the day's urine being examined. It is as well always to remember the urine is most acid after a long fast, such as takes place during the night, and therefore one ought to examine an early-morning specimen.

In cases where the precipitation of uric acid takes place in the urinary tubules it irritates their epithelial lining and hence causes the formation of hyaline casts. In some cases the irritation is to such an extent as to cause albumin or even blood to appear in the urine.

Ultymann and Leube say that the so-called periodical albuminuria is often due to uric acid sand.

I think all observers who have employed the centrifuge in the separation of the urinary deposit are agreed that hyaline casts are a common accompaniment of uric acid crystals. I have frequently met with them as well as occasionally cases in which uric acid crystals were embedded in granular casts. These uric acid casts are best found in urine passed in the early morning and centrifuged while fresh. *Débris* of epithelial cells are nearly always found when the centrifuge is employed, and in some cases the deposit reveals the existence of a pyelitis.

In cases belonging to the second group, in which the uric acid is not in excess, the urine is nearly always very acid, and generally much paler than normal urine. In fact it is what one would call a very watery urine.

A good rough test to recognise a tendency to uric acid deposit, even when no precipitate occurs, is to pour very slowly into a test tube nitric acid so that a layer forms. The urine thus treated, if it shows a cloudy ring above the junction of the two liquids before it has stood five minutes has a tendency to deposit uric acid; if between five and ten minutes it is normal; while when it takes longer than ten minutes either the total quantity of uric acid is below normal or it contains more than the usual amount of solvents. This uric acid ring lies above the ring formed when albumin is present, so in such cases one gets two rings.

The symptoms of uric acid gravel vary from being most marked and pointing definitely to the urinary tract to very doubtful ones. I only intend here to mention those symptoms which arise from the presence of uric acid crystals in the urine, and not those due to its excess or otherwise in the blood. In a typical attack lumbago-like pain in the kidney region extends down in front, along the course of the ureters, into the groin, accompanied by pain in and retraction of the testicles (in women pain in the ovary). This pain is accompanied by a frequent desire to pass water. There is inability to stretch down the legs, and the necessity of keeping them in a flexed position, with the feet towards the scrotum, and the knees thrown outwards. Great relief is here obtained by putting a pillow under the knee and bending the leg over it.

When gravel is impacted in a ureter pain may be intense, and the tenderness on pressure apt to be mistaken for peritonitis. The tenderness does not radiate so much over the abdomen. Vomiting frequently occurs, and when pain is very acute one may even have delirium. These symptoms are so closely allied to those of renal calculus, and as I am now only dealing with the smaller forms of uric acid gravel, I will now turn to the more indefinite ones.

In slight cases the lumbar pain may be expressed by the patient as merely a "tender feeling" over the loins, or it may be a heavy, dull pain which ceases on going to bed, to return on rising in the morning. This pain may diminish somewhat during the day, but never entirely goes away. It is aggravated each time the patient assumes a new position, and is often on that account mistaken for a lumbago.

The pain may radiate from the back in various directions, either towards the stomach or the shoulders, and even occasionally, according to Levison, down the arms. I oftener find it in the legs, and have had it described to me as a sciatica, which it can as a rule be distinguished from by the course it takes being more towards the front than the back of the thigh.

Various forms of neuralgia—as, for example, migraine, angina, asthma, etc.—are said by Da Costa to accompany uric acid gravel. Irregular action of the heart is a frequent accompaniment of the passing of gravel. Levison says constipation is a common occurrence; but this as a rule is, I think, due to some other cause than mere gravel. Frequent micturition is an accompaniment of even the mildest forms of uric acid gravel, and can be explained by reflex irritation.

In children, in mild cases the presence of uric acid sand is often overlooked on account of the child never complaining of any actual pain. Such cases only are recognised by examination of the urine on account of the child suffering from a frequent desire to micturate, which may be attended with sudden fruitless desires to go to stool, and a general restless nature. An ordinary examination of the urine often fails to discover anything abnormal about it. If, however, a fresh specimen of the morning urine is examined by means of the centrifuge, crystals are recognised and the case easily diagnosed.

In more severe cases, as pointed out by Sutherland, Goodhart, etc., the symptoms are more marked. Pain commonly occurs, which is as a rule not referred to the kidneys but to the umbilical or iliac region. The children are restless and active, sleep badly, and often talk while asleep. Besides the presence of uric acid crystals in the urine, albumin is often intermittently present, and tube casts, when properly looked for, are usually found. Frequent desire to micturate and the desire to go to stool also accompany these cases.

TREATMENT.

The treatment of uric acid gravel takes two directions, according as we desire to increase the solubility or decrease the amount of uric acid formed. It is well to remember that in the majority of cases uric acid deposits are due to an increased tendency to precipitation, and not to excessive formation of uric acid.

In cases due to an increased tendency to precipitation, we have to give drugs which help to hold uric acid in solution. In spite of the recent outcry against piperazin, I must say I have found it of great service, particularly in all cases in which gravel has been due to diminished solvents and not excessive formation of uric acid. In fact it appears to me to have no action whatsoever on the quantity of uric acid daily formed in the organism, but merely on its solubility. On this account I always give it in such cases in combination with alkalies either in the shape of alkaline waters, or potash bicarbonate combined with iodides. It is as well to remember that as the urine is naturally most acid at night and early morning, and therefore most likely to deposit uric acid, we can get over this by following Sir William Roberts's advice, and give the alkalies at bedtime. The diet in these cases is not of so much importance except in favour of salines and vegetables.

In cases, again, when the uric acid deposit is due to excessive formation, a carbohydrate diet is the most useful. Starch, sugar, and vegetables should, therefore, be the staple diet, and meat and fish only in small amounts. The old idea that sugar causes an increase of uric acid has no foundation, as I found in a series of experiments performed on myself when I took as much as a quarter or even a pound of sugar a day without causing any noticeable increase in the uric acid passed. Alcohol, on the other hand, should be prohibited, as it causes an increase in the quantity of uric acid voided.

Quinine and arsenic decrease the quantity of uric acid because they diminish the quantity of leucocytes, and therefore in cases where gravel is due to an excessive formation of uric acid they are most valuable. While moderate muscular exercise is of service, excessive exercise is, on the other hand, harmful.

In cases of excessive formation, although alkalies are of some assistance, they, like piperazin, are only of secondary importance by increasing the solubility of the uric acid formed.

The subject of treatment could well be gone into much more fully, but I think I have said sufficient to indicate the general principles on which it should be conducted.

IN WHAT WAY DO DIET AND DRUGS WHICH CLEAR THE BLOOD OF URIC ACID AFFECT THE ARTHRITIS IT PRODUCES?

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It appears to have been concluded by some of those who have read my previous writings that drugs which clear the blood of uric acid, and may under certain circumstances produce arthritis in doing so, must of necessity produce arthritis under all circumstances whenever administered. And so I have been asked to explain how it is that iodides and other drugs which I have shown clear the blood of uric acid are nevertheless useful in uric acid arthritis.

A similar question has also been recently raised in the *Medical Record*, January 26th, 1895, p. 113, with regard to the effects of meat diet in arthritis in connection with my paper on the direct introduction of uric acid in the *BRITISH MEDICAL JOURNAL* of December, 1894; and it is there evidently concluded that as meat diet introduces a lot of uric acid into the body, it must of necessity produce arthritis, and cannot possibly cure or prevent it.

I believe that a very brief consideration of the actual causation of arthritis by uric acid will suffice to show that these difficulties and apparent contradictions are without any foundation in fact.

I have often produced arthritis in myself working under conditions where, all the factors being recorded day after day, I could see every move in the process; I have unintentionally done the same in others, and have seen it done very often indeed by others. The patient is of course said to have had a relapse; but look at the list of drugs used, and note their effects on the solubility and excretion of uric acid, and you will often have no difficulty in saying why the relapse occurred.¹

From such experience I see that if I was going to produce an arthritis—and I have complete confidence that I can do so at pleasure—I must bring about two things: (1) A considerable excess of uric acid in the blood, in solution probably with some salt of potash or soda; (2) the sudden supervention on (1) of some condition unfavourable to the solubility of uric acid in the blood so as to precipitate it on the joints. Unless (2) duly supervenes on (1) no arthritis results; and either excess of uric acid in the blood, or its absence from the blood, may occur alone without any arthritis.

Now as to mineral waters containing sulphates, it is, I believe, well known that their first effect is often to precipitate an attack of gout², that is to say, the patient comes to the Spa with (1) and the water taken produces (2), and the result is a more or less severe attack of arthritis according to the amount of uric acid present, and the rapidity with which it is driven into the joints. But when this attack has passed over, absence of urates from the blood continues, the sulphate water being continued; and there is no further arthritis as (1) is now absent, and the gout is said to be cured. With (2), and as its result, there is a general stimulation of nutrition and metabolism throughout the body³, and the blood is kept clear of urates for a considerable time, perhaps till the following spring or summer; but then, if not sooner, a repetition of the water is required, and the same sequence of events is repeated.

I believe, further, that a considerable number of drugs, or combinations of drugs, which I have no space to mention, owe their reputation for the cure of gout and rheumatism to their power of keeping the blood clear of uric acid. Now, it follows from what I have just said about drugs, and have previously said about diet, and am quoted as saying in the *Medical Record*, January 26th, 1895, p. 113, that meat diet, if it is well taken, well digested, and if the patient is young

¹ Excretion of Uric Acid in a Case of Gout, *St. Bartholomew's Hospital Reports*, vol. xxiv, p. 217; and *Uric Acid*, 2nd edition, pp. 84, 160, 292, and 315.

² I believe that physicians at these Spas tell their patients that the attack is a sign that the water is going to do good, and so it is. See also *Uric Acid*, pp. 31 and 292.

³ *Uric Acid*, 2nd edition, Ch. iv.