trousers of the same material. He told us he always made them himself. They were washed every week; some of them were actually hanging on a line in the room to dry. From Blareau's we went to the house of M. Paniels in the Rue Croix-Blanche. Neither the master nor his wife were at home, but a young daughter showed us into a dwelling room, the window of which served to display several sweet stuffs—for a little shop of these things was kept by them. Everything was very clean. She showed us a blouse with hood attached, and said her father wore two of them every week; he also wore leggings; and she showed us what we had not previously seen—a piece of clean stuff which her father and all other sweeps there wear over the lower part of the face when they sweep. She demonstrated the manner of wearing the cloth so as to cover the mouth and nose of the wearer. The machines used by the Belgian sweeps are a brush similar to that used in this country, but with a weight in the middle, a broom, a cord, sack, and shovel. In the Brussels Directory there were the names and addresses of twenty-four *ramoneurs-jurés*. We found that it was possible to employ other sweeps than these men; but if a fire occurred in the chimney of a house the last receipt of the *ramoneur* was required, and only that of a *ramoneur-juré* was recognised. In some towns a holly-bush is used for the cleansing of the flues from soot, as it was formerly used in this country.

Of the habits of the sweeps, so far as personal cleanliness is concerned, I believe I am correct in saying that the general custom is to wash down to the waist daily, and to wash the whole body from head to foot once, or at the most twice, a week.

As I was unable to go myself, I sent to the north of Germany during September of last year, and the information obtained was most satisfactory. Hanover, Hamburg, Kiel, and Göttingen were visited. In the first two towns hard coal is generally burned not only in the factories, but for the heating of dwellings; it is brought there from Westphalia, Belgium, and England. In the last two a great deal of stone coal is also burned, but in addition peat and wood. Stoves are used in the dwelling houses of all these towns, and there are few open grates. But the kitchen chimneys are often climbed by the men.

In Hanover a master sweep, Herr Fricke, was visited. He lived on the third floor of a tall house in a small street. The living-rooms were exceedingly clean. The journeymen washed after their work was over in a small room, where there were three or four wooden tubs. They stood in the tubs, and washed with warm water, soap, and even soda, from head to foot every day. The clothes in which they swept consisted of a coat and trousers made of a stout kind of cloth, to which they give the name of "English leather." During sweeping the feet are naked, the trousers fit not very closely, and are not tied around the ankles. They button down the front, and are fastened at the waist by a strong leather belt, and the knees are protected by stout leather patches. The coat also buttons down the front. It fits pretty closely at the neck, and the sleeves, which fit close at the wrists, are made to fit still closer by tying them with tape. The bottom of the short coat is tucked inside the trousers, so that the trouser-belt knits it close around the body. A small skull-cap of coarse linen is worn on the head, and over this a hood, which covers the head, neck and chin, and is fastened closely round the neck; and, during sweeping, the mouth and nose are covered with a cloth after the manner of the Belgian sweeps. The clothes are made in the house, and the suit which I have here was made for my messenger by Herr Fricke's people.

The same make and arrangement of clothes was used in the other towns which were visited, and the same material was employed; and in every house the same excellent arrangements for daily washing in large wooden tubs in a special room were observed. It appeared to be the custom for the journeymen to sleep in the house of the master sweep. In the house of Herr Puschmann, in Göttingen, my messenger was shown the bedroom of one of the journeymen, which opened out of the bathroom. The bed was made, and the sheets and pillow were quite white and clean.

The clothes are only washed from time to time, perhaps not more than once in many weeks. The nature of the material is not favourable to frequent washings. But it was found that the coarse shirt which was worn beneath the

jacket was washed every day by some of the men after they had washed themselves.

The dwelling rooms were exceedingly clean in all the houses which were entered, and the furniture was in some of them even handsome, while the master sweeps were a very superior class of men. Herr Puschmann's daughter had been governess in an Irish family for some time. There was not one of them who had ever heard tell of a case of cancer in a sweep. Herr Schikorrer, of Kiel, believed they were among the most healthy of the population because they washed so much more than men in other trades.

The protection afforded by means of clothing and washing was displayed in a manner and to an extent I had not conceived. In the first lecture I told how the supposed decline of chimney-sweeps' cancer has been attributed by some persons—I might almost say by many persons—to the fact that "climbing boys" have not been permitted in this country since the year 1840 or thereabout. It was not that the boys themselves were liable to cancer of the scrotum, but it was suggested, with some show of reason, that the exposure of the scrotum to the daily contact of soot from childhood upwards, beginning when the skin is soft and tender, rendered the sweeps much more liable to the disease than they would otherwise have been; and this belief received support from the fact that warts occurred on the scrotum of some of the boys who were employed in "climbing." To my surprise I discovered that climbing boys are largely employed on the Continent. In the north of Germany boys of 14 years, and sometimes younger, are employed, and in Belgium, perhaps more than in any country in Europe, the employment of climbing boys is of daily occurrence. In Brussels and Antwerp we saw several of these boys, black with soot and dressed like the men. At Mechlin a boy, 7 years old, was seen standing with his mother at the door of the sweep's house. The woman said he was employed in climbing chimneys but, as he was rather delicate, and had a cough, the doctor had advised her not to permit him to "climb," any longer. At one house we were told that the boys began at the age of 4 years to "climb." And the chimney-sweeps' signs in the Belgian towns usually present three figures of sweeps in their working clothes, carrying their implements. Foremost stands a man, next follows a boy of about 15 years of age, and last comes a tiny boy.

THE CROONIAN LECTURES ON THE CHEMISTRY AND THERAPEUTICS OF URIC ACID GRAVEL AND GOUT.

Delivered before the Royal College of Physicians of London.

By SIR WILLIAM ROBERTS, M.D., F.R.S.

LECTURE III.—CHEMISTRY OF URATIC PRECIPITATION IN GOUT.

THE chemistry of gout in its full extension embraces changes of the most diverse character in the blood and tissues. I do not propose to deal with the subject in this comprehensive sense, but to confine myself entirely to the relations of gout with uric acid. By far the most characteristic feature of gout is the formation of chalk-like deposits in certain parts and tissues of the body, especially in and about the joints. The essential component of these deposits is the biurate of sodium, and it is always present in the crystalline condition. The crystals are distributed through the implicated tissue in the form of delicate needles, aggregated into tufts, bundles, and stars. The arthritic incidents of gout may be said, not improperly, to be simply incidents pertaining to the precipitation of these crystals in the structures of the joints. Without the occurrence of this precipitation the gouty paroxysm could not take place, nor could the more chronic changes in the joints, with their train of attendant symptoms, follow after. Were it possible for us to keep the sodium biurate in a state of solution in the bodily fluids, the clinical portraiture of gout would be completely transfigured. Whatever other manifestations of the gouty constitution we might have

to deal with, we should not have to contend with this most grievous outcome of the diathesis. The evidence brought forward by Sir Alfred Garrod on this point appears to me to be conclusive, and justifies the deduction that the deposition of the crystalline biurates is not merely a concomitant, but is the actual cause of the joint troubles of gout.

Hence it is that the history and chemical properties of sodium biurate have acquired a capital importance in the pathology of gout. We are interested to know how this compound arises in the body from nascent uric acid, what are its relations of solubility in diverse media, and more particularly in the blood and lymph and synovia, what are the factors which tend to determine its precipitation in the body, or tend to prevent its precipitation.

I have before adduced evidence to show that the normal or physiological condition of uric acid in the body is that of a quadriurate, and that any departure from this condition must be regarded as pathological. In the last lecture I traced the changes which the quadriurate undergoes in the urine, and which lead up to the separation of uric acid in the free state as gravel and urinary sediments. In the present lecture I shall endeavour to trace the converse changes which the quadriurate undergoes in the blood and lymph, and which lead up to the formation and deposition of sodium biurate in the tissues.

I propose, first, to examine the solubility of the material of gouty concretions, namely, sodium biurate in various media, in the serum of the blood, in synovia, and in diverse saline solutions, then to examine and compare the behaviour of free or combined uric acid with the same media. Upon the basis of the results thus obtained I shall be able to formulate a general theory of uratic precipitation.

SOLUBILITY OF SODIUM BIURATE IN DIVERSE MEDIA: (a) IN WATER. (b) IN BLOOD SERUM AND KINDRED MEDIA, (c) IN VARIOUS SALINE SOLUTIONS.

(a) *Solubility of Sodium Biurate in Water.*—When sodium biurate is digested at blood heat with pure water, it enters pretty freely into solution. Careful experiments indicated that the solubility of sodium biurate in distilled water, at 100° F., approximated very closely to the proportion of 1 part in 1000. This was taken as the standard of comparison in estimating the solubility of this compound in all other media.

(b) *Solubility of Sodium Biurate in Blood Serum.*—Sodium biurate is very sparingly soluble in the serum of the blood, as is shown by the following experiments: Sodium biurate in excess was treated with blood serum of the horse and pig in corked phials. The phials were placed in the warm chamber and frequently agitated. After a digestion of twelve hours the supernatant serum was filtered twice through a threefold filter.¹ The filtrate thus obtained when acidulated with acetic acid gave not the slightest precipitation of uric acid. Nevertheless some slight solution had taken place. For when a portion of the filtrate was evaporated on a watch glass in the warm chamber to near dryness, needles of biurate could be readily detected in it under the microscope; or when the filtrate was tested with Garrod's thread experiment, crystals of uric acid were always found sprinkled on the thread. It thus appears that sodium biurate, although very sparingly soluble, is not altogether insoluble in blood serum. From a number of comparative experiments I estimated that at blood heat the amount dissolved was probably about 1 part in 10,000.

The behaviour of sodium biurate with synovia corresponded exactly with its behaviour with blood serum; only minute traces went into solution. It was ascertained by direct experiment that the behaviour of uric acid and its compounds with blood serum depended entirely on the saline ingredients contained in it, and had no reference to its albuminous constituents. When the serum was deprived of its salts by dialysis, it was found that it reacted with uric acid and the urates like simple water, and the same rule holds good, no doubt, with regard to all the bodily fluids. An examination of the saline components of these fluids is, therefore, of prime importance in the study of the chemistry of gout.

¹ The needles of sodium biurate are so minute and delicate that some of them pass through the filter unless the most stringent precautions are taken.

The serum of the blood, and its derivatives, lymph and synovia, although differing considerably from each other in their albuminous elements, are almost identical in regard to both the quantity and the quality of their saline constituents. These latter are remarkable for the immense preponderance of sodium salts. The subjoined table exhibits the average proportion of the several saline ingredients contained in blood serum.

TABLE XI.—Showing the Percentages of the Several Salts in Blood Serum.

Sodium chloride	... 0.50 per cent.	} Sodium salts=0.73 per cent.
Sodium bicarbonate	... 0.20 "	
Sodium phosphate	... 0.03 "	
Potassium salts	... 0.06 "	} All other salts=0.11 per cent.
Calcium salts	... 0.05 "	
Magnesium salts	... 0.05 "	

The fact just mentioned—namely, that the reactions of uric acid and the urates with the bodily fluids depend exclusively on the saline ingredients contained in them, suggested the idea that advantage might be taken of this circumstance to facilitate the chemical study of gouty precipitation. If a solution in water of the salines of blood serum were prepared, such a solution might be expected to behave with uric acid and the urates like the serum itself, and this proved on trial to be the case. An examination of the above table shows that the salts of sodium exceed the aggregate of all the other salts of blood serum in the proportion of seven to one. And practically, for the purpose in view, the saline basis of blood serum might be considered as consisting essentially of sodium chloride and sodium carbonate, so greatly do these preponderate over the sum of all the other salts put together. From these particulars it may be deduced that a solution in water containing chloride and bicarbonate of sodium in the proportion specified in the table would be a fairly exact representation of blood serum, in so far as its saline ingredients are concerned. And it was found experimentally that such a solution reacted with uric acid and the urates in the same manner as blood serum itself, and in the same manner as a solution comprising all the salines of the serum in their due proportions, as ascertained by the best analyses. Accordingly a solution was prepared in conformity with these indications, and was designated as the standard solvent or standard solution. Its composition was as follows:

TABLE XII.—Showing the Composition of the Standard Solvent.

Sodium chloride	... 0.5 grammes
Sodium bicarbonate	... 0.2 grammes
Distilled water	... 100 cubic centimetres.

This solution was much used in the present research, especially as a pioneer. For experimental purposes it possessed certain advantages over serum and synovia. Its composition could be more easily modified by additions or subtractions from it—the quantities of uric acid and urates taken up by it could be more exactly estimated, and its limpidity permitted the first signs of precipitation to be more readily detected. The behaviour of uric acid and the urates with this solvent was studied in detail, under varying conditions of temperature and time, and with varying modifications of its composition. The results thus obtained were afterwards collated with those obtained with blood serum in similar circumstances, and with parallel modifications of its composition.

The standard solvent was found to behave with sodium biurate in exactly the same way as blood serum. Only the minutest traces of the biurate were taken up by it at 100° F. Such a solution, when carefully filtered, gave no precipitate of uric acid when treated with hydrochloric acid.

(c) *Solubility of Sodium Biurate in Saline Solutions.*—The influence of different saline substances on the solubility of sodium biurate has not only a pathological, but also a therapeutical bearing. Saline substances are largely used in the treatment of gout, both in the guise of pharmaceutical preparations and as constituents of mineral springs, under the belief that they promote the holding in solution of the peccant biurate, and thereby hinder its deposition as gouty concretions, and even favour the resolution of concretions already formed. It is, therefore, of practical interest for us to know what kinds of salts, if any, act favourably, and what kinds act unfavourably in this respect. A large series of experi-

Behaviour of Uric Acid with Blood Serum and the Standard Solvent.—When uric acid is digested at the temperature of the

body with blood serum or with the standard solvent it passes into solution in combination with a base. In the course of an hour, with due agitation, the liquids will, on analysis, be found to have taken up uric acid in the proportion of about 1 part in 500. The chemical and solvent power of these media on uric acid depends on the sodium carbonate contained in them, and not on the sodium chloride, for a solution of the latter salt alone has no more action on uric acid than pure water. On the other hand, a solution containing sodium bicarbonate alone has precisely the same action on uric acid as when it is associated, as in the serum and standard solvent, with sodium chloride. The question now arose, what is the combination in which uric acid enters into solution? It could not be biurate, because sodium biurate is almost insoluble in these media; nor could it be neutral urate, because the neutral urates cannot arise in the presence of carbonates. The presumption remained that the combination was a quadriurate. It was, however, highly desirable to have direct proof that such was the case. This was obtained by taking advantage of the great difference of solubility of quadriurates at different temperatures. The following experiment appears to be conclusive on this point: Uric acid in excess was digested at blood heat with a 1 per cent. solution of sodium bicarbonate, under constant agitation, for twenty minutes. The filtered product was rapidly cooled on ice. It threw down a copious amorphous deposit, which, when duly washed on the filter with rectified spirit, to free it from adherent carbonate, gave the characteristic reaction of quadriurate, that is to say, it was decomposed by water with abundant emission of uric acid crystals. A corresponding experiment with a 0.5 per cent. solution of potassium bicarbonate yielded exactly the same results.²

We may, therefore, conclude with certainty that when uric acid comes into contact with blood serum or the standard solvent it enters into solution in the first instance as a quadriurate. But the process does not stop here. The quadriurate gradually takes up an additional atom of base, and is thereby converted into biurate, and the biurate thus formed is, after some delay, eventually precipitated in the crystalline form.

In order to bring this remarkable succession of events more vividly before your minds I will relate the particulars of two actual experiments.

EXPERIMENT I.—Uric acid in excess was digested, with frequent agitation, in the standard solvent, at 100° F. for twenty minutes. The excess of uric acid was then filtered off, and the clear solution was placed in a corked phial in the warm chamber. It remained unaltered for two days. On the third day it began to precipitate, and on the fourth day a copious deposition of crystalline biurate took place. On the fifth day the process was completed, and the supernatant liquor was found on acidulation to contain only traces of uric acid.

EXPERIMENT II.—Blood serum of the horse was digested at 100° F. with excess of uric acid for fifteen minutes, with constant agitation. It was then filtered and placed in a corked phial in the warm chamber. In about twelve hours the serum, previously clear, began to lose transparency, and fine needles of biurate were detected in it with the microscope. On the next day copious precipitation took place. On the fourth day the process seemed to be completed, and the supernatant serum was found to be almost free from uric acid.

It was impossible not to be struck with a certain rough resemblance between the results observed in these experiments and the phenomena of the gouty paroxysm. In the gouty subject it is assumed that the blood becomes more and more impregnated with uric acid until, after a certain period of incubation has been accomplished, sudden precipitation of sodium biurate takes place in and about the joints, and the "fit of the gout" is declared. Then follows a process of recovery, with restoration of the blood to a purer state, that is, with a lessened impregnation of uric acid. In the artificial counterfeit we observe a similar succession of events: first, impregnation of the medium with sodium quadriurate; secondly, a period of incubation or maturation, during which the quadriurate passes into biurate; thirdly, somewhat sudden precipitation of sodium biurate in the crystalline form; and lastly, restoration of the medium to comparative purity.

Behaviour of Uric Acid with Synovia.—It is a marked peculiarity of the uratic phenomena of gout, that the deposits occur most commonly in and about the joints; and it was a matter of interest in the present inquiry to ascertain how

synovia behaved when impregnated with uric acid; and especially whether synovia, as compared with blood serum and when impregnated to an equal degree, had the property of retarding or hastening the precipitation of biurate. This part of the investigation is hampered by the difficulty of obtaining an adequate supply of materials, and my information thereupon is scanty. I have so far only been able to make satisfactory experiments with synovial fluid drawn from the hip of the ox. From this source about a couple of ounces may be obtained from the two joints. Butchers tell me that the synovia from the hip is thinner as well as more abundant than that obtained from the other joints.

On two occasions I was able to examine and compare the synovial fluid of the hip-joint with the blood serum of the same ox. The behaviour of the two fluids with uric acid was substantially the same, but in both instances I found that, when impregnated with uric acid in an equal degree, precipitation of biurate began distinctly a little earlier in the synovia than in the serum. And my impression is, but it is only an impression, that with the thicker and more concentrated synovia of the smaller joints this difference would be more pronounced. Whether there is in this distinction between serum and synovia a key to the preference of uratic deposition for the joints is a question well worthy of further inquiry. It is at any rate conceivable, supposing the blood and its derivative fluids to be equally impregnated with uric acid, and supposing the synovial fluids to be more largely charged than their congeners with salts, and especially with sodium salts, that precipitation of biurate would take place earlier and by preference in and about the joints than elsewhere. This point will be again touched on in my next lecture when I come to speak of the topographical distribution of uratic deposits.

GELATINOUS OR HYDRATED MODIFICATIONS OF THE URATES.

There is a point of considerable interest in connection with the chemistry of the urates which may be conveniently considered in this place, and that is the occurrence of gelatinous modifications of these compounds, which differ both in physical condition and in solubility from the more common granular and crystalline forms.

The existence of these gelatinous modifications was first noted by Dr. Ord in the course of his well-known researches on the influence of colloids upon crystalline form and cohesion.³ He observed that when hot saturated solutions of the urates of soda or ammonia were mixed with an equal bulk of strong solutions of the alkaline chlorides or phosphates, the urates were thrown down on cooling in a gelatinous state. Dr. Ord further observed that this condition was not a permanent one, and that the gelatinous matter, after a time, changed into a mass of crystals. The interest for us, in our present inquiry, of these observations lies in the probability that these gelatinous modifications of the urates intervene, perhaps importantly, in the succession of changes which lead up to the formation of uratic deposits in gout. I must, therefore, ask your attention to some additional particulars which I have gathered on this subject.

Crystalline sodium biurate is very much more soluble in hot water than in cold water. Nevertheless such a hot solution, fully saturated, does not deposit its surplus biurate on becoming cold; it continues perfectly clear, and remains so. But if the solution be evaporated down on the hot water bath, the biurate is again recovered in the crystalline form. It is obvious, therefore, that the biurate in passing into hot solution undergoes some notable change, whereby its solubility is greatly enhanced. This change consists in the assumption of the gelatinous modification, and herein lies the explanation of the enhanced solubility. These deductions are substantiated by the following experiment: Crystalline sodium biurate is dissolved to saturation in hot water. The filtered solution, when cold, is mixed with an equal volume of a 20 per cent. solution of common salt. A voluminous jelly-like precipitate is thrown down.⁴ This is caught on a filter and allowed to drain, and then cautiously washed on the filter with cold

² Solutions of the common (dimetallic) phosphates of soda and potash, and of the alkaline acetates, also take up uric acid very freely at blood heat, and the combination formed in these cases in the first instance is likewise a quadriurate, as may be shown by the above-described method of cooling on ice.

³ *On the Influence of Colloids upon Crystalline Form and Cohesion*, by W. M. Ord. London, 1879. Pp. 72, et seq.

⁴ The gelatinous biurates may be thrown out of their solutions in several ways. Instead of common salt, a concentrated solution of the phosphate, chloride or acetate of sodium potassium or ammonium may be used, or any of these salts in crystals may be added to saturation to the solution.

water. The gelatinous biurate is thus obtained in a condition of approximate purity. Now when this substance is digested at 100° F. with blood serum, or with the standard solvent, it goes freely into solution—so freely that when the filtered product is treated with acetic acid it throws down, on standing, a considerable deposit of uric acid. But it has before been shown that these same media, when digested under similar conditions with the crystalline sodium biurate, take it up so sparingly that the filtered products do not yield any deposit of uric acid when acidulated.

Dr. Ord noticed, as above stated, that the gelatinous biurate collected as a mass on a filter passes after a time into the crystalline condition. The same transformation occurs when the gelatinous matter is held in solution in blood serum or the standard solvent. Such solutions when set aside continue clear and unchanged for a certain time, but after the lapse of a day or two the biurate is reprecipitated in the crystalline form. The obvious explanation is this. The dissolved gelatinous modification reverts by slow degrees to the anhydrous crystalline condition, and the biurate in this condition is, as we know, almost insoluble in these media. Consequently, when the transformation reaches a certain point, the biurate is necessarily precipitated.

As to the nature of the gelatinous modifications of the urates, Dr. Ord is inclined to regard them as true colloids, and he remarks on their resemblance to the colloidal modification of silica. Their jellylike appearance is certainly strongly suggestive of this idea, but they differ radically from true colloids in passing with ease, and unchanged, through the dialyser. Their real nature is, I believe, that of hydrated salts. The crystalline biurates are anhydrous; the gelatinous modifications are highly hydrated. It is well known that certain salts can be obtained in several degrees of hydration, and that these several hydrations possess diverse degrees of solubility.

The quadriurates likewise readily assume the gelatinous modification. Sodium quadriurate may be obtained in the gelatinous state in the following manner. A 5 per cent. solution of the common phosphate of soda is heated to boiling with excess of uric acid. The mixture is filtered hot. On cooling the filtrate sets into a jelly. The gelatinous substance thus obtained, pressed between blotting paper to deprive it of its mother liquor, possesses the characteristic reaction of a quadriurate—that is to say, it is rapidly decomposed by water with copious emission of uric acid crystals.

Summary of the History of Uric Acid in the Body: (a) in the Normal State, (b) in the Gouty State.—The facts elicited in this and the preceding lectures enable us to obtain a coherent view of the state and destiny of uric acid in the body. It has been shown that in normal urine uric acid always exists as a quadriurate, and that in animals which eliminate their nitrogen as uric acid, like birds and serpents, the urinary secretion is composed entirely of the same combination. Proof has also been furnished that in liquids containing alkaline carbonates—such as the serum of the blood and its derivatives, lymph and synovia—uric acid passes into solution in the first instance as a quadriurate. From these considerations it may be inferred that in the normal state uric acid is primarily taken up in the system as a quadriurate, that it circulates in the blood as a quadriurate, and that it is finally voided with the urine as a quadriurate. In perfect health the elimination of the quadriurate proceeds with sufficient speed and completeness to prevent any undue detention or any accumulation of it in the blood; but in the gouty state this tranquil process is interrupted, either from deficient action of the kidneys, or from excessive introduction of urates into the circulation, or from some other cause, and the quadriurate lingers unduly in the blood, and accumulates therein. The detained quadriurate, circulating in a medium which is rich in sodium carbonate, gradually takes up an additional atom of base, and is thereby transformed into biurate. This transformation alters the physiological problem. The uric acid, or, rather, a portion of it, circulates no longer as the more soluble and presumably easily secreted quadriurate, but as biurate, which is less soluble, and probably also—either for that reason or because it is a compound foreign to the normal economy—less easy of removal by the kidneys. The biurate thus produced exists at first in the gelatinous modification, but with the lapse of time and increasing accumula-

tion it passes on into the almost insoluble crystalline condition, and then precipitation becomes imminent, or actually takes place.

The Conditions which Accelerate or Retard the Processes which Culminate in the Precipitation of Sodium Biurate.—Assuming a real analogy to exist between the processes which go on in serum or synovia artificially impregnated with uric acid and the processes which go on in the blood and synovia of a gouty patient, and which culminate in the deposition of uratic concretions, it is a matter of interest, as bearing on the pathology and treatment of gout, to investigate the conditions which, in the artificial parallel, accelerate or retard these processes.

As already explained, these processes consist of three distinct chemical changes. First the quadriurate originally formed is converted into hydrated biurate; next the hydrated biurate is changed into anhydrous biurate; and finally this anhydrous biurate is precipitated in the crystalline form. For the present purpose it will be more convenient to consider these changes as one continuous process, and for the sake of brevity and ease of expression this process may be designated as "maturation."

The investigation embraced a study of the effects of temperature, percentage of uric acid in the medium, and the addition of various saline and other substances to the maturing medium.

(a) *Temperature.*—It was found invariably that the stage of maturation was more quickly accomplished in the warm chamber at 100° than at the temperature of the room; but the ultimate result was exactly the same in both cases. For example, serum charged with 1 part uric acid in 600 began to precipitate in the warm chamber in four hours, and precipitated copiously in six hours. A duplicate specimen kept at the temperature of the room began to precipitate in eight hours, and did not precipitate copiously for sixteen hours. Another sample of serum, impregnated with 1 part of uric acid in 1,000, began to precipitate in the warm chamber in six hours, and deposited copiously in fourteen hours, while a duplicate kept at the temperature of the room only began to precipitate in thirty hours, and copious precipitation did not take place for forty-eight hours.

The absolute constancy of these results led to the idea that maturation would go on more rapidly at a febrile temperature (104° to 105°) than at the normal temperature of the body, and that herein might be found an explanation of the circumstance that gouty outbreaks sometimes follow immediately on the heels of an injury. When, however, this notion was tested experimentally no support was found for it.

It was also conceived that, although maturation itself was favoured by warmth, the terminal act of the process—namely, the act of precipitation—might, on the contrary (seeing that the biurate is more soluble at higher than at lower temperatures), be favoured by cold, and that this might account for the fact that gouty concretions tend to be deposited in the cooler and more exposed parts of the body, in the joints and subcutaneous tissues rather than in the warmer interior regions. I failed, however, to obtain any direct experimental evidence in favour of this conception.

TABLE XVII.—*Showing the Influence of Percentage of Uric Acid in the Medium on the Speed of Maturation, and the Time of Advent of Precipitation.*

Quantity of Uric Acid contained in the Serum.	Time of Precipitation of Sodium Biurate.
1 in 1,000	Precipitation began in six hours. Copious precipitation in fourteen hours.
1 in 2,000	Precipitation began in thirty-three hours. Copious precipitation in three days.
1 in 3,000	Slight precipitation began in three days, which became a little more copious in twelve days.
1 in 4,000	A few needles of biurate were detected on the sixth day; more needles and a few tufts in twelve days.
1 in 5,000	A few short needles were detected on the thirteenth day. In thirty days the needles were somewhat more numerous.
1 in 6,000	No needles were discoverable in fourteen days; a few were detected in forty days.
1 in 8,000	No needles could be detected after the lapse of forty days.

(b) *Quantity of Uric Acid in Solution.*—It was found that no condition exercised so great and decisive an influence on the speed of maturation and the advent of precipitation as the proportion of uric acid in solution. The experiment with blood serum, the results of which are arranged in a tabular form (see p. 10), illustrates these points in a striking manner. The phials containing the serum were placed in the warm chamber for fourteen days, and were afterwards kept at the temperature of the room. Chloroform was added to prevent putrefactive changes.

Assuming that the inflammatory arthritic attacks in gout are directly due to copious and sudden precipitation of crystalline stars and needles of sodic biurate in the cartilages and fibrous structures of the joints, the evidence before me indicates that such copious sudden precipitation can only take place when the fluids bathing these structures are impregnated with uric acid in at least the proportion of 1 part in 2,500. Below this point the precipitation occurs slowly and scantily, and only in the form of short scattered needles. When the proportion of uric acid in the serum was only 1 part in 5,000, the deposited needles were mostly about as long as the diameter of a red blood disc, some were twice this length, and a few three times this length, and all were of extreme tenuity. It is quite conceivable that this slighter precipitation in the tissues, of short scattered needles, might account for certain irritations in the various organs, such as characterise irregular or larval gout; but it could scarcely engender downright inflammatory attacks. It is further conceivable that the presence in the blood of such scattered needles might constitute foci, around which clotting might take place; and that the thrombosis not infrequently observed in gouty cases might thus be accounted for.

The impregnation of the blood in gouty persons with uric acid to the extent of these lesser degrees is within the range of observed actualities. Sir Alfred Garrod obtained, by quantitative analysis from the blood serum of one of his patients, uric acid to the amount of 1 part in 5714; and he remarks that the quantities thus recoverable from the blood are probably much under the actual amounts, as considerable loss is liable to occur from unavoidable causes.

These considerations lead to the suggestion that a microscopical examination of the blood in gouty persons might sometimes reveal the existence of needles of biurate in that fluid. I tested this point in ten cases of chronic gout by examining a drop of blood drawn from the finger, but I failed to obtain positive results.

(c) *Influence of Saline Substances.*—The effect of saline substances on the maturing process was tested by adding small quantities of various salts to serum impregnated with uric acid and observing whether these additions accelerated or retarded precipitation. The experiments were carried out in the following manner: Uric acid was dissolved at blood heat in blood serum in the proportion of 1 per 1,000 or 1 per 2,000. A number of phials capable of holding 25 cubic centimetres were charged with the serum thus impregnated. One phial had no further addition made to it—this was the control phial. To the others small quantities, varying from 0.05 per cent. to 0.2 per cent. of the salts to be tested, were added. The phials were then chloroformed to prevent decomposition and placed in the warm chamber. The occurrence of precipitation was noted at two points, namely, at its very onset, as revealed by the detection on microscopical examination of needles of biurate, and, secondly, when precipitation became copious and was recognisable by the naked eye.

A large number of experiments were made on this plan. The state of the medium during precipitation was that of a supersaturated solution, and, consequently, a very slight, often inappreciable, inequality in the conditions of the experiment was sufficient to disturb the time and rate of precipitation. For this reason it was frequently found necessary to repeat the observations once and again to get the correct indication. I need not trouble you with details; the following summary indicates sufficiently the conclusions deduced from the experiments.

(a) The addition of sodium salts to the maturing medium hastened precipitation. An idea of the degree of acceleration may be gathered from the following examples. Serum impregnated with uric acid to the extent of 1 part per 1,000 commenced to precipitate in seven hours, and precipitated

copiously in 16 hours. A parallel experiment, in which 0.2 per cent. of sodium chloride had been added to the serum, began to precipitate in five hours, and precipitated copiously in twelve hours. Another sample of serum was impregnated with uric acid to the extent of 1 part in 2,000. This began to deposit crystals in 30 hours, and deposited freely in 96 hours. In a parallel experiment, in which 0.2 per cent. of sodium bicarbonate had been added to the medium, precipitation began in 20 hours and free precipitation took place in 40 hours. The alkaline reacting salts—the carbonate and phosphate—had exactly the same effect as the chloride and sulphate which are neutral in reaction.

(b) The addition of potassium salts sensibly retarded precipitation, but did not appreciably diminish the eventual amount of it. Here again the carbonate and phosphate, which are alkaline, produced just the same effects as the chloride, iodide, and bromide, which are neutral. Both with potassium and sodium salts the results were entirely dominated by the nature and quantity of the bases added, and had no reference to the acidulous radicle with which the bases were combined.

(c) The addition of calcium and magnesium salts appeared to delay precipitation, but their action in this respect was quite insignificant or even doubtful.

ABSTRACTS OF LECTURES ON THE TREATMENT OF SURGICAL TUBERCULOUS DISEASES.

Delivered at the Royal College of Surgeons of England.

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LECTURE III.

THE modes of complete removal of the disease in cases of joint affections are three in number, namely: (1) Complete removal of the diseased tissues along with as little as possible of the healthy structures, in other words arthrectomy; (2) removal of the diseased tissues along with certain portions of the ends of the bones, whether diseased or not—excision; and (3) amputation above the affected joint. Intermediate between arthrectomy and arthrectomy we have partial arthrectomy, where only portions of the disease are removed, parts being left behind either intentionally in order to avoid division of ligaments and breaking up of the joint, or unintentionally, where scraping or other imperfect methods are employed. In cases where I formerly would have performed arthrotomy, I have of late done a partial arthrectomy, thus combining the principle of removal of the diseased tissue with that on which we suppose that arthrotomy acts—namely, relief of tension, and consequent diminution of the inflammation. We must now consider the relative advantages and disadvantages of these methods of treatment, and the principles which guide us in making our choice. Many circumstances influence our choice of operative measures, and of these I may refer to the influence of age, of the general condition of the patient, and of the local condition.

Beginning with the influence of the local condition, we may consider it (1) as to chronic suppuration, (2) as to sepsis, and (3) as to the distribution and character of the local disease.

The occurrence of chronic suppuration in connection with tuberculous diseases of bones and joints greatly increases the gravity of the case, and exercises an important influence on the question of treatment. It usually indicates a progressive form of the disease, while the opening of the abscesses, if large and if not performed aseptically, exposes the patient to very great dangers in consequence of the resulting decomposition of the contents and septic inflammation of the wall. So impressed are some surgeons with the unfavourable character of these cases, that they recommend the most radical operations (excision or amputation) in cases where suppuration has occurred. For example, König states that in the case of