ON THE STATE
IN WHICH THE
URIC ACID EXISTS IN THE URINE.

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IN the following paper I shall mention, 1st, the opinions of Berzelius, Prout, Simon, and Becquerel.

2nd. The appearance and properties of that deposit containing uric acid, which may be obtained from urine by evaporation under the air-pump.

3rd. Appearance and properties of pure urate of ammonia.

4th. How urate of ammonia may be modified, so as to have the appearance and properties of that deposit, which may be obtained by evaporating urine.

1st. Berzelius, in the "Lehrbuch der Chemie," vol. ix. p. 417, mentions Dr. Prout's view of the uric acid existing as urate of ammonia, and then states his own, that uric acid most frequently is in an uncombined state; but perhaps modified by the presence of other matters in the urine. On this point he says, "We know moreover that iodine is

more soluble in water which contains common salt, or muriate of ammonia, than it is in distilled water, although we know of no combination of these salts with iodine." Dr. Prout, in the 4th edition, p. 531, after giving Berzelius's view, states his own reasons for differing. Dr. Simon, in the "*Handbuch der Medizinischen Chemie*," vol. ii. p. 340, after mentioning the views of Berzelius and Prout, says, that the truth may be that healthy urine contains free uric acid and also urate of ammonia. He gives no reasons for so thinking. M. Becquerel, in the "*Sémeiotique des Urines*," p. 45, says, that the ordinary fine amorphous powder which is deposited from acid urine consists of uric acid combined with colouring matter and (the so-called) extractive matters of the urine.

2nd. Appearance and properties of that deposit containing uric acid which may be obtained from urine by evaporation under the air-pump.

When examined with a microscope of a moderate power, this deposit is seen always in the form of a most minute globular powder. As the particles are smaller in diameter than the hair of the micrometer eyepiece they cannot be measured. The particles exhibit rapid molecular motions. No crystalline appearance whatever can be detected. The powder is soluble in warm water, and is again deposited on cooling, of the same form as before. Any acid gradually changes the minute globules into angular crystals, which are considerably larger than the granules. The smallest of these crystals which I

have measured was $\frac{1}{9000}$ of an inch in length. Their breadth is from a third to half their length.

Some deposit obtained from healthy urine by evaporation under the air-pump was washed with alcohol. It was then dried and dissolved in boiling water. After standing ten hours no deposit took place, so that the fluid might not have been saturated.

Bottle full at 64 Fahr. = 64·836 grammes.

Evaporated to dryness in a water-bath.

Residue + Bason . = 30·688 grammes.

Bason . . . = 30·640

Residue . . . = ·048

Hence water . . . = 64·788

Hence one part of the residue would remain dissolved in at most 1349 parts of water at 64 F.

Some urine which gave a deposit on standing twelve hours was filtered.

Bottle full at 64 F. = 66·767.

Hydrochloric acid was added in great excess, and after forty-eight hours the clear liquor was poured off; the crystals were thrown on a filter and washed with acidulated water.

The uric acid = ·026 grammes.

Hence one part of uric acid remained in at most 2567 parts of urine after it had been allowed to stand twelve hours to deposit sediment.

Healthy urine of sp. gr. 1027 gave no deposit on standing in the air twenty-four hours, whilst some placed under the air-pump, and evaporated for

twelve hours, gave a plentiful precipitate. When filtered, bottle full at 68 F. = 66·959: strong hydrochloric acid was added in excess, and it was left at rest forty-eight hours. Uric acid = ·024. Hence one part of uric acid remained in at most 2789 of urine after it had been concentrated by evaporation *in vacuo*, over sulphuric acid.

Lecanu says, one part of uric acid exists in between 780 and 1030 water.

Becquerel says, one uric acid to between 2000 and 3333 water.

3rd. Appearance and properties of pure urate of ammonia.

When pure uric acid is boiled with strong liquor ammoniæ, sp. gr. 0·884, a compound forms, which if dissolved in boiling distilled water, and filtered whilst hot, gives a copious white precipitate on cooling. Examined by the microscope this is seen to consist of small needles which form tufts and crosses. The slower the deposit, usually the larger the crystals, but I never obtained them large enough to be seen by the naked eye, though it requires only a low power to detect the crystalline structure.

The ammoniacal mother liquor, from which some urate of ammonia had crystallised, after standing many hours was filtered.

Bottle full at 65 F. = 64·924 grammes.

Evaporated to dryness in a water-bath :—

Urate of ammonia = ·058

Hence water . = 64·866

or one part of urate of ammonia required 1118 of this dilute ammoniacal water to hold it dissolved.

The needles which were deposited from this mother liquor as it cooled, were dried *in vacuo* over sulphuric acid: when perfectly dry, they were re-dissolved in hot distilled water, and the solution was distinctly acid to test-paper, when it dried upon it.

To render the acid reaction of urate of ammonia as certain as possible, some serpent's urine was powdered, boiled with water, and filtered whilst hot. The solution when dry reddened blue litmus-paper. It deposited on cooling, a multitude of small and large globules; these gradually formed a crust at the bottom of the vessel in which the deposit took place. Some of this was boiled with liq. ammoniæ fort., of which fresh quantities were added from time to time. It was then left at rest many hours; fresh ammonia was again poured on, and it was again boiled. Distilled water then was added, and the whole boiled and filtered whilst hot: on cooling, numbers of little tufts of needles were seen with the microscope, and no globules. These tufts were evaporated to dryness under the air-pump; dissolved again in boiling distilled water, and tested with litmus-paper, which was reddened as it dried about as strongly as by healthy urine.*

* This acid reaction on test-paper as the fluid dried, was thought to indicate that a minute quantity of free ammonia was present, which hindered the acid reaction of the salt until the ammonia escaped. Later experiments have proved that not only

As the mode of preparation shows, pure urate of ammonia is much more soluble in hot than in cold water. When quite dry, some of the needles were dissolved in boiling distilled water; the solution was set aside to deposit the excess of urate of ammonia. After twelve hours, the clear fluid was filtered.

Bottle full at 69 F. = 64·720 grammes.

Evaporated to dryness in water-bath:—

Residue of urate of ammonia = ·072

Water = 64·648

Hence one part of urate of ammonia remains in 897 parts of water at 69 F.

Some needles were dissolved as before, and left to deposit urate of ammonia twelve hours.

Bottle full of clear solution at 67 F. = 64·854

Residue = ·064 Water = 64·790

Hence one part of urate of ammonia remains in 1012 water, at 67 F.

Needles prepared at another time were treated as in the last experiment.

Bottle full at 69 F. = 64·824

Residue = ·065 Water = 64·759

Hence one part of urate of ammonia required 996 parts of water at 69 F. for solution.

By lengthened exposure to heat even below 212°, the needles of urate of ammonia are decomposed; thus in the residue or evaporation in the above ex-

urate of ammonia, but all salts of ammonia are decomposed by evaporation at ordinary temperatures. These experiments will be read to the Chemical Society at their next meeting.

periments a change took place, although in all cases the sides of the bason were prevented by cork from touching the water-bath; still, after about four hours, which were required before the water was evaporated, the residue was found to be not so soluble as it had been, and when dissolved and left to deposit crystals, the microscope detected crystals of uric acid.

To avoid the decomposition, a solution of needles, prepared as before, was evaporated under the air-pump, over sulphuric acid.

Bottle full at 59 F. = 62·205.

Residue of urate of ammonia = ·061

Water = 62·144

or one part of urate of ammonia required 1018 parts of water at 59 F. to dissolve it.

If to a solution of these needles, which is just so strong that it gives no precipitate on standing twenty-four hours, the smallest quantity of most dilute liquor ammonia, or small quantities of muriate, sulphate or acetate of ammonia, are added, a deposit in a very few minutes falls. The precipitate with the two last re-agents is changed in form, no needles are seen, only globules. Sulphate of soda and sulphate of magnesia gave no precipitate when added in small quantity to the solution of needles.

On the addition of any acid, the needles may be observed under the microscope to undergo a change: this is not instantaneous. Usually, rectangular plates form singly or in groups. It is rarely that angular crystals, similar to those in urine, are found.

In order to admit of comparison with the experiments on the urine, some needles were dissolved in water at a boiling temperature. After standing twelve hours the solution was filtered.

Bottle full at $72\frac{1}{2}$ F. = 64.712 grammes.
Hydrochloric acid was added in excess, and left at rest forty-eight hours. The crystals of uric acid washed and dried = .029. By washing, some of the uric acid was dissolved, so that there was one part of uric acid in at most 2231 parts of the solution.

In a second experiment,

Bottle nearly full at 71 F. = 61.801.
Treated as before, uric acid = .026, or 1 uric acid in at most 2399 parts of solution.

The correspondence between these experiments and the similar ones on the urine is to be noted. The loss of uric acid in all, from washing the precipitate, though it makes the experiments of little value as regards the actual quantity present, yet it does not affect the comparative results. The error being common to all.

The next object was to determine the composition of these needles:—some very carefully-prepared needles were dried under the air-pump, and very gently warmed in a water-bath; of these .397 grammes were taken, mixed with moderately dilute hydrochloric acid, allowed to stand forty-eight hours, then thrown on a filter and slightly washed.

Uric acid = .368.

The clear acid fluid was mixed with a solution of ammonio-chloride of platinum in excess, evaporated

to dryness in a water-bath, thrown on a filter, washed with a mixture of æther and alcohol, dried, and weighed :

Ammon.-chloride of platinum = $\cdot 487$

Hence ammonia = $\cdot 037$

And in 100 parts of needles of urate of ammonia we have, uric acid = $87\cdot 65$, ammonia = $9\cdot 32$. In this analysis I thought the whole of the urate of ammonia was not decomposed. In the following one made with needles prepared at another time, stronger acid was used :

Substance = $\cdot 457$, uric acid = $\cdot 398$

Ammonio-chloride of platinum = $\cdot 557$

Hence in 100 parts,

Uric Acid = $87\cdot 09$, ammonia = $9\cdot 29$.

Another analysis was made with needles dried only over sulphuric acid :

Substance = $\cdot 353$.

This was put into a flask with distilled water, and heated to near the boiling point : hydrochloric acid was then added in large excess. After forty-eight hours, uric acid = $\cdot 305$, chlor. amm. plat. = $\cdot 422$. Hence, in 100 parts,

Uric Acid = $86\cdot 40$, ammonia = $9\cdot 12$.

In the three analyses, then, we have in 100 parts of substance :—

	1st.	2nd.	3rd.	Theory.	
Uric Acid	$87\cdot 65$	$87\cdot 09$	$86\cdot 40$	$86\cdot 58$	1 equivalent uric acid.
Ammonia	$9\cdot 32$	$9\cdot 29$	$9\cdot 12$	$8\cdot 77$	1 equivalent ammonia.
Loss	$3\cdot 03$	$3\cdot 62$	$4\cdot 48$	$4\cdot 68$	1 equivalent water.

From these analyses the needles consist of one

equivalent of uric acid combined with one equivalent of the oxide of ammonium.

It was thought that another urate of ammonia might be formed, containing more uric acid. Such a compound has been called superlithate of ammonia by Coindet. In various ways I tried to obtain this substance. Some uric acid was boiled with very little ammonia, so that the solution whilst boiling was acid to test-paper. This was filtered when hot. It deposited, on cooling gradually, a white curdy mass, which, under the microscope, consisted of short thick needles, mixed with long rectangular crystals of uric acid.

By mixing urate of potash with muriate of ammonia in solution, I still found a deposit of needles. The only way I thought I obtained a different substance was by heating the needles for some hours about 212 degrees, so that partial decomposition took place; boiling water was then poured on, and filtered whilst hot: no deposit fell on cooling, in one experiment not for forty-eight hours. At the end of this time, when shaken, a deposit of globules, and globules with projecting angular crystals, was seen, mixed with crystals of uric acid; after standing some hours, the mother liquor was separated by filtration.

Bottle full of clear liquid at 64 F. = 64·801.
Evaporated in water-bath:—

Residue = ·061 Water = 64·740.

Hence, one part of the residue required 1060 parts of water, at 64 F., to retain it in solution.

This solubility agrees so nearly with that of the needles, as to make it probable that no new compound was in solution. I could not obtain it free from uric acid, so as to admit of analysis.

Failing to obtain another urate of ammonia, I tried if the needles could be modified, so as to have the appearance of the ordinary urinary sediment.

4th. Some long needles of urate of ammonia were boiled with some healthy acid urine. The needles were dissolved, and, whilst hot, the solution was filtered; on cooling, no trace of needles could be seen, but the usual small granules only were visible, precisely similar to those that are seen in the ordinary deposit from urine. When cold, the clear urine was poured off from the sediment, and again boiled with a fresh quantity of needles: the same granular deposit again ensued on cooling. The clear fluid again poured off, and, boiled with fresh needles, again gave granules. Some of the same needles were boiled with water, a deposit took place on cooling, which consisted of needles; these were again dissolved, and so little urine added, that the deposit on cooling was quite colourless. When examined with the microscope it consisted no more of needles, but of granules. Some of the needles were dissolved in hot water, and some pure urea was added, still the deposit on cooling consisted of needles.

In the attempt to form another urate of ammonia, excess of uric acid was added, and still needles

were deposited. As then neither urea nor uric acid altered the form of the crystals, I tried common salt.

Some long needles of urate of ammonia were dissolved in boiling water, and a thickish white precipitate of needles occurred on cooling. These were again heated, and a little common salt added to the solution. No deposit took place on cooling, or in twenty-four hours. More needles were boiled with the saline fluid, and still no deposit took place on cooling. Some of the liquid was poured on a plate of glass, and, on spontaneous evaporation, granules were observed precisely similar to those in the ordinary urinary deposit. Some more of the liquid was evaporated over sulphuric acid *in vacuo*, and a deposit took place which consisted of granules only.

A large excess of needles was boiled with distilled water, and filtered whilst hot, a little salt was added, and after some hours largish globules were deposited, and no needles.

Some of the needles, prepared as before, were dissolved in distilled water: the solution was filtered, and gave a plentiful deposit of needles on cooling. These were re-dissolved, and the solution divided into three portions. To one a few drops of healthy urine was added, to another a small quantity of salt, to the third some pure urea. In this last a deposit fell on cooling, which, under the microscope, consisted of needles, and in quite as large

quantity as before. In the other portions the deposit was very much smaller in quantity. It was in both cases white, and consisted only of granules. Moreover, by boiling some urine, which contained the ordinary globular deposit soluble by heat, with ammonia, and filtering whilst hot, the deposit on cooling consisted of thickish needles and crosses. The same thing happened when urate of ammonia, salt, distilled water, and excess of ammonia were used. Here then seemed to be a satisfactory explanation of the difference which exists in the appearance, under the microscope, of the ordinary deposit, and of pure urate of ammonia. The salt seemed to be the cause of the difference.

It remains to be shown how far the same cause can account for the different quantities of uric acid which have been found in urine and in pure water. The greatest quantity in urine is, one part uric acid to 780 urine, according to Lecanu.

The greatest solubility of the needles which I observed was 1 needles to 897 pure water. Hence urine sometimes contains even more uric acid than would remain in a solution of urate of ammonia in distilled water after it has been left to crystallize.

Some needles were dissolved with some salt in boiling water: after standing twelve hours for crystallization, the mother liquor was filtered.

Bottle full at 71 F. = 64·909 grammes.

Evaporated in a water bath :—

Salt + urate of amm. = ·301 Water = 64·608

The salt and urate of ammonia were heated to redness in a covered platinum crucible.

Salt = $\cdot 162$

Hence urate of ammonia = $\cdot 139$

Or one part of urate of ammonia with rather more than one part of salt, require 466 parts of water at 71 F. to hold it dissolved after crystals have been deposited.

In the above analysis the salt is to the water as 2·50 to 1000. In the analysis of the urine of three grown-up men, Lecanu found in 1000 parts of urine 4·60, 2·40, 3·76 common salt.

The above experiment was then made with more salt and with less.

Bottle full at 67 F. = 64·125.

Salt + urate amm. = $\cdot 382$ Water = 63·743

Salt = $\cdot 246$ Hence urate of amm. = $\cdot 136$

Or one part of urate of ammonia with nearly two parts of salt, require 468 parts of water at 67 F. The salt is to the water as 3·86 to 1000.

Bottle full at 68 F. = 64·862.

Salt + urate of amm. = $\cdot 159$ Water = 64·703

Salt = $\cdot 067$ Urate of amm. = $\cdot 092$

Or one part of urate of ammonia with two-thirds of one part of salt, require 703 parts of water at 68 F. The salt is to the water as 1·03 to 1000.

If a great excess of salt was used, the urate of ammonia appeared not to be more soluble than in pure water.

These and the previous results may be compared in the following Table ; the experiments having all

been made on hot saturated solutions, which were allowed to stand many hours to deposit crystals.

In ammoniacal mother liq. at 65 F., there was 1 pt. urate of amm. to 1118 water.

In pure distilled water	67 F.,	1	1012
	59 F.,	1	1018
	69 F.,	1	897
	69 F.,	1	996
Distilled water with little salt	68 F.,	1	703
with more salt	71 F.,	1	465
and more salt	67 F.,	1	468

From these experiments it appears, that urate of ammonia, when dissolved with about an equal weight of salt, acquires a greater degree of solubility in water, and a difference in appearance from pure urate of ammonia. The appearance is identical with that deposit which can be obtained from urine, and the solubility is more than double the solubility in distilled water.

To render the conclusion still more certain, some pure uric acid was boiled with distilled water: in ten hours it was filtered.

Bottle full at 68 F. = 62·597 grammes.

Evaporated to dryness in water-bath:—

Uric Acid = ·007 Water = 62·590

Or one part of uric acid remained in 8941 parts of water at 68 F.

Pure uric acid was boiled with salt and distilled water: in ten hours it was filtered.

Bottle full at 64 F. = 64·974.

Salt and uric acid = ·177 Salt = ·168

Hence, Uric acid = ·009 Water = 64·797

Or one part of uric acid, with salt, remained in

7199 parts of water, at 64 F. The quantity of salt was nearly the same as had been found to dissolve most urate of ammonia. The salt being to the water as 2·59 to 1000.

Hence,

1	part of uric acid remains in 8941 parts of water at 68 F.	
1	7199	64 F. with salt [added.
1	was found in 2231 pts. of solution at 71½ F. when urate [of ammonia was decomposed.	
1	2399	71 F.
1	2567 parts of urine at 64 F.	

Whilst,

1	part of urate of ammonia was found in 1000 parts of water at 65 F.	
1	450	with salt added.

Now,

Berzelius gives 1 part of uric acid in 1000 parts of urine.	
Lehmann	1 917 to 980
Lecanu	1 780 to 1030
Becquerel	1 2000 to 3333 urine

This was Dr. Prout's first reason for believing that urate of ammonia exists in the urine. The results I have given tend only to establish his opinion, by showing how urate of ammonia is modified in form and solubility.

The higher solubility which Dr. Prout gives to urate of ammonia possibly arises from the solution not being left to deposit crystals. In the above experiments, if no deposit took place in twelve hours, a fresh quantity of urate of ammonia was added, and the solution was set aside to crystallize. In some of these solutions, and also not unfrequently in urine, I have observed that when cooled even below 60 degrees, no deposit took place ;

but if left a few hours, in even a little higher temperature, or when agitated, a large deposit fell.

The experiments which I have made may give a further insight into the various causes of that frequent deposit of urate of ammonia which occurs in health.

A small quantity of salt increases the solubility of this substance; the muriate, the sulphate, and the acetate of ammonia, lessen the dissolving power of distilled water. The red deposit from urine was diluted and heated until a clear solution was formed. It was filtered whilst hot, and divided into two portions; to one a little muriate of ammonia was added, and the temperature of both was taken as soon as a cloud began to appear in either.

Tube with muriate of ammonia.		Without muriate of ammonia.	
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97	F. cloud appeared	95	F. clear
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93	very thick	91	clear
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88	very thick	86	cloud
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86	very thick	84	thick
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In a second experiment, with a rather stronger solution of urate of ammonia :

103	very thick	98	clear
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It is most probable, that each salt that occurs in the urine has some effect on the solubility of the urate of ammonia; and it may be by a very extended inquiry into the relative re-action of the different salts, more particularly the phosphates and sulphates, that we may arrive at an accurate knowledge of the causes of the frequent deposit of urate of ammonia in the urine.