Second Communication.

ON THE
BLOOD AND EFFUSED FLUIDS
IN
GOUT, RHEUMATISM, AND BRIGHT'S DISEASE.

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IN February, 1848, I had the honour to communicate to the Society a paper on the condition of the Blood and Urine in Gout, Rheumatism, and Bright's Disease, which appeared in the volume of the 'Transactions' for that year; I now offer one intended as supplementary to the first, and introductory to a third paper, which I hope in a few weeks to bring before your notice.

The principal points established in the first paper having reference to the subject matter of the present communication are as follow :

1. The discovery of uric acid in the blood.
2. Its existence in very minute quantities, mere traces, in healthy human blood, and in that of some of the lower animals, as the duck.
3. Its augmentation in that fluid in certain pathological conditions of the habit.

The mode then recommended for its discovery and estimation was, to extract from carefully dried blood serum, by

means of hot alcohol, such matters as are soluble in that menstruum; then taking up, by hot water, the urate of soda, and after evaporation, either crystallising that salt, or by the addition of a foreign acid, liberating the uric acid, and afterwards collecting and weighing. This process requires considerable time and care in the manipulation, especially if any attempt be made at determining the quantity; and hence, although it is a method most desirable to have recourse to, in investigating the pathology of disease, yet it is one which cannot readily be employed in clinical medicine.

To obviate this difficulty, I have devised another mode of ascertaining the presence of uric acid in the blood, which I have been in the constant habit of using clinically during the last four years, and with the results of which I have every reason to be well satisfied; it is a method which can be readily employed by every medical practitioner, and which has the advantage of requiring for its performance the abstraction of only a very small amount of blood. I have named the process the "Uric Acid Thread" experiment, which is thus performed.

"Take from one to two fluid drachms of the serum of blood, and put it into a flattened glass dish or capsule; those which I prefer are about three inches in diameter, and about one third of an inch deep, which can be readily procured at any glass house; to this is added the strong acetic acid of the London Pharmacopœia, in the proportion of about six minims to each fluid drachm of the serum; a few bubbles of gas are generally evolved at first; when the fluids are well mixed, a very fine thread is introduced, consisting of from one to three ultimate fibres, from a piece of unwashed huckaback or other linen fabric, about one inch in length, which should be depressed by means of a small rod, as a probe or point of a pencil. The glass is then put aside in a moderately warm place, until the serum is quite set and almost dry; the mantelpiece in a room of the ordinary temperature answers very well, the time varying from eighteen to forty-eight hours, depending on the warmth and dryness of the atmosphere.

“Should uric acid be present in the serum in quantities above a certain small amount noticed below, it will crystallise, and during its crystallisation will be attracted to the thread, and assume a form not unlike that presented by stone sugar upon a string (see fig. 1). To observe this appearance, a linear magnifying power of about fifty or sixty, procured with an inch object-glass and low eye-piece, or a single lens of one sixth of an inch focus, answers perfectly. The uric acid is found in the form of rhombs, the size of the crystals varying with the rapidity with which the drying of the serum has been effected.”

To ensure perfect success, several precautions are necessary.

1. The glasses should be broad and flat, as above described: watch-glasses of the ordinary kind are not good, being too small, thus allowing the fluid to be frequently spilt; and too much curved, causing the film of partially dried serum to curl up and split.

2. The acetic acid should be neither very strong nor weak. Glacial acid often forms a gelatinous compound with the albumen of the serum, and the appearance of flakes; and very weak acid adds unnecessarily to the bulk of the fluid. By experience I find the *acidum aceticum* (*Pharmacopœia Londinensis*) to be well suited for the experiment.

3. The character of the thread and its quantity is of some moment. Very smooth substances, as hairs or fine wire, but imperfectly attract the crystals: if the number or length of the fibres be too great, and the amount of uric acid small, the crystals become much scattered, and therefore but few appear in the field of the microscope. The glass should not be disturbed during the drying of the serum, or the crystals become detached from the thread.

4. Some attention to temperature is necessary; if the serum be evaporated at a high temperature, above 75° Fahr. for example, the drying may take place too rapidly to allow crystallisation; the temperature of an ordinary sitting room answers well for the purpose.

5. If the serum is allowed to dry too much before the examination takes place, the surface becomes covered with a

white efflorescence consisting of phosphates (see fig. 2), which may obscure the thread; this can be removed by the addition of a few drops of water before putting the glass under the microscope; sometimes over-drying causes the serous film to become cracked or fissured throughout, as well as covered with the phosphatic efflorescence.

6. It is well, when practicable, to put up two or more glasses with the same serum.

7. The blood should be recently drawn; that is, no change or decomposition should have been allowed to take place before the experiment is made; the reason for this precaution will be spoken of below.

Delicacy of the above Test for Uric Acid.—The serum of healthy blood, and that of blood from patients suffering from most diseases, gives no indication of the presence of uric acid by the “uric acid thread” experiment; and this absence of very extreme delicacy is of itself a most valuable quality, as only in blood containing an abnormal amount of this principle, will the acid be indicated. In my first communication, where the results of several quantitative determinations of the amount of uric acid in the blood in gout and albuminuria were given, it will be seen, that in 1000 grains of serum it varied usually from 0·045 to 0·175 grain; these numbers were necessarily smaller than the quantities which really existed, being those actually separated and weighed; guided by these results, I have endeavoured to ascertain the value of the “uric acid thread” experiment by the following series of observations. For this purpose I have taken serum of blood from the healthy subject, in which the most careful analysis could with difficulty show the presence even of a trace of uric acid, and to this serum have added the acid in the form of urate of soda in certain definite proportions. After testing such serum in the manner above detailed, the following results were arrived at:

1. Serum with the addition of uric acid in the proportion of 0·010 grain in 1000 grains	{ gave no indication of uric acid.
2. Serum, containing 0·020 grain in 1000 grains	{ „ no crystals of uric acid.

3.	Serum, containing	0.0250	grain in 1000 grains	{	gave 2 or 3 crystals on thread.
4.	"	"	0.030 " 1000 "	"	" a few crystals.
5.	"	"	0.040 " 1000 "	"	" several crystals.
6.	"	"	0.050 " 1000 "	{	" moderate sprinkling of crystals on thread.
7.	"	"	0.060 " 1000 "	{	" thread pretty freely covered with crystals.
8.	"	"	0.080 " 1000 "	{	" very numerous crystals on thread.
9.	"	"	0.100 " 1000 "	{	" abundance of crystals, more than usually found in serum.
10.	"	"	0.200 " 1000 "	{	" thread completely covered with crystals of uric acid, and numerous scattered crystals.

It appears, therefore, that an amount of uric acid equal to 0.025 gr. in 1000 grains of serum, in addition to the trace existing in healthy serum, is required to be present in the blood before the "uric acid thread" experiment gives indications of its presence, and hence the appearance of the uric acid on the thread becomes complete evidence of an abnormal or morbid quantity in that fluid.

Changes which Uric Acid undergoes in the Blood when removed from the Body.

In enumerating the precautions which should be observed in making the "uric acid thread" experiment, it was stated that recently drawn blood should be employed, and the importance of this will be seen from the following observations, which at first perplexed me not a little. Having ascertained the presence of uric acid in the blood in many cases, and put aside the serum for a time, it was found that on repeating the experiments, no indication of the

presence of that acid could be discovered ; this circumstance more frequently happened in the summer months. On closer examination I found that the serum had usually undergone some slight decomposition, which gave me at once a clue to the explanation of the phenomenon, namely, that uric acid existing in blood is broken up, or undergoes a species of fermentation, when the albuminous portion of the serum becomes altered in character. In order to verify this, the following experiment was repeatedly made, and with uniform results. Uric acid in the form of urate of soda was dissolved in serum in the proportion of from 0·10 gr. to 0·30 gr. to 1000 grains of serum, and the fluid allowed to become putrid. The whole of the acid was found to be destroyed, no indications being afforded by the “uric acid thread” experiment, although at first abundance of crystals were obtained.

I have made some few experiments in order to discover the change which the uric acid undergoes under the above-mentioned circumstances.

When submitted to the action of certain oxidising agents, as the puce-coloured or per-oxide of lead, it is broken up into oxalic acid, urea, and allantoin ; and when the oxide is in excess, the oxalic acid is further oxidised and converted into carbonic acid. This fact led me to try whether oxalic acid might not be formed in the blood-serum from a change in the uric acid, and for this purpose I made daily observations on such serum during its decomposition, and found evidence of the formation of oxalic acid in the occurrence of octohedral crystals of oxalate of lime ; after a time these crystals appeared to become less numerous, and at last to vanish. I have also evaporated the serum when decomposition was taking place, and treated the residue in the manner described in my paper on ‘The occurrence of Oxalic Acid in the Blood,’ published in the 32d volume of the ‘Medico-Chirurgical Transactions.’ Many crystals of oxalate of lime were thus obtained for the most part octohedra, some agglomerated into oval bodies, some similar to dumb-bells. To make the experiment more conclusive, I have taken serum

of blood not containing an appreciable amount of uric acid, divided into two parts, and to one portion have added urate of soda in small amount, and allowed both quantities to decompose ; it was found that in the portion of serum to which the urate had been added, oxalate of lime octohedra were formed, but not in that portion free from uric acid. The microscopic examinations were made with object-glasses giving a linear magnifying power of from 200 to 400. Much further investigation is required on this subject ; enough, however, has been done to show that the study of these changes is not without interest to the pathologist, for there can be little doubt that oxalic acid is formed in the animal body, not, as formerly supposed, from the oxidation of saccharine matters, but from the decomposition of uric acid. Very many observations on the occurrence of oxalic acid in the blood of man and the lower animals, since the publication of the paper above referred to, have convinced me that such is the case.

Non-occurrence of Uric Acid in the Perspiration of the Gouty Subject.

There are several instances on record in which a whitish powder has been noticed as occurring on the skin of gouty patients, especially after profuse perspirations, and this has not unfrequently been supposed to consist of some combination of uric acid, but no proof of the presence of this body in the excretion from the skin has, I believe, ever been given. In 1853, I adopted the following plan, in order to discover if uric acid is thrown out by the skin of gouty patients. A man was selected suffering from a severe attack of gout, who had been subjected to the disease for a long time, who had many tophi or concretions of urate of soda, and in whom the blood gave, at the time, abundant evidence of containing a large excess of uric acid. Several folds of white bibulous paper were steeped in a very weak solution of potash, and applied for about thirty hours to the abdomen, protected by oil-silk. The papers were rendered acid, and were found to

be strongly impregnated with the perspiration, and to contain much organic matter; these were treated with rectified spirit, and afterwards with hot water, and the watery solution, when evaporated, carefully examined for uric acid. No trace of this body could be discovered, by the murexide test, nor any crystals separated by the addition of acetic acid.

When we consider that the excretion from the skin is very acid in character, and very deficient in saline matters, it would hardly be thought probable that a substance having the properties of uric acid would be excreted with it, either in the free state or that of a saline combination.

Discovery of Uric Acid in certain Morbid Effusions.

I am unacquainted with any published analyses which have demonstrated the presence of uric acid in fluids effused into cavities in disease; but as far back as the year 1848, soon after my first communication to the society, I made some investigations upon this subject, and found indisputable proof of its occurrence. The first of these were made on the abdominal and pericardial fluids in a case of granular kidney, with cirrhosis of the liver, and extensive cardiac disease; for some days prior to death, suppression of urine had supervened.

Abdominal Fluid.—Golden yellow colour, rather thick and turbid; slightly acid in reaction at first, but becoming alkaline on partial evaporation. Odour during evaporation similar to the perspiration. Sp. gravity, 1013·54.

In 1000 parts were contained	{	Solids	.	.	.	36·40
		Water	.	.	.	963·60

In the 36·40 parts of solids, there were 10·79 parts of albumen, and, on incineration, 5·94 parts of ash were left, the salts consisting of phosphates, chlorides, and sulphates; evidence of uric acid was obtained, in its separation in the

crystalline form, and also of urea; the weights of these bodies, however, were not determined.

Pericardial Fluid.—This was lighter in colour than the above, in other respects similar. Reaction acid. Sp. gravity, 1010·60.

1000 grains gave {	Solids	.	.	.	24·53
	Water	.	.	.	975·47
					<hr/>
					1000·00

The solids yielded, of—

Albumen	.	.	.	.	.	10·53
Salts (ash)	.	.	.	.	.	9·70
Uric Acid	.	.	.	.	.	0·069
Urea	.	.	.	.	weight not determined.	

Since the time the above analyses were made, I have ascertained the existence of uric acid in effused fluids in several cases where the blood gave evidence of containing an abnormal amount of that principle. I have many times crystallised it from such fluids by the “uric acid thread” experiment.

Discovery of Uric Acid in the fluid artificially effused by the application of Blistering Agents, or in Blister-Serum.

Not unfrequently in practice, for the sake of diagnosis, it is desirable to ascertain the condition of the blood, as to the presence or absence of uric acid, in cases where, from the state of the patient or other causes, the abstraction of that fluid cannot well be effected, and it occurred to me that, probably, the fluid effused by the application of a blister would contain this acid, if the circulating fluid were impregnated with it; experience has proved the truth of this conjecture. The following are some of the results I have obtained by the use of the “uric acid thread” experiment, which may be employed for the discovery of uric acid in blister-serum as well as in blood-serum :

1853. Feb. 9. E. W.	{ Serum of blood. Sp. gr. 1029·2, at 46° Fahr. Abundance of uric acid on thread.	Feb. 11. E. W.	{ Serum of blister. Abundance of uric acid.
March 5. J. W.	{ Serum of blood. Sp. gr. 1026·4, at 51° Fahr. Abundance of uric acid.	March 6. J. W.	{ Serum of blister. Abundance of uric acid.
March 25. — R.	{ Serum of blood. Sp. gr. 1028, at 41° Fahr. Abundance of uric acid.	March 28. — R. Attack pass- ing off.	{ Serum of blister. Sp. gr. 1022·8, at 46° Fahr. Crystals of uric acid.
March 29. J. H.	{ Serum of blood. Sp. gr. 1029·6, at 47° Fahr. Abundance of uric acid.	April 1. J. H.	{ Serum of blister. Sp. gr. 1024·8, at 54° Fahr. Abundance of uric acid.
June 30. C. S.	{ No blood taken.	June 30. C. S.	{ Serum of blister. Numerous crystals of uric acid.
Nov. 8. M. J.	{ Serum of blood. Sp. gr. 1026·8, at 62° Fahr. Crystals of uric acid not very numerous.	Nov. 11. M. J.	{ Serum of blister. Sp. gr. 1024·0, at 65° Fahr. Crystals of uric acid several in number.
1854. January 2. C. F.	{ Serum of blood. Sp. gr. 1026·8, at 50° Fahr. Abundance of uric acid.	Jan. 13. C. F.	{ Serum of blister. Moderate amount of uric acid.

It appears, then, from these results, that the fluid effused by the action of a blistering agent applied to the skin, will give evidence of the presence of uric acid when the blood from the same patient exhibits the phenomena, and in the performance of the experiment the same precautions must be taken as have been before indicated when the process with blood-serum was detailed; but, in addition to these, one more circumstance must be attended to, namely, that the application of the blister should not be made to an inflamed part, for it seems that the existence of inflammation¹ has the power of preventing the appearance of

¹ The inflammation attending the production of a blister does not appear to destroy the uric acid.

uric acid in the effused serum, as shown by the subjoined results :

1854. January 2. C. F. patient be- fore referred to.	{ Serum of blood. Abundance of uric acid.	January 2. C. F. ditto.	{ Serum from blister on inflamed (gouty) dorsum of hand. No trace of uric acid.
1853. Dec. 21. C. C. F.	{ Serum of blood. Abundance of uric acid.	Dec. 23. C. C. F.	{ Serum of blister from inflamed (gouty) knee. No trace of uric acid.
1854. Jan. 15. F. P.	{ Serum of blood. Abundance of uric acid.	Jan. 15. F. P.	{ Serum from blister to inflamed (gouty) knee. No trace of uric acid.

Should further inquiry confirm the result which the above limited number of observations appear to point to, namely, that during the existence of inflammation in a part, there is a destruction of the uric acid (when such exists) in the blood of that locality, and other independent researches which I have made appear to favour much this idea, it may hereafter throw no small amount of light on the pathology of certain morbid conditions of the system; in the present paper, however, I have abstained, as much as possible, from connecting the condition of the blood with any specific disease, reserving that subject for my next communication on "Gout and Rheumatism," when their differential diagnosis, and the nature of the so-called "rheumatic gout," will be discussed.

With regard to artificially effused fluids, I may observe that, during crystallisation, the uric acid usually assumes a form slightly different from that in which it occurs in blood-serum, the crystals having a greater tendency to become agglutinated, and form irregular masses, as seen in fig. 3. Lastly, these effused fluids may be employed, not only to ascertain the existence of uric acid, but likewise of other principles, as urea and sugar, which are contained and can be detected in them, when, in the blood of the patient, their presence is capable of demonstration.

Fig 1a.

Fig 1

Uric Acid crystallized on fibre from
Blood Serum (very slowly dried.)

Uric Acid crystallized on fibre from Blood Serum.

Fig 2

Fig 3

Uric Acid crystallized on fibre from blood serum

Uric Acid crystallized on fibre from blood serum