

OBSERVATIONS
ON
CERTAIN PATHOLOGICAL CONDITIONS
OF
THE BLOOD AND URINE
IN
GOUT, RHEUMATISM AND BRIGHT'S DISEASE.

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IN the present paper I purpose to make known some researches on the condition of the blood and urine in gout, rheumatism and Bright's disease, which appear to throw considerable light on their pathology.

The ancients considered *gout* to depend on the presence of some morbid humour in the blood, which, becoming deposited in weak parts, gave rise to the affections of the joints: as to the nature of this matter their ideas greatly varied. At the present time, gout is regarded by some as depending on vascular plethora, by others as due to local debility, accompanied with general plethora; but the balance of opinion appears to be in favour of its arising from some alteration in the circulating fluids. The nature of this change, however, has not been defined, although most agree in regarding it as connected with an excessive formation of uric acid in the system; the frequent presence of chalk-stones or tophaceous deposits in

and around the joints, the liability of gouty patients to uric acid deposits in the urine, and the formation of urinary calculi consisting of the same acid, strongly favouring the idea. But as gout sometimes occurs in patients not having such deposits in their urine, and also in broken-down constitutions not generally considered prone to an excessive formation of uric acid, it has been doubted by many whether this substance is the "*materies morbi*," or only an occasional accompaniment. Those who look upon gout as depending on a uric acid diathesis, have entertained various views as to the cause of this abnormal state, and the presence of the acid in the blood has hitherto never been proved.

As far as my experiments regarding the nature of this disease have been prosecuted, they appear to show that—

1st. The blood in gout contains *uric acid* in the form of urate of soda, which salt can be obtained from it, in a crystalline state.

2nd. The uric acid is diminished in the urine, immediately before the gouty paroxysm.

3rd. In patients subject to chronic gout with tophaceous deposits, the uric acid is always present in the blood, and deficient in the urine, both absolutely and relatively to the other organic matters, and the chalk-like deposits appear to depend on an action in and around the joints, &c., vicarious of the "*uric-acid-excreting*" function of the kidneys.

4th. The blood in gout sometimes yields a small portion of urea (no albumen being present in the urine).

The experiments and analyses which favour these conclusions were chiefly made on patients in University College Hospital. In support of the 1st conclusion viz., that *in gout the blood contains uric acid*, the following analyses were performed.

In June 1847, a male patient, R. Hartley, was admitted into the hospital suffering from gout. During the three last years he had been subject to repeated attacks of the disease, and several chalk-stones had formed about the fingers, and a few in other parts. At the time of his admission, many

joints in the right hand were inflamed and swollen, and after a few days new tophaceous deposits began to form. At this time blood was taken from the arm for the purpose of examination. The clot was small, firm, and exhibited upon its surface a buffy coat, about an eighth of an inch in thickness, such as appears in the blood of patients suffering from some slight inflammatory disease. The serum was strongly alkaline. Specific gravity 1028.

1000 grains of the serum were taken for examination, and evaporated to dryness in thin layers in a water-bath. It was then powdered and treated with rectified spirit, boiled for about ten or fifteen minutes, again treated in the same way, and the spirit solutions preserved for examination. After again washing with spirit, the dried serum was exhausted by means of boiling distilled water, the operation being repeated two or three times, and the watery solutions mixed. When a small quantity of this fluid was evaporated with the addition of nitric acid, and afterwards held over the vapour of ammonia, distinct evidence of the existence of uric acid was afforded by the production of the beautiful purple tint of murexide or purpurate of ammonia. The watery solution was then evaporated till it became slightly thick, and, when cool, was acidulated with pure hydrochloric acid. On standing for some hours, crystals of *uric acid* were deposited,* which were afterwards collected, washed with alcohol and weighed.

1000 grains of serum gave of uric acid 0.050 grain.

From another quantity of blood drawn soon after the first, 1000 grains of serum was taken, and treated in the same manner, except that no hydrochloric acid was added. The concentrated watery solution was allowed to stand for some hours, when, on examination, innumerable tufts of crystals were found deposited on the sides of the vessel, and the surface of the fluid. These crystals were proved to consist of urate of soda;† for crystallised uric acid could be produced

* Plate I. fig. 1.

† Plate I. fig. 2.

from them, and they left an alkaline ash, soluble in water, and not consisting of potash.

I may remark, that I have always employed this method in seeking for uric acid and urate of soda in the blood.

1000 grains of serum gave of urate of soda 0·050 grain.

But in this experiment some was lost from the solubility of the salt in water, and from its examination previous to weighing.

The next analysis was made on the blood of a man (May), admitted into the hospital, suffering from an attack of gout in the knee; he had for many years been afflicted with this disease, and a small chalky deposit had formed on the cartilage of one ear. When the blood was taken, the attack had begun to subside.

1000 grains of serum gave of uric acid 0·025 grain.

The blood of a male out-patient (Appleby), suffering from an attack of gout of the knees and ankles, was next examined.

1000 grains of serum gave of uric acid 0·045 grain.

The next analysis was performed with the blood of an in-patient (Ansell), admitted for an affection of the heart, with symptoms of angina, who, during his stay in the hospital, had an attack of acute gout in the great toe. Serum, specific gravity 1026.

1000 grains of serum gave of uric acid 0·030 grain.

But much was lost accidentally: it also gave crystals of urate of soda.

I think these cases are sufficient to prove "that *uric acid* is present in the blood in cases of gout," and that "it exists there in the form of urate of soda;" for it was obtained in this form without the serum being acted on by any chemical agent capable of altering the composition of that salt.

2nd. *The uric acid is diminished in the urine immediately before the gouty paroxysm.*—The urine of the patient (Ansell), spoken of above, was carefully examined for uric acid, and

for *several* days at the commencement of the gouty attack, the addition of hydrochloric acid did not cause any deposit of uric acid; although by much evaporation on the third day a trace could be discovered by the murexide test, and a few crystals were deposited. During this time the blood gave abundant evidence of the presence of this body. When the attack had subsided, the *uric acid* was present in the urine in its normal quantity, and could be readily precipitated by means of a strong acid without any previous evaporation. Before leaving the hospital this patient's urine threw down natural deposits of uric acid.

Hartley's urine, when examined during the attack, did not give evidence of containing a trace of uric acid, although a large quantity was evaporated, and carefully examined: the re-action of the urine was very acid.

May's urine was examined when the attack was passing off. Specific gravity 1021; acid.

1000 grains gave of uric acid 0.050 grain.

1000 grains of healthy urine, when of the same specific gravity, yields about 0.60 grain.

So that the uric acid did not amount to more than one-twelfth the normal quantity.

I have examined the urine of other patients suffering from gout, and have found that at the commencement of an attack the amount of uric acid is much below the normal average.

When the affection of the joints has produced excitement in the system, then uric acid and urate of ammonia are frequently thrown out in abundance; especially where an attack of the disease produces, for a time, an improved state of health; but in those persons who have suffered during many years, from repeated attacks, the urine, after the fit, often ceases to be loaded with these matters, and then the disease becomes more frequent in its appearance, and tophaceous deposits are often formed in and about the joints.

3rd. *In patients subject to chronic gout with tophaceous deposits, the uric acid is always present in the blood and defi-*

cient in the urine, both absolutely and relatively to the other organic matters; and the chalk-like deposits appear to depend on an action in and around the joints, &c., vicarious of the "uric-acid-excreting" function of the kidneys.—Hartley's blood was examined at other periods, when not suffering from any acute attack, and uric acid was always found in it in considerable quantities. His urine also was always very deficient in uric acid, scarcely ever allowing it to be deposited when a strong acid was added, unless very considerably concentrated by evaporation: the other organic solids, however, were not much deficient, for frequently, on examination, it was found that the amount of urine varied from 40 to 45 oz. while its specific gravity was 1014, and that it contained, of

Solids, in the 1000 parts	31·5
Urea	12·5
Other organic compounds	13·5
Fixed salts	5·5

Thus it appears that the kidneys had almost entirely lost their power of excreting uric acid, but not the other solids of the urine.

The uric acid is, however, frequently thrown out of the blood by another process, giving rise to the formation of chalk-stones or gouty concretions. These always contain uric acid; and when first effused appear in the form of a milky fluid, from which the watery portion afterwards is absorbed.

Lehmann gives the following analysis of a deposit on the metacarpus:—

Urate of soda	52·12
Urate of lime	1·25
Fixed salts	14·16
Cellular tissue, water, &c.	32·47
	<hr/>
	100·00

Lehmann found in such deposits innumerable four-sided prisms of urate of soda. But although the analysis of them gives fixed salts, and other matters, yet when first effused they

consist only of a clear fluid containing multitudes of crystals of urate of soda, and it is to the reflections from the surfaces of these crystals that the opacity of the fluid is owing: the phosphate of lime, found in large quantities in some gouty concretions, is probably due to an after deposition from the occurrence of common inflammation around the parts. The appearance, under the microscope, of a drop of fluid effused under the cuticle, in Hartley's case, and of a small quantity of the concentrated watery solution of his serum, was almost identical.* I have examined a great number of these concretions from different parts of the body, and find that all of them consist of bundles of crystals (urate of soda) united into masses. The size of the crystals varies much, apparently depending on the degree of rapidity with which the effusion takes place. Some white matter deposited on the metatarsal bones of a gouty patient, under the microscope, gave evidence of being entirely composed of very minute crystals of this salt.†

It thus appears that sometimes, when the kidneys have lost their power of excreting uric acid, parts in and around the joints, and in other situations, often perform that function vicariously.

4th. *In gout, the blood sometimes contains a little urea (no albumen being present in the urine).*—The alcoholic solution of the serum of Hartley's blood was examined, and found to yield urea. When crystallized with nitric acid,

1000 grains of serum gave of nitrate of urea 0·03 grain.

I have not yet been able to crystallise urea from the blood in other cases of gout, but as it exists in such minute quantities, it may frequently escape detection; perhaps the urea being retained in *small* quantities in the blood, may explain one of the symptoms of gouty inflammation, viz., the frequent presence of slight œdema; since this symptom is so constantly produced when the blood contains a *large* amount of urea, as in cases of Bright's disease.

* Plate I. figs. 2, 3.

† Plate I. fig. 4.

Having obtained uric acid from the blood in all cases of gout, I next examined that fluid in other diseases, and also in health. The blood, which I selected for the purpose of discovering whether this acid exists in its healthy state, was usually procured from patients suffering from slight headache, or some other very trifling affection, yet of sufficient importance to make them apply for relief.

1000 grains of serum, from such blood, specific gravity 1029, gave of uric acid 0·007 grain.

Again, from the blood of a girl *æt.* 19, apparently in good health, but complaining of headache,

1000 grains of the serum gave a *trace* of uric acid, but too small to be weighed.

In two cases of patients suffering from slight paralysis, and in an ill-conditioned habit of body,

1000 grains of serum gave of uric acid 0·010 grain.

The blood of the sheep was next examined.

1000 grains of serum gave *no trace* of uric acid,

and this acid forms no part of their urinary secretion.

Afterwards, the blood from the pigeon, whose urine consists entirely of urate of ammonia,* was analysed.

1000 grains of serum gave *no trace* of uric acid.

It appears, then, from these experiments, that in health (or tolerable health), uric acid can be detected in the blood of the human subject; perhaps its quantity may vary with the length of time which has elapsed between taking food and the abstraction of the blood. It also appears, that when the function of excretion is very perfectly performed, no trace can be detected, although, as is the case with birds, the amount of uric acid formed in the system is very large.

The blood in *acute rheumatism* was next examined, for the purpose of seeing the relation between this affection and gout,

* Under the microscope, the urine presents the appearance shown in Plate I. fig. 5.

two diseases which have usually been considered as nearly allied.

The results which I obtained appear to indicate that—

In rheumatism, the blood contains no more uric acid than in health; and no urea can be detected in 1000 grains of serum.

Many cases were taken to prove this conclusion.

An in-patient (Friend), suffering from acute rheumatism, with most of the large joints affected.

1000 grains of serum gave only a trace of uric acid, too small to weigh.

A male patient (Exley), with acute rheumatism. The right wrist inflamed the day before the bleeding; the knee for two or three days previously. A buffy coat on the clot, about one-third of an inch thick.

1000 grains of serum gave traces of uric acid, but the quantity too small for weighing.

A male patient (Barret), with acute rheumatism; blood very much buffed, and cupped.

1000 grains of serum gave of uric acid a mere trace, too small to weigh.

A girl (Holloway), with acute rheumatism, who had lived low for some time.

1000 grains of serum gave no indication of either uric acid or urea.

A male patient (Smith), with acute rheumatism, affecting the knees, ankles, elbows, and wrists: the clot firm, with a buffy coat about three-eighths of an inch thick, and cupped: serum alkaline; specific gravity 1028.

1000 grains of serum gave of uric acid numerous crystals, but they could not be collected for weighing.

1000 grains of serum gave no trace of urea.

This patient had been in good health previous to the attack.

In acute rheumatism there is no evidence of any deficient

“uric-acid-secreting” power in the kidneys, and the urine is also generally loaded with urea.

Blood from patients suffering from *Bright's disease*, and *albuminuria after scarlatina*, was then examined: the results of these analyses appear to show, that—

1st. *Uric acid is always present in the blood in albuminuria. The quantity, however, greatly varies: when the functions of the kidneys are much impaired, it exists in quantities almost as great as in gout; in other cases its amount is small, but it usually exceeds that found in ordinary blood.*

2nd. *Urea always exists in large quantities in this blood, (a fact which has been long since proved,) and no relation is found between the amounts of urea and uric acid.*

3rd. *The kidneys are always deficient in their power of throwing off urea; but with regard to the uric acid, their excreting function may be impaired or not.*

In a male patient, (McCarty,) suffering from albuminuria, with anasarca (an advanced case),

1000 grains of serum gave of uric acid 0·037 grain.

Much urea was contained in the blood.

In a male patient (Peter Skelley), suffering from albuminuria, with anasarca, the disease not being far advanced, œdema of legs not having been noticed more than a few weeks.—Specific gravity of serum 1028.

1000 grains gave of uric acid 0·005 grain.

1000 grains gave of urea (nitrate) 0·192 „

1000 grains, at another examination, gave of nitrate of urea 0·145 „

The urine from this patient usually contained a precipitate consisting of uric acid crystals and the lining of the tubuli; a further quantity of uric acid was precipitated on the addition of a strong acid.

In Richard Cole, a patient with albuminuria and anasarca,

1000 grains of serum (specific gravity 1026) gave of uric acid 0·012 grain.

In Mary Cockburn, æt. 9, with albuminuria after scarlatina,

1000 grains of serum gave of uric acid 0·027 grain.

The blood also contained a large amount of urea. The urine was very albuminous, and the anarsarca considerable.

I may remark, that during the evaporation of the serum of blood in albuminuria, a peculiar *odour* of urine was frequently detected; this was not observed in healthy serum, or in that taken from gouty or rheumatic patients. Some of the *colouring* matter of the urine seemed, however, to be thrown down with the uric acid in all cases.

The results of these experiments on the condition of the blood and urine, prove that uric acid is not a product of the action of the kidneys, as is frequently supposed, but that it is merely excreted from the system by these organs. They also appear to indicate that the excreting function of the kidneys, with regard to the solid portion of the urine, is not simple, but that the urea and uric acid are separately eliminated; also that one of these functions may be impaired or destroyed, the other remaining entire. With regard to the solid and fluid portions of the urine, Mr. Bowman has already shown the probability of different structures in the kidneys being concerned in their excretion.

It appears also probable that as, in albuminuria, the "urea-excreting-function" being chiefly impaired, we find a vicarious discharge of this body in the dropsical effusions; so, in gout, the "uric-acid-excreting function" being defective, the chalk-like deposits are produced, by a similar vicarious discharge of urate of soda.

Gout would thus appear partly to depend on a loss of power (temporary or permanent) of the "uric-acid-excreting function" of the kidneys; the premonitory symptoms, and those also which constitute the paroxysm, arising from an excess of this acid in the blood, and from the effort to expel the "materies morbi" from the system. Any undue *formation* of this compound would favour the occurrence of the disease; and hence the connection between gout and uric acid, gravel and calculi; and hence, the influence of high living, wine, porter, want of exercise, &c., in inducing it.

This hypothesis would also explain two facts which have been regarded as militating against its humoral pathology; viz. the *hereditary* nature of the affection, and also its frequent occurrence in *low states* of the system; for we can understand that the peculiarity of the kidney, with reference to the excretion of uric acid, may be transmitted; and, likewise, that when the function in question is permanently injured, it will not require an excessive *formation* of the acid to cause its accumulation in the blood.

Dr. Todd's observations on what he terms the "gouty kidney," appear to favour this view. This hypothesis would also remove gout from acute rheumatism, for no excess of uric acid was found in the blood in this affection. Again, if we take into consideration the causes of the latter affection and the subjects in whom it occurs, we must be led to consider the two diseases as analogous only as far as they both affect similar structures. What greater analogy exists between gout and rheumatism, than between any two skin diseases?

In conclusion I must beg to express my thanks to Dr. C. J. B. Williams for his kindness in affording me every facility for the prosecution of my researches in patients under his care, and also in communicating this paper to the Society.

The following preparations illustrative of the paper were exhibited when it was read.

1. Uric acid from blood in gout.
2. Urate of soda from blood in gout.
3. Uric acid from blood in health.
4. Uric acid from blood in Bright's disease.
5. Chalk-like deposit from great toe.
6. Pieces of deposits (tophaceous).
7. Deposit on cartilages of tarsal bones.
8. Nitrate of urea from blood in gout.
9. Nitrate of urea from blood in Bright's disease.

Postscript, July 26, 1848.—At the discussion which ensued after the reading of the above paper to the Society, some remarks were made which implied that I was understood as considering gout to be entirely dependent on a deficient power in the kidneys for the excretion of uric acid; such, however, is not my opinion: and, at present, I do not wish to advance any hypothesis as to the cause and nature of gout, considering that many further researches should be made on the subject before a theory of the disease could be advanced with safety. The conclusions which I stated were such as seemed to me, at once, to arise from the data given.

The discovery of uric acid in blood, and the finding that its amount is much greater in gouty than in healthy blood, and that the kidneys may temporarily or permanently lose their power of excreting this acid, are facts to my mind important.

With regard to the *weights* which have been given, I may observe that in the earlier determinations they doubtless were below the real quantities, a circumstance which arose from the watery solutions of the serum not being sufficiently concentrated, and from sufficient time not being allowed for the deposition of the uric acid. In the experiments now made, I do not collect the crystals until after forty-eight hours have elapsed. Such slight errors are however unavoidable in new investigations on any subject.

Since the above paper was written, some further experiments have been made.

A young man, *æt.* 28, died of phthisis. He had suffered from gout for eight years, had many tophaceous deposits upon his hands and feet, some of which had taken place a few days only before his death. The blood used for the analysis was taken a few hours after death.

1000 grains of serum gave of uric acid 0.175 grain;
a greater amount than I had ever obtained.

In some other cases of old standing gout, the patients being afflicted with extensive depositions of chalk-stones, the urine was examined to ascertain the quantity of uric acid.

In one case, a female,

1000 grains of urine, specific gravity 1010, gave *no* trace of uric acid, although much evaporated.

In another case, a man,

1000 grains of urine gave only 0·02 grain of uric acid.

These results confirm those stated in the paper.

I have also lately many times repeated the analysis for detecting uric acid in healthy blood; and have always succeeded in finding it, even when the individuals were in most perfect health, and were only bled for the purpose of experiment. I have also succeeded in finding *urea* in *perfectly healthy human blood*.

In one case,

1500 grains of serum gave of nitrate of urea 0·015 grain.

The detection of urea in healthy human blood will easily explain why it was found in some cases of gout; and, probably, urea may sometimes be retained in the system to a considerable extent, without the existence of any such disease of the kidneys as is made known by the presence of albumen in the urine.

Very lately I have examined the blood of a patient who came to me for an affection which he called gout, but which, for many reasons, viz. the history of the case, the subject of the disease, the parts affected (the side of the foot and hands), I considered to be rheumatism. The serum gave only traces of the presence of uric acid, which could not be weighed. The solution of the blood had also certain peculiarities which I have observed in rheumatism, but not in gout.

Might it not, in doubtful cases, be possible to determine the nature of the affection from an examination of the blood?

Some of the results contained in the paper appear to me to be interesting in a physiological as well as pathological point of view; especially the occurrence of opposite conditions of the blood and urine, as we find—

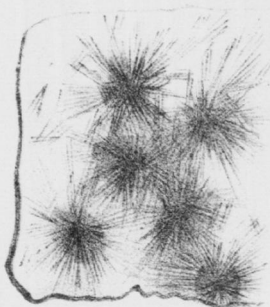


Fig. 4.
L. M. P. 670.

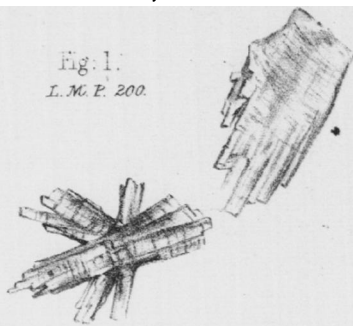


Fig. 1.
L. M. P. 200.

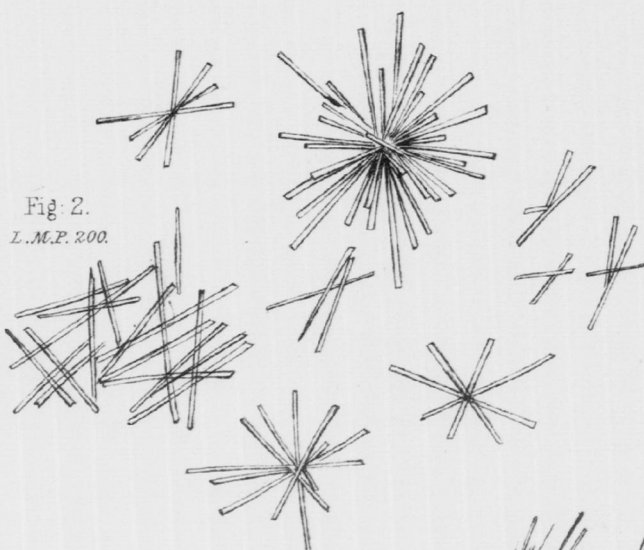


Fig. 2.
L. M. P. 200.

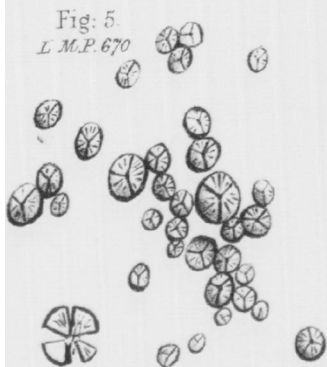


Fig. 5.
L. M. P. 670.

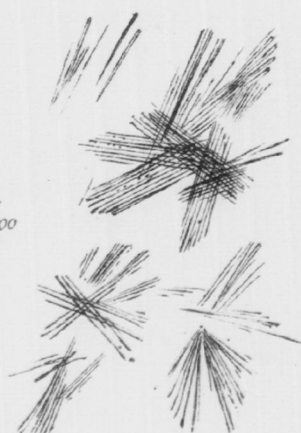


Fig. 3.
L. M. P. 200.

In certain cases (Bright's disease),

Blood—rich in *urea*, but with little *uric acid*.

Urine—deficient in *urea*, but not so in *uric acid*.

In other cases (gout),

Blood—with little or no increase of *urea*, but rich in *uric acid*.

Urine—with little or no decrease of *urea*, but very deficient in *uric acid*.

At some future time I hope to bring before the Society some further researches on the pathology of uric acid.

EXPLANATION OF PLATE I.

Fig. 1. Uric acid from blood.

Fig. 2. Urate of soda deposited from the solution of the watery extract of gouty blood.

Fig. 3. Urate of soda from chalk-stones in gouty subjects.

Fig. 4. Urate of soda deposited on articular cartilage.

Fig. 5. Urine of the pigeon, exhibiting the form in which the urate of ammonia occurs.