URINARY CRYSTALS AND CALCULI:

BEING

OBSERVATIONS ON SOME OF THE CIRCUMSTANCES
DETERMINING THE FORMS OF CRYSTALLINE
DEPOSITS IN URINE,

AND

ON SOME OF THE CONDITIONS UNDER WHICH RENAL
AND VESICAL CALCULI ARE PRODUCED.

BY

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To Mr. George Rainey, my former teacher and deeply respected friend, are owed the inspirations which have led to this and similar investigations. His perfectly original observations on molecular coalescence constitute, as I believe, a discovery the value of which will be abundantly proved in time to come. In the present memoir I record some results of a pathological extension of his physical and developmental researches.

The starting-point of the observations and inferences recorded in this paper is that uric acid assumes remarkably different forms accordingly as it is deposited pure from solution in distilled water on the one hand, or coloured and impure from urine on the other. I beg, leave, therefore,

in the outset to remind the Society of the general nature of this difference.

If some of the colourless or nearly colourless uric acid prepared from guano or serpent's urine be boiled in distilled water, and, after filtration, be left to crystallise from solution, the acid will be found in tabular crystals. Some of the tablets will be oblong in outline, and about six times as long as thick; such tablets, being perfectly transparent and homogeneous, may be compared to the oblong pieces of glass sold as paper-weights; they are the "oblong-square plates" of Dr. Thudichum.¹ Others will be much thinner, much longer, six-sided in outline, with acute points, and may be compared to the common form of glass hand-plates on doors. There will be a number of intermediate forms connecting these extremes. It will be important to notice that the tablets remain generally separate and distinct from one another, or, if here and there aggregated, do not form regular star-shaped masses of crystals radiating from a common centre.

Uric acid deposited from urine differs from the pure uric acid in colour, form, and aggregation.

The crystals are always of a strong yellow or brownish colour, and are most commonly rhombohedra or modifications of the rhombohedron in which that form is easily made out. Prout ('Stomach and Urinary Diseases,' 1840) gives two figures of uric acid. "The first represents," to use his words, "the ordinary appearance of lithic acid crystals under the microscope. The crystals are rhomboidal prisms, thin, transparent, and of a yellow colour." Fig. 2 represents "rhomboidal prisms of lithic acid, thicker than those depicted in the preceding figure, and, in some instances, approaching to the cubic form. The cubic is much more rare than the rhomboidal variety of crystal." There is here no mention of the tabular forms. Dr. Beale, in his well-known work on 'Urinary Deposits,' describes or figures more than thirty forms of uric acid. The edition of 1869 does not contain

¹ 'Pathology of the Urine,' 1858, p. 80.

one drawing of the perfect oblong tablets and only one of hexagonal crystals. A descriptive note beneath the latter points out that this form occurs in urine very rarely.

There must exist, therefore, in urine causes leading to a complete turning away of uric acid from its pure crystalline form. The change, too, is in a definite direction. The faces and angles of a crystal of urinary uric acid are almost always curved and rounded. Such a crystal is clearly the resultant of the operation of two distinct influences,—of crystalline polarity, under which flat surfaces and sharp angles are determined, and of molecular coalescence, in which polarity is lost and particles are arranged in spherical masses by virtue of their unimpeded mutual attractions. Furthermore, in urine the crystals are very frequently gathered into larger glomeruli, to which such names as “gravel” and “cayenne pepper grains” are given. These, on examination, are found to be regularly constructed of radiating rhombs or prisms. The difference, therefore, between the *urinary* acid and the *pure* is very pronounced. So also is the difference among the forms of urinary acid. From Prout’s two figures the record has gone on growing till as many as forty or fifty distinct varieties can be reckoned. Dr. Miller, Dr. Beale, and other writers on micrology and chemistry have suggested that the substances associated with uric acid in urine are the determining causes of the several differences; and the original observations of Mr. Rainey on the influence of colloids upon crystalline form—observations recently confirmed in a remarkable way by Harting’s independent researches—have pointed the way to a solution of the problem. In the ‘St. Thomas’s Hospital Reports’ for the year 1870 I have published an account of a number of experiments and observations which led me to the following general conclusions:

1. That, in the presence of albumen and other colloids, uric acid was deposited in small, thick, subcubical crystals with much-curved faces, or in some kind of dumb-bell, or

in some kind of spheroid. The forms plainly tended to sphericity.

2. That, in the presence of grape sugar and other crystalloids, the acid was deposited in large tabulate or foliaceous crystals with flat sides and sharp edges.

The first experiments were made with artificial solutions from which, in each case, everything but pure acid and one associate substance was excluded; but at the end of the paper a few drawings were given of forms of uric acid taken from albuminous and sugary urine respectively. The figures confirmed in a general way the principle obtained in the exclusive experiments, but left evidently much to be explained.

The present communication relates the results of further investigations, affecting not only uric acid, but also urate of ammonia, oxalate of lime, and triple phosphate.

I. It appeared to me that one of the first subjects of inquiry should be the cause or causes of the difference between the pure and the urinary form of uric acid. Four groups of substances to which determining influence might probably be referred were to be found in urine,—mucus, urea and extractive, colouring matters, and salts. Mucus among these seemed most likely to mould uric acid. Mucus is a colloid, prone to decomposition, and active in promoting the decomposition of organic substances associated with it in solution. On the other hand, mucus in its fresh state is not actually held in solution in the urine, but merely suspended in a very much gelatinised condition. The first experiment consisted in removing the mucus from urine and observing the crystals of uric acid deposited after such removal. Absolute alcohol was added in equal bulk to fresh urine, of specific gravity 1020, clear, of a light sherry colour, and free from sugar or albumen. After standing some time the mixture was filtered, the mucus and some of the salts being thus removed from the liquid, which was afterwards heated to expel the alcohol. After all the alcohol was driven off, the remaining liquid was diluted with distilled water till the specific gravity of 1020 was restored.

The liquid was next divided into four portions. To one a few drops of hydrochloric acid were added; in a second a few grains of pure uric acid were dissolved by the aid of heat; in a third and fourth washed uric acid from urine was dissolved, with and without the addition of two drops of glacial acetic acid. The four solutions were clear, and possessed the characteristic colour and smell of urine. Crystals were obtained from all four; they were in each case small rhombohedra with rounded angles, very much like those represented in Prout's first figure. To complete the experiment, the precipitate of mucus, &c., remaining upon the filter was washed with distilled water till the filtrate was colourless. The precipitate was then washed off the filter-paper and digested in three ounces of distilled water with three drops of hydrochloric acid; one ounce of a solution of pure uric acid in boiling water was added. The crystals deposited from this mixture were small; they were partly thick rhombohedra and partly short four-sided prisms with pointed ends, having therefore often a six-sided outline. They were not aggregated in any way, and were not adherent to the vessel.

The removal of the mucus from the urine, therefore, did not decidedly affect the form of the individual crystals. But their mode of deposit was different from the mode of deposit of uric acid from natural urine. They were caked on the sides of the vessel, and had to be detached for examination, and they were not in spherical radiating masses. Uric acid deposited from urine is rarely caked in this way, and is only in part attached to the side of the vessel. It usually lies in a loose powder among the mucus at the bottom of the vessel, and it is most commonly in radiating masses. The mucus probably arrests, by mechanical opposition, the fall of the crystals as they are formed in the solution, and places them in a favorable position for the addition of fresh crystalline matter on all sides of them. The spherical form of the crystalline masses indicates, I believe, more than a mechanical influence; indicates the molecule-disturbing influence of a colloid. The

complementary experiment proves that the mucus does, in fact, affect the form of the crystals, and that the affection is like that of other colloids. But the necessary processes of the experiment cook the mucus, and tend decidedly to weaken its power. It is no more the same mucus that works in natural urine than boiled salt beef is living flesh. It is less putrefiable than fresh mucus, and has therefore less energy in transformation. If, thus weakened, it is capable of transforming uric acid, its natural influence must be considerable.

Supposing the uric acid of human urine and the uric acid having another source to be the same substance, the experiments showed conclusively that mucus with earthy phosphates, &c., was capable of impressing upon it the rhombohedral form, and that urine deprived of its mucus and earthy phosphates had the same power. It was necessary to pass to further exclusions.

Uric acid spontaneously deposited from urine was separated from the other constituents of urine by decantation and repeated washings. It was then thrown upon a filter and washed with distilled water containing a little acetic acid. There would remain then on the filter the uric acid, with perhaps a trace of mucus and epithelium. The prevailing forms of crystal in the uric acid used are drawn in fig. 2. Boiling distilled water was poured upon the filter, and the filtrate was collected and cooled. The solution was of a golden sherry colour, and yielded a large crop of yellow crystals.

Four further recrystallizations were made, each time with loss of colour, and the forms accompanying each loss of colour were noted and drawn (figs. 3, 4, 5 and 6). In the last all colour had disappeared, and the tabular forms of the pure acid were obtained in great beauty.¹ Separate

¹ Uric acid and urates are notable among urinary deposits for carrying down with them the colouring matter. They seem to take the dye much as animal fibres take dyes; and uric acid at least appears to be changed in its crystalline polarities by the dye in a degree corresponding to the amount of dye present with it in solution.

experiments were afterwards made with the various salts of urine. The influence of urea was known before to be in favour of the tablets, and the salts made little or no difference either way. The possibility of some of the constituents of the extractive combining with uric acid and modifying its form had occurred to me; but the experiments noted, and the fact that the form of the acid is the same when deposited in the presence of considerable excess of other acids, were against the supposition.

The final conclusion was that mucus and colouring matter were certainly both agents in determining the ordinary urinary form of uric acid, and that they were probably the sole agents.

ii. *Forms of uric acid in albuminous urine.*—These are always different from the forms found in ordinary urine, but they differ remarkably among themselves. They are small, rounded, and compact, presenting many gradations from the subcubical crystal with curved sides, such as is drawn in Prout's second figure, to the sphere. I have not been able to trace any connection between the variations of form and variations in the quantity of albumen present. Neither have I any observations recording the influence of isomeric varieties of albumen. Urea, however, does appear to be one among the causes of variation. Urea alone, in solutions of specific gravity less than 1040, promotes the formation of large, very thin plates of uric acid, and numerous observations indicate that a large proportionate quantity of urea in albuminous urine constitutes *pro rata* an obstacle to the sphere-forming process.

Thus, in albuminous urine of specific gravity 1027 or upwards, yielding a free precipitate of nitrate of urea, on the addition of an equal bulk of nitric acid and subsequent cooling to 60° Fahr., I have constantly found the forms shown in the adjoined figures (fig. 7). These have been drawn for me by Dr. Donkin, who was kind enough to help me in a series of observations made at St. Thomas's Hospital. They may be arranged in three groups:—

1. Small, thick, sharp-edged rhombohedra; almost cubical.

2. Rhombohedra having the obtuse angles rounded, and the axis joining the flat sides lengthened, whereby a long cylinder with flat ends is produced. (Compare fig. 3, p. 339, 'St. Thomas's Hospital Reports,' 1870.)

3. Rhombohedra having the margins of the flat sides swollen and rounded, the crystal between being thinned and marked with diagonal lines. (Compare fig. 5, a, d, and e, at p. 340 of the 'Reports,' above quoted.)

Secondly, with a lower specific gravity (1015 to 1021) the forms drawn in fig. 8 by Dr. Donkin, and in fig. 9 by myself, occur. The cylinders are thicker and shorter.

Lastly, in albuminous urine of still lower specific gravity (1009 to 1015) there are found, associated with very small rhombohedra, tub- or cask-shaped crystals (*doliola*). The rhombohedron is still to be detected under the disguise of the *doliolum*. The alternate obtuse and acute angles are rounded off, making the section parallel to the flat end-faces first lozenge-shaped, then broadly ovate, then circular. A deeply shaded line frequently runs like a hoop across the middle of the cask, and this is again bisected by faint diagonal markings. The ends of the *doliolum* are rarely quite flat. Sometimes they are excavated between the diagonals, and become a double cup (*ἀμφικύπελλον*) like the wooden egg-cups to be seen in some country inns. Sometimes the head of the cask is projected into a bundle of spicular crystals, the substance of the cask giving at the same time indications of the formation of longitudinal lines of crystallisation (fig. 10). Sometimes the cask is so short and its ends are so rounded that it has become a sphere with a long spike projecting from each end. The perfect spherical form of uric acid is not often found in urine; the dumb-bell is even more rare. I have, however, found both in albuminous urine of very low specific gravity. The spheres are always very small and homogeneous when deposited in urine. But in experiments made with watery solutions of egg-albumen I have obtained large and beau-

tiful spheres, some equalling fat-cells in size and displaying a brilliant radiating crystalline structure. I conclude that even in small quantities urea still hinders the completion of the collospheres of uric acid. Urea is known to modify by its presence the form of the crystals of chloride of sodium, and its influence may be in part merely such an influence as we have seen it exerting on uric acid in exclusive experiments. It may also, like saline matter in solution, retard the decompositions of albumen.

iii. *Forms of uric acid in sugary urine.*—Here the crystals tend to be tabular. Whereas with albumen the acute angles grow larger and the obtuse angles smaller till equality is attained and the cube prevails, with sugar the obtuseness of obtuse angles and the acuteness of acute angles are increased; whereas with albumen the axis joining the flat sides of the rhombohedra is lengthened, with sugar that axis is shortened. Two forms of uric acid may be noted in connection with sugar in urine; one oblong or square in outline, with fine chiselled ends and thicker middle; the other much less common, with flat parallel surfaces and diamond-shaped or hexagonal outline. Drawings of both are annexed (figs. 11 and 12).

iv. *Forms of uric acid in purulent mucus.*—Colloidal substances allied in composition or reactions to purulent mucus contribute, if my observations are correct, to the formation of stone in the kidney and bladder. The urine of chronic cystitis, abounding in purulent mucus, is mostly advanced in decomposition far enough to have become ammoniacal, and filled with precipitated phosphates at the time when examination has been possible. Urine of this kind, secured early, and, after gentle warning, treated with a few drops of hydrochloric acid, gives very interesting forms. In the fluid portion of such urine rhombs and rosettes are formed just as in natural urine. In the mucus, cubes and rounded bodies and dense stalactitic agglomerations of uric acid are deposited, the precipitate within the mucus being much larger than in the surround-

ing fluid. Artificial conjunctions show very clearly that the actively changing colloids entering into the matter of purulent mucus exert a strong converting and cementing influence on uric acid. For instance, the stringy sediment from some cystitic urine was separated on a filter, and treated successively with liquor potassæ, hydrochloric acid, and distilled water, until no crystalline forms could be seen under the microscope. The residue, flaky and much less cohesive than before, was heated in a solution of pure uric acid. The liquor being cooled was found to be full of six-sided and long thin halbert-shaped crystals. The mucus, where thin and but little cohesive, contained small subcubical and rounded forms; where thicker and more gummy it contained the same forms, with the addition of a stalactitic and columnar growth of large irregular crystals with rounded margins. These sticky flakes were hard and gritty when compressed between the fingers, and were practically the beginnings of calculi formed under one's eye. The larger columnar crystals, resembling nothing that I had seen in urine before, find their counter-part in a drawing by Dr. Vandyke Carter, of "crystals forming columns," from a urethral calculus. This drawing occurs in fig. 5 of Plate I, illustrating Dr. Carter's valuable book on the "Microscopic Structure and Mode of Formation of Urinary Calculi." The main point demonstrated in that book by Dr. Carter is, that in calculi the crystalloids are found in spheroidal forms, or in forms tending to be spheroidal associated with a colloid bed. The form and the cohesion of the crystalloids are explained according to the principles of Mr. Rainey's theory of molecular coalescence. Dr. Carter suggests that "an excess of mucus, perhaps altered in character, in the urinary passages, or the effusion of albumen, fibrin, or blood and the like, say from congestion of the kidneys, or from irritation of the urinary tract, would furnish a colloid medium with which uric acid, the urates or oxalates, themselves perhaps in excess would combine in the manner before described." Mucus in particular commends itself to Dr. Carter as a colloid most

likely to be actively concerned in the formation of calculi. The purulent mucus poured out in irritation of the urinary passages should certainly be just the substance to effect the formation of calculi, if the inferences which I have elsewhere drawn from the observed influence of colloids upon oxalate of lime and other salts are correct.¹ A fact upon which I was led to lay great stress was, that whereas oxalate of lime was turned into dumb-bells and spheroids by gelatin, the conversion was much more active and complete where the gelatin was undergoing decomposition and when the temperature was raised. In experiments I have not had opportunities of observing uric acid deposited at the temperature of the body. But it is of course quite certain that under particular circumstances uric acid is frequently deposited in the urinary passages, and is therefore deposited at temperatures ranging near 100° Fahr. I entertain no doubt whatever that if uric acid in the act of crystallisation, or during its stage in the body after crystallisation, meet, at such temperature, with purulent mucus in full activity of molecular change, the formation of calculous bodies, more compact than those which I have been able to obtain outside the body at ordinary atmospheric temperatures, will follow. Two thirds of all urinary calculi are in bulk composed of or start from concretions of uric acid. Writers on the stone have, therefore, directed their attention to the causes of the formation and deposit of uric acid as the most important considerations in explaining the occurrence of calculi, but if Dr. Carter's examinations of calculi and my experiments, here and elsewhere related, have any value, it is necessary to take into account besides the deposit of uric acid the existence of conditions sending colloids into the urine. The pebbles of the concrete would not hold together without the cement to bind them, and act on their surface. To make calculi of uric acid without colloids would be as hopeless a task as making ropes of sea sand. Therefore, if the causes of the varying prevalence of calculus disease in different communities and

¹ 'St. Thos. Hosp. Rep.,' 1871.

regions are to be fully and usefully examined, such subjects as constitutional proneness or indisposition to vesical catarrh, habits of life, diet and regimen, or local conditions of soil, water, and climate which can hinder or promote the secretion of mucus, or the occurrence of irritation in the urinary tract, must be very carefully treated. And if such observations be applied to practice, we may hope to find that the prevention of stone becomes partly possible through the prevention of the local conditions which constitute the soil in which it is sown and grows.

v. *Forms of urates*.—In many cases I have observed small brown spherules, soluble at moderate temperature, in albuminous urine depositing uric acid. They dissolved much more readily than the acid, and were either urate of soda or urate of ammonia.

In ammoniacal urine containing much purulent mucus I have frequently seen urates in three forms: 1, perfect spheres; 2, spheres with regular radiating raphides; 3, spheres with an investment of branched and irregular or bristly raphides ("hedge-hog" crystals) (fig. 15).¹ I have procured these in great abundance by adding to an acid urine containing large quantities of urate of ammonia the stringy mucus from ammoniacal urine of chronic cystitis. The mixture being first warmed to dissolve the urates, they are found, after cooling, deposited in two forms; within the mucus as spheres and hedge-hog crystals, elsewhere as granules. I have also often observed the spherules of urate of ammonia which have been described by Dr. Roberts as formed in decomposing urine, and have no doubt of their being formed under the influence of the chemically-active mucus.

A spherical form of urate of soda was figured, at first under the name of urate of ammonia, by Dr. Golding Bird in his urinary deposits. He described it as follows:—"Spherules of urate of ammonia with crystals of uric acid adhering." And he stated that this form was occasionally observed in albuminous urine occur-

¹ "Thom-apples" of German authors.

ring in scarlatina. Dr. Thudichum, Dr. Beale, Dr. Roberts, and Drs. Ultzmann and Hofmann, have since figured similar forms. There is no further note of albumen, but the associated conditions were usually febrile attacks in children. Drs. Thudichum and Roberts have added a third condition, evidently of much importance—delay of the urine in the urinary passages. In all the cases where any history or explanation is given there have been states favouring the presence of colloids, either of albumen or of mucus, or of other results of rapid febrile action. And delay in the urinary passages, keeping the urates long in contact with putrescent colloids, at a temperature most probably above 100° Fahr., must have added a very strong impulse to the forces determining spherical form.

The urates, though the most common of all deposits from cooled urine, enter much less frequently than uric acid into the composition of calculi. Their comparative solubility, and their habit of assuming a fine molecular (amorphous?) state without running into masses, will account for this. Their solubility has been shown by Dr. Bence Jones¹ to be increased by the presence of chloride of sodium, distilled water being rendered capable of taking up double the quantity of urate of ammonia when the chloride is added in small quantity. The same addition prevents urate of ammonia from taking the crystalline form. Dr. Bence Jones states, that if urine is added to a warm solution of needles of urate of ammonia in such small quantity as not to cause any discoloration of the subsequent deposit, that deposit is always amorphous. He traces this to the chloride of sodium. Whether the colouring matter, which adheres with such tenacity to the urates that it is best obtained from them (Golding Bird, Thudichum), affects the form of urates, I have not as yet determined.

vi. *Oxalate of lime*.—Dr. Beale has figured dumb-bells of oxalate of lime in casts of urinary tubules. His remarks upon these figures, indeed, directed my thoughts to the pre-

¹ 'Trans. Roy. Med.-Chir. Soc.,' 1844, p. 102.

sent investigation. Following up Dr. Beale's¹ hints, I have shown elsewhere that oxalate of lime is much modified in its crystalline form by the presence of colloids, exchanging the octohedron for various tablets, dumb-bells, "wheat-sheaves," and spheres.²

I have a few notes of modifications of oxalate of lime in urine. One instance is so remarkable that I must quote it at length. A friend sent me one day a slide of beautifully mounted crystals of oxalate of lime; mixed with variously altered octohedra were multitudes of large lustrous "wheat-sheaves," or crystalline dumb-bells. He told me that they had been mounted by the gentleman who had passed them. This gentleman was subject to violent attacks of headache, during which he passed very turbid urine. Being accustomed to make much use of the microscope, he examined the deposit for himself, and found these beautiful crystals. On receiving the specimen I wrote at once to ask if the urine contained albumen or mucus, and was informed that during the attacks the urine did contain albumen, and that it was free from albumen at other times. Dr. Thudichum gives figures of dumb-bells of oxalate of lime from albuminous urine.

I adjoin two more illustrations of altered oxalate from urine. The first (fig. 17) of oxalate taken from slightly acid urine of sp. gr. 1016, containing both albumen and stringy mucus; the second (fig. 18) from neutral urine of sp. gr. 1021, containing much mucus and vaginal epithelium. There was no sugar present in either case.

To mould oxalate of lime into calculi would seem to require denser colloids than are usually present in vesical urine, and it is probable that the beginnings of oxalic calculi take place in the recesses of the kidney, among less diluted colloids. Certainly, in my own experience I have found the small calculi passed with so much pain from the kidneys much more frequently composed of oxalate of lime than are vesical and urethral calculi.

¹ 'Urine and Urinary Deposits,' 2nd edit., p. 347, W. S. C.

² 'St. Thos. Hosp. Rep.,' 1871.

vii. *Triple phosphate*.—The crystals of this and other phosphates are much less influenced by colloids than the substances with which I have been so far dealing. In urine containing much albumen or purulent mucus I have often found crystals rounded at the angles and altered considerably from their natural beauty. But only a part of the crystals have been so changed, and there has been no observation of spherical or agglomerated forms. By the use of a temperature a little higher than that of the body I have been enabled to effect the moulding of these crystals into calculous masses. If ammoniacal urine of chronic cystitis containing plenty of purulent mucus be digested for twenty-four hours at a temperature ranging between 100° and 110° Fahrenheit, the mucus is afterwards found full of spheroidal forms, many of them very large. The reactions of these indicate them to be in part phosphates, but the presence of urates deprives the experiment of conclusiveness. The mucus must be separated, treated with caustic alkali and hydrochloric acid, and after good washing be placed in a slightly acid solution containing triple phosphate. A small excess of ammonia is added after a while, and the mixture is then digested for twenty-four hours at 110° Fahrenheit. The flaky and much coagulated mucus is found then to contain rosettes of crystals almost identical in form with certain figures given by Dr Vandyke Carter at Plate IV, fig. 2 *b* and. fig. 3 *a*, *b* of his book. Dr. Carter's crystals were from the outer layer of a small pale calculus and from the nucleus of a small pale calculus respectively.

viii. *Influence of albumen on nitrate of urea*.—Nitrate of urea, as is well known, can often be obtained from urine without previous concentration. The crystals thrown down from urine of a specific gravity exceeding 1037 after the addition of an equal bulk of nitric acid are shining flakes, often cohering in irregular masses and distinctly darker than the urine. If urine of such specific gravity contain a moderate quantity of albumen, the addition of an equal bulk of nitric acid causes the solution

of the first precipitate, and a perfectly clear liquid is obtained. The process of crystallization is in this case very different. Instead of dark flakes, tiny globes of a light colour are suddenly seen suspended at several points in the liquid and grow rapidly under the eye. They are composed of fine radiating acicular crystals, and look like little drops of fat. That albumen is the cause of this growth of spheres may be readily proved. Another portion of the fresh urine is freed from albumen by boiling, the addition of two drops of nitric acid, and filtration. The filtrate, treated as before with nitric acid, yields flaky crystals.

ix. *Bearing of the foregoing observations on microscopic morphology.*—Dr. Carter in his remarks on the formation of calculi does not fail to recognise the importance of the higher temperature of the body as a condition of the process. How far this influence is to be attributed to the unchanged movements of heat, and how far to induced molecular changes in the colloids, cannot be decided or calculated at present. Both of these will, of course, come under the head of molecular disturbances, but whether one or other form of molecular movement is more apt to blur the lines of crystallization I do not pretend to suggest. It is only necessary now to point out that heat plays a remarkable part in determining the assumption of spheroidal shape by crystalloids in the presence of colloids. I have already, in the paper referred to, shown this to be the case when oxalate of lime is deposited in albumen. Experiments with phosphate of lime and carbonate of lime in albumen have since confirmed the first inductions.

I have long felt that the present inquiry is only part of a much larger questioning of nature—of an inquiry into the causes, general and particular, by which the morphology of tissues is determined. Microscopists have been content for the most part to record the forms of the tissues with constantly increasing research and accuracy. This is undoubtedly a work of importance, indeed of necessity, but is, to

my mind, only a preliminary process, bearing to the higher morphology of the future the sort of relation borne by the Linnæan to the Natural system in Botany. There must follow a natural system, interpreting the meanings of forms, compelling form to tell the story of growth and function, recording the relations between form and substance, and proceeding to the discovery of the laws of tissue formation. The line of thought into which my observations have directed me leads to the belief that such further research will put us in possession of new methods in diagnosis and therapeutics.

DESCRIPTION OF PLATES V AND VI.

PLATE V.

- FIG. 1.—Purified uric acid. Deposited from solution in boiling water. The forms are the same with and without the addition of acetic acid. Experiment.
- FIG. 2.—Uric acid, from urine of sp. gr. 1030, containing mucus and much coloring matter, but no albumen or sugar. Observation.
- FIG. 3.—The same uric acid separated with the mucus by filtration, and precipitated from solution in boiling water. Exp.
- FIG. 4.—The same, second and third boilings; less colour. Exp.
- FIG. 5.—The same, fourth boiling; still less colour. Exp.
- FIG. 6.—Fifth boiling; no colour. Exp.
- FIG. 7.—Uric acid from albuminous urine of sp. gr. 1027 and upwards (Dr. Donkin). Obs.
- FIG. 8.—Uric acid, from albuminous urine of sp. gr. 1015 to 1021 (Dr. Donkin). Obs.
- FIG. 9.—Uric acid, from albuminous urine of sp. gr. 1015 to 1021 (W. M. O.). Obs.
- FIG. 10.—Uric acid, from albuminous urine of sp. gr. 1009 to 1015 (Dr. Donkin and W. M. O.). Obs.
- FIG. 11.—Uric acid, from sugary urine, sp. gr. 1042; no albumen; not much colour. Obs.
- FIG. 12.—Uric acid, from sugary urine, sp. gr. 1023; no albumen; very acid. Obs.

PLATE VI.

- FIG. 13.—Uric acid.—In watery fluid round mucus. Experiment.
- FIG. 14.—Uric acid.—In mucus. Exp.
- FIG. 15.—Urates (probably urate of ammonia) in purulent mucus. Obs.
- FIG. 16.—Oxalate of lime, from albuminous urine. Obs.
- FIG. 17.—Oxalate of lime, from urine containing much mucus; acid; sp. gr. 1016. Obs.
- FIG. 18.—Oxalate of lime, from urine containing much mucus and vaginal discharge; neutral; sp. gr. 1021. Obs.
- FIG. 19.—Triple phosphate. Deposited in flaky mucus at temperature of 100° to 110° Fahr. Exp.