ON THE INFLUENCE

OF

COLLOIDS

UPON

CRYSTALLINE FORM AND COHESION

WITH OBSERVATIONS
ON THE STRUCTURE AND MODE OF FORMATION OF
URINARY AND OTHER CALCULI

BY

WILLIAM MILLER ORD, M.D., LOND.
FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS IN LONDON,
OF THE LINNÆAN SOCIETY, OF THE ROYAL MEDICO-CHIRURGICAL SOCIETY, OF THE ROYAL
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AT ST. THOMAS'S HOSPITAL, LONDON, ETC.

LONDON
EDWARD STANFORD, 55 CHARING CROSS
1879

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1879

THIS WORK IS DEDICATED

TO

MY FATHER AND MY MOTHER

NOW IN THE FORTY-EIGHTH YEAR

OF THEIR WEDDED LIFE

"Illâ sunt annis juncti juvenilibus, illâ consenuere casâ.

PREFACE.

THE subject of the following Treatise has occupied much of my attention during the last twelve years. From time to time I have published, through various channels, accounts of observations in various subordinate lines. These are now collected, and, so far as continuity is possible in a study which is not more than inchoate, are connected. The story which they tell is rather suggestive than instructive; the results to which they lead are more in the direction of aid to investigation, than of practical application to medicine or therapeutics. If the work obtain some attention as a record of the phenomena observed, it will have served its end. The record has not been made to prove things outside itself, but to serve in future endeavours towards the comprehension of the physical processes associated with life.

W. M. ORD.

November 1879.

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I. INTRODUCTORY CHAPTER,

CONTAINING A SHORT HISTORICAL SKETCH OF THE SUBJECT OF "MOLECULAR COALESCENCE," WITH AN ACCOUNT OF SOME ALLIED OBSERVATIONS, AND OF PROCESSES ADOPTED BY VARIOUS EXPERIMENTERS.

As far back as the year 1857, Mr. George Rainey, Lecturer and Demonstrator on Anatomy at St. Thomas's Hospital, began to show that certain crystalline matters, when deposited in viscous or gummy solutions, assumed globular and cell-like forms. In the "British and Foreign Medico-Chirurgical Review" of that year, in the "Quarterly Journal of Microscopic Science" for January 1858, and in a short treatise published at the end of the same year, "On the mode of Formation of Shells of Animals, of Bone, and of several other structures by a process of Molecular Coalescence, demonstrable in certain artificially-formed products," he put forward the following original statements and arguments; first, a "statement of a process by which carbonate of lime could be made to assume a globular form, and the explanation of the nature of the process, "molecular coalescence," by which that form was produced; secondly, the explanation of the probable cause of crystallisation, and the manner in which the rectilinear form of crystals is effected ; thirdly, the discovery of a process of "molecular disintegration" of the globules of carbonate of lime by inverting the mechanical conditions upon which their previous globular form had depended; fourthly, the recognition, in animal tissues, of forms of earthy matter analogous to those produced artificially; and fifthly, the deduction, from the above facts and considerations, of the dependence of the rounded forms of organised bodies on physical and not on vital agencies."

Mr. Rainey, it will be seen, made a bold step into regions as yet hardly trodden. The synthetic method had been but little applied to the investigation of vital phenomena, though Ascherson had indeed already, in 1840, achieved something like an artificial imitation of an organic cell. Not content, however, with making the imitation, Mr. Rainey persistently followed up the analogy thus placed in his hands, and went so far as to assert that many of the so-called vital processes were in their essence purely physical. As a dweller in the dissecting-room he had the question of the lost vitality constantly before him; and he set to work to sift away from the processes subservient to and associated with life all that could be proved or assumed to be of a physical nature, until at length he had abstracted so much that he came to the assertion with which his analysis of his treatise ends—that the rounded forms of organised bodies depend upon physical and not on vital agencies. The rejection of the latter by that emphatic "not" was a remarkable act of decision. It was characteristic of the man of powerful and concentrated thought, of the man who after long mathematical training had come to form his own conclusions from his own observations, and who felt himself strong enough to accept them and to stand by them.

Hitherto Mr. Rainey's work, though received with respect, has not exercised a wide influence on physiology, either as regards the interpretation of phenomena, or as affects microscopical technics. And at the present moment, when, to quote an example, the question of the structure of blood-corpuscles is attempted to be solved by the use of all kinds of destructive and coagulating agents, it might be well for observers thus employed to read and re-read Mr. Rainey's little book, and to think well over Mr. Savory's observations on the structure of the fresh blood-corpuscles of the frog ("Proc. Roy. Soc." vol. xvii. 1869, page 346), observations which are conceived in a spirit akin to that of Mr. Rainey's treatise.

I propose now to describe pretty fully the synthetic process adopted by Mr. Rainey. "It consists," to use his own words, "in introducing into a two-ounce phial, about three inches in height, with a mouth about one inch and a quarter in width, half an ounce by measure of a solution of gum-arabic saturated with carbonate of potash (the sub-carbonate of the old pharmacopœias). The specific gravity of the compound solution should be 1·4068, when one ounce will weigh 672 grains. This solution should be perfectly clear; all the carbonate of lime which had been formed by the decomposition of the malate of lime contained in the gum, and also all the triple phosphate set free by the alkali, must have been allowed completely to subside. Next, two clean microscopic slides of glass, of the ordinary dimensions, are to be introduced, with the upper end of one slide resting against that of the other, and with their lower end separated as far as the width of the phial will permit; and, lastly, the bottle is to be filled up with a solution of gum-arabic in common water of 1·0844 specific gravity, of which one ounce will weigh 520 grains. This solution must be also perfectly clear, having been first strained through cloth, and afterwards left to stand for some days to allow of the subsidence of all the floating vegetable matter. It must be also added carefully to the alkaline solution, so that the two solutions may be mixed as little as possible in this part of the process. The bottle must now be kept perfectly still, covered with a piece of paper to exclude the dust, for three weeks or a month." At the end of this period the slides are removed, and are found covered with deposit of carbonate of lime on both sides. The most perfect forms are found on the lower face of slides, and therefore it is directed that the upper face be first thoroughly cleaned, after which the lower face is washed, dried, and the deposit on it subsequently mounted *in situ* in Canada balsam. The most perfect spheres, some separate and distinct, others in all stages of coalescence with each other, and all of the hardness of pearls, are thus obtained; and, by examination of the mingling fluids at various epochs, Mr. Rainey demonstrates that they are built up by the slow coalescence of minute molecules. The perfect spheres exhibit both radial and concentric markings, and in polarised light present a strongly-marked cross. Where two spheres are brought into contact, they gradually coalesce, or form one perfect sphere; and, where the spheres are in contact with the glass, a distinct erosion of the surface of the glass occurs, so that a shallow pit is formed. In both cases, according to Mr. Rainey, a new arrangement of the molecules, previously balanced in relation to a separate centre of gravity in each mass, now occurs around a new centre of gravity common to the two masses. He considers that the "viscosity" of the gum, in a way hereafter to be considered, annuls the polarity of the crystal, and allows the molecules of the crystal to obey simple laws of common and mutual attraction. He shows that in the calculous spheres thus formed a portion of the gum is enclosed or intermixed. The process thus described is called by our author "molecular coalescence." When the spheres thus formed are plunged into new solutions of gum of different specific gravity, most effectively of greater specific gravity, the spheres lose their concentric arrangement and break up into radial lines, and subsequently into molecules. This is "molecular disintegration." Mr. Rainey shows that carbonate of baryta and strontia give similar results, but that carbonate of magnesia only forms crystals; and that the most beautiful spheres of all are formed by a combination of carbonate of lime with a little triple phosphate. He then shows how forms such as are here artificially produced can be seen in bone, in shell, in ossified tendons of birds, in the apodemata and external skeleton of small crustacea, etc.; the tail of the shrimp and the inner layer of the shell of the young lobster being rich in globules and masses of globules exactly resembling the artificial products just described; and proceeds to argue that bone, starch, and the crystalline lens, are severally wrought according to the same principles out of mixtures of various substances with colloids.

In the year 1872 an abridged report of a work by Professor Harting of the University of Utrecht, "On the Artificial Production of some of the Principal Organic Calcareous Formations," appeared in the "Quarterly Journal of Microscopic Science." As regards this work I am bound to recant some observations which I made at the time in the same journal, to the effect that to those who were acquainted with Mr. Rainey's work it offers little that is new. I am bound, on reperusal, to acknowledge that it is deeply interesting, full of important facts, and most suggestive. Professor Harting, it may be stated, claims to have published matter on this subject even before Mr. Rainey; but certainly his large work appeared thirteen years after Mr. Rainey's. There can at least be no doubt of the independence and originality of the work. Professor Harting used a method which is less elegant than Mr. Rainey's, placing the salts that were to be mutually reactive in the solid form at different points in an albuminous or colloid solution, sometimes interposing a membrane, sometimes not. The carbonate of lime spheres he called "calcosphærites," and his drawings have a wonderful resemblance to Mr. Rainey's. He states that the albumen contained in the calcosphærites undergoes a chemical change bringing it near to chitin, and says that the same change is effected in albumen by chloride of calcium. To this modification he gives the name calcoglobulin. He finds in his experiments explanations of the structure of the shells of Lamellibranchiata and some Gasteropoda, of the calcareous plates of the bone of sepia, of the shells of Foraminifera and loculi of Bryozoa, the spicules or sclerites of Alcyonaria; and states that the last-mentioned forms are produced when cartilage previously impregnated with calcium chloride is placed in a solution of potassium carbonate mixed with a little sodium phosphate. The formation commences in the interior of the cellular capsules of the cartilage, and then extends into the fundamental intercellular substance.

In observations of my own, which also preceded Harting's both in time of execution and of publication, I have used freely a modification of Mr. Rainey's method, which appears to me of sufficient importance to warrant its being fully described. I use glass tubes of about ¾ inch diameter and of 6 to 8 inches length, open at both ends. One end is plugged to a thickness of from ¾ inch to 1½ inch with clear jelly melted into it, or with albumen coagulated in it, or with albumen, gum, vitreous humour, or soap-solution, retained by a muslin cap. The tube is filled with one solution, say of carbonate of soda, the plugged end being then immersed in another solution, say of chloride of calcium. These two solubles rapidly diffuse through the gelatin, meet in it, and decompose one another. The carbonate of lime deposited in the jelly takes crystalline or spherical form in various parts of the plug, according to the preponderance of one or other of the solutions, and according to the strength of the solutions; the best spheres being found where the solutions balance each other, and when they are so diluted as to favour slow and gradual decomposition. The plugs being solid allow of the making of sections at different levels, and also of the application of various external influences, such as heat and cold, electricity and magnetism; but it is seldom that individual spheres are found equal in perfection to those obtained by Mr. Rainey's own process.

Professor Guthrie has recently attained a somewhat similar set of results by the evaporation of gelatinous solutions of various salts, particularly of sulphate of copper. In the "Philosophical Magazine" for July and August 1878, under the title "On Salt Solutions and attached Water," Professor F. Guthrie writes as follows (p. 18 of paper):—"Among the jellies which I then prepared was a stiff gelatine jelly saturated with sulphate of copper. This jelly was of a bright emerald green by transmitted light. On exposure to the air of a portion which had not been subjected to electrolysis, the water gradually evaporated, and the salt began to crystallise out. The form of the crystalline masses was curiously modified by the jelly. Rounded masses were formed, reminding one of my friends of the coccoliths of the deep-sea dredgings—another, of the mineral or uric concretions which occur in mucous media—and yet another, of 'chlorite.' Whether there be, as is most likely, a common cause, a colloid medium, in all the three cases, I must not here discuss. The ultimate crystalline element is too minute for determination, but the elements of secondary form invariably resemble a bean-shaped mass with deep hilum. These elements are frequently linked two by two in one plane, or at right angles to one another. The convex sides are generally very deeply furrowed, so as to give the impression of their being four secondary elements. These concretions can be picked out of the jelly in which they form, like almonds out of a cake. So clean is their separation, and so feeble their blackening when heated with oil of vitriol, that they must be regarded as homogeneous bodies free from gelatine; and their composition is therefore of no common interest. Ten of these concretions, which are remarkably uniform in size, weighed 0·5024 gramme; the loss on heating to 200° C. in an air-current was 0·1432 gramme, showing 28·504 per cent of water."

There are yet several observations to which attention may be drawn in relation to the general subject of which "molecular coalescence" forms a part.

In 1866, Dr. Montgomery, at that time Curator of the Museum of St. Thomas's Hospital, recorded in the Proceedings of the Royal Society some observations made by him on the behaviour of "myelin" when brought into contact with water. By "myelin" Dr. Montgomery indicated a substance obtained by digestion of the yolk of an egg in hot alcohol, and the subsequent cooling of the alcohol till an extract or deposit was formed. This was brought by heat to a tolerably firm consistence, but not to dryness. A small quantity of the extract being placed upon a glass slide and covered with thin glass, was examined through a tolerably high objective. The mass was seen to be shapeless and indistinguishable from crushed grease or similar structureless substances until a drop of water was allowed to run beneath the thin glass, and to come in contact with the edges of the "myelin." Then a multitude of minute processes began to sprout from all parts of the surface of the myelin exposed to the action of the water. These processes when fully formed were tube-like in appearance, with rounded or bulbous extremities; the walls of the tubes were thick and refractile with marked double contour, and the contents appeared to be fluid. The processes reminded the observer of nerve-tubes, or, still more closely, of the tubular and rounded processes which are seen under the microscope to issue from the cut ends of nerves in contact with water. Dr. Montgomery varied the experiment in many ways, and showed in particular that, if albuminous fluid were used instead of water, spheroidal protrusions were formed and floated free. The late Dr. Hughes Bennett in his "Manual of Physiology" drew special attention to these fascinating experiments, and related how he used year after year in the appropriate stage of his lectures to reproduce them for the benefit and amusement of his class. In working with cholesterin and acetic acid in presence of colloids, I have obtained forms exceedingly like those of Dr. Montgomery, and have been able to reproduce them all with certain matters extracted from ox-brains by Dr. Thudichum,[1] called by him "Kephalin" and "Buttery Matters" respectively. The Kephalin gives the reaction slowly, and sends out only small tubes; the "Buttery Matter," which is an impure extract containing a great deal of free cholesterin, yields really magnificent processes. If some of the same "Buttery Matter" be heated to ebullition with glacial acetic acid, the cholesterin is at first dissolved, and afterwards precipitated in irregular points, lines, and spherules, which gradually coalesce to form the most beautiful spheres, more nearly approaching the perfection of Mr. Rainey's spheres of carbonate of lime than anything else. This takes place during a period of

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[1] See "Rep. Med. Off. to H.M. Privy Council, 1874."

three or four days, on the glass slide, so that a rapid illustration of molecular coalescence is obtained.

Among synthetic experiments it is impossible to pass without notice those of Ascherson on the "Haptogen Membrane," and the forms observed in emulsions of oil and albumen. Ascherson's paper "Ueber den physiologischen Nutzen der Fettstoffe, etc.," was published in Müller's "Archiv" for 1840, p. 44. The paper shows that when oil and albumen are brought together, a membrane consisting apparently of coagulated albumen is formed wherever there is contact between the two substances. When oil and albumen are shaken together, an emulsion is formed which is permanent, because every globule of oil is instantly invested by a pellicle. The forms thus produced correspond with the condition in which fat is found in milk, in the fat-masses of animals, in eggs, and in plants. He calls fat drops so invested "Elementarzellen," and argues that the tissues of the animal organism are made up of fat-cells which may be regarded as the results of the metamorphosis of oil-drops or elementary cells; the blood-corpuscles are cells which, besides colouring matter, contain fat; it is their principal function to carry the fat wherever the formation of new cells shall be proceeding; the primitive condition of the ovule of animals is that of an oil-drop, and Wagner's germinal spot is the remains of that drop; the cells of plants are also formed by means of a heterogeneous fluid, but it remains to be determined whether only fat oil or some others in addition play an active part in the process.

A repetition of Ascherson's experiments, and a renewed observation of chyle, milk, and other emulsions under the microscope, have led me to investigations into some of the causes of Brownian movements, and to the conclusion that in a large degree those movements are related with the causes that bring about sphericity in crystalloids deposited within colloids.

The extreme activity of the Brownian movements exhibited in chyle under the microscope must be familiar to every one who has examined that fluid. But when Aschersonian emulsions of much inferior comminution are examined, the Brownian movements can be seen to affect not only tiny immeasurable molecules, but globules up to the diameter of half a red blood-corpuscle. The unusual force of motor impulse necessary to sway such comparatively large granules appears to me to be due to the existence of a chemical relation between the oil and albumen, such as is in fact demonstrated to exist by the formation of the pellicle on the surface of each oil-drop. And further experiments have led me to the following conclusions :—1. That whatever favours the decomposition of the albumen favours the activity of the movements ; 2. That the addition of alkalies, which at one and the same time favour the decomposition of albumen and react chemically on the fat, accelerates and intensifies the movements ; 3. That the addition of strong acids, which, while keeping the albumen in solution, hinder its decomposition, and which have little or only slow action on the fat, hinders or actually annihilates the movements. I infer from this that just as the vibrations set going by heat generally distributed are known to intensify Brownian movements, so disturbances or molecular movements set going by chemical change in the containing fluid tend to intensify the movements, independently of, and in addition to the motor influence arising out of surface tension between the oil-drops and the chemically aggressive fluid in which they are suspended. A comparison of this sort of mixture with mixtures of soap-solutions and solid molecular matters having no chemical relation with them, such as carbon or china clay, justifies the belief that the chemical constitution of the containing fluid has much to do with the activity of the contained molecules, and that it is when we use colloids, prone to chemico-molecular change within themselves, that we get most active movements, and when, as Professor Jevons has shown, we use acids and salt solution not prone to internal commotion that we get weaker movements or none. The solution of soap is a liquid that observation will show to be constantly undergoing change, visible even to the eye, and though Professor Jevons considers the influence of this and the other solutions to be explained by electrical relations, the chemical explanation appears to me to cover the facts thoroughly, and to be consistent with the influence, which occupies my attention in this treatise, of colloids in destroying crystalline form. This part of my subject has been recently treated by me at greater length in a paper which I had the honour of reading before the Royal Microscopical Society in June last, and which appeared in the October number of the Transactions of that Society. I may note in passing that if alkalised Aschersonian emulsions be kept for a fortnight or so in test tubes, enough oil accumulates on the surface to prevent putrefaction in the solution beneath, and that cell-like bodies of considerable size with thick walls and contents variously composed of oil, molecules, and watery or albuminous fluid, are then found in abundance in the cream floating above the solution of alkali-albumen.

Finally, before the general subject is discussed, we may be reminded of two interesting lines of experiment—1st, Of Dr. Heaton's remarks on "Dendroidal Forms assumed by Minerals" ("Trans. Brit. Assoc. for Promotion of Science, 1869, p. 127"), in which the results of suspending a crystal of sulphate of copper or iron in a solution of silicate of sodium are described. A crystal being suspended in a weak solution of the silicate, branches shoot perpendicularly downward, presenting a remarkable resemblance to the branches of some vegetation. These branches are fine hollow threads, composed of non-crystalline silicate of iron or copper, and the whole formation looks like a seaweed or conferva. With denser solutions the tubes run vertically upwards. Here, in both cases, the colloid influence of the silicate of sodium plays a part in the production of the phenomenon. 2d, Traube's experiments on the formation of artificial cells, in imitation of vegetable cells, by means of "pellicle precipitates," produced by copper-salts in a solution of ferrocyanide of potassium, or on drops of gelatin in solutions of tannin, with the remarkable results as to the degrees of diffusibility of various solutions through the membranes so formed. (See Sachs' "Text Book of Botany," tr. by A. Bennett, p. 594.)

CHAPTER II.

CONTAINING A DISCUSSION OF THE CAUSES OF MOLECULAR COALESCENCE, AND AN APPLICATION OF THE PRINCIPLES ESTABLISHED TO SOME STRUCTURAL PHENOMENA OF LIVING BODIES.

In the general consideration of the questions involved in the relation between colloids and crystalline form frequent reference will necessarily be made to the second or practical division of this book, and both statements and arguments will be found repeated at various places in the two parts. In one part observations are used to illustrate arguments; in another, arguments are founded upon observations.

It will be useful first to review the more important of the processes by which the modification of the crystalloid to the spheroidal form is effected.

1. A new salt is formed by decomposition, and caused to combine in its nascent state with the colloid. Such is the condition in Mr. Rainey's typical experiment and in Professor Harting's processes. The colloid may be of the proteid or gelatinous kind, or amyloid, or pectous, or an isomeric modification of an organic crystalloid, as uric acid, or of an inorganic crystalloid, as silica and silicates, peroxide of iron, etc. Thus Mr. Rainey mixes two gummy solutions of the reacting salts; Professor Harting places the solid salts at different points of an albuminous solu-

tion; in my own plugged tubes the reacting solutions are placed on opposite sides of a thick colloid dialyser, within which they meet and undergo mutual decomposition. A modification of this condition is employed when urate of soda is formed by boiling uric acid with strong solutions of chloride of sodium or phosphate of sodium. The urate comes down in a colloidal state, and affects included crystals as any other colloid would (see page 77).

2. A crystalloid is deposited from solution in the presence of a colloid. This occurs in Dr. Guthrie's experiment with sulphate of copper and gelatin, in uric acid and urates mixed with albumen and mucus, in nitrate of urea crystallised from albuminous urine.

3. Crystals are broken down and turned into spheres or spheroids or molecules, by the action of colloids into which they are introduced—a condition constantly seen in microscopical preparations. Crystals of uric acid, carbonate or oxalate of lime, etc., when preserved in gelatin or glycerine or glycerine-jelly, speedily lose their transparency, lose their sharp outline, and progress in various degrees towards sphericity. I have drawn attention to this in respect of glycerine in particular, in the "Quarterly Journal of Microscopic Science" for 1873. The transformation of crystals of murexide put up in glycerine is a particularly beautiful phenomenon, exquisite tufts of black-looking needles growing at the expense of the brilliant purple prisms.

When we seek the causes of the spheroidal modification, several possible influences present themselves for consideration.

1. *The "Nascent" State.*—Professor Harting lays

great stress upon the fact that in the experiments of the first group the crystalline substance is in a "nascent" state, and appears to regard the spheres as a result of the combination of the nascent crystalloid with the colloid, which incidentally undergoes a chemical change. If we stretch the use of the term "nascent," so as to include the state of substances in the act of separating from solution, thereby making it apply to the second group, we have still the third group to bring under the genus. On the supposition that a process of partial solution is followed by recrystallisation, we may in part include this group, and murexide and uric acid may readily be dissolved at one temperature and separated at another; but as far as I know, this does not apply to carbonate of lime, still less to the oxalate. Yet a review of the behaviour of the various salts and matrices favours the idea that the nascent modification of substances is an important element in the production of changes of form. This I have pointed out in earlier papers in relation to uric acid, which is certainly precipitated in a colloid form when freshly dispossessed of its combinations by other acids. This colloid state has been called its hydrate by Prout; and, while in aqueous solutions it is short-lived, in colloidal solutions or mixtures it endures for a long time. An analysis of the phenomena in a great number of experiments made with various media makes me incline to believe that hydrated colloids and strong solutions of very soluble salts have a power of prolonging the colloid state of certain crystals. In respect of the present inquiry, any prolongation of the colloidal state in the substances precipitated must favour the production of spheroidal forms. Our knowledge, indeed, of the ways of the higher colloids must be admitted elementary. Of the albumens, for instance, we know really little more than their rough chemical reactions; and though the reports of various Societies embalm fragments of what may be more properly called their natural history, most of these fragments remain unnoticed or useless. Whenever these fragments shall be put together, and supplemented by further investigation, the collection between colloidality and hydration will require to be carefully worked out. With this the meaning of the "nascent" stage of substances will form a congenial object of inquiry; and at present the probability suggests itself to me that the nascent state is allied to or even identical with the colloid state of matters. Just as chemical substances may be either gaseous, fluid, or solid, as some are commonly seen in all states, some only in one, while many which we are accustomed to see only in one may by special experiments be brought into the other forms, so it seems to me probable that all matters, when deposited from solution, or otherwise assuming a solid form, a liquid or gaseous form, have, or tend to have, a colloid and a crystalloid stage, both of which may be well marked, as in silica, or one of which may be more marked than the other, as in uric acid, or one only of which may at present be recognised, as in chloride of zinc on one side, in albumen on the other. For instance, the state of sulphate of soda in the well-known experiment in which a saturated hot solution, being kept in a corked bottle, fails to crystallise till the bottle is uncorked, is worthy of careful investigation. Besides the question of hydration manifestly involved, the experiment offers that of the molecular condition of the salt and its molecular relation to the water. How far, again, is the energy of nascent bodies due to some sort of colloid state, allowing of more ready interpenetration of their molecules by combining substances—to something like a spongy state, offering enormous and facile contact ?

2. *Hydration.*—Professor Guthrie, in the interesting paper already referred to, throws out a suggestion that the partial dehydration of the sulphate of copper has to do with the forms found in the evaporated gelatine solution. The idea is valuable, and certainly points to a good line of investigation. But, as Dr. Guthrie has remarked to me in conversation, sulphate of barium contains no water, yet undergoes the spheroidal change in the most complete way. The same may be said of carbonate of barium, of carbonate and sulphate of strontium, and of cholesterin, all of which readily form spheres. Nitrate of urea, also, when thrown down by excess of strong nitric acid, is anhydrous, although, when crystallised from neutral solutions, it contains water, and has a different form. Dehydration, partial or complete, can cover, therefore, only a part of the facts.

3. *Crystalline Form.*—I have sought in vain for any indications of any difference in the tendency to sphericity, or in the modifications of spheroidal form assumed by different substances, which might be attributable to their belonging to one or other group of crystalline forms.

4. *Relative Solubility.*—The best spheres are certainly obtained when substances of little or no solubility are deposited by double decomposition; and

when a very moderate degree of insolubility is reached, as in triple phosphate, spherical forms are only with much difficulty obtained by that process. But by evaporation (Guthrie), and by deposition from hot, concentrated solutions (nitrate of urea, ferrocyanide of potassium), very soluble matters may be made spheroidal. The influence of solubility extends, therefore, only so far as to involve different modes of preparation, when solubles and insolubles are respectively dealt with.

5. *Influence of the Colloid.*—Mr. Rainey throughout his book uses the term "viscous" when he speaks of colloids, and argues that the "viscosity" of such matters acts as an impediment to the movements of polarity by which crystallisation is determined, so allowing of the unhindered operation of simple attraction. This at least is the inference to be drawn from the following passage:—"When the molecules of pure carbonate of lime, that is, carbonate uncombined with a viscid substance, come into existence, they immediately commence arranging themselves in straight lines, and thus, when collected together, form rectilinear figures or crystals; but when the impure carbonate, that is, carbonate combined with a viscid substance, comes into existence under similar circumstances, its molecules assume a curvilinear disposition, and hence become collected into globules. Now, as these forms of arrangement are exactly the reverse of one another, and as the curvilinear form has been shown to be the effect of attraction, the rectilinear form might have been inferred to be the effect of repulsion, or at least of some force causing the separation of the molecules of the pure carbonate. Hence it appears that when

the gum or albumen is intimately combined with the ultimate particles or molecules of the carbonate of lime, it confers upon them a property capable of neutralising this inferred repulsion, and thus, making the molecules of this compound indifferent in respect to any inherent attraction or repulsion existing among themselves, they become amenable to the effective operation of gravity, a force which is ever in action, either effectively or ineffectively, upon the molecules of all bodies."[1] Mr. Rainey goes on to explain the action of the gum, or albumen, with which he associates "glycerine and probably all other viscid substances if only they are capable of combining with the nascent carbonate," as follows:—" Hence this effect of viscidity may depend upon some property of animal or vegetable matter, which is no other than a form of attraction peculiar to organic products, differing from chemical attraction in producing its effects, independently of any chemical change in the substances acted upon; as, for instance, when two recently exposed surfaces of elastic gum are brought together, they unite without any sensible development of chemical action, differing from the attractions of gravitation in taking place only at insensible distances, and lastly differing from that force which acts indiscriminately upon all substances, organic and inorganic, called cohesion, in possessing in connection with a certain amount of adhesiveness, a degree of elasticity, the two making up together the property called viscidity or tenacity, a property occurring only, with the exception of certain compounds of silica, in substances of animal or

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[1] *Op. cit.* pp. 31, 32.

vegetable origin."[1] This property is called afterwards by Mr. Rainey " the attraction of tenacity."

To me, in long thought on the subject, the influence of the colloid has come to present itself as a result of intestinal molecular movement inherent to the constitution of the colloid. The assumption of the spheroidal state, and the throwing off of the crystalline state, are both consistent with the idea of a state of movement possessing the molecules, engrossing them so fully as to render them insusceptible to attractions by which, being at rest, they would be held and controlled. Such a state of movement is seen in the gyroscope and in the revolving bullet; something close akin to it is seen in the condition of water thrown on a red-hot metal plate, where not only is the earthward tendency arrested, but the spheroidal form results from the unhindered mutual attractions of the molecules of the fluid; the same principle is to be found in the opposition of heat to crystallisation, and not impossibly in the hindrance offered to the freezing of water by pressure; lastly, it may be remembered that fine and perfect crystals are only formed where the solutions from which they are separated are kept perfectly at rest.

Graham has spoken of colloid, as the dynamic form of matter. The constituents of their large molecules are in a perpetual movement or strain tending to ultimate rest in crystallinity, either by isomeric change or by decomposition. The viscosity characteristic of them in their most perfect state, instead of appearing to me as a peculiarity related with their animal and vegetable origin, is partly due to the size and im-

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[1] *Op. cit.* p. 32.

mobility of their chemical molecule, partly also to their intestinal movements, belonging so far to the same class of conditions as the spheroidal state of water. It accords with this, that we should find, as is related farther on (pp. 124, 125) — 1st, that spheres are more readily formed when the colloid is placed in conditions favourable to decomposition; 2d, that when the temperature of the mixture of colloid and crystalloid is raised, spheres are more perfect, and crystals smaller and less perfect; 3d, that when the temperature is lowered spheres are fewer, crystals larger and more perfect. When carbonate of lime, for instance, is formed in gelatine or albumen at temperatures near 40° Fahr., crystals are abundant; and, what is most instructive, when spheres exceed a certain diameter, crystalline spicules are formed on their surface, looking like transparent rose-thorns. With this result of my own experiments may be compared Professor Harting's statement that in mixtures kept for many successive days at a low temperature, forms resembling the spicules of corals were obtained having central masses or cylinders upon which were seated lateral pointed processes. Read by the side of Mr. Rainey's experience that finer spheres were obtained when to tractable carbonate of lime a small quantity of intractable triple phosphate was added, these observations indicate that when the action of the colloid is most energetic and complete, smaller forms are found, and then more and more spheres and fewer and fewer crystals; the reverse occurring, as respects both size and proportion of numbers of the two forms, when the action of the colloid is less perfect. Whatever favours internal molecular movement intensifies the working of the colloid, and may therefore be presumed to act in harmony with its mode of action, and *vice versa.* The presumption, therefore, that the influence of the colloid depends upon its intestinal molecular movements is greatly strengthened by experimental observation.

In a later chapter some experiments on the influence of electricity and magnetism on the mode of deposit are related. They are only referred to here, being incomplete and tentative. But the reason which induced me to try the effect of magnetism may be stated. The "viscosity" of the magnetic arc suggested itself to me as likely to intensify the power of the viscosity of the colloid. At the time I accepted Mr. Rainey's views as expressed above. I subsequently found that there was reason, from suggestions of the late Mr. Charles Brooke, to believe that this viscosity was due to the existence in the arc of numerous "spiral waves," and that in fact the same sort of principle was here at work as I was coming to recognise in the working of the colloid.[1]

The idea of a "combination" between the colloid and the crystalloid as constituting an essential part of the whole phenomenon is insisted on both by Mr. Rainey and Professor Harting. If by this is meant chemical combination, the idea does not seem to me well founded. The observation of Professor Harting that albumen undergoes a chemical change where the spheres are formed—an observation which agrees with what occurs in urinary calculi—does indeed go to show that a chemical interaction goes on between the two substances. This might be expected to occur when

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[1] See Proc. Roy. Soc. xv. 1867, p. 409.

they have been so intimately commingled. But the fact that variations in the density of the colloid solutions produce the phenomena of molecular disintegration alone shows the union to be of physical and not of chemical nature; and the history of long-formed spheres, of urinary and of cholesterin calculi in particular, shows that in process of time there is an actual mechanical separation of the colloid from the crystalloid within the substance of the spheres, without loss of the spherical form, so far as it is possessed by the whole mass. The idea is also opposed by the plasticity and capacity for growth possessed by the spheres, and by such a fact as that recorded by Mr. Rainey in the observation that the surface of the glass slides is eroded by the calculi where they are formed upon it. The quantity also of colloid present in a sphere is extremely small in proportion to the crystalloid, as is shown by Dr. Guthrie's observation already quoted. Such a fact, it is true, is not decisive, but it is at least opposed to the ordinary laws of combination between colloids and crystalloids, a small proportion of the latter usually combining with a large proportion of the former. And, if a combination takes place, why is it limited only to an area of the colloid collimitary with the area of the densely-packed saline matter?

Some Physiological Applications of the Observations here reported or recorded.

1. Although a number of instances have been already quoted from Mr. Rainey and Professor Harting of hard tissues evidently formed by the same process in various animals, it is evident that the list is incom-

plete and the survey as yet very limited. A careful study and enumeration of the hard structures of animals, plants, and minerals, in which indications of sphere-formation present themselves, would be of great value. Here I may mention two striking illustrations to be found in the human body—one brain-sand (mentioned by Harting), the other the interglobular spaces of dentine, or rather the globular dentine forming the margin of the spaces.

As regards bone I have elsewhere recorded some speculations and experiments regarding its relative compactness in different animals. Briefly I find reason to suggest that the relative compactness of bone in different classes of vertebrata is dependent on three factors—(*a*), The nature of the colloid matrix; (*b*), the nature of the earthy salts; (*c*), the temperature of the body—the greatest compaction being attained with albuminoid matrix, with a mixture of carbonate and phosphate of calcium, and with the highest temperature, as in the bird. In the lower vertebrata, and in the invertebrata, where the tissue is mostly an external investment incapable of interstitial change, carbonate of lime is the almost exclusive constituent. The extreme hardness of external investments, of which pearl is a good type, and with which (as regards position, not structure or composition) the enamel of our teeth may be compared, is interesting as contrasted with the toughness belonging to bone. But the great difference lies in the capacity which bone possesses of being absorbed and reproduced interstitially. With this it appears to me certain that the process of "molecular disintegration," perhaps the most strikingly original of Mr. Rainey's discoveries, has much to do. To make clear what is meant by the phrase I will again quote from Mr. Rainey. Well-formed spheres, composed of carbonate of lime and triple phosphate, are exposed to the action of the same gum-solution in which they have been deposited, after it has undergone concentration by evaporation, and has therefore become denser. "This process of disintegration is first indicated by the radiating lines becoming more distinct, especially near the margin of the globules. Afterwards separations occur between these lines, so that the circumference of a globule, in the place of being one sharp line, is made up of their projecting ends, giving the appearance of a ciliated fibrous zone, whose breadth depends upon the degree of disintegration. As this process progresses this zone disappears in certain parts, leaving the periphery uneven, and afterwards it disappears altogether, when the globule becomes reduced in size according to the width of the disintegrated zone. And thus the disintegration proceeds until the entire calculus is removed. The disintegrated molecules, deprived of the whole or a great part of their triple phosphate, are dispersed through the solution, where some again coalesce, but into much smaller oval and globular particles, exhibiting all the stages of molecular coalescence described at the beginning of this paper, while others reassume a crystalline form." The disintegration takes place only in the spheres of mixed composition, those of pure carbonate being unaffected. Mr. Rainey argues that "in those (mixed) globules" the "attraction of tenacity is neutralised by the combination of triple phosphate with the globular carbonate;" and therefore "it can be only with gravity that the disintegrating force has to contend; and as the conditions of the experiment are such as to exclude the action of all other forces upon these calculi excepting that of gravitation, it must follow, of necessity, that gravity is the disintegrating agent;" "the surrounding dense medium attracting the molecules of the bodies with a force exceeding that by which they are attracted by the bodies themselves." Whatever be the true explanation of the process, Mr. Rainey shows that such calculi may be readily disintegrated in the way mentioned above, or by immersion in gum-solutions of varying density, or in glycerine, or in oil, or by exposure to heat. Applying this to bone, it is not difficult to suppose that the Haversian spaces formed as a preliminary step to the deposit of new bone may be excavated by a process of molecular disintegration set going by a variation in the constitution of the colloid matrix—either by a change of a senile character, or by the introduction of new material in consequence of altered vascular relations.

The process is abundantly seen wherever microscopical calculi are put up in glycerine, and is the probable cause of the softening of bone and teeth by that reagent to which Dr. Beale has drawn attention. It offers a reasonable explanation of the excavation of the interior and lips of many of the spiral shells of Gasteropoda, and is not improbably the process by which the boring sponges make their way into the substance of shells.

Although in the observations hitherto made the behaviour of crystalline matters in the presence of colloids has been chiefly examined, Mr. Rainey has extended his regard to the formation of starch-granules and of the crystalline lens, and has stated his reasons for believing that a process of molecular coalescence is involved in both cases. In animal and vegetable bodies colloids of different composition and reactions are everywhere intermingled, and sometimes, as in blood-corpuscles, most intimately. The structures going by the name of "nuclei" in organic tissues have just the characters likely to arise out of their being composed of masses of one kind of colloid suspended in another. Their naturally spherical form is one character of importance. Another interesting point is the limitation of their size, and their adherence to one size in each kind of animal. Regarding them as masses of colloid, having, as their relations show, great functional activity, we can be certain that their internal molecular movements are active. With this their limitation as regards size is very possibly connected. As we have already seen (page 23), and as is farther on (page 125) stated in greater detail, the spheres of carbonate or oxalate of lime, though more abundant, are of smaller size when formed in mixtures kept warm for days together. This appears to me to depend upon the activity of the molecular movements, which, in proportion as they increase in range relatively to the radius of any sphere, tend to throw the peripheral molecules beyond the range of the common attraction. When a mass has grown to such a size that the peripheral molecules are in this way regularly swung out of the reach of the original centre, new centres must form, and therefore new spheres. Applying this to nuclei and cells, we can see the necessity of their dividing fissiparously when their growth reaches a certain size, so that rapidity of growth is rather marked by small spheres in great multitudes than by large spheres.

The necessity that the granular or less soluble colloids of a complex body should in early stages of growth and development take the spherical form, and go on to the production of cells by the action of each sphere on the surrounding matrix, appears from these considerations; and I am strongly inclined to believe that the movements of nuclear bodies which we can see in the amœboid corpuscles of the blood, and which almost certainly occur in all similar structures, are just marks of their molecular activity, are resultants of the forces swaying about the centre.

In the fission of the yelk the principle seems to me most beautifully and strikingly illustrated. The ovum before impregnation is one of the largest organic cells that we meet with. Although it be a mixture of colloids, these are for some reason not in active molecular movement. But, on the entry of the spermatozoon and the starting of the process of development, when, as we must suppose, new chemical relations are introduced, a peristaltic contraction of the yelk follows. This marks the vigour of the internal molecular movements, and leads speedily to a fission of the mass first into two, then into four, then into many spherules, the degree of comminution corresponding with the degree of intensity of reaction, till the mulberry mass is formed.

I do not expect these views to be readily adopted, for in the present state of histological investigation the structure of parts is mainly investigated by the use of reagents and of processes which harden colloid matters. Such methods are of the greatest value, I admit. They teach us much of the healthy structures; they afford the readiest means of comparing normal and diseased tissues. But they also tend to fix in the mind ideas of the form and still more of the consistence of the elements of tissues which are far removed from their living form and consistence. And too often it is assumed that because certain appearances are obtained by the use of reagents they represent structural existences. But surely the fact of coagulation of one out of three or four intimately mixed chemical principles does not prove that the substance so coagulated represents a distinct structural form. For instance, if I take a drop of a mixture of gelatin and albumen, perfectly clear and structureless to the eye, and heat it, the albumen is coagulated and speedily contracts to a little lump lying in the gelatin, but now quite separate from it. Is this to be called a "nucleus"? Or is the clot which forms, contracts, and floats in the serum of blood a "nucleus"? No one will, I think, say "Yes" to either question; yet when blood-corpuscles are treated in an analogous way, and are variously broken up by reagents, the changes produced by solution or coagulation of one kind or another are put forth as indications of a complexity of structure, when, for the most part at least, they indicate only a complexity of chemical composition.

In the Practical Division of this treatise which follows, the most familiar kinds of urinary crystals are successively studied, in respect of their varieties of form, of the causes of the varieties, of the modifications which may be brought about by experiment, and of further considerations arising from time to time out of the changes and processes observed.

CHAPTER III.

URIC ACID.

Under the microscope uric acid is found in three forms :—1st, in rectangular oblong colourless plates; 2d, in rhombohedra and modifications of the rhomb; 3d, in spheres, and in fibrous masses forming parts of spheres. The first form belongs to pure uric acid, the second to urinary uric acid, the third to calculous uric acid. These may with advantage be examined in detail.

I. If some of the colourless, or nearly colourless, acid prepared from the urine of serpents 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 homogeneous and transparent, may be compared to the oblong pieces of glass sold as paper-weights; they are the "oblong square plates" of Dr. Thudichum[1] (Pl. I. Fig. 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, separated 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.

II. When deposited from urine, uric acid differs from its pure form in colour, shape, and aggregation. The crystals are always of a yellow or brownish colour, and are most commonly rhombohedra, or modifications of the rhombohedron in which that form can be readily made out. Prout ("Stomach and Urinary Diseases," 1860) gives two figures of uric acid. "The first," to use his words, "represents the ordinary appearance of lithic acid crystals under the microscope. The crystals are rhomboidal prisms, thin, transparent, and of a yellow colour." His 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 the crystal." There is here no mention of the tabular form. Dr. Beale, in his well-known work on

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[1] "Pathology of the Urine." Churchill, 1877, p. 60.

"Urinary Deposits," describes or figures more than thirty forms of uric acid. The edition of 1869 did not contain 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.

It follows from this comparison of the pure and urinary acids that there must exist in urine causes leading to a complete turning away of the substance from its proper crystalline form. The change is also in a definite direction. The faces and angles of a crystal from urine are almost always some or all of them curved and rounded. Such a crystal is a resultant of the operation of two distinct influences—of crystalline polarity under which the flat surfaces and sharp angles are determined, and of "molecular coalescence," in which polarity is lost and particles become arranged in spherical masses by virtue of their unhindered mutual attractions. Furthermore, in urine the crystals are very frequently gathered into large 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. While the difference between the urinary and the pure acid is so pronounced, the differences among the forms of urinary acid are both extensive and remarkable. 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. Beal, 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 researches of Mr. Rainey have pointed the way to a solution of the problem.

The first series of observations made by me on this subject were directed chiefly to the experimental determination of the way in which and the extent to which the form of uric acid might be altered by other substances present in solution with it. They arose out of the consideration of some curious uric acid crystals occurring in the urine of a patient suffering from subacute nephritis, apparently of syphilitic origin, and with the case may now be set forth.[1]

The patient, a young man of four-and-twenty, had been, for nearly five years, affected with secondary syphilis. Two years ago, when covered with tubercles and lepra, he was for a short time paralysed on the left side. In connection with the paralysis there existed pain and tenderness at the back of the head and neck, extending round towards the right mastoid process. These symptoms were attributed, first by myself, and afterwards by Mr. Solly, whose opinion was obtained in consultation, to syphilitic periostitis in the base of the skull on the right side, causing some pressure on the motor columns above their decussation. He was treated with the perchloride of mercury and tonics, and the paralysis speedily disappeared; the pain however remaining, complicated with occasional attacks of vertigo. Shortly afterwards, while still under treatment, he caught cold, and the kidneys appeared to become involved in the mischief, the urine being for many days albuminous. At length his health amended in all respects. He

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[1] The above series of observations was related in the "St. Thomas's Hospital Reports." New Series. Vol. i. 1870.

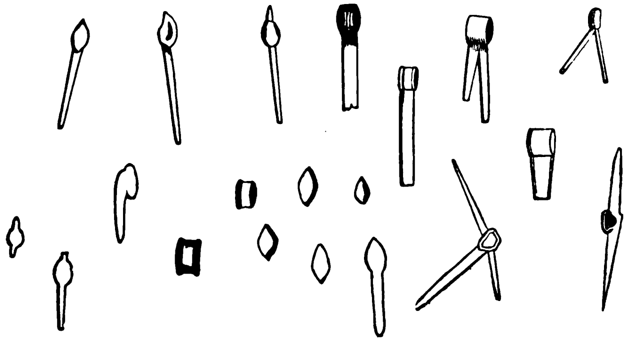
lost the pain and regained his strength, the albumen disappeared from the urine, and, except for the recurrence from time to time of easily healed ulcers in the fauces, it might have been supposed that he was quite well.

In the beginning of November 1869, an abscess was suddenly formed on the outside of the left ear, spread rapidly, and was opened, but nevertheless discharged itself after a few days through the ear. No bone could be felt exposed, but the scalp was undermined nearly to the vertex. With this attack there was a return of kidney-trouble; the urine became bloody, there was great loin-pain, and the face and limbs were puffy. Matters had been going on thus for nearly ten days, when he came under my observation, and my attention was of course directed at once to the state of the urine. It was nearly natural in colour, but was obscure with solid matter, which collected after a time in a singularly sharp-bordered whitish layer at the bottom of the vessel. The specific gravity was 1012. On boiling the urine a gelatinous albumen was slowly thrown down; the addition of nitric acid produced little further change at first, but after a time a further deposit of the same character took place. In the filtrate, after boiling there were traces of sugar.

In the deposit, as examined under the microscope, were great numbers of cells from the uriniferous tubules, some loose, some contained in casts of transparent substance; there were few traces of degeneration, hardly any fat, a little pus, and not many blood-corpuscles. Mixed with these were crystals (Fig. 1) of three kinds—(1) small octohedra of oxalate of lime;

(2) small thick rhombs of uric acid; (3) forms looking at first sight like stiffened spermatozoa, but in reality crystals, behaving with reagents like uric acid. They were easily soluble in liquor potassæ, and resisted acetic acid. The most characteristic of these had an oval, refractile head, with a long stiff tail or process attached, sometimes to one end of the oval, and continuing its long axis, sometimes obliquely. By careful examination of transitional forms it was determined that the head was a modified thick rhomb, and the tail a modified and elongated chisel-shaped or wedge-like crystal, such as is often seen in deposits of uric acid. Sometimes two or three processes were attached to one little rhomb, and there were great variations in thickness and flatness of the processes. Similarly the rhombs varied in their condition, some having sharp edges and angles, others exhibiting all degrees of rounding up to the production of oval bodies.

Fig. 1.

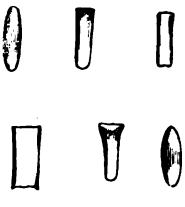


The rarity of the forms here observed, and the corresponding rarity—or at least unusual condition—of the fluid portion of the urine, suggested the existence of some definite mutual relation, while the complica tions of the case itself rendered all information to be derived from examination of the urine most important. The condition of the urine appeared to indicate that the liver was discharging its functions imperfectly, and that the kidneys were in a state of subacute inflammation, the syphilitic poisoning being probably the origin of both troubles; directly as concerned the kidneys; indirectly, as I judged from symptoms, as concerned the liver. It seemed to me not unreasonable to suppose that the difficultly-coagulable albumen, the sugar, and other unusual but less easily recognised constituents of the urine, had determined by their presence the unusual crystallisation of the uric acid. From previous investigations with regard to the influence of colloid substances upon crystalline form, I had supposed that the forms of uric acid, as deposited from urine, must often be determined by the nature of other constituents of the fluid, and I now determined to institute some experiments bearing upon this point. The great number of forms of uric acid hitherto observed had been noted and described in such comprehensive books as Dr. Beale's, chiefly, if not entirely, to aid in the ready identification of the substance when occurring in urinary deposit. If there were any value in the present experiments, they might be expected to lead to some diagnostic use of the varieties of uric acid.

Exp. 1.—Urine passed by the same patient on 15th December 1869. Dark in colour; of specific gravity 1006; slightly acid; the deposit flocculent, not in a defined layer, and not containing crystals; albumen freely precipitated on boiling, and in the usual form; no sugar.

(*a*) A portion was gently warmed with a few drops of hydrochloric acid, and left to cool. At the end of twenty-four hours a thin white deposit was found coating the sides of the beaker (Fig. 2). It could be detached in flakes, which under the microscope were found to be entirely composed of small crystals matted together, much as in Plate XXIX. Fig. 163, of Beale's "Urinary Deposits," Ed. 1869. The crystals when separated were of an elongated prismatic shape, some flattened and rectangular, some with rounded ends; most of them were thicker at one part than another, either in the middle or at one end, so that, thinning away to fine rounded edges at both ends or one, they looked like chisels or kelts. There was a striking resemblance between the thinner and more elongated of these and the flattened spicular processes observed in the first specimen. But there were no isolated thick rhombs, and no combinations of thick rhombs with spicules. On the other hand, it was not difficult to determine that these crystals bore a very strong likeness to rhombs much drawn out in the direction of their long axis, with excessive widening and rounding of their obtuse angles.

Fig2.



(*b*) A portion boiled, filtered, and treated with a few drops of hydrochloric acid during cooling. At the end of twenty-four hours large rosette crystals were found in no large quantity, some free, some deposited around fibres from the filtering paper (Fig. 3). The rosettes were built up of large broadened yellow rhombohedra, with the flattened (as opposed to the chiselled) ends outward. On the third day some patches of film such as constituted the whole deposit in (*a*) were observed; and on the fourth day the larger crystals were found bristling with attached smaller ones having the chiselled ends outwards; so that here was presented a curious modification of the crystals observed in the original specimen, and it was indicated that the combination of two forms therein observed was due to crystallisation occurring in two stages.

For the further experiments a solution of uric acid in caustic potash was used, and was decomposed by hydrochloric acid.

The crystals formed when only the solution and the acid were used, were large thin oblong plates, rarely perfect or regular, but generally marked with diagonal lines very clear at their decussation, and fading towards the angles.

Exp. 2.—Some egg-albumen was diluted with twice its bulk of water, and placed in a narrow test tube; upon this an equal bulk of the uric acid solution was poured, without mixing; hydrochloric acid was then added in excess. Next day there were

Fig3.

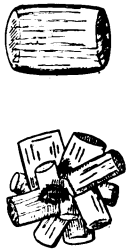
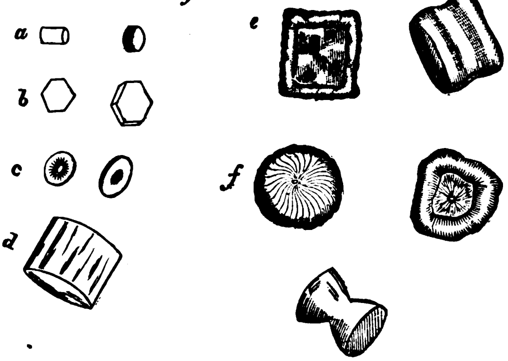


Fig4.

found on the surface of the albumen beautiful lamellar crystals of great size, having four diagonal, and two or four intermediate rays; some perfect, some not they resembled in a general way the crystals deposited from the simple solution, but were far more perfect in outline, and more regularly and minutely figured upon the surface (Fig. 4).

Exp. 3.—Egg-albumen similarly diluted; mixed with equal bulk of uric acid solution; hydrochloric acid added in excess. Under the microscope there were no lamellar crystals; the forms present were various, viz. (*a*) small thick rhombs with the obtuse angles rounded; (*b*) thinner rhombs, with the acute angles truncate, producing an approach to hexagonal form; (*c*) oval plates produced by rounding of all the angles of (*b*), with a central depression, perforation, or cavity; two-thirds of the deposit consisting of such forms; (*d*, *e*, *f*) large flat rhombohedra of yellow colour, exhibiting numerous degrees of transition to spherical or subspherical bodies with radiating striation on the one hand, and to dumb-bells on the other (Fig. 5).

Fig. 5.



Exp. 4.—Egg-albumen boiled hard, and digested for some time with pepsine and a drop of hydrochloric acid, at a temperature of 90° to 100° Fahr. The resulting peptone mixed with twice its bulk of water, and afterwards with the uric acid solution and hydrochloric acid. Next day a precipitate was found composed entirely of large, perfect, very thick, but quite homogeneous, halbert-shaped crystals (Fig. 6).

Fig.6.

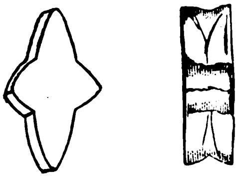
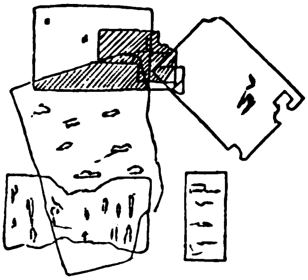


Fig.7.



From these results it became evident that albumen in different conditions had a remarkable influence in determining the kind of crystal deposited. But in the original specimen sugar and most probably other substances not naturally present in the urine might have contributed to the unusual crystallisation. The effect of some of these must therefore be seen.

Exp. 5.—Solution of refined cane sugar, treated as above. Result: very thin lamellar crystals of long oblong shape with unbroken angles, mostly perfect edges, and tolerably homogeneous internal structure; diagonal lines indicated (Fig. 7).

Exp. 6.—Solution of impure grape sugar. Delicate, flat, elongated plates, with three-sided ends, perfectly unbroken contour, and perfect internal homogeneity.

All uniform in size, but varying in the rounding of the terminal angles (Fig. 8).

Fig. 8.

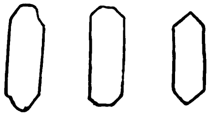
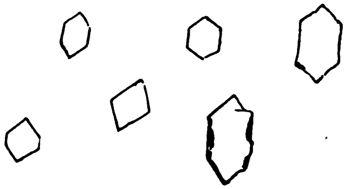


Fig. 9



Exp. 7.—Solution of brown cane sugar. Six-sided plates of all sizes; the smallest the most perfect (Fig. 9).

Exp. 8.—Solution of gum-arabic. Forms chiefly lamellar; viz., extremely elongated, oblong plates, often slightly curved inwards between the angles; outline often jagged, and surface much figured. By much drawing out of the angles some large feathered crystals were obtained; and besides these some curious compound crystals, reminding one of windmill-sails (Fig. 10). Mixed with the large plates were small spherical bodies looking like tiny spores, each presenting a bright spot.

Fig. 10.

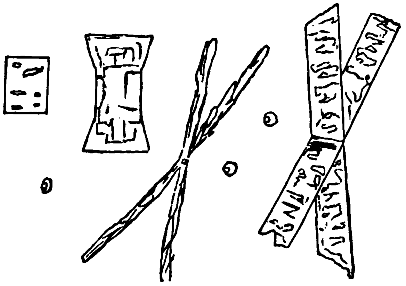
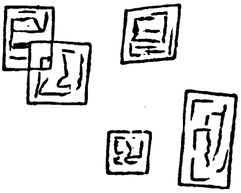


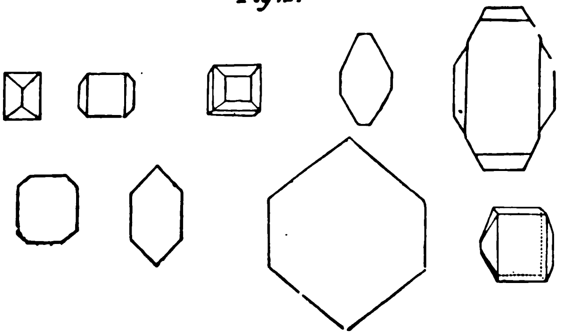
Fig. 11.



Exp. 9.—Solution of starch. Plates, some square, most oblong, chiefly rectangular, but in some cases slightly oblique; of uniform thickness, figured surface, continuous outline (Fig. 11).

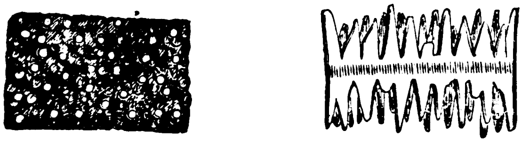
Exp. 10.—Weak solution of gelatine. Two extreme forms. (*a*) Large, very thin, but in all respects perfect hexagonal plates. (*b*) Sub-cubical crystals much smaller than the plates; seen one way they had a square outline; turned on to their sides a hexagonal or octagonal outline; so that they were apparently modified dodecahedra. The plates and the crystals were clearly linked by a series of transitional forms produced by gradual cutting away of layers of the square surface (Fig. 12).

Fig 12.



Exp. 11.—Thicker solution of gelatine. The mixture effected while the solution was warm, and the jelly examined when perfectly set. The uric acid was deposited in large, coarse, oblong masses,

Fig. 13.



having at first sight a much figured surface. Seen sideways these masses were resolved into an oblong axial plane, bristling on both surfaces with stout acicular crystals (Fig. 13).

Exp. 12.—Some strong clear gelatine jelly was melted, mixed with an alkaline solution of uric acid, and allowed to cool. Upon this, when fully set, diluted hydrochloric acid was poured in such quantity as to be in excess of the alkali present in the jelly. In the morning the gelatine was filled with thick halberts, and with curious lamellar crystals connecting the halbert with the rhombohedron and oblique octohedron. It is worthy of remark that in this series, while the outer surface of the rhomboidal plate is undergoing indentation so as to approach the halbert-shape, a halbert is also growing up within to meet it; the perfect halbert ultimately obtained being the result of the double process. This illustrates what I elsewhere found occasion to note, that crystalline are altered by two processes, by modifications of surfaces and angles, and by corresponding internal re-arrangement of molecules (Fig. 14).

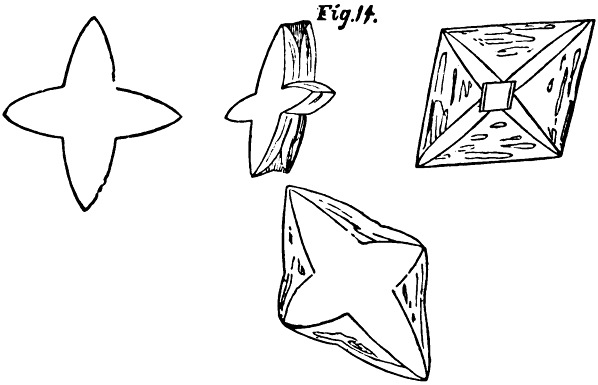


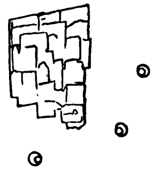
Fig. 14.

Exp. 13.—In relation to the original question, it was important to notice the effect of the presence of glycogen and liver-sugar upon uric acid. Some fresh bullock's liver was crushed and boiled in water. The decoction after filtration was clear, of a dark brown colour, reduced oxide of copper freely, and gave, with hydrochloric acid, a dense amorphous precipitate, chiefly, of course, glycogen.

To a portion of the decoction some strong solution of uric acid in liq. potassæ was added, and then the usual excess of hydrochloric acid.

In the precipitate (Fig. 15), mixed with the amorphous glycogen, were lamellar crystals, with a broken oblong outline, and much figuring of the plane surface, by the presence of small imperfect lamellæ. The amount of crystalline deposit did not at all correspond with the amount of uric acid used, no precipitate being in fact produced when the ordinary solution was used, so that it was concluded that the uric acid had in part entered into some not easily crystallisable compound with certain constituents of the decoction.

Fig 15.



Excepting where it is specially stated otherwise, the same conditions of temperature, the same strength of solution of uric acid, and the same degree of excess of hydrochloric acid were secured in these experiments. Dr. Sansom had already shown the form of the uric acid to be much affected by the strength of the urate solution and the concentration and excess of the acid; and therefore all care was taken to preserve uniformity of conditions in this respect.

Time, too, was most important. Dr. Beale very justly observes that crystals of uric acid often acquire entirely different characters if allowed to remain a longer time immersed in the urine. In the course of experiment it was observed that the crystals deposited on the second day were different from those deposited on the first. And when crystals were put aside for further examination, they were often found changed beyond recognition after a few days. Uric acid in many of its aspects closely verges upon the colloids, affecting their heavy molecule, and prevalent quaternary composition, their proneness to change under slight, or scarcely visible provocation, their slight diffusibility, and, in part at least, their rounded form. In dealing with it, therefore, in respect of the forms assumed under given circumstances, time, so important an element in all reactions of colloid matter, required most careful attention. The observations were made as nearly as possible at the end of twenty-four hours from the institution of each experiment. Sources of fallacy arising from this side being eliminated, the variety of the forms obtained in the experiments still required explanation, and the chief cause of this variety seemed to be found in the character of the solution from which the acid in each case was precipitated. Having regard to diagnosis, the remarkable difference of the crystals obtained in the presence of albumen and sugar respectively could not pass unnoticed. In the sugar solutions of all kinds lamellar and micaceous forms prevailed. Compared with the acid as precipitated from the simple or unmixed solution, these forms were more regular and more definite, but they became more definite and smaller as the sugar solution deviated from purity; the crystals deposited from the solution of pure sugar resembling very closely the crystals from the simple solution. On the other hand, in the grasp of the albumen the colloid nature of the acid was easily asserted; small stout sub-cubical crystals passed, through all degrees of rounding, to spherical and calculous forms, even within twenty-four hours; a few days always sufficing to obliterate all angularity and sharpness of outline in the crystals, and to turn them into such shapes as are seen in Fig. 5, *e*, *f*, very faithful repetitions of Fig. 158 in Pl. XXVIII. of Beale's "Deposits" (1869). The difference in the influence of egg-albumen and peptone, particularly when compared with the difference in the crystals deposited in dense gelatin and thin gelatin respectively, illustrates very beautifully the greater power of a more typical colloid in neutralising crystallising force. Egg-albumen, whether soluble or coagulated, exercises, as far as my observations go, a more powerful influence of this kind than any other substance, excepting, perhaps, some of the pigments of blood, urine, and bile; and though the present inquiry is at the moment limited in its scope, the wider bearing of this fact upon questions of structure-formation in animal bodies is suggested, and will at a subsequent stage of the investigations be considered.

It cannot be supposed, however, that the conditions, so far considered, suffice to explain all the phenomena observed, or to exclude other causes of modification. The well-known aptness of sugar to combine with other crystalline substances, and to modify their solubility and other properties, renders t not improbable that some of the marked differences observed in experimenting with the saccharine group of matters may have been due to some such combinations; the suggestion gaining much force from what occurred in the attempt at crystallisation from the liver-decoction. And the fact that the coloured crystals deposited from urine, both spontaneously and after the addition of acids, differ materially in shape and character from the colourless crystals deposited from the artificial solutions, probably indicates that combinations of extractive and colouring matter with uric acid, have much to do with the mode of its crystallisation. Considerations of this kind made it evident at the time that much close observation and experiment upon uric acid, as crystallised from urine of all sorts, would be required in order that any effective use might be made of the indications afforded by this series of experiments.

But one suggestion arising out of these inquiries was to the effect that the difference between uric and urinary acid, as seen under the microscope, would be likely to result from the association of colloids with the latter. In the attempt to resolve this problem the method of difference was applicable, as well as the method of agreement, and the results are therefore, according to the rules of the inductive logic, the more trustworthy.

A review of the circumstances showed that 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 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, in one with, in one 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, etc., 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 favourable 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 experiment showed conclusively that mucus with earthy phosphates, etc., 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 recrystallisations were made, each time with loss of colour, and the forms accompanying each loss of colour were noted and drawn (Pl. I., 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 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

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[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.

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. And when it is remembered that the pigment of urine is a colloid of high molecule, related with the pigment of blood, and that this pigment has a special combining affinity with uric acid, the inference follows that this pigment is the main efficient of the rhombohedral form. The twofold position thus obtained by experiment is supported by the observation of natural urines, and the result is that several of the modifications of uric acid found in urine can be scientifically explained.

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 ratâ* 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 (Pl. I., 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. 40).

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, p. 41).

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

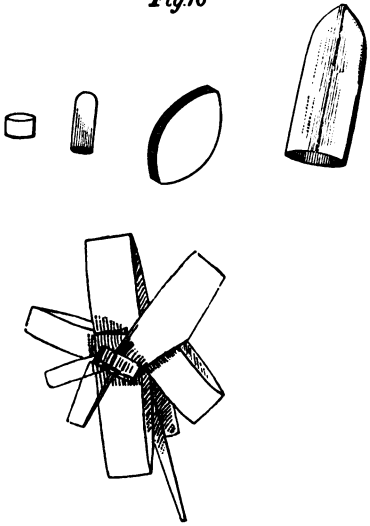
Lastly, in albuminous urine of still lower specific gravity (1009 to 1015) there are found, associated with very small rhombohedra, tub- or cask-shaped crystals (doliola). The rhombohedron is still to be detected under the disguise of the doliolum. The alternate obtuse and acute angles are rounded off, 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 (Pl. I., 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 beautiful 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.

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 (Pl. I., Figs. 11 and 12).

Three observations of the influence of sugar with and without albumen on the form of uric acid are annexed.

Obs. 1.—Diabetic urine; spec. grav. 1045; contains albumen. Forms; (*a*) small thick rhombs, often

Fig.16



elongated to spicular shape; (*b*) large lozenge rhombs, with corresponding spicular shape; (*c*) aggregations of the above, with the chiselled ends outwards (Fig. 16).

Obs. 2.—Diabetic urine; sp. gr. 1028; no albumen. Forms; (*a*) large thin plates of oblong outline, with rounded ends and thinned edges, depressed rhombs; sometimes hexagonal; (*b*) combinations of these into rosettes, with the chiselled ends outwards; (*c*) small rhombs and chisels free or attached to the larger. Nearly every one of the larger plates had a little thick rhomb in the centre (Fig. 17).

Fig. 17.

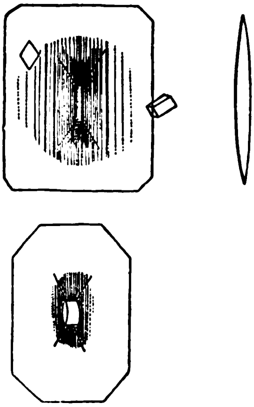
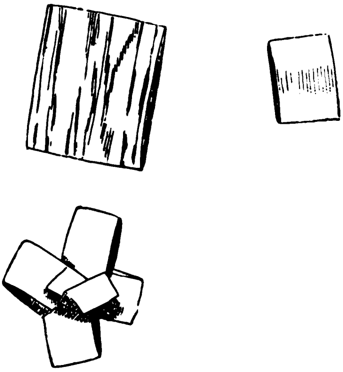


Fig. 18.



Obs. 3.—Diabetic urine; spec. grav. 1053; no albumen; very pale. Hydrochloric acid added. Forms, large thin oblong crystals with chiselled ends; colour, deep yellow. They resembled the crystals of the preceding observation, but were less regular both in internal composition and outline. When combined, they had the chiselled ends outwards (Fig. 18).

In the first observation the presence of the albumen had so far prevailed as to lead to the production of the stouter forms of crystal, but in both the second and third observations the plate-producing influence of the sugar was evident, the beautiful crystals of the second case bearing a strong resemblance to the forms produced with the brown sugar and impure grape sugar.

Forms of Uric Acid in Purulent Mucus.—Production of Calculi.—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 warming, 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 surrounding 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 counterpart 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 shall hereafter draw from the observed influence of colloids upon oxalate of lime and other salts be 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

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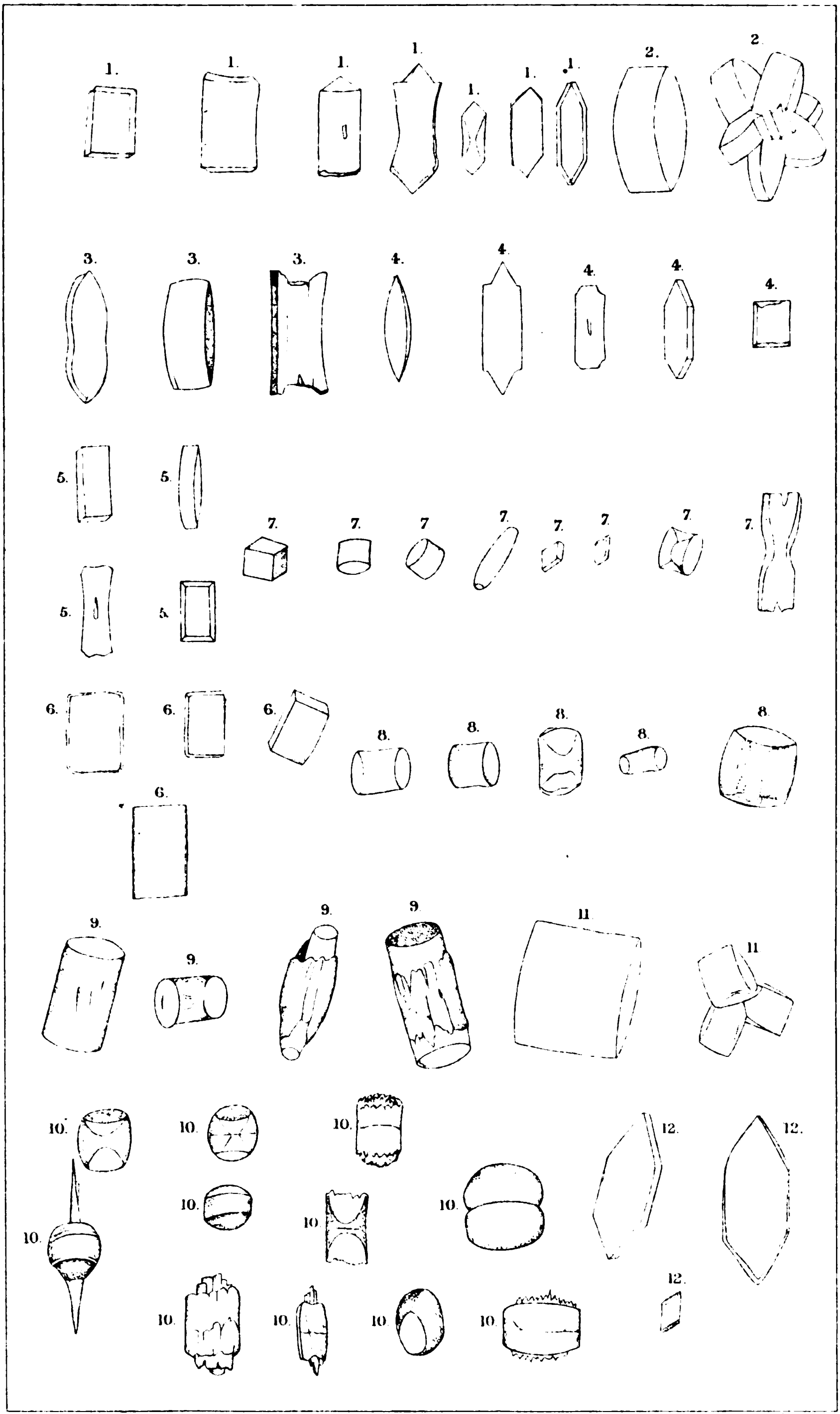
[1] "St. Thos. Hosp. Rep.," 1871.

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 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.

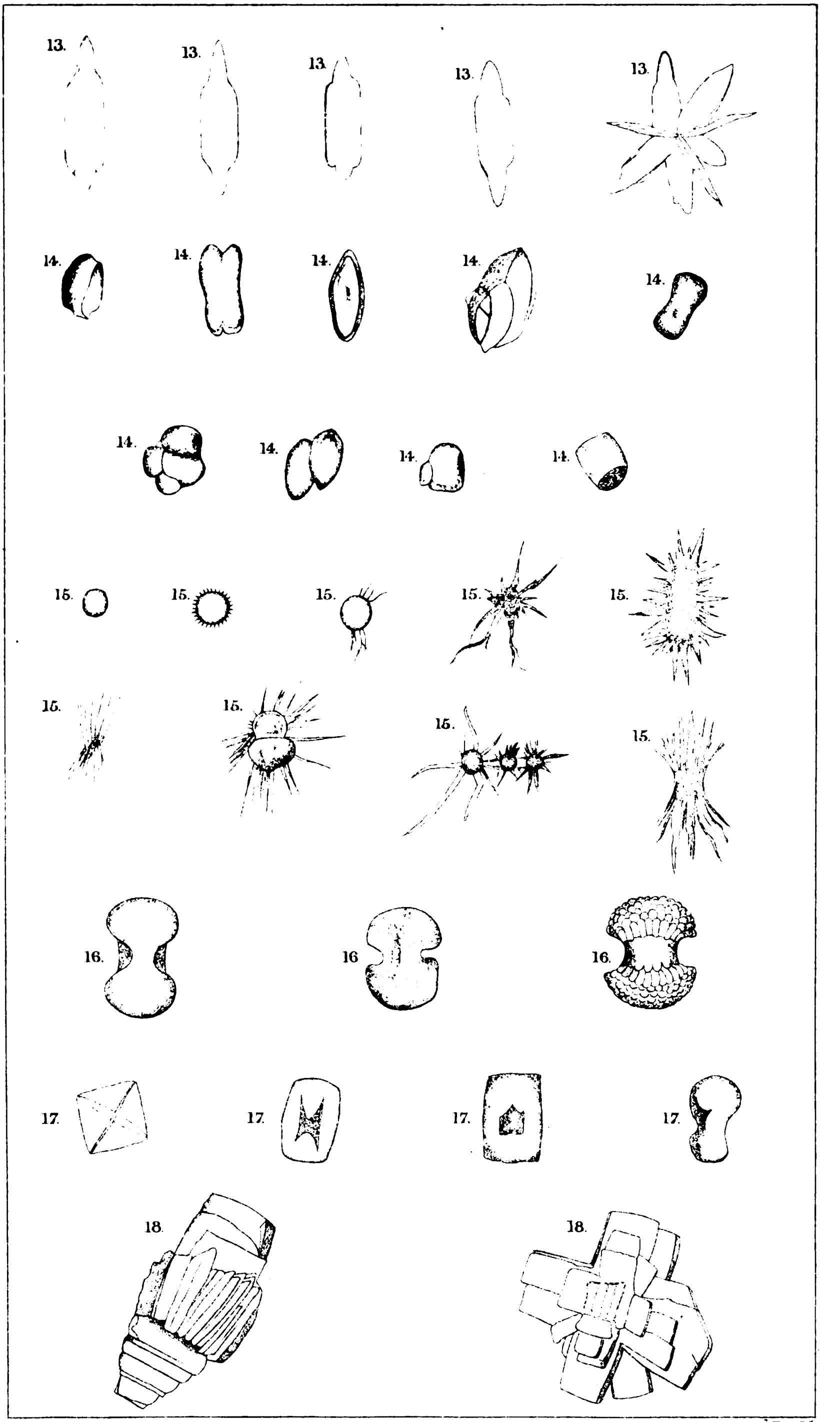
Uric Acid in Calculi.—Separate crystals and spheres of uric acid can sometimes be found in the nuclei of calculi having the same composition, and are not infrequently found scattered through calculi mainly composed of other substances, in particular of oxalate of lime. But the substance has a different arrangement in the bulk of uric acid calculi. Take, for instance, one of the typical forms of uric acid calculi, a pisiform calculus of Prout, and carry a section through its centre. The surface of the section presents a number of concentric bands, differing in colour from yellow to dark fawn-colour. These are sections of concentric laminæ of uric acid intimately mixed with a non-crystalline organic matrix. Each lamina is found under the microscope to consist of fibrous crystalline matter, the fibration being radial, and the fibres extending through the thickness of the laminæ. The appearance is figured by Dr. Carter (*op. cit.* Plate I., Figs. 6, 7), and may be instructively compared with a drawing (Fig. 5 A) of a section of crab-shell in Mr. Rainey's "Molecular Coalescence," page 85. Mr. Rainey demonstrates that the lamellæ and radiating lines of the shell are produced by the coalescence of spheres of carbonate of lime (with some phosphate) in the animal organic matter. If Mr. Rainey be right, as I believe him to be, in the one case, the applicability of the reasoning to the other is evident. The conclusions which, two pages back, were reached synthetically, are now confirmed by analytic observation.

Plate I.



Stanford's Geog^l Estab^t.

Plate II.



Stanford's Geog^l Estab^t.

DESCRIPTION OF PLATES I. AND II.

PLATE I.

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 colouring 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 II.

FIG. 13.—Uric acid.—In watery fluid round mucus. Exp.

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.—Triple phosphate. Deposited in flaky mucus at temperature of 100° to 110° Fahr. Exp.

CHAPTER IV.

URATES.

THERE is as marked a difference between the form of pure urates and the form of urinary urates, as has been just illustrated in the case of uric acid. In healthy urine the urates are deposited in fine molecules, decidedly not crystalline, and not certainly spherical. The normal form being prismatic it is to be presumed that other substances present in solution determine molecularity. A series of experiments and observations on the behaviour of urates under varying conditions[1] may with advantage be first related.

1. *Urate of Soda.*—Uric acid, combined in various proportions with soda, and probably, as the experiments now to be related indicate, with other substances, presents itself to observation in three forms at least as a pathological phenomenon. Urate of soda is crystalline in tophaceous concretions and in cartilage, spherical in certain somewhat rare conditions of the urine, amorphous in cartilage, tophi, and urine.

In a slice of the cartilage from a gouty great-toe joint the urate occurs in long needles usually bent, and pointed at both ends. These are sometimes scattered, sometimes in parallel bundles, sometimes in

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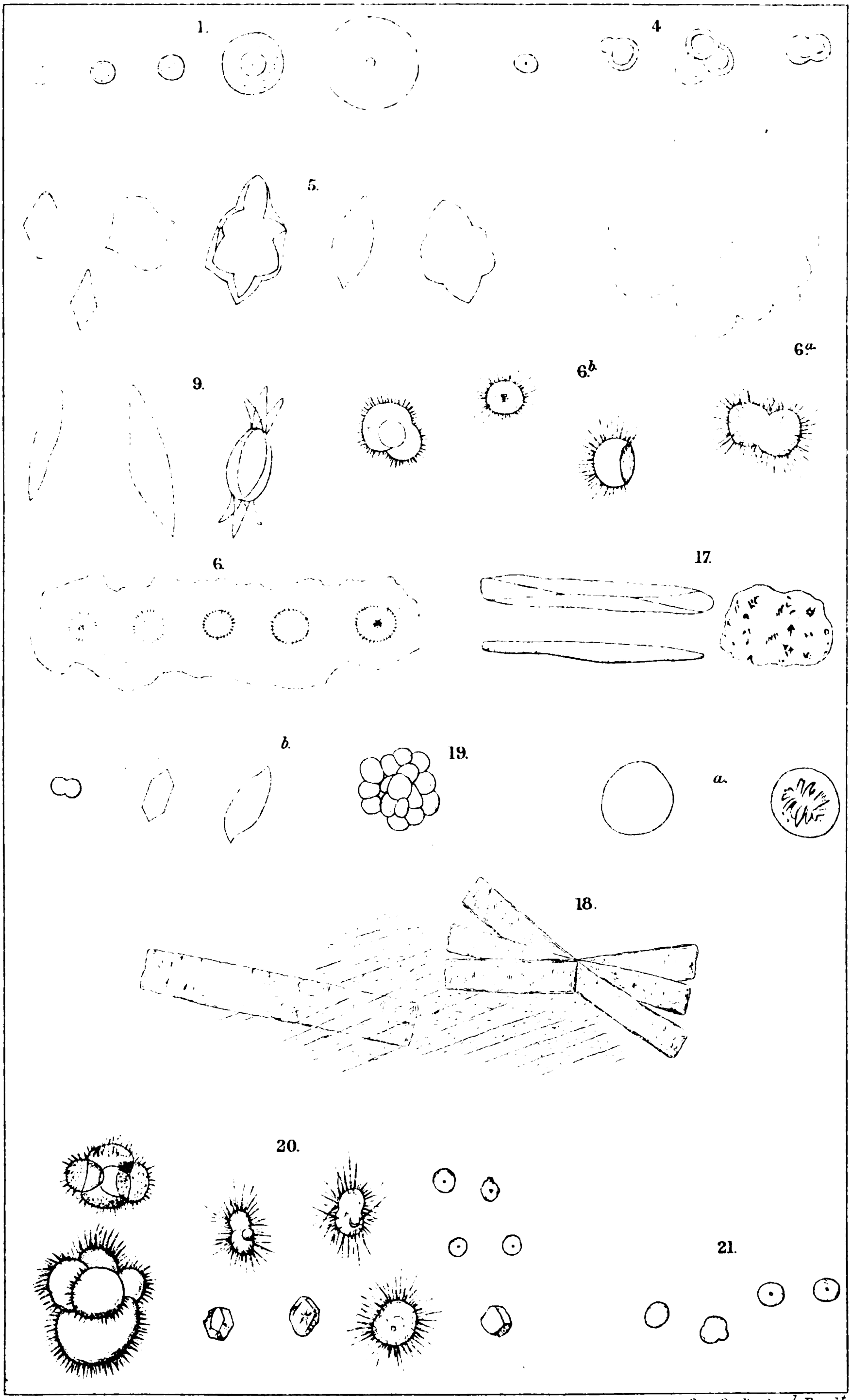
[1] The following observations were in part published in the "Monthly Microscopical Journal" for March 1875, and in the "St. Thomas's Hospital Reports" of the same year respectively.

Plate III



Stanford's Geog^l Estab^t.

radiating tufts, sometimes woven and matted irregularly. Dr. Garrod,[1] Dr. Roberts, Drs. Cornil and Ranvier, and others, have figured this form of deposit, and as it agrees with the form in which neutral urate is artificially deposited, also figured by Dr. Roberts,[2] Dr. Beale,[3] and Drs. Ultzmann and Hofmann,[4] I do not propose here to put forward any fresh drawing of a so-well-recognised form.

EXPLANATION OF PLATE III.

Fig. 1.—Urate of soda, deposited in liquor sodæ.
„ 4.—Biurate (?) of soda, in gelatin.
„ 5.—Uric acid in gelatin.
„ 6 *a*.—Urate of soda, with uric acid, in gelatin.
„ 6 *b*.—Ditto.
„ 6 *c*.—Ditto.
„ 9.—Uric acid and urate of soda, in water.
„ 17.—Uric acid and urate of soda in presence of concentrated solution of chloride of sodium.
„ 18.—Urate of soda and uric acid with concentrated solution of chloride of ammonium.
„ 19.—Deposit from solution of urate of ammonia after rapid evaporation—*a*, first day; *b*, second day.
„ 20.—Urate of soda in concentrated solution of chloride of sodium.
„ 21.—Urate of soda in concentrated solution of chloride of potassium.

Mixed with the crystals, masses and clouds of fine granular matter having a brownish tint by transmitted

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[1] "Med. Chir. Trans.," vol. xiii., 1848, p. 97.

[2] "Urinary and Renal Diseases," p. 71.

[3] "Urinary Deposits," pl. xviii., figs. 98 and 100.

[4] "Atlas der Physiologischen und Pathologischen Harnsedimente," Taf. viii.

light may be observed. These agree with the amorphous form of urate of soda, and are, like the crystals, slowly extracted by water. The amorphous form is well represented in the coloured figure No. 2, Taf. viii., in Ultzmann and Hofmann's Atlas.

A spherical form of what is generally supposed to be urate of soda has been represented by Dr. Golding Bird, Dr. Thudichum, Dr. Roberts, Dr. Beale, and Drs. Ultzmann and Hofmann. It consists of small, very perfectly-outlined spheres, which, as Dr. Beale describes them, are of great lustre, and which have usually spikelets of uric acid deposited on their surface. They are said to be found chiefly in the urine of children, and of persons in a feverish state (Dr. Beale); in the long-retained urine of children in fever (Dr. Roberts); in the urine of persons labouring under fever who were treated with carbonate of soda (Dr. Golding Bird); in the urine of children suffering from petechial typhus not treated by carbonate of soda, from measles, and from scarlatina (Dr. Thudichum). Drs. Ultzmann and Hofmann give, besides these, figures of large, somewhat irregular crystalline dumb-bells from the urine of a child suffering from intestinal catarrh.

Dr. Thudichum[1] states that if a solution of urate of soda be allowed to evaporate spontaneously, the salt is deposited in simple spherical masses and granules. Dr. Beale[2] gives twice a drawing of large spheres of urate of soda with halo of fine radiating needles, obtained by concentrating healthy urine; and also a drawing of some very large spheres from a case of remittent fever (sent by Dr. Kennion).

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[1] "Pathology of the Urine," p. 91.

[2] "Kidney Diseases, Urinary Deposits," etc., 1868.

It may be assumed that the needles are to be regarded as crystals, though their appearance of flexibility, their remarkable tenuity, and the absence from them of indications of angularity of section are departures from the typical qualities of the crystal. They are to my mind crystals with definite colloidal affinities.

Assuming that the needles are crystals, they occur where, *primâ facie,* crystals ought not to be looked for. Crystallisable matters of low solubility deposited in a colloid, such as the substance of cartilage, deposited, moreover, at the comparatively high temperature of the body, might, according to our experience, be expected to affect a spheroidal form. The departure from the rule is so startling as to make it probable that when the conditions are fully known much addition to our knowledge of the working of the rule may be hoped for.

Conversely, the same substance which forms crystals in the presence of colloids, forms spheres where the influence of colloids is less manifest, or is absent. Here again extended observation of conditions is necessary.

I will now relate a series of experiments affecting the habits of urate of soda under various conditions, and endeavour to draw therefrom inferences in explanation of the aberrations above noted.

1. Uric acid from the urine of the boa, white in colour, crystallised in long rectangular plates, was dissolved with the aid of heat in liquor sodæ (Br. Ph.) The acid was added in small quantities until no more was dissolved. The liquor was filtered and left to crystallise. The urate was deposited entirely in

spheres. The spheres were sharply outlined, brownish, very regular; in diameter from $\frac{1}{800}$ inch downwards; some were clear in their interior, some granular; some marked with concentric zones of lighter and darker colour; some gathered in conglobate masses.

Fig. 1. Smallest; clear; $\frac{1}{2000}$ inch.
Next, granular, $\frac{1}{2000}$ to $\frac{1}{1000}$ inch.
Larger, zonate, $\frac{1}{1000}$ to $\frac{1}{800}$ inch or more.

These forms did not affect polarised light.

2. The precipitate from the above was collected on a filter, washed with cold water, and afterwards dissolved in boiling water. The solution was neutral. On cooling, long, curved, pointed needles were deposited. They were partly matted, were partly in not very regular radiating masses, and resembled very closely the needles of gouty deposit in cartilage.

3. A weak solution of gelatin, which formed only a very thin scarcely coherent jelly on cooling, was prepared. It was clarified by albumen, but not further purified. In this a portion of the precipitate of No. 2 was boiled, the quantity of precipitate being in excess of the solvent powers of the liquid. The liquor was gradually cooled to 40° Fahr., and then formed a soft jelly. The urate was deposited in a fine molecular condition. The molecules were gathered into irregularly spherical masses, which were soft and friable on the least pressure. There were no firm, separable spheres, and there were no crystalline or other structural forms.

4. To a solution prepared and treated as in 3, acetic acid was cautiously added before cooling, till a faint acid reaction was obtained. The next day there was a large deposit of brilliant, highly-refractile

spheres with smooth surface, some homogeneous, some with faint, radiant, internal disturbance. These spheres were of about twice the diameter of blood-corpuscles, and were mixed with molecular deposit as in 3 (see Pl. III. Fig. 4).

5. A similar solution treated with large excess of acetic acid. The forms were now decidedly the forms of uric acid, as known to be deposited in gelatin. They included large halberds, diamonds, pointed ovals, and small rhombohedra (see Pl. III. Fig. 5).

The foregoing experiments tending to show that with acid urates spherical forms were assumed, further investigation was made in this direction. And with very interesting result.

6. Pure urate of soda and pure uric acid were added in equal quantities to a weak non-gelatinising solution of gelatin. Mixture boiled and filtered. In the filtrate there appeared at the end of twenty-four hours (temp. 45°) forms as in No. 4. At the end of forty-eight hours, the temperature having meanwhile fallen to 40°, the spheres were found covered with a dense deposit of needles (Pl. III. Fig. 6). The precipitate included three groups of forms: *a*, large irregular masses, looking by transmitted light like black velvet; *b*, dark brown spheres, with a halo of densely-packed fine bristles; *c*, curious pale spheres, looking very much like pus-globules in partial decomposition. They were composed of a thin crust of tiny radiating rods and a cavity within containing a few granules not having any obvious regularity of arrangement. All these forms were imbedded in a gelatinous matrix distinctly defined from the original solution. This matrix may have been hardened gela-

tin, or a compound of urate or uric acid and gelatin, or a colloidal form of uric acid or urate. And the deposit of needles may have been either a further crystallisation or a metamorphosis. The fact that where they could be seen the spheres round which the bristles were arranged were imperfect on one side and reduced to crescents is important (see Pl. III. Fig. 6, *b*).

7. The whole mixture of No. 6 was boiled for some time, but without perfect solution of the precipitate. It was filtered, and the solution was divided into two equal portions, *a* and *b*.

To *a* a solution of 20 grains of chloride of sodium in half an ounce of distilled water was added. The next day (temp. 45°) there was a brownish granular deposit resolved under high powers of the microscope (300 diam.) into fine matted needles and molecular matter. To *b* acetic acid in excess was added. Result next day (temp. 45°), long slender wheat-sheaves; circular radiant tufts of needles; large, very perfect rhombohedra; and very large foliaceous and pennate crystals.

8. To fresh urate, of alkaline reaction, uric acid added in decided excess. This, after boiling in distilled water and filtering, deposited at 45° dense tufts of needles. The solution was only faintly acid.

9. Neutral urate of soda with equal quantity of uric acid boiled in distilled water. Solution acid. Filtrate deposited delicate navicular crystals, single, in bunches and in stars.

10. To boiling solution of urate of soda with slight excess of uric acid an equal quantity of boiling distilled water added. Solution cooled by next day

to 38°. A small deposit, chiefly on the surface, of thick navicular crystals with central hollow; no other forms.

11. Mixture in 10 boiled, evaporated to $\frac{1}{3}$, and then divided into two portions; one rendered alkaline by four drops of liq. sodæ, the other left acid. Cooled to 38°. The first day produced soft much-conglobate spheres, in semi-gelatinous matrix, in both solutions; the spheres being larger in the alkaline solution. Both solutions were left in a temperature ranging between 50° and 60° for a week, and at the end of that time the whole deposit was found transformed into needles.

A parallel series of observations was next made with albumen.

12. To a clear filtered solution of urate of soda in boiling water, one-third bulk of egg albumen was added when the temperature had fallen to 120°. On complete cooling, tufts of the ordinary form of needle were deposited.

13. Slightly alkaline urate was digested in distilled water at 100° Fahr., and one-third bulk of egg albumen added. No crystalline or formed precipitate, but formless tracts of molecular matter.

14. Alkaline urate boiled in distilled water and filtered. Half bulk of egg albumen added to hot solution and the coagulated mixture cooled. Needles both in fluid and coagulum, with much molecular matter in coagulum.

15. The mixture in 14 was now boiled for some time, in order that the coagulum might be fully saturated with the urate solution. On cooling, the flakes of albumen were found to have absorbed most of the

urate. They contained large brown tracts of molecular matter, with faint indications of the presence of very small delicate needles. The solution contained no needles.

16. The mixture was again heated, and a small excess of acetic acid added. Now there occurred granular deposit in the albumen, and a free formation of small thick rhombohedra on the surface of the flakes. On again heating and adding more acetic acid, rhombohedra and bright spheroids were formed.

The influence of chlorides was now examined. Dr. Bence Jones in the year 1844 showed that the presence of chloride of sodium in solution with urate of ammonia prevented the formation of crystals and determined the occurrence of the molecular urate; and that the solubility of urate of ammonia was doubled by the presence of chloride of sodium.

17. To a solution of urate with free uric acid, as in 10, a strong, nearly saturated, solution of chloride of sodium was added in equal bulk. On cooling, the liquid was found almost filled with a gelatinous precipitate, which did not subside. It had just the appearance of freshly precipitated gelatinous silica. Under the microscope the gelatinous matter was found in well-defined masses, quite distinct from the liquid; it had a mottling of bright points and obscurely indicated acicular crystals, which were often gathered into rounded groups. The crystals were irregularly interlaced, and gave rise to an appearance of polygonal cellular structure. Imbedded in the gelatinous matter were numerous lengthened navicellæ, and chisel-ended three-sided prisms (see Pl. III. Fig. 7).

18. A similar experiment to 17 was made, with

the substitution of chloride of ammonium for chloride of sodium. A light semi-gelatinous substance was at once perceived to be formed in the liquid. This was boiled for several minutes, but was not dissolved. On cooling, it was found to consist of a brownish matrix, richly moleculate, and having imbedded numerous long, flat, quadrangular plates like those of uric acid in sugary solutions (see Pl. III. Fig. 18).

19. To solution of alkaline urate of soda at 100° Fahr., a hot concentrated solution of chloride of ammonium was added. A white gelatinous precipitate fell at once. It was amorphous, and molecular both when formed and after cooling.

20. To solution of alkaline urate at 100°, a hot concentrated solution of chloride of sodium was added. No precipitate occurred at the time; but next day a gelatinous mass was found filling two-thirds of the liquid. It contained (*a*) small refractile spheres, almost homogeneous, with a tiny central cavity; these were about as large as lymph-corpuscles, and were very like the spheres of carbonate of lime in gelatin; they did not affect polarised light; (*b*) large brown spheres variously aggregated; granular, not fibrous; not refractile; denser at the surface than at the centre; covered with radiating needles, just like cilia round an infusorium; these with the rest of the forms were imbedded in a gelatinous stuff which was apparently condensed among the cilia, so that the cilia corresponded to an outer sphere of partly condensed matter aggregated round the dark spheres; (*c*) rhombohedra, clear, thick, colourless, separate; with forms intermediate between them and the spheres (*a*) (see Pl. III. Fig. 20).

21. To a solution of alkaline urate at 100°, a hot concentrated solution of chloride of potassium was added. A precipitate fell at once. It was, under the microscope, a mixture of semi-transparent, waxy-looking stuff, with bright granules and dark solid spheres in large coalesced masses. The spheres had central points (cavities) and indications of radial striation, but there were no needles (see Pl. III. Fig. 21).

22. A hot but not very strong solution of phosphate of soda and a hot alkaline solution of urate of soda being mixed, no precipitate occurred till the mixture was cooled. The whole mixture then became a firm jelly, which did not liquefy or subside after a portion had been scooped out, but remained with sharp edges after twenty-four hours. Under the microscope it consisted of soft compressible spheres and a transparent structureless gelatinous matrix.

23. A very strong solution of phosphate of soda was mixed with equal bulk of solution of urate of soda at 100°. A precipitate speedily appeared. At the end of four hours this was found to contain large, beautiful, homogeneous, yellow spheres, presenting a black cross on pale white ground in the polariscope. The next day only half the spheres remained as at first, the other half being opaque and granular, or radiatingly fibrous, or expanded into tufts of fine needles. And at the end of a week the spheres were altogether replaced by tufts of needles.

II. *Urate of Ammonia.*

1. Uric acid was digested in liq. ammoniæ at 150 for two hours; left for twenty-four hours at temperature of laboratory; then, water being added, the mix-

ture was boiled and filtered. The salt was deposited in tufts of fine needles.

2. The filtrate was evaporated somewhat rapidly to a small bulk. It was then discoloured, having a pinkish brown tint, and had exchanged its former alkaline for a very decided acid reaction. On cooling, it deposited dark brown spheres with strongly-marked radiating crystalline tendency within, and an outer layer of dense, homogeneous, non-crystalline character. They looked as though in a state of tension. On examining the deposit next day I found the spheres all broken up into delicate six-sided plates, rhombs, and diamonds, with masses of small, bright, coalescing spheres, mixed with small dumb-bells and octohedra of oxalate of lime. There was apparently a mixture of uric acid, acid urate, and perhaps neutral urate (see Pl. III. Fig. 19, *a*, *b*).

3. With albumen used in many ways I obtained urate of ammonia always in the finely molecular form.

4. Gelatin had the same effect.

5. A strong hot solution of chloride of ammonium being added to a hot solution of urate of ammonia, a large, soft, light precipitate was formed at once. It consisted of coarse granules which did not sink or run together, being held apart by a gelatinous deposit containing very fine needles irregularly arranged. The granules were spherular, dumb-bell-shaped and irregular. The deposit had not altered when examined after several days. The solution was faintly acid.

6. Hot strong solutions of urate of ammonia and chloride of sodium were mixed. The solution was still clear while hot, and was faintly acid. Next day a bulky gelatinous precipitate had fallen, and filled

three-fourths of the fluid. The precipitate was composed of bright spheres of various sizes, and bright spheroidal granules imbedded in a clear gelatinous stuff. The spheres were in appearance a little denser than white blood-corpuscles, and were a little more refractile. They looked soft, were easily altered in shape without being broken up by compression, and appeared to consist of fine molecules. The next day they were all altered, being replaced by dense masses of tufts of needles, and small, bright, firm, homogeneous spheres.

This precipitate was thrown on a filter, and washed with distilled water. Under the process of washing it lost its gelatinous character, and became a tough pasty mass. A portion of this was incinerated on platinum foil, and the fused residue was dissolved in distilled water. It did not yield the least trace of chlorine, but consisted apparently only of soda with a little carbonate. It occurred to me that chlorine might have been sublimed with ammonia, and I now took some of the precipitate formed by mixing hot solutions of urate of soda and chloride of sodium. This was thrown on a filter, and washed thrice. A portion of this was incinerated; the rest was then well washed and again incinerated.

The first incineration of the possible double soda salt yielded free indications of chlorine.

The salt was then compressed for some time between blotting paper, and was afterwards incinerated. There were again good indications of chlorine; so that the spheres were possibly a combination of urate of soda and chloride of sodium. But the combination, if it really existed, was destroyed by prolonged washing with distilled water; the salt left yielding no chlorine reaction.

As far as may be judged at the present stage of the inquiry, two forms at least must be added to the three forms of urate of soda already observed. And I am inclined to arrange the five forms thus obtained in the following order, according to their several degrees of departure from the colloidal or quasi-living state, to the crystalline or not-living state:

1. Gelatinous colloid.
2. Molecular urate.
3. Spherules of first kind, soft, and tending after a time to crystallise.
4. Needles.
5. Spherules of second kind; composed, as I believe, of matter originally crystalline, but subdued by colloid around to colloid form.

i. The gelatinous colloid form has been observed both in solutions containing only urate with uric acid, and in solutions of urate with chlorides or phosphates. It appears to correspond with the gelatinous form in which uric acid is deposited from alkaline solutions after the addition of acids, and, like that gelatinous form, has an impulse to crystallisation. The gelatinous form of uric acid is called a "hydrate" by Prout and others. I am disposed to call it simply the colloid form, leaving the question of any chemical distinction between a colloid and a crystalline form, such as would consist in hydration or non-hydration, an open question: though, as it seems to me, the alterations of molecular arrangement must be larger and more comprehensive than hydrations.

ii. The urate assumes the molecular form where as a crystalloid it should take the spherical. The molecules may be either small spheroids or small crystals. They show the mark of two several influences—the influence of a recognised colloid such as gelatin in one case, and in the other the influence of the colloidal forms of their own substance, from which they are departing in different degrees towards crystallinity.

iii. The large soft spherules, breaking up after a time into needles, appear to be magnified spherical molecules. They occur under two conditions—in acid urates, of soda and ammonia, and in the combinations of hot saturated solutions of urates with chlorides or phosphates of alkalies. In both cases they are transitional between the gelatinous colloid and the needle. In the second case it is open to considerable doubt whether they are merely urates having their molecular arrangement altered by the presence of strong saline solutions, or whether they are urates in combination with chlorides or phosphates. The medium of solution being the same in both cases, I incline to the latter view. But this part of the inquiry, full of suggestion and analogy, requires a great deal of experimental testing. It may be noted that these spheres closely resemble Dr. Garrod's drawings of urate of soda from pigeon's urine ("Med. Chir. Tr.," 1848).

iv. The needle, though a crystalline form, is not by any means the true or perfect crystalline form of urate of soda. The true form is a short six-sided prism. The needle of urate of soda occurs where uric acid would be found in spheres, and urate of ammonia in molecules. But it also occurs where uric acid would be in crystals—that is to say, where no colloid save colloidal modifications of itself exists.

In the cartilage the long, bent, rounded, pointed needle may be a parallel to the rhombohedron of uric acid in urine, and may be fairly supposed to represent some corresponding change to the change from flat rectangular plate to rhombohedron with rounded angles.

But the influence of alkali in altering the behaviour of uric acid has yet to be understood. First, what do the light spheres of urate in strong liq. sodæ mean? Do they mean that a strong solution of a crystalloid exerts some of the power of a colloid upon crystalline polarity? Or do they mean that the liquor sodæ, being able in excess and with the aid of heat to break up uric acid, exercises some of the molecule-disturbing power possessed by colloids beyond and above the influence of its density? Second, why are the needles formed in weaker alkaline solutions? Further observation is needed to explain this; but it is not unlikely that these needles are also the outcome of transient sphere formations; and after crystallisation the alkali may hold the uric acid in a crystalline state.

v. The bright compact spheres formed by acid urate in gelatin approach closely to the urinary forms recorded by several observers. They are in appearance like the spheres of crystalloids such as carbonate of lime, sulphate of baryta, iodide of mercury, and oxalate of copper, all of which when small are bright and homogeneous. Acid urates therefore assume shapes indicating that their form and polarities revert towards uric acid. In particular, where uric acid is used in large excess, as compared with its soda or ammonia, the crystals deposited from watery solutions are always navicular plates of great beauty and delicacy, and sometimes of great size, making the fluid in which they are suspended sparkle with bright flakes.

It is evident that with regard to causation these phenomena are open to some variety of interpretation.

First, for example, a strong solution of a crystalloid may, by its viscidity, oppose crystallisation in associated substances and act like a colloid in promoting the formation of spheres.

Secondly, the precipitate may be either a urate or a combination of urate with the other salt in solution.

Thirdly, the gelatinous substance first thrown down (often at boiling temperature) may act as a colloid in determining the form of later precipitates, whether of the same or of different chemical composition.

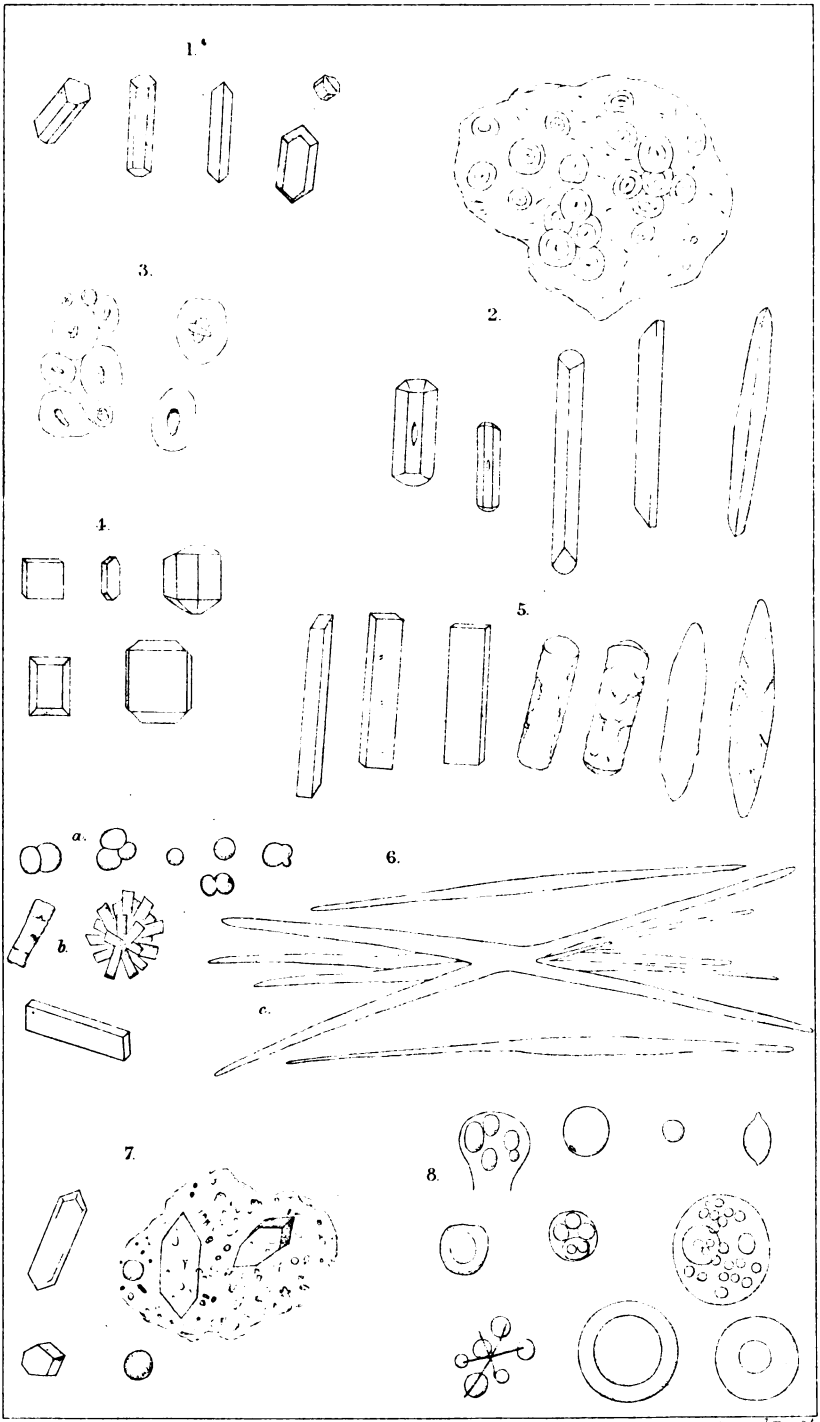
The experiments now to be related bear chiefly upon the first interpretation, and began with the substitution of uric acid for urates in solution of the chlorides. Would uric acid become spherical in presence of strong saline solution?

Exp. 1.—Boiling saturated solutions of uric acid and chloride of sodium were mixed in equal bulks, and left to crystallise.

Neither gelatinous matter nor spheres were observed in any stage of the precipitate, which consisted entirely of very regular and perfect prismatic crystals. The prisms were six-sided and sharp-ended, and were about three or four times as long as broad (see Pl. IV. Fig. 1). These crystals agree with the descriptions of urate of soda given by Thudichum and others, and supposing them to be composed of that substance, the process adopted is certainly the best I have yet tried for obtaining good investigable crystals.

Exp. 2.—Uric acid in excess was boiled for some

Plate IV.



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time in a strong solution of chloride of sodium, so far saturated as to deposit a small quantity of salt on cooling. The solution was filtered and cooled slowly.

DESCRIPTION OF PLATE IV.

FIG. 1.—Prismatic crystals of urate of soda.
„ 2.—Spheres and prisms of urate of soda, formed by boiling uric acid in strong solution of chloride of sodium.
„ 3.—Spheres from the same, formed six days later.
„ 4.—Uric acid deposited from same on addition of hydrochloric acid.
„ 5.—Acid urate of ammonia.
„ 6.—Urates and uric acid in gelatinous silica and in solution. (*a*) in solution; (*b*) in substance of silica; (*c*) in thinner silica.
„ 7.—Urate of soda in gelatin and chloride of sodium.
„ 8.—The same after boiling, evaporation and cooling.

At the end of three hours a precipitate of long three-sided prisms was formed, and lay in a powder at the bottom of the beaker. After twenty-four hours a second, much lighter, and granular precipitate was found overlying the first, and floating loosely upon it. This was found to be a mixture of gelatinous matter and spheres very like the deposit after the mixture of hot solutions of urate of soda and chloride of sodium. The spheres were lustrous, soft, and compressible, and in the centre of each was a bright rod. Among the crystals were now many with flattening of one or more sides, and many of them had a tiny rod in their middle, the axis of the rod corresponding with the long axis of the crystal. There were also many spindle-outlined and navicellar crystals, still with sharp angles (see Pl. IV. Fig. 2). At the end of six days the gelatinous matter had decreased considerably in quantity. The spheres were larger, were more closely aggregated, and were altered in character; whereas they were at first homogeneous, they were now granular, with distinct indications of radiating arrangement of granules, and in some cases with radiant striation. The central rod had now become an ovoid with pointed ends; sometimes there were two ovoids crossing each other at right angles (Pl. IV., Fig. 3). The prisms were now obscured by incrustations. At the end of six days more every sphere had disappeared, or was converted into a ball of fine radiating needles, and there was no remaining trace of gelatinous matter.

The decomposition of the chloride by the uric acid was doubtless carried much further during the prolonged boiling.

The different result in the two cases is probably due to two causes—1st, the greater production of urate; 2d, the formation of a lower urate.

In both experiments, however, the original question was unanswered as far as uric acid was concerned.

Exp. 3.—In Exp. 3, after the uric acid had been boiled in solution of chloride of sodium as in Exp. 2, some hydrochloric acid was added to the still hot filtrate, before the commencement of crystallisation. The forms thrown down on cooling were now clearly forms of uric acid. But they were, although tabular, much thicker tablets than are usually observed. They were tablets affecting the form of chloride of sodium; in fact, at first, I thought that some of them were chloride of sodium, and I only dismissed the idea when I found them resisting, after the manner of uric acid, the solvent influences of dilution and warmth (see Pl. IV. Fig. 4).

Exp. 4.—Strong, hot solutions of uric acid and of chloride of ammonium were mixed. Crystals were thrown down abundantly on cooling. They included a regular series of forms, from long slightly oblique four-sided prisms to large, very thin plates of navicular outline; these agreed with the forms of acid urate of ammonia (see Fig. 5).

Exp. 5.—On boiling uric acid in solution of chloride of ammonium, gelatinous matter and abundant needles were produced. Spheres were observed, but the needles were mainly in round tufts. It is, however, quite possible that there was a transient sphere formation preceding the period (twenty-four hours) at which the examination of the deposit was made.

Exp. 6.—Uric acid was boiled in solution of chloride of ammonium, and hydrochloric acid was added to the solution before cooling. Then elongated six-sided tablets were deposited, exactly resembling a common form of uric acid, and also resembling the form in which the chloride was deposited from acid solutions.

The answer given by these six experiments, so far as it goes, is, therefore, to the effect, that in the case of uric acid the presence of strong saline solutions does not materially determine towards spherical form. I say "not materially," because the subcubical crystal is certainly the first stage in the journey of uric acid towards sphericity in the presence of organic colloids.

Some observations which I have carried on for some time on the behaviour of uric acid in the presence of silica may be here quoted with advantage. They illustrate the influences of one substance in different molecular states upon the form of uric acid, and may throw light upon several of the appearances of conflict in preceding observations.

Uric acid and urate of soda dissolve with great facility in warm solutions of silicate of potash, more easily, I think (but have not proved), than in very strong liquor potassæ. The deposit which falls on cooling is always finely acicular.

When cool weak solutions of uric acid in silicate of potash or warm stronger solutions are cautiously neutralised with acetic, hydrochloric, or nitric acid, so that a precipitate of gelatinous silica falls at once, the uric acid is found afterwards in three well-marked forms. (*a*) In the solution, in plates—long, thin, rectangular—single, or gathered into radiating groups. (*b*) In the thickest gelatinous silica in small, brownish, granular, sharp-outlined spheres, separate or aggregate. (*c*) In the thinner silica, in remarkable long spicular crystals, mostly gathered in beautiful spherical or sub-spherical tufts (see Pl. IV. Fig. 6, *a*, *b*, and *c*).

Now, as is well known, when hydrochloric acid is suddenly added in large excess to warm solutions of silicate, the silica is not deposited in the semi-opaque gelatinous form, but is held in a sort of solution, which after a time becomes gelatinous, retaining for a long time its transparency.

A solution of uric acid in silicate of potash was poured, while hot, into hydrochloric acid. The solution remained clear, but was somewhat viscid. As it cooled it began to sparkle with bright points of light, which on examination proved to be exceedingly large plates of uric acid. They were the largest and most perfect plates of the substance that I had ever seen. They were rectangular, a little longer than broad, and without flaw or unevenness. Many of them more than filled the whole field of a quarter-inch of large aperture, and in the polariscope they behaved like the most carefully prepared selenites, giving at each turn one unbroken field of colour.

When six weeks had passed the solution had become semi-solid. It did not run when the vessel was inverted. Its transparency was exchanged for a bluish opalescence. Under the microscope the silica was not granular, but much like white of egg. The crystals were much broken at their edges, and were thickened. In the densest part of the silica were many small rather thick rhombs. There were no spheres, no needles, no elongated prismatic forms.

It is hardly necessary to point out the remarkable contrast of result in the two experiments. The marked tendency to spherical formation in the gelatinous silica is almost like what one has formerly and again found in albumen and its allies; the perfect development of the tabular form exceeds what one has formerly and again found in saccharine solutions.

One and the same substance in opposed states of crystallinity and colloidality works this curious process of opposed results.

The further history of the second solution will be of much interest and importance. But even now it is strongly indicated that the sphere-forming influence is not merely an inert opposition, such as may be offered by the single quality of viscidity. The plates of uric acid flashed out in the crystalline silica, while the spheres and their allies formed in the same time only clouds of whitish matter in the gelatinous silica. The molecular arrangement of the two silicas must evidently be the chief determining condition of this difference, and the gradual change in the crystals in the second experiment, corresponding to the change in the molecular condition of the silica, is very eloquent in support of this idea.

Throughout a long series, comprehending several hundreds, of experiments, many of them frequently repeated, viscidity as a sign of mere close package of molecules has appeared to me to be of little influence in disturbing crystalline polarities. Throughout there has been an evidence of the working of active forces rather than of inertiæ—of tensions, in solutions at crystallising point, in solutions of substances subject to mutual decompositions; of movements in substances undergoing internal molecular redistribution or re-arrangement, in change of temperature, in currents of electricity. Enclosed in the hydrochloric solution of silica, the uric acid, at first typical in its crystalline character, is seen slowly bent and distorted by the molecular whirls and eddies which are slowly transforming its bed.

The acid urates themselves pass rapidly through phases of consistence even more comprehensive than those of silica. By bringing to bear upon them the combined influence of strong solutions of chloride of sodium and of gelatin, I have obtained them in a very plastic state.

Exp. 7.—A saturated solution of urate of soda and uric acid was mixed with gelatin and chloride of sodium while still close to boiling temperature. The usual soft spheres were at once thrown down and were filtered off. Almost immediately after a granular precipitate was formed in the solution, and was found to consist of a gelatinous matter, fine bright granules, homogeneous spheres, and flat tablets with sharp ends (six-sided outline) (Pl. IV. Fig. 7.)

While this was under observation a number of tiny bright spots appeared in the solution, outside the gelatinous deposit. These grew rapidly till they became distinctly spherical bodies, perfect in outline and homogeneous. When the plate was quite cooled these ceased to grow, and at the end of about half an hour they were transformed into masses of needles.

Exp. 8.—The above was further evaporated and cooled. Then among masses of gelatinous matter enclosing dense aggregations of soft brownish feebly refractile spheres, with needles scattered and in most beautiful radiant tufts, were found great numbers of large pale spheres of perfectly homogeneous matter looking like fixed spherical amœbæ, with numerous vacuoles in their centre. It was difficult to believe that they were not amœbæ introduced accidentally, but for the fact that they existed everywhere under the hard superficial evaporation crust. They were of all sizes and had vacuoles of all sizes; and they were put out of shape by the least pressure (Pl. IV. Fig. 8). These existed during the morning of the day on which they were formed, but had entirely disappeared by evening.

Exp. 9.—Distilled water was now added to the mass, and the mixture was boiled and filtered. It was then again slowly evaporated till it began to be thick.

A portion of it placed under the microscope consisted entirely of spheres of two kinds floating in thick fluid.

The first were large spheres, perfectly transparent, looking like oil in Canada balsam, very compressible, and full of vacuoles. While they were watched the vacuoles would often contract and disappear, leaving no trace. Around the vacuoles there appeared after a time small, bright, seemingly crystalline granules. As the gelatin became solidified these spheres faded away at their margins and were lost, and then numbers of little vacuoles were found gathered beneath the covering glass in groups corresponding to the position of the spheres. The second spheres were smaller, quite homogeneous, and looked as refractile as oil in weak glycerine. They were like urate spheres as seen often before.

III. *Of a supposed Urate of Urea.*

It has been seen that in urine, urea, in proportion as its quantity increases, favours the formation of large and perfect forms of uric acid. The same effect is seen when uric acid is crystallised from solutions of pure urea in distilled water, so long as the solution does not contain more than 5 per cent of urea. But when this proportion is exceeded, and particularly if solutions containing 8 or 10 per cent of urea are used, beautiful spheres are deposited, which break up after a time into fine needles from the centre outwards. The composition of these spheres has puzzled me very much. Several suppositions might be reasonably entertained. First, they might be urate of urea; or, second, urate of ammonia formed by decomposition of urea; or, third, uric acid. A hydrochlorate of urea is known to chemists, being formed by the contact of pure hydrochloric acid gas with urea, and being decomposed by water. Is it possible that in strong solutions a colloid urate of urea is formed, and is decomposed afterwards by addition of fresh water? The effect of washing this precipitate with water is to leave pure uric acid on the filter. If washed with alcohol and afterwards analysed by combustion, it yields a result which corresponds neither with urea, nor uric acid, nor urate of urea, but to a mixture of urea and uric acid in non-equivalent proportions. It leaves a little urea in solution if redissolved and treated with an acid. The spheres are formed when the solution is acidulated, clearly showing that they are not urate of ammonia. The probability is, therefore, that this is a form of uric acid, and that it takes such form because it is thrown down as colloid (or hydrate) from the strong solution of urea, carrying some of the urea with it.

The foregoing observations being applied to the interpretation of urinary urates, the molecular form of these matters appears to depend upon at least two causes. To the influence of the chloride of sodium, advocated by Dr. Bence Jones, must be added that of colloids. The colouring matter or matters of urine, always strongly attracted by urates—so much so, that in the case of uroerythrin they withdraw it in great proportion from solution when they themselves are deposited—cannot fail to be active in opposing crystallisation. And, as on uric acid, so on urates, mucus will assert its crystal-destroying power. The molecular urate is, however, not the only form found in urine. The globular form has already been in part discussed. 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 ("hedgehog" crystals) (Pl. II. 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 hedgehog 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.

Influence of Albumen in the Form of Nitrate of Urea.—This is a suitable place for a short note on the form in which nitrate of urea is precipitated from solutions containing albumen. 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 1027, after the addition of an equal bulk of nitric acid, are shining

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[1] "Thorn-apples" of German authors.

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 crystallisation 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. The conditions of the experiment may be further simplified by making a solution of pure urea having a specific gravity of 1026, and by observing first the result of the addition of strong nitric acid in equal bulk, when white incoherent crystals of the nitrate are rapidly formed; and by subsequently adding a little egg-albumen to the urea solution before mixture with the acid. The spheres then formed (if cooling be not too rapidly effected) are of the greatest beauty, floating like snowballs in the yellowish liquid. This experiment has a great interest in addition to the beauty of the phenomenon, since it is the first process as yet devised by which Mr. Rainey's theory can be illustrated rapidly and on a large scale, fitted for the lecture-theatre.

Urates in Calculi.

The urates, although the most common of all deposits from cooled urine, enter much less frequently than uric acid into the composition of urinary calculi. Their comparative solubility, increased, as Dr. Bence Jones has shown, by the presence of chloride of sodium, and their habit of assuming the fine molecular state, without running into masses, will help to account for this. But they are found entering into the composition of mixed calculi, particularly with triple phosphate, sometimes as needles, sometimes as spheres, sometimes as hedgehog masses, sometimes in fibrous laminæ. The spherical forms drawn by Dr. Vandyke Carter in Plate II. of his book will be seen to resemble with extraordinary accuracy many of the forms resulting from experiment. (See Pl. II. Fig. 15; Pl. III. Figs. 1, 4.)

The difference between crystalline forms may be turned to use in the analysis of calculi. If a piece of a calculus known to contain uric acid be powdered and boiled in distilled water, and if crystallisation be subsequently effected, of course after filtration, supposing the calculus consist of uncombined uric acid, that substance is thrown down in rectangular tablets. But if ever so little ammonia be combined, we have lancet-ended plates, often of great size. If much ammonia or alkali be combined, we get needles, and with intermediate proportions we find intermediate forms.

In analysing the several laminæ of a calculus, we may often find different forms prevailing in one or another, and can draw inferences as to the conditions under which each lamina was deposited. Thus we may find sometimes a nucleus of pure uric acid encrusted by laminæ of urate of ammonia. In proportion as the ammonia increases, we shall be able to note the exchange of the radiating fibrous structure of a compact uric acid calculus for fine molecular, spherical, or tufted acicular forms, and crystallisation from hot solutions will give us the range of forms from rectangular tablets to tufts of needles. We have often evidence thus given of a diminishing acidity of the urine, going on possibly to complete alkalinity, in which case we can often find traces of triple phosphate mingled with the urate.

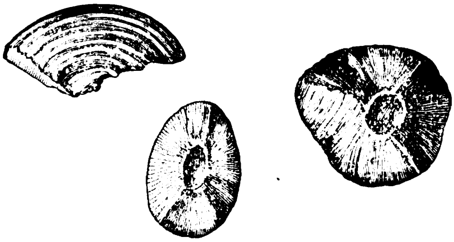
I may quote here some illustrative cases:—

Case I. *Spontaneous Disruption of Uric Acid Calculi.*—(Quoted from Clinical Lecture, March 1877. Published in "Brit. Med. Journal," June 2, 1877.)—"The specimens exhibited were passed by a gentleman aged 84, who, three years ago, weighed 25 st. He had been in his early days a hard worker, and, as he alleged, a small eater, particularly of meats. For the last twenty years, however, he had been leading a sedentary life, chiefly because of his bulk. His general health has been good, and, though there is gouty enlargement of his knuckles, he has never had any acute gouty or rheumatic illness. One day, when passing urine, he observed two round stones fall into the chamber-utensil he was using. He was rather amused than frightened, and, feeling no inconvenience, took no notice of the matter. Not long afterwards, his urethra was for some hours obstructed by a calculus. A catheter was introduced, but only as far as the calculus, which barred the way to the bladder. The stone ultimately came away, and was, like the first passed, perfectly spherical. For a year after this, his health was bad. He lost all appetite, took very little food, and wasted considerably. Then he began to pass stones in fragments. The number passed was very large, enough, as he said, to gravel the path to his house. He is not aware that there was any change in the quality of his urine. He felt no unusual sensations in the bladder; nothing like an explosion. He had no violent fall or jerk that he remembers. Most of the stones thus passed were in fragments.

"After the stones had come away, his health underwent a fresh change. He was attacked with eczema and senile prurigo, and at the same time regained his appetite. Then he began to grow fat again, and his legs, which had become œdematous, resumed their natural state.

"At present he is well and cheerful, his only complaint being of 'heaps of sand' in his eyelids. His urine, otherwise healthy, always contains crystals of uric acid, and sometimes small friable concretions of the same. The calculi exhibited are only a few out of hundreds that he has passed; some are round, some irregular; but it is evident that the majority are fragments of larger calculi; they are such fragments as might be compared to segments of an exploded spherical shell. Each has a pyramidal form, with the base of the pyramid convex, the apex slightly hollowed. The calculi of which they would appear to have formed parts must have been mostly about half to three-quarters of an inch in diameter, and each sphere must have split up from the centre outwards into seven or eight segments. It is evident, on close examination, that the fracture occurred some time before the stones were voided. The surfaces are not fresh or sharp, and the whole stone is covered with an uniform grey deposit. A section being carried in a radial direction through any one of them, the surface exposed is marked by concentric lines, by fragments of a concentric system of which the rounded base would be the outermost circle, and of which the centre would be the apex of the fragment, if it remained perfect. Such a section demonstrates at once the fact that the seeming segments are, in fact, segments of a calculus built up of many concentric layers. The section-surface is of a reddish-grey colour, very compact, and exhibits no cracks or irregularities of consistence. The crust which invests the whole fragment, and which is moulded to all the irregularities left by the fracture, is much lighter in colour than the substance of the calculi. (See Fig. 19.)

Fig. 19.



"The calculi are composed of uric acid and urate of ammonia intimately mixed. The outer light portion, which has the look of a phosphatic deposit, is, in fact, urate of ammonia. When this is dissolved in liquor potassæ, it leaves a gelatinous matrix and a great abundance of spores and mycelium, strongly resembling those of microsporon furfur. The central portion of the original calculus is wanting in all the fragments. Under the microscope, the mass of the calculus is found to consist of compact crystalline matter with a radial fibration. No separate crystals are to be obtained.

"The cause of the original fracture of the calculi appears to me to have been an expansion of the central portion, or some expansion at the centre, acting as the exploding powder in a shell. There is evidence that, for some time preceding the appearance of the fragments, there was enough disturbance of the general health to render it probable that the chemical constitution of the urine was altered. There is also evidence in the nature of the secondary deposit that the state of the urine was different after the fracture from the state accompanying the formation of the calculi. I infer that such change was accompanied with a tendency to alkalinity, and that as a result a chemical influence was exerted upon the calculi, tending to cause swelling of any mucoid matters which might enter into their composition; that the centre which has disappeared was different in some respects from the circumference which remains; and that this difference determined an unequal swelling of the centre, resulting in disruption of the spheres.

"That this was the case rather than a disintegration or falling to pieces through general failure of cohesion, is an idea supported by the perfection of the individual segments and the compactness of their structure. The regular form of the fragments opposes the idea of fracture having arisen through collisions among calculi. Such conditions would produce irregular chipping rather than radial fissure and segmentation. An inspection of the fragments resulting from lithotripsy will show the essential nature of the difference. It is not uncommon, indeed, to find calculi that have been cut in two and preserved, as commonly found in museums, fissured radially round the centre. This is, to my mind, usually an acquired, and not an originally present, condition, not existing when the calculi were in the bladder, due to the unequal drying of the centre and circumference. The condition, however, indicates that under exposure to certain circumstances of altered moisture, radial splitting, beginning from the centre, may occur in calculi; and what I suggest is, that a similar sort of process led to the segmentation in this case under circumstances which determined swelling instead of shrinking of the nucleus.

"The spontaneous fracture of vesical calculi is apparently not a common event. The late Mr. Southam, however, published in the 'British Medical Journal' two cases observed by himself and one of Mr. Luke, quoting also a case of Mr. Liston and giving a drawing of a calculus from the Dupuytren Museum of Paris. The paper was illustrated by excellent drawings, which have been reproduced in Dr. Beale's work on the "Urine." The calculi in Mr. Southam's two cases were larger than those now exhibited, and the hypothesis of rupture by internally developed gas was advanced. The fragments were only two in each case, and were less regular segments of spheres. One was composed of lithic acid with a coating of hard oxalate of lime, and the fragments, after disruption, had become coated with fresh phosphate. It is, therefore, quite possible that changes in the composition of the urine played a part in producing disruption. The composition of Mr.

Southam's second calculus is not stated. In Mr. Luke's case, the calculus was composed of triple phosphate, and there was no history of violence. In Mr. Liston's case, the calculus is supposed to have broken up suddenly under the influence of a violent bodily shock. The fragments were numerous, and the result was fatal. No analysis is given. In the last case only the drawing is given, showing a fragment separated by fissures, but not detached. The fissures do not reach the nucleus, and the fragment is held in place by fresh enveloping deposit. Mr. Coulson has also recorded a case in which a sort of natural lithotripsy occurred, two or more calculi being crushed together and broken by one another, as nuts may be broken in the hand. In such cases, the calculi are mostly of loose consistence, and the fragments are irregular and not segmented. ('Pathological Transactions,' vol. xv. p. 143.)

"I have been fortunate enough to find in the Museum of the Royal College of Surgeons a preparation (Calculi, A 177) very closely resembling my own. It is figured at the end of the catalogue in Plate I. Figs. 6, 7, and 8. There is no history, but the preparation is described as a pisiform calculus (Prout's term) 'separated into triangular portions, possibly the result of spontaneous disintegration.' The segments are pointed, instead of being, like these, truncate; that is to say, the centre remains. They are composed, according to Mr. Taylor's analysis, of uric acid, and appear to have been coated by fresh material after fracture.

"In relation to the analysis of these calculi, I may add a few remarks illustrating the use of the microscope in these processes. After the general facts of organic composition, of the presence of uric acid and ammonia had been determined, some of the central part was chipped and examined under the microscope. The characters of the fragments have been already noted, and it may be observed that the whole of the original portion of the calculus was built up of fine concentric laminæ, perfectly compact, perfectly continuous with one another, and showing a radial crystalline structure. The superficial portion, on the other hand, consisted of spherules imbedded in a clear matrix, the spherules being dense at their centre, less dense and lighter in colour, with marked radial crystalline structure, at their circumference. This is the form taken by urate of ammonia in the presence of colloids. The spheres were slowly disintegrated by hydrochloric acid, and rapidly dissolved by caustic potash, leaving the matrix and the contained fungoid structures.

"The central mass, on being powdered and boiled in distilled water, dissolves sparingly, giving a strongly acid solution, from which large very thin flat lancet-ended crystals are thrown down. These are exactly like the crystals which I have shown elsewhere to be produced when uric acid is added in large excess to hot solutions of urate of ammonia. As I believe them to be crystals of a highly acid urate, they will indicate that only a comparatively small relative quantity of ammonia is present. After three or four exhaustions of the powder with boiling distilled water, rectangular plates of pure uric acid are deposited. There is clearly, then, also a large proportion of uncombined uric acid, representing, in fact, more than half the bulk of the calculus. The solution yielded by the surface is neutral. The quantity of material being small, and the material itself comparatively soluble, crystallisation was not effected. No oxalate crystals were obtained in any process.

Case II. *Spontaneous Disruption of Calculi.*—(Quoted from Clinical Lecture, May 1878. Published in the "Brit. Med. Journal" Sept. 7, 1878.)—"Soon after the publication of my last lecture, I received two parcels of fragments of disrupted calculi, closely resembling those described by me. They were sent by Mr. Lockhart of Blackheath and by Mr. G. Buckston Browne respectively.

"Mr. Lockhart sent me twelve fragments, which he regarded as portions of three or four calculi. They had been passed as they were sent to me, and as I now exhibit them, at different times, between two and three years ago, by a gentleman of the age of fifty-six, who experienced great pain during their passage, but not before or after. The urine at the time was copious, limpid, free from deposits, from albumen, and from sugar. Before his death, which was caused by bronchitis about a year ago, he manifested symptoms of vesical calculus; but his fatal illness occurred before a contemplated exploration of the bladder was effected. Mr. Lockhart has kindly allowed me to make use of the specimens, but proposes to make them, or part of them, over to the Museum of the Royal College of Surgeons afterwards.

"The fragments were, as has been said, twelve in number, but one has been used for examination. They are all evidently fragments—segmental fragments—of hollow spheroidal calculi, and appeared to Mr. Lockhart, as they appear to me, to have been produced by the disrupture of two or more calculi. This has evidently occurred within the bladder, since six of the calculi are covered unconformably, to use a geological term, with a thin white powdery layer of urate of ammonia, covering a yellowish-grey mass with concentric layers; and the remainder are yellowish-red, with the edges of fractures rounded and smoothed as though by mutual friction. They are composed of uric acid, combined with ammonia, and mixed with a little oxalate of lime. When a fragment was powdered and treated with boiling water, it yielded a very acid solution, from which, on cooling, large narrow lancet-headed plates were thrown down. These, as I have shown elsewhere as a result of direct experiment, are forms produced where a little ammonia is present in combination with great excess of uric acid. Ammonia is set free by caustic alkali. There are no organic forms to be found in the watery solution after standing, or after complete solution in liquor potassæ. The structure is fibrous crystalline. The fact that one portion of the fragments is coated by neutral ammonic urate shows that, as in the case mentioned before, a difference in the reaction of the lime existed after the disrupture of the calculi from that which existed before. That is to say, an acid was exchanged for a neutral or alkaline reaction. And here I am glad to find Mr. Lockhart agreeing with me, that the missing nucleus underwent expansion or swelling, and so burst its envelope into fragments.

Case III.—(Quoted from same Lecture.)—"On

July 13, 1877, I received from Mr. G. Buckston Browne a box of calculous fragments, described in a note by Mr. Browne accompanying them 'as evidently the results of the spontaneous fracture of several moderate-sized calculi, and curiously water-worn and polished.' A few facts as to history were also communicated by Mr. Browne, as follows: 'H. H., aged 63. 1870. Movements began to cause pain.—1873. Sounded by Mr. Quain. Nothing found. —1874. Sounded by Mr. Quain. Nothing found.—1875 (April). Began to pass little pieces of calculi.—1876. Sounded by Sir Henry Thompson. "Numerous rather largish calculi."—No operation was performed, the patient being too ill. Died of uræmia August 12th.

"The fragments were thirty-two in number, large and small, and were to all appearance portions of rather large pisiform calculi. Some, as you see, have a sharp-edged fracture, having perhaps been broken since emission; others correspond to Mr. Browne's suggestive description, and are 'water-worn and polished.' Most are uniformly fawn-coloured and free from superficial deposit; but six, in which the edges are little, if at all, worn down, are coated with a thin and not quite complete film of white matter, are slightly whitewashed. They consist of almost pure uric acid, with not even a small admixture of ammonia; for, when powdered and boiled in distilled water, they yield a very acid solution, from which the oblong plates of pure uric acid are thrown down on cooling. I show you some of the plates. If any ammonia had been present, these would have had lancet ends instead of square. Here, too, are the affirmative results of the murexide tests for uric acid. When a piece of the mass is broken and examined under the microscope, the structure is found to be fibrous crystalline, in concentric layers, with the fibres radiating from the original centre of the calculus. The coating on the six mentioned is granular under the microscope, and readily dissolves in water with a little heating. It is probably urate of ammonia.

If you will compare the two sets of fragments now exhibited with those described in my former lecture, which are here placed alongside of them, you will, I think, have no hesitation in recognising a strong family likeness between the three. All are segmental fragments of pisiform calculi, composed of either uric acid or acid urate of ammonia; in all, the nucleus is wanting; in many specimens of all three groups indications are afforded—in the presence of an investing unconformable layer of more alkaline material —of a change in the reaction of the urine immediately after, if not at the very time of, disruption. Where this coating is wanting, there are unmistakable proofs of denudation by attrition, and it is only where these proofs exist that the coating is wanting. I maintain, therefore, that the fresh specimens support the idea which I advanced upon examination of the first: that in a changed state of urine the nucleus had become swollen, and acted as a bursting charge in a shell.

Case IV. *Calculus composed of Mixture of Uric Acid, Urate of Ammonia, and Triple Phosphate.*—A long narrow calculus, pointed at both ends, and resembling in shape a large orange-pip. It was passed by the urethra. The patient, a young man aged 29, had been healthy and free from bladder troubles till about four years previously, when, by an injury to the neck, he became paralysed in the lower part of the trunk, and in the lower limbs. For many months the bladder was totally paralysed, and the urine became alkaline, and was loaded with purulent mucus. After a time he began to pass calculi. The calculus now described is one of the largest. When cut through, it shows a white polishable surface, marked with concentric bands, while its surface is crusted with a reddish material, chiefly uric acid.

The substance gives the following reactions:—

1. Heated on platinum-foil in the flame of a Bunsen's burner, it first turns black and then fuses. The fused matter is soluble in hydrochloric acid, and yields triple phosphate, giving no precipitate afterwards with oxalate of ammonia. The nature of the precipitate is verified by the microscope, which shows the house-top crystals only.

2. Liquor potassæ causes the evolution of fumes of ammonia.

3. The nitric acid (murexide) test gives feeble indications of the presence of uric acid.

4. A piece of the calculus dissolved in weak hydrochloric acid leaves a small pinkish residue consisting of spherules, glomeruli, wheat-sheaves, and six-sided tables of uric acid, all of them such forms as would be assumed by it in the presence of mucus or albumen. See Fig. 25, p. 141.

The urine, when examined a day or two after the passage of the calculus, was said by the patient to be in its ordinary state. It was alkaline, very offensive, of sp. gr. 1026, and contained albumen and much purulent mucus. In the mucus were crystals of triple phosphate, and dark-brown spherules of urate of ammonia. The state of the urine was, in fact, a commentary on the structure of the calculus. The crystals and the spherules were here to be seen blending into masses within the substance of the mucus. Without the albumen and the mucus the crystals would no more have become fused into calculi than do the crystals of carbonate and oxalate of lime, found constantly present in thousands in the urine of the healthy horse. The history is instructive in a high degree. First comes the paralysis leading to retention; retention permits decomposition and the formation of carbonate of ammonia; then come cystitis and the mixture of mucus and albuminous fluid with the triple phosphate and the spherical urates; and so a calculus is formed. This patient suffered when seen two years later from "surgical kidney," and was in considerable danger through the occurrence of pyonephrosis, which at length discharged through the ureter. As regards treatment, the case raises considerations of great importance. First, that wherever the urine is for any length of time purulent and ammoniacal, the formation of calculus is to be looked for. Second, that whenever the urine is persistently ammoniacal, means should be taken to neutralise the alkali, and avert the destructive effects exercised by it directly on bladder and kidney, remotely in the formation of calculus. The regular washing out of the bladder from an early period with weak solutions of mineral acids or of salicylic acid, would seem to be the best mode of meeting the double danger.

CHAPTER V.

OXALATE OF LIME.

This salt occurs in urine under three shapes—that of the perfect octohedron, that of the dumb-bell, and, rarely, that of flat tables, with rounded or angular ends. And although, as we shall subsequently see, oxalate of lime calculi have a very dark colour in section, the isolated forms are not in the least degree tinted with urinary pigment.

It will be convenient to begin by a statement of synthetic experiments, by which I have sought to explain the variations of form.—And I may be permitted to draw special attention to this statement. Although oxalate of lime was the principal object of experiment, the whole subject of the influence of colloids upon crystalline form is raised and abundantly illustrated.

In December 1868, while examining some urine, I met with dumb-bells of a kind quite new to me; and consulting Dr. Beale's work on "Urinary Deposits" (3d ed.), I found that he had made drawings of dumb-bells of oxalate of lime contained in transparent casts of renal tubes, accompanied by octohedra floating in the surrounding fluid. In his remarks upon these forms I found arguments adduced—1st, to prove that the dumb-bells were, in fact, composed of oxalate of lime; 2d, to explain the assumption of the dumb-bell form in such cases by considerations founded upon the investigations of Mr. Rainey. I resolved to apply a modification of Mr. Rainey's plan of experiment to the determination of some of the conditions under which dumb-bells might be formed; to fix with more certainty the relations between the octohedron and the dumb-bell of oxalate of lime; to try, in fact, to turn the one into the other, and set at rest any remaining doubt as to their identity. The first experiments were made in a way already in part described, but now given more fully.

Some perfectly clear jelly, prepared from isinglass, was melted in a flat-bottomed jar, in quantity enough to form a layer about three-quarters of an inch deep. In this while still liquid a number of glass tubes, each about four inches long half an inch in diameter and open at both ends, were placed upright, so that each tube was immersed to the depth of nearly three quarters of an inch. After cooling, the tubes were removed, and each was found plugged with firm clear jelly, so as to be thoroughly water-tight. Six of these tubes were next filled with a slightly alkaline solution of potassium oxalate, and placed with their plugged ends in a weak solution (about 6 grs. to 1 oz.) of chloride of calcium, the level of the solution in the tubes being much higher than the level of the calcium solution. The plug of jelly was thus interposed between the two solutions, in the hope that, diffusion slowly occurring, the results of the mutual decomposition of the oxalate and calcium salt might be found after a time in the jelly, a fair representative, as far as consistence was concerned, of the casts of the kidney tubes. This experiment was performed in a room of the average temperature of 57° Fahr.

On the second day the plugs were clouded with white deposit, and fragments removed from one of them were found to contain a large number of crystalline and rounded forms, including both octohedra and dumb-bells.

The process was then allowed to go on for three months, till, on the 12th March 1869, an entire and uninjured plug was removed and submitted to careful examination. The oxalic solution was still clear; the calcium solution was thickened with deposit of calcium oxalate, but the relative levels of the solutions were unaltered. The plug was found free from decomposition, and opaque with earthy deposit. The deposit was not uniform, but somewhat stratified, forming a layer of greatest density near the calcium solution, a layer of less density, with some opalescence near the oxalic solution, and several intermediate layers of still less density, with alternate spaces of extreme scantiness of deposit.

Transverse sections of the plug were made at thirteen points; the sections were transferred to glass slides, melted with the gentlest possible heat, and examined under the microscope with a half-inch objective. For preservation they were afterwards slightly dried at a gentle heat, and mounted in solution of Canada balsam in chloroform. In this course of preparation it was found that, although a great variety of forms were present in the several sections, one only, the octohedron, was altered; the rest remained for many weeks unchanged, a point which was easily determined by comparison with fine sections of subsequently prepared plugs placed on slides without use of heat or balsam.

To sum up the results of the examination of the thirteen sections, it was found that the forms existing on the side of the oxalate were very different from those on the side of the calcium salt, and that a remarkable series of gradations led easily from the one set of forms to the other. At the calcic end two forms were most abundant — perfect octohedra, and large tabular crystals of oblong outline with rounded angles. The tablets, when seen lying flat, were colourless, marked with diagonal lines and faint concentric shadings; when tilted up on one side, were yellowish in colour, highly refractile, longitudinally laminated, and again marked with diagonal lines; their thickness was about one-third of their breadth. They might be described as consisting of a number of fine oblong plates bound together face to face, the outermost larger in all dimensions, the innermost shorter by one-twelfth and narrower in proportion (Pl. V. Fig. 1, *a*, *b*, *c*). At this point also were found in smaller numbers forms transitional between crystals and coalescence bodies (non-crystalline, rounded, calculous); two paths being taken. By one the dumb-bell form was reached without loss of outline of the crystals, the molecules undergoing re-arrangement within, so that a large flattened dumb-bell, with sharply cut edges, was found enclosed in the outline of a tablet (Pl. V. Fig. 2); by another much more frequented path the dumb-bell was reached through entire disintegration. In this second case smaller tablets were found to lose their sharpness of outline and to become granular, at the same time that they became marked by a line of slight continuous constriction round the middle of their long axis, the result being the formation of a small, not very perfect dumb-bell, and beyond this of complicated masses built up by the coalescence of a number of the smaller ones, and taking sometimes the form of double, sometimes of single, simple, or tuberculated spheres—mulberry calculi on a small scale (Pl. V. Fig. 3). The large dumb-bells were, as is already remarked, very perfect, their outline sharp and running in a bold unbroken sweep; their substance nearly homogeneous—though there were often indications of a tendency to radiating fibrillation—and very refractile; they usually presented in each half a large cavity joined to its fellow by a canal running through the isthmus. As successive sections were examined, the tablets and the octohedra steadily diminished in size to the junction of the lower and middle third of the plug, and mixed with them were found small spherical molecules increasing in size as the others grew less, until they were moulded into large bodies in which the rhomboidal and spherical forms were engaged in a well-balanced struggle for superiority. They were at first sight oval, but were, in fact, rhomboidal with much-rounded angles. Each had a tiny central cavity like that of a starch-grain, and at the level of this a line corresponding to the plane which would join the obtuse angles divided the crystal into halves. Internally, the structure was apparently fibrous; it was, in fact, laminar, the laminæ being curiously bent and twisted in a spiral way, the little central cavity marking the axis of torsion (Pl. V. Fig. 4). Above the middle of the plug these bodies, having attained their full development, were suddenly lost.

Tablets, in some respects resembling the first, next appeared (Pl. V. Fig. 5). They were, however, much longer, and much thicker in proportion to their breadth. These, as they grew, were also modified. They became longer and expanded at their extremities, the middle transverse line being unaffected. At first each half was split, as it were, into two crystals, firmly bound together at the middle, slightly divergent at the end; then by the continuation of the same process, each half became broken up into a number of flat rods bound together at the middle, so that the whole mass had a great resemblance to a wheatsheaf. Further subdivision, with curving and flattening of the rods, turned the wheatsheaf into a crystalline dumb-bell; still further, as the oxalic surface was approached, the forms rapidly fell in size, acquired a sharper outline, thicker waist, and, to all appearance, a central cavity. In some cases, by extreme arching over of the points, the two halves of the dumb-bell met round the middle, and so a sort of sphere was formed. Here also the octohedra which had been present throughout, and had followed the variations in the size of the associated bodies, underwent a change of form. They were flattened in the direction of one diagonal, and expanded in other directions. They next exhibited indentations midway between the angles, with corresponding outgrowth of the angles until they became distinctly cruciform. The rays of the cross presently lost their sharpness, and by transverse splitting (which never reached the axis of any ray) became feathered. In the central mass of the crystal the octohedral form could still be made out (Pl. V. Fig. 6). The principal forms altogether observed were five, viz. — 1, octohedra; 2, tablets; 3, ovoid rhombohedra; 4, calculous (coalescing) dumb-bells; 5, wheatsheaves, and crystalline dumb-bells. The coalescent forms were characteristic of the calcic end, the crystalline of the oxalic end of the plug. It was further evident that certain kinds of tablet were in distinct constructive relation with the two kinds of dumb-bell and the ovoid bodies respectively. It was evident also that the object originally proposed had been attained; in the presence of such a colloid as gelatin oxalate of calcium did assume the form of the dumb-bell and of allied calculi; and, further, a comparison of the bodies now obtained with figures given by Dr. Beale and others left no doubt that many, at least, of the dumb-bells found in urine by different observers were composed of oxalate of lime.

But more than this was to be learnt. The meaning of the great variety of the crystals, the conditions determining the formation of each, and the relations held by them each to each, must be sought for.

To begin, similar experiments were instituted with solutions of calcic chloride and sodic bicarbonate, with a view of reproducing the beautiful spheres originally figured by Mr. Rainey. It was here noticed that when the sodic carbonate was in considerable excess only a few spheres were formed in the neighbourhood of the calcium solution, the middle of the plug being filled with large ovoid rhombohedra closely resembling the bodies in Pl. V. Fig. 4. The suspicion then arose that some alkaline carbonate might have been present in the oxalic solution in the first experiments, and that calcic carbonate might have been formed and modified the results. The remarkable facility with which this salt was brought into spherical form by colloids made it possible that the form of the oxalate might have been affected by the presence of the carbonate. The solution of oxalate of potassium had, in fact, been rendered alkaline by a little liquor potassæ, and here was a very probable source of error.

A new series of experiments was accordingly instituted.

1. Acetic acid was added in considerable excess to the solution of oxalate of potash and all the carbonic acid expelled. The solutions being now used as before, the plug was found at the end of five days white and opaque with deposit in its lower fourth, adjoining the calcium solution. Above this it was almost clear, the acetic acid having, apparently in virtue of its greater diffusibility, driven back, as it were—outstripped (?)—the calcium salt. The deposit corresponded in the main to the oxalic end of the first plug (Pl. VI. Fig. 1). At the calcic end were "wheatsheaves" and the crystalline kind of dumb-bell, mixed with long, narrow-pointed, and very regular tablets; the octohedra were few and small. In the clear part of the plug were smaller oval tablets, and small, beautifully-rounded, thick-waisted dumb-bells of nearly transparent substance enclosing a dumb-bell-shaped cavity. These forms dwindled down at the oxalic end to tiny granules, still resolved by the one-eighth-inch objective into dumb-bells, and then found surrounded with still more tiny granules, possibly demonstrable as dumb-bells by a higher magnifying power.

2. Solutions of pure oxalic acid were placed in the tubes.

(*a*) Oxalic acid was used in large excess of the chloride of calcium. The plug was examined at the end of two days, experience having now shown, in the case, at least, of oxalate of calcium, such an interval to be sufficient.

Three several lines of forms were here observed (Pl. VI. Figs. 2, 3).

(1.) Beginning at the oxalic end, small spicules of no very definite form were followed through many stages of aggregation to, first, the perfect and, next, the feathered octohedron.

(2.) Beginning also at the oxalic end, small rounded but irregular masses were shaped into thick-waisted, clear-coloured, homogeneous dumb-bells, which became thinner-waisted and more characteristic at the point where the perfect octohedra were found; underwent sudden enlargement and radial crystallisation where the octohedron became feathered, and finally assumed the "wheatsheaf" condition.

(3.) At the point where the foregoing series were completed, tiny crystalline bodies appeared, soon seen as they grew to be octohedra, much split up into planes parallel with the basial plane (which was oblong), and partly divided by a superficial incision perpendicular to the long axis of the oblong plane (Pl. II. Fig. 4). The full development of this series is seen in Pl. II. Fig. 4, in the shape of very large ovoid much faceted and laminated crystals not unlike the large tablets of Pl. I. Fig. 1. We seemed to have here before us the changes leading from the octohedron to the tablet. Here also the "wheatsheaves" had become compressed into spheres with radiating texture and with rough spiked surface.

Just at this point the density of the deposit was so great as to draw a perfectly opaque white line across the middle of the plug, with a comparatively clear stratum below. In most of the plugs such a line existed, and appeared to indicate the point at which the two solutions balanced one another. I shall call it the line of greatest deposit. In this line only crystalline forms occurred, viz. small rhombohedra, large ovoid tablets, and large perfect octohedra. Below the line all the forms rapidly decreased in size; the ovoid crystals thinned away, by casting off their outer laminæ, till they were reduced to delicate hexagonal plates or lozenges, very transparent and symmetrical; a further simplification of outline by growth of certain sides at the expense of others produced the rhombic form; and finally, at the calcic extremity, the only crystals left were three-sided prisms with shallow pyramidic ends (Pl. II. Fig. 5).

The series constructive of the large octohedra requires some special description. The little spicules before mentioned as having no very definite shape were first gathered into radiating tufts; the tufts became cruciform, with very irregularly outlined arms; then six-rayed, with arrangement of rays corresponding to the angle-joining lines of an octohedron; by the filling up of the interradial spaces, and simultaneous smoothing of surfaces and pointing of angles, the perfect crystal was obtained.

It was constantly to be observed that the cruciform bodies were joined in pairs face to face by a bar, so as to resemble the amphidisci of Spongilla; the two halves then correspond to the two pyramids into which an octohedron can be divided, and the bar joining them to the line joining the apices of the pyramids, or third axis of the octohedron.

(*b*) Chloride of calcium was used in large excess of the oxalic acid.

The line of greatest deposit was here removed to the upper end of the plug. The constituents of the deposit were the same as in the preceding experiments, but above it very few of the forms seen in the corresponding part of the plug in the preceding experiment had been deposited; there were no octohedra, their place being taken by little rhombs. It was found that all the oxalic acid had been withdrawn from the solution, and the predominance of the calcic solution seems to have driven away all the forms characteristic of the oxalic side.

3. Solutions of ammonium oxalate carefully purified by repeated crystallisations, and of chloride of calcium of known strength, were prepared.

The formula of ammonium oxalate is given in Miller's "Elements of Chemistry" as follows:—

$$(H_4N)_2C_2O_4,\ H_2O = 142;$$

of calcic chloride in the fusible form as follows:

$$CaCl_2,\ 6H_2O = 219.$$

from which it can be calculated that 100 parts of calcic chloride will be decomposed by 65 parts of ammonium oxalate. The solutions were therefore made to contain respectively 100 grains of calcic chloride and 65 grains of ammonium oxalate in four ounces of distilled water.

Experiments were now carried on with more exactness:—

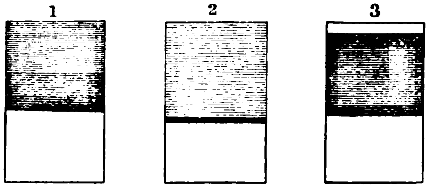
1st, with equivalents of the two salts;

2d, with 4 equivalents of oxalate to 1 of chloride;

3d, with 1 equivalent of oxalate to 4 of chloride.

The plugs, removed simultaneously at the end of six days, were found very differently charged with deposit. In all, the precipitate was confined to the upper (oxalic) half of the plug, leaving the lower (calcic) half quite clear.

Fig. 20.



In No. 1 the deposit was divided into two strata; the lower, a little less than half, denser; the upper, rather more than half, more scanty.

In No. 2 a narrow line of excessive density ran along the lowest part of the deposit, leaving the portion above rather less dense than the upper part of No. 1.

In No. 3 a very dense deposit filled the upper half of the plug, except at a very thin line in contact with the oxalic solution. In all three cases the denser tract of the plug contained coalescence forms with octohedra. On the side of the oxalate were large wheatsheaves, bundles of crystalline plates looking like packets of docketed letters tied tightly round the middle, and octohedra of moderate size with much-broken angles (Pl. VI. Fig. 9).

On the calcic side the wheatsheaves were replaced by smaller, rounded, homogeneous dumb-bells of great beauty; the octohedra were much larger, flattened in the direction of their perpendicular axes, and much drawn out at their angles, their internal structure being at the same time disturbed. The upper scantier layer of deposit contained in all three cases the same forms—a series running from granular aggregations of crystalline matter to tolerably perfect octohedra, without any associated coalescence forms. In the lower half of the plug, just below the dense line, was a shallow layer of exquisitely perfect small octohedra, with their three axes nearly equal. Below this layer the plug contained nothing. Comparing the plugs in other respects it was noted that the coalescence forms were most abundant in the broad tract of No. 3, most perfect in the thin dense line of No. 2, where the wheatsheaves were so luxuriant as to form spheres of radiant crystal, and the dumb-bells were compacted into lustrous spherical beads.

4. Lime water and oxalic acid were now used in the beaker and tubes respectively. But the oxalic acid was evidently much more diffusible than the lime, and the plugs were filled with a slight deposit, corresponding in the main to the upper scantier deposit of the foregoing experiments, and contained only a few tables and bundles of plates at the very lowest point. When equivalents were used, all the forms were small, and the tablets were little oval-pointed lozenges. When two equivalents of oxalic acid and one of lime were used, the tablets were rounded at the ends, thicker, often laminated and compressed or constricted in the middle, indicating the early stages of wheatsheaf formation.

Reviewing the whole group of experiments, it is evident—

1. That when deposited in gelatin, calcium oxalate

assumes many forms, including, besides the characteristic octohedron, dumb-bells of two kinds, crystalline and homogeneous, tablets and prisms of several kinds, and variously shaped calculi.

2. That the octohedra, tablets, wheatsheaves, and crystalline dumb-bells appear to stand in direct serial relation to one another; the granules, calculi, and homogeneous dumb-bells having among themselves a similar relation. Crystals, however, may be resolved into homogeneous dumb-bells in two ways—either by a formation of dumb-bell within the outline of the crystal, or by total disintegration of the crystal, which is converted in mass into a non-crystalline dumb-bell.

3. That there is usually observed in the plugs a "line of greater deposit," corresponding, apparently, to the point at which the diffusive force of the two solutions is balanced. On the calcic side of this line homogeneous or "coalescence" forms, on the oxalic crystalline forms, predominate. Excess of oxalic or oxalates is favourable to the size and perfection of the form generally; with excess of calcic salt, the coalescence forms are immensely increased in numbers, but decreased in size.

Where the oxalic acid predominates, crystals are mostly broken up at their angles and laminated; where calcic salt predominates, they are flattened, drawn out at their angles, feathered, or are small, perfect, and extremely symmetrical. The causes which may produce these differences may be, and are probably, of several kinds, namely—

a. The formation of basic, neutral, or acid salts, according as the solutions balance or in turn prevail.

b. The formation of double salts.

c. Alterations in the firmness or chemical constitution of the gelatin. It was generally noticed, in reference to this, that the chloride of calcium tended to soften the gelatin, the oxalic acid and oxalates to harden it.

d. The presence of undecomposed salts of different solubilities, and containing bases of different solubilities, would probably, in each case, tend to modify the form in which deposit occurred.

4. That in the first experiment the presence of calcium carbonate rendered the results different from those observed when the presence of carbonic anhydride was avoided. And here new questions arose:—Why should carbonate and oxalate of calcium, when they had once ceased to be crystalline, assume different coalescence forms? This might be due to the fact that, their crystalline form being different, their molecules still tended to repulsions or attractions among themselves in certain directions, and so modified the sphere-forming force; or their different degrees of hydration or of solubility might have influence. The lines of weakening of the cohesion of crystals must evidently be carefully noted.

Before complicating the evidence by using solutions of other salts than those mentioned, it became desirable to determine whether the action of the colloid upon the oxalate and carbonate of calcium could be modified by the influence of the various physical forces. The curious viscosity of magnetism—first, I believe, demonstrated by Faraday, and clearly described by Prof. Tyndall in his work on heat—here suggested itself as not unlikely to intensify the viscosity of the colloid.

Common horseshoe magnets of moderate power were at first used. In some experiments, the plugged tubes being arranged as in the first experiment, the magnets were so placed that the line of greatest deposit would run between their poles, in other cases so that the length of the plug would be parallel to the line joining the poles. In other experiments little jars were partly filled with gelatin imbued with chloride of calcium, the poles thrust into the gelatin while warm, and the jars, on cooling, filled up with solution of oxalate of ammonia. The general result was that there was an extraordinary increase in the size of all the forms, crystalline and non-crystalline, where the plug or gelatin was subjected to the action of magnetism, but that there was no production of new forms or greater tendency to sphericity (Pl. II. Fig. 7).

Similar experiments were made with an electro-magnet capable, with the means at hand, of sustaining a weight of thirty pounds. Some of the crystals in several cases appeared to have their axes slightly twisted; it would be very interesting to know if this and the direction of the axis generally bore any relation to the direction of the interpolar line, a point to which I intend to recur at some future period.

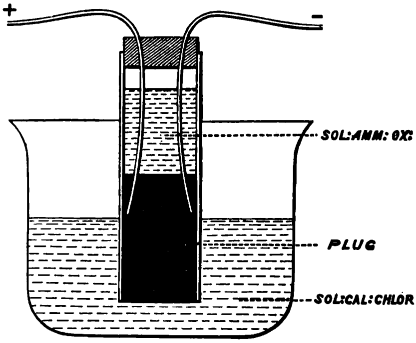
The influence of electric currents was next to be investigated.

A battery of four small cells, each containing a plate of platinised silver, a little amalgamated zinc, with excess of mercury, and about two drachms of weak sulphuric acid, was constructed, and found to produce a weak current lasting for several weeks.

Copper wires, carefully coated with shellac except at their extreme ends, were taken from the poles of the battery into a plug, and their points placed at opposite sides of the line of greatest deposit. The solutions were used as usual, and the plug removed at the end of five days.

The plug, when cut across, was found divided into two unequal portions by a thin, curved, bluish line, the smaller portion enclosed within the concavity of the line corresponding to the negative pole. The appearance and consistence of the two parts were very dissimilar. The larger was softer than the plug before experiment, more particularly in the neighbourhood of the wire (positive), and was of a purplish colour, darkest near the line of separation, shading off towards the wire.

Fig. 21.



The line of separation was a firm transparent elastic membrane, of a brilliant emerald green colour when removed and viewed by transmitted light, well defined and easily separable from the surrounding gelatin, especially on its convex side.

The smaller portion of the section was exceedingly firm and elastic, required a great deal more heat to melt it than the original gelatin, and was of a ligh green colour. Under the microscope the differences were equally marked. On the positive side the forms were chiefly crystalline, on the negative side all were spherical, the membrane constituting an abrupt line of demarcation like the so-called basement membrane in skin and mucous membrane.

The crystals were chiefly depressed octohedra, with a few sharp-ended tablets; the spherical bodies were opaque, greenish in colour, perfectly circular from all aspects, of sharp and perfectly unbroken outline, and marked internally by a radiating striation.

In the membrane at the level of the points of the wires, bodies of the same appearance, and flattened spheres with fimbriated margin were found giving to the structure under the microscope much of the appearance to be seen in the shells of some Cyprids. Lower down all forms disappeared from the membrane and from the negative side of the line, the crystals on the positive side remaining abundant.

The unexpected conditions here met with were in great part due to electrolytic action. It was found, in some comparative observations, that oxalate of copper deposited in gelatin took a form exactly like that of the beautiful green spheres (Pl. II. Fig. 8); and when carbonate of copper was formed by placing sulphate of copper and bicarbonate of sodium on opposite sides of a gelatin plug, no deposit occurred, but the middle of the plug assumed a brilliant emerald-green colour, and became excessively firm and resilient; the sodic side of the plug was softened and purplish in colour, the copper side not altered. In subsequent experiments, where platinum and silver wire were used and the solution of the copper avoided, it appeared that the influence of electricity was to favour the production of small, very perfect crystals, chiefly octohedra. But these experiments were open to the objection that the occurrence of electrolysis was certain, and the advice of some able experimenter in electricity can alone help one to more satisfactory results.

Effects of Temperature.—In some plugs prepared during the second week of February 1870, when very firm and strong gelatin was rendered still firmer by the prevailing cold, hardly anything except octohedra and their immediate derivatives (macles, etc.,) were found. It was then remembered that coalescence forms had been abundant and well formed in the softened plugs of the summer experiments; and although experience had shown that, other things being equal, a denser plug was favourable to the perfection of the coalescence forms, it was now evident that the vibrations of heat, and possibly of light, must be looked to as likely to aid the production of spherical forms by disturbing the lines of crystallisation and throwing the molecules into the power of the colloid. Five different positions were secured for strong plugs placed between equivalent solutions of oxalate and chloride.

1. Kitchen, mantelpiece, temperature 55°–65° Fahr., in bad light.
2. Study, near window, temp. 53°–56°, good light.
3. Study, cupboard.
4. Garden, good light, temp. 27°–45°.
5. Garden, dark shed.

It was intended to take into consideration here the effect of light as well as of heat, but no decisive results were obtained with regard to the former force.

On the other hand, the influence of temperature was made beautifully evident. In the kitchen specimen the coalescence forms were three or four times as numerous as the crystalline. In the garden specimen this condition was more than reversed. The crystals were at least ten times as numerous as the coalescence forms, and were, on the average, more than twice the diameter of the crystals in the warmer specimens. It will be noticed that the crystalline form here remains perfect as long as the crystal does not exceed a certain size. In the small crystals the force of crystallisation is strong enough to resist the surrounding forces of disturbance. When the length of the axes is extended, and the relations between the more widely separated molecules become weaker, the line is broken and disintegration of more or less completeness follows; just as liquids in small quantities will form drops, but only drops of a certain limit of size for each kind of liquid.

After varying the consistence of the colloid, it appeared desirable to vary the nature of the colloid. Some experiments made with triple phosphate and phosphate of lime showed that gelatin did not turn them into spherical forms. Yet it was known that in animal bodies phosphates were found in spheres or spheroids. And albumen now was suggested as the common associate of organisation, and as capable, when coagulated, of forming a matrix in experiments carried on at temperatures which would melt jelly, and yet corresponded with the temperatures of the human body.

Tubes were therefore plugged with albumen on the same principle as the tubes had before been plugged with gelatin.

Beakers were filled to the depth of three-quarters of an inch with fresh white of egg, the tubes were introduced, and heat gradually applied by means of a water bath till the albumen was thoroughly coagulated. When this was carefully carried out, with a temperature not exceeding 200° Fahr., the plugs were firm, homogeneous, and water-tight, no leakage occurring after the tubes had been filled with water and left for twenty-four hours.

Oxalate of lime, deposited in these plugs at a temperature of from 50°–60°, took almost entirely the coalescence form.

When a plug was carefully examined, it was found firm and bluish in colour at the oxalic end, soft and yellowish at the calcic. In the third next the oxalate, no forms whatever of crystalline or coalescence order existed, but the albumen was remarkably fibrillated.[1] Below this appeared, in small numbers, large perfect homogeneous spheres, isolated, refracting light energetically, and polarising with one very perfect cross. Lower down these had decreased in size, increased in number, and begun to coalesce with each other, forming here and there very perfect dumb-bells, and further on, large confused calculi, of which the line of greatest deposit was in chief part composed. As to crystalline forms, only one was present—the feathered octohedron, much depressed and much drawn out at angles, large enough to fill, when seen flat, the field of a half-inch of considerable angle of aperture; composed, when seen sideways, of two plates joined face to face, with a boss or enlargement at the middle, where generally a small coalescence sphere could be seen. Albumen

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[1] *Query.*—Did this indicate combination ?

Plate V.

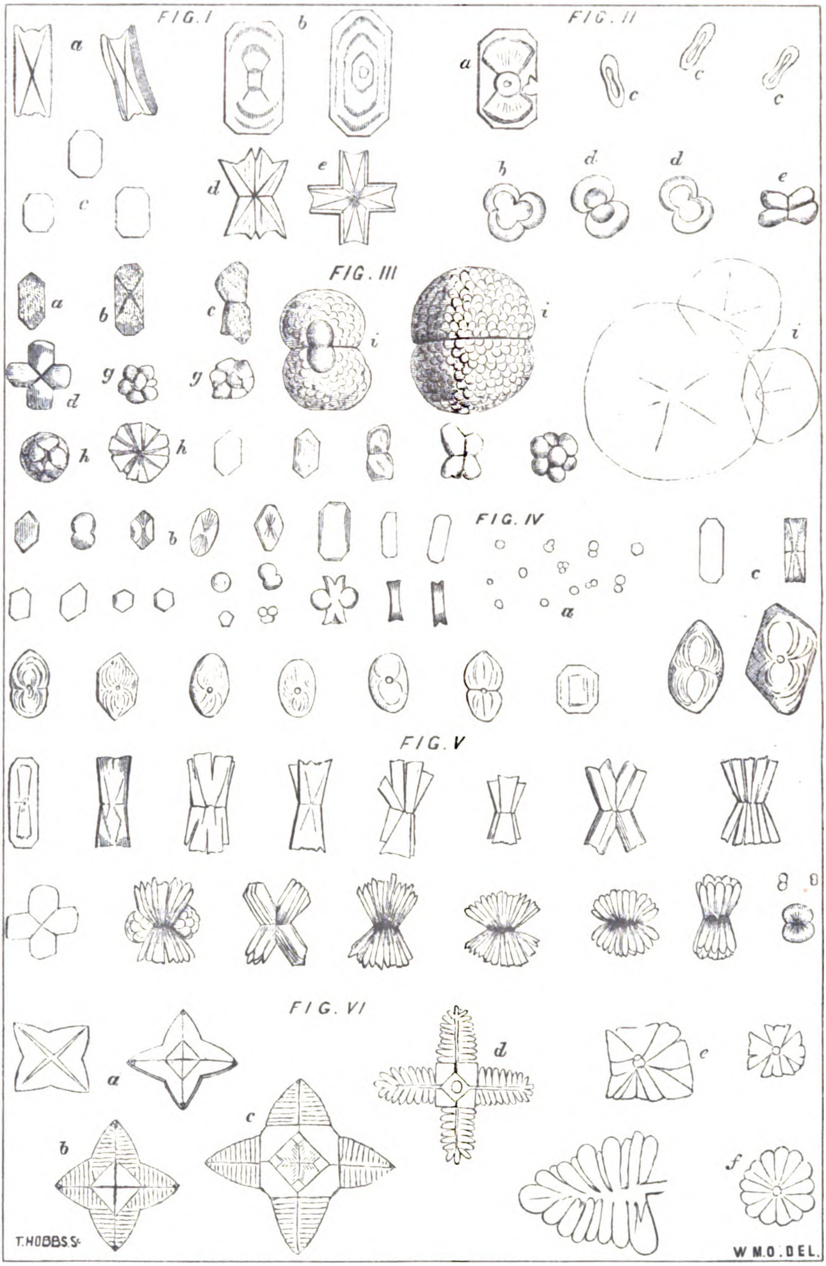
FIG. I
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FIG. IV
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FIG. VI
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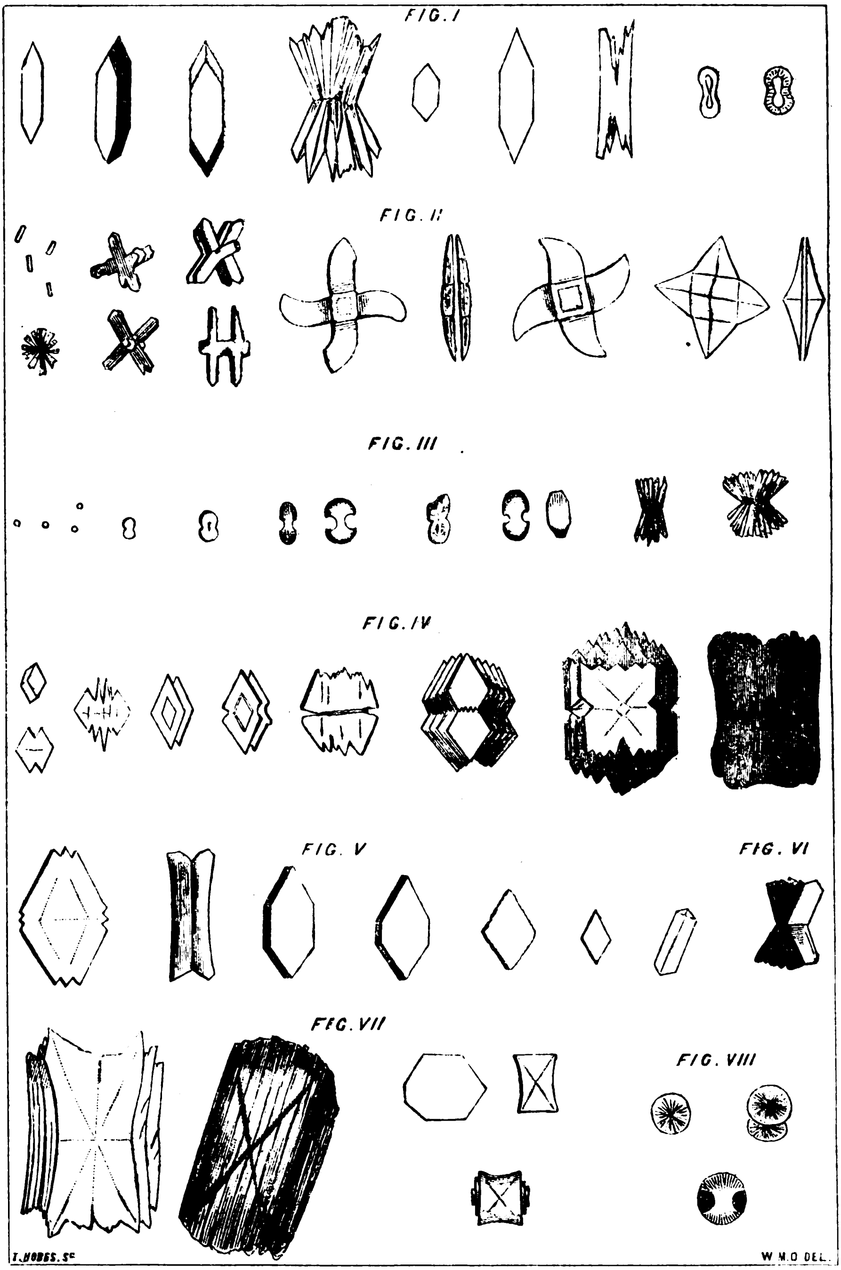
T. HOBBS Sc.
W. M. O. DEL.

Plate VI.



T. HOBBS. Sc

W. M. O DEL.

was evidently much more active than gelatin in controlling crystallising force.

DESCRIPTION OF PLATES.

PLATE V.

Forms observed in thirteen sections of the gelatin plug used in the first experiment.

FIG. 1.—First slide, from calcic end.
a, Large tables of oxalate of lime seen sidewise; *b*, the same, flat; *c*, smaller tablets; *d*, compound tablets.

„ 2.—*a*, Homogeneous dumb-bell formed within large tablet; *b*, *c*, *d*, *e*, dumb-bells and allied spheroidal homogeneous bodies.

„ 3.—Various forms of coalescence-bodies, showing their relation to tablets. (Slide 2.)

„ 4.—Tablets and spherules of a new series; the spherules (*a*, *b*, and *c*) growing to large rounded, fibrous rhombohedra, composed of calcic carbonate; the tablets growing, further on, to "wheatsheaves." (Slides 3 to 7.)

„ 5. Formation of "wheatsheaves" from the thick tablets. (Slides 8 to 13.)

„ 6. Flattening and feathering of octohedra. (Slide 13.)

PLATE VI.

„ 1.—Forms assumed by calcic oxalate in gelatin, acetic acid being present in excess.

„ 2.—Oxalic acid in excess of calcium salt. Series constructive of flattened octohedron.

„ 3.—Oxalic acid in excess. Series of dumb-bells from calcic end, where they are homogeneous and rounded, to oxalic end, where they are crystalline ("wheatsheaves").

„ 4.—Oxalic acid in excess. Octohedra passing into much-facetted tablets.

Fig. 5.—Thinning of tablets on calcic side of plug.

„ 6.—Oxalate of ammonia and calcic chloride. Form of "wheatsheaf" observed in oxalic region of plug. Note, that I have, since this was drawn, observed similar forms twice in urine.

„ 7.—Comparison of forms observed in magnetised plug with those formed at the same time, all other conditions being perfectly equal, in non-magnetised plug. The large tablet-shaped bodies were formed in the magnetic arc.

„ 8.—Oxalate of copper, as deposited in gelatin.

Urinary Modifications. Case I.—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 "wheatsheaves," 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.

Cases II. and III.—I have twice observed flattened tablets of oxalate of lime in urine. On both occasions the patients voiding the urine were out-patients at St. Thomas's Hospital. Both were dyspeptic, and the urine in both cases contained albumen.

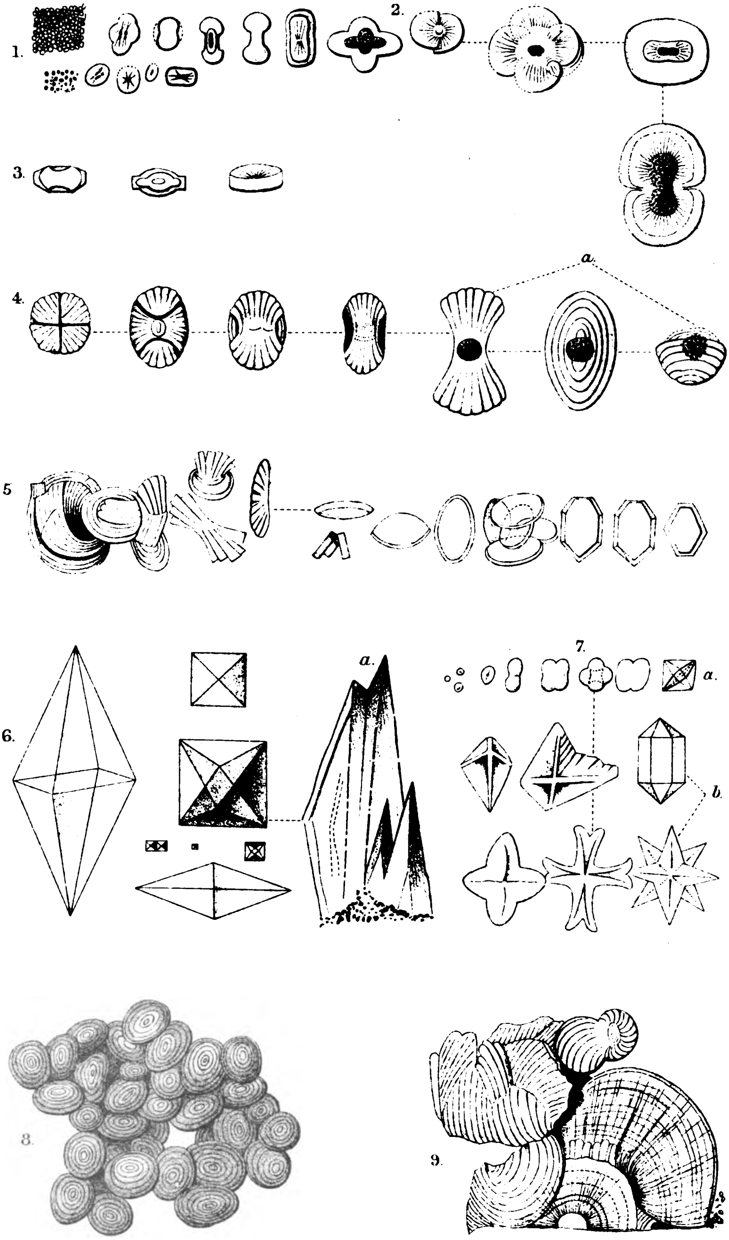
My experience is that the homogeneous, sharp-margined dumb-bell is more common in urine than the "wheatsheaf." And, to judge from the drawings in various books on the subject, the experience of other observers is to the same effect.

Oxalate of Lime in Calculi.—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.

Dr. Vandyke Carter ("Microscopic Structure and Mode of Formation of Urinary Calculi," 1873) has so fully treated this part of the subject that I can add nothing to his description. He demonstrates the existence in calculi, of oxalate of lime in the form of granules, of octohedra, of rounded ovoid and dumb-bell forms, of spheroids or globules, and of laminæ having a tendency to break up radially. And, speaking of my then recently-published drawings of oxalate of lime deposited in colloids, he proceeds to say: "So remarkably indeed do my figures correspond to those given by Dr. Ord that it seems almost needless to insist upon the identity of the crystalline forms referred to; yet, should this be allowed, there follows the great probability that it was under conditions not less alike in character that both forms arose. Had these rhomboid plates alone been in question, the argument in favour of identity would have been a forcible one, but when it appears (see the Figures) that several collateral forms also closely correspond, I confess but little doubt remains in my own mind that phenomenon and explanation here stand side by side." The coincidence is the more interesting for the circumstance that Dr. Carter's observations had been made before he saw my figures. Dr. Carter has handsomely accorded me permission to introduce here the figures in question, so that the results of the analytical process may be at once compared with the synthetic forms (see Plate VII.)

AFTER DR. VANDYKE CARTER.

STRUCTURAL ELEMENTS OF CALCULI — OXALATE OF LIME.



Stanford's Geog^{l} Estab^{t}.

CHAPTER VI.

PHOSPHATES.

Triple Phosphate.—This salt proves much less plastic than the oxalate of lime. In order to be able to compare results, triple phosphate was first deposited in a gelatin plug, which was interposed for the purpose between a mixed solution of phosphate of soda and chloride of ammonium on one side, and a solution of sulphate of magnesia on the other.

After several days' exposure the plug was found to contain at the magnesic end small, but not very perfect, "house-top" crystals. At the middle were large scattered masses, plainly visible to the naked eye, often more than a line in diameter, each consisting of a central spherical body with many radiating stalactitic arms, composed of aggregated and overlapping prisms. On the magnesic side the edges and angles were sharp; on the phosphatic, all the masses were greatly reduced in size, and the angles were rounded. Near the phosphatic end were subspherical, or crescentic or unsymmetrical sheaf-like tufts of fine radiating needles or raphides, easily broken up by pressure. All these forms depolarised light, the larger with brilliant play of colour, the smaller with alternations of light and darkness.

When the experiment was repeated with an albumen plug the stalactitic crystals were found turned into rounded rods, bulging at many points into beads, and variously bent, twisted, and interwoven, so as to bear a remarkable resemblance to the form in which earthy matter is deposited in the skin of the echinodermata.

When this experiment was repeated at temperatures from 80° to 85°, the stalactites were replaced by smaller irregular masses, but I have rarely obtained any distinct spherical forms.

In Urine the crystals of triple phosphate are not uncommonly rounded at their angles. This occurs, so far as I have observed, only when albumen or much mucus are present. And even then no spheres are formed, and there is hardly any indication of agglomeration of the round-edged crystals into calculous masses. But, by the use of a temperature a little higher than that of the body, I have been able to effect the moulding of these crystals into calculous masses. If some 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 spherical forms, many of them very large. The reactions of these under the microscope indicate them to be in part phosphates, but the presence of urates deprives the experiment of conclusiveness. To get rid of the uric acid a further experiment can be made, though at the expense of the perfection of the mucus as a colloid. The mucus being separated from the urine is treated successively with liquor potassæ and hydrochloric acid. It is then thoroughly washed, and placed in a slightly acid solution containing triple phosphate. After the lapse of an hour a slight excess of ammonia is added, and the mixture is digested for twenty-four hours at 110° Fahrenheit. The flaky and much-coagulated mucus is then found to contain rosettes of crystals almost identical in form with figures given by Dr. Vandyke Carter in Plate IV. Fig. 26, 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.

In addition to these forms I have seen in some small elongated friable triple phosphate calculi passed in great numbers, apparently from the pelvis of the kidney, in a case of chronic pyelitis, small brilliant spherules densely aggregated and mixed with darker spherules, the former soluble in acetic acid without effervescence, the latter insoluble, but slowly decomposed with the precipitation of uric acid. These calculi were fusible, and the spheres were evidently composed of triple phosphate. The same patient had pyonephrosis on one occasion, and when relief was obtained by discharge through the ureter, passed fragments of what looked like false membranes, having rounded "house-tops," urate spherules, and hedgehog crystals imbedded in large quantities. These forms under the microscope presented a great similarity to the forms yielded by the crushed calculi.

In a calculus passed from the alimentary canal of a horse, triple phosphate was found arranged in most perfectly circular laminæ, and homogeneously distributed through an abundant organic matrix. No crystals and no straight lines of fracture existed; the fragments seen under the microscope having conchoidal fractures, and looking like fragments of wax.

The active colloids of the alimentary canal would appear therefore to be able to abolish crystallinity altogether, even in so determinedly a crystalline matter as triple phosphate.

Phosphate of Lime.—The behaviour of this salt accords so completely with what has been related of triple phosphate in the presence of colloids, that no special description is needed.

CHAPTER VII.

CARBONATE OF LIME.

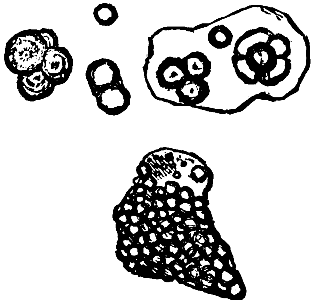
THIS salt was, as we have seen, the subject of Mr. Rainey's first investigations in molecular coalescence. Experimentally it is found to assume the spherical form in all kinds of colloids—in gum, in gelatin, in albumen; and the spheres are mostly the only forms produced; crystals being absent, excepting in a limited part of the gelatin plug. In this respect it offers a marked contrast with oxalate of lime. This substance occurs with the greatest rarity, if indeed ever, in human urine. It is frequently found in the urine of the horse, and mostly, though not always, in the spherical form.

As a constituent of urinary calculi also it is rare in the human subject. The Hunterian Museum contains only one specimen of carbonate of lime urinary calculus from man, presented recently by Dr. Bird of York. Most commonly the carbonate is found combined with phosphate of lime or triple phosphate. I adjoin illustrative cases.

CASES I. II. and III.—"Last year I exhibited at the Pathological Society of London three small carbonate of lime calculi. They were passed by a young man of twenty-two after symptoms of considerable prostatic irritation. They had the hempseed form characteristic of prostatic calculi, and this, taken together with the symptoms, made it probable that they came from the prostate.

"The calculi were originally six in number. Of these one was crushed to form the microscopic preparation on the table, one had been chemically examined by Dr. Bernays, and one by myself. The chemical examination showed them to consist of carbonate and phosphate of lime with an organic matrix. Their microscopy was extremely interesting. They were composed entirely of minute spherules, in diameter twice or thrice the size of blood-corpuscles. The spherules were closely aggregated in most parts, and were slightly flattened at their points of mutual contact. They refracted light very powerfully, and, when one was seen separate from the rest, it usually exhibited concentric internal lines—lines of lamination. The matrix was clear, transparent, and structureless. The forms were altogether like the spherical forms obtained in Mr. Rainey's original experiments, when mixtures of carbonate and phosphate of lime were slowly deposited in gum. The regularity of form and size indicated that the calculi were formed slowly

Fig. 22.



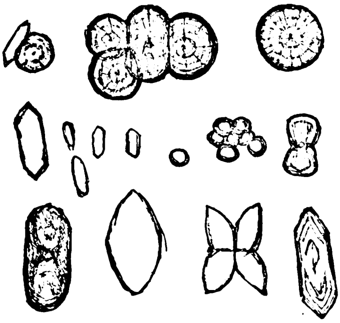
in a muciform colloid, and they illustrated also the influence of the high temperature of the body (see Fig. 22).

"As useful subjects of comparison, two calculi composed of carbonate of lime taken from the urinary passages of the horse were exhibited, one irregular, nodulated, evidently moulded to the form of its place of formation, and extremely compact, from the pelvis of the kidney; the other, soft, friable, and roundish, from the bladder.

"In the friable vesical calculus, the earthy matter was held together by only a small proportion of not very adhesive animal matter. Small pieces could be easily picked off with the finger-nail and crumbled to dust between the fingers. The dust, on drying and examination under the microscope, consisted of minute crystals and spheres. The spheres were beautifully perfect bodies, of all sizes up to the $\frac{1}{800}$th of an inch, or even larger. They were marked with concentric shadings and with radiating fibration, indicating a tendency to centrifugal crystallisation. They are not described in further detail, because they had every character belonging to the spheres of carbonate of lime formed artificially by Mr. Rainey. The spheres were mostly separate from each other; here and there a string of three or four was found, and some few little globular aggregations of very tiny spheres occurred. With the spheres were found a long series of forms linking them on to the rhombohedral crystal. This form itself was not found perfect. There were found — 1. Dumb-bells; 2. Rounded bodies, partly crystalline, partly rounded, with central cavity; 3. Rounded rhombohedra without central cavity; 4.

Six-sided crystals, some with a little rounding, some with sharp angles (see Fig. 23).

Fig. 23.



"1. Of the dumb-bells, some were clearly such as are produced by the coalescence of spheres of equal size. Others had every indication of an origin in modified hexagonal prisms. Both kinds usually presented a very small central cavity.

"2. The rounded rhombohedron with central cavity was sometimes found single, sometimes in the form of a St. Andrew's cross. The central cavity was the starting-point of a number of markings, which would tend to make oval figures. These rhombohedra exactly resembled forms which I have drawn and described in the 'St. Thomas's Hospital Reports' for 1871 and in the 'Quarterly Journal of Microscopical Science,' 1872 (see Pl. V. Fig. 4). They were composed of carbonate of lime, and were deposited in gelatine.

"3. The simple crystal was here more declared and in varying degrees of perfection. With the central cavity the oval markings were also absent. When the earthy matter was dissolved by an acid, the organic matrix still remained perfectly transparent and structureless, retaining the form of sphere or crystal.

"A large, hard, irregular, and tuberculated calculus from the pelvis of the kidney of a horse was next shown. Its section showed it to be capable of taking a polish, on account of the great compactness of its structure. It had several nuclei, around which the laminæ wound irregularly, like the layers in walnut-wood, and it had all the appearance of having been formed by the binding together of several original calculi by subsequent enveloping deposit. One side of it was flattened, smooth, and pale, looking as though it had been in contact with another calculus. Probably, if time had been allowed, this would also have been cemented to the general mass. The surface of the section was whitey-brown, in lighter and darker lines; the external surface a dark blackish brown. The earthy matter in this calculus was carbonate of lime. Associated with it was a large proportion of organic matter, which formed thick rich-brown flakes after solution of the earthy matter in acid. The figure shows a section of the calculus at right angles to the surface prepared for the microscope. It presents in some parts dense agglomerations of spherules of all sizes, with a few oblong forms. In other parts, thick laminæ are seen running parallel to the surface. They are transparent, and are evidently composed of completely fused crystallised spheres. They have smaller secondary laminæ, reminding one of the circumferential laminæ of bone (see Fig. 24).

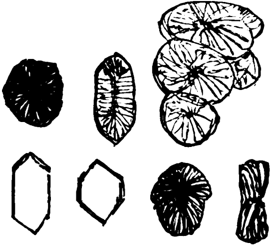
"The animal matrix looked exceedingly like soft vegetable structure that has undergone partial decay in water. Under the microscope it was brown, and was completely occupied by round and roundish cavities of various sizes, corresponding evidently to the spherules. In some places the structure was almost fibrous, and here probably it corresponded to laminæ."

The following remarks were made at the time:—"These three carbonate of lime calculi can be advantageously compared. You will observe that they present three degrees of hardness and compactness, the calculus from man holding in these respects a middle position, but inclining to friability. The readiness to disintegration in the first is not, indeed, to be measured by its present condition. When first examined *in situ*, it was soft and plastic, like a lump of clay. This condition is associated with the presence of but little colloid, and that of a thin, and not tenacious, quality. Now, I have no hesitation in laying down the rule that, in proportion as a colloid departs from the typical form of colloid albumen, it has less power in disturbing the molecular arrangements of crystals and in binding the molecules after the first disturbance into spheres and masses of spheres.

"Carbonate of lime is more easily turned than most crystalloids from the crystalline into the spherical forms by colloids. And the weak influence of the colloid in this case is shown, first, by the presence of many crystalline forms, and, secondly, by the marked individual perfection of the spheres. A stronger colloid would have subdued all the crystals, and matted and cemented, and still further compacted by actual coalescence, the resulting spheres. This is exactly what we see in the hard renal calculus, where the colloid is present in large quantity and of considerable strength, in spite of the great condensation of the earthy material. The calculus from man has much colloid; but, while the crystals are entirely replaced by beautiful spheres, these latter are only slightly united together, and are nowhere fused into laminæ. The presence of phosphate in this calculus probably influences the form and increases the cohesiveness of the spheres. In Mr. Rainey's experiments, the most beautiful and perfect spheres were formed when mixtures of carbonate and triple phosphate were used. It seems to me a clear corollary from these observations that the question whether calculi shall be formed in the urinary passages is very much determined by the amount and character of the colloids present in the urine, or shed into it by the surfaces. Colloid was present, gluing these spheres and calculi together into a soft clay. A little less colloid, or a little softer one, being present, the clay would have been soft mud. And with less colloid, the mud would have been only a turbidity in the urine. If it were otherwise, calculi, as Dr. Thudichum has well pointed out, would be exceedingly common, or almost invariably formed in the herbivora. The urine of these animals is mostly alkaline, and full of large crystalline forms of carbonate and oxalate of lime.

Fig. 24.

Fig. 25.



"So with human beings. Here the crystalline constituent is most commonly uric acid, less commonly oxalate of lime. Both are constantly found present in fresh urine; both are frequently passed for years together by a single patient without the production of calculi. It is only when some colloid nidus, like a clot or mucus, or colloid impregnation of the urine by albumen, or the like, is added, that the formation of calculi takes place.

"Whether, indeed, carbonate of lime calculi are ever deposited from the urine or in the direct tract of the urinary passages, is very doubtful. Dr. Thudichum is of opinion that they are only deposited when the influence of the urine is cut off. The present specimens are just such as might have been deposited in prostatic diverticula, although the two examined by me gave no indication of being built upon any structure resembling the prostatic concretions described by Sir Henry Thompson. The calcareous prostatic calculi described by the same author are, again, very different from these, being very firm, hard, and polished, looking like pearl-barley. On the whole, these calculi rather correspond with some carbonate of lime calculi briefly described by Mr. Smith in the eleventh volume of the 'Medico-Chirurgical Transactions,' p. 14, which were, like these small bodies, composed of carbonate of lime held together by animal mucus. To my mind, the calculi now in question are probably deposited in large ducts of the prostatic, and are to be compared to the earthy concretions formed in the ducts of racemose glands, though it is true that such bodies are generally more completely composed of phosphates."

Case IV. *Calculus containing Carbonate and*

Phosphate of Lime.—A branched coral-like calculus, found in the pelvis of a kidney, destroyed, so far as its glandular structure was concerned, by a sarcoma which had obstructed the ureter. The calculus was firm and hard at its surface, laminated in its crust, friable in the interior and without lamination. The interior consisted of spheroidal particles of phosphate of lime with a little carbonate, mixed with urate of lime and soda in beautiful needles and prisms. Such forms as these latter are rare in calculi, not being coherent enough to subsist in a moving stream, and being turned into spherules or fibrous masses when made to cohere by colloids. And this particular deposit was so friable that there could be little doubt as to its being formed after a partial occlusion of the ureter had produced dilatation in the pelvis, so as to allow sediments to accumulate in some diverticular sac out of the track of the urine. The small quantity of carbonate of lime found confirms this idea. The particular crystalline forms of which the deposit was composed were such as would be formed only in limpid urine. If, then, mucus or other colloid had been present, there would have been spheroidal masses and cementation.

The crust of the calculus contained alternate strata of urates and of phosphates with carbonates, the latter predominating on the surface. The most superficial layers were very compact, and the carbonate was so intimately mixed with organic matter as to offer much resistance to the action of acetic acid. This predominance of carbonate most probably indicated that the ureter had been completely blocked when the crust of the calculus was formed, and the completeness of coalescence marked the presence of albuminous matters in the surrounding fluid.

CHAPTER VIII.

ON SOME OTHER KINDS OF CALCULI, RENAL AND BILIARY.

A CHAPTER may now be devoted to a description of some calculi not treated of in preceding chapters, but offering points of interest.

CASE I. *Indigo Calculus, from the Kidney.*—I was fortunate enough to light upon this specimen last year, and subjoin the account of it published in the "Trans. Path. Soc." 1878:—

"The specimen was removed *post mortem* from the pelvis of the right kidney of a woman of middle age by Dr. Bloxam, who sent it to me, with other parts, for examination. The clinical facts of the case are as follow:—The left kidney was destroyed by a soft, round-celled sarcoma, which had ended by obstructing the ureter and reducing the kidney to a lobulated cyst, containing a long, branched, earthy calculus. The right kidney was hypertrophied and somewhat hyperæmic, but its structure was healthy.

"The calculus is a flat hard cake, of the shape and size of a fruit lozenge, and weighs forty grains. It is partly of a dark-brown colour, but on three-fourths of its surface a blue-black colour, granular and without polish, is spread. Drawn across a sheet of white paper it leaves a rough blue-black mark. Its section is grey, polished, and stratified.

"1. In examining the calculus I first heated a portion on platinum foil. It was in great part consumed, giving off a vapour of an offensive and pungent quality, reminding one partly of burnt feathers, partly of soot, but having also a character of its own. I did not know at the time what this character was, but in a later experiment found that indigo during sublimation yielded exactly the same odour. There was left on the foil a white, infusible ash, composed of phosphate of lime.

"2. The next step in the process was to examine some of the calculus under the microscope. A small portion was scraped and powdered, and placed in water for examination. It showed a matrix of a dark reddish-brown colour, containing fibrous crystalline matter and masses of pigment. The pigment looked mostly black, but at the edge of masses, or in small detached granules, a deep blue colour was observed. At first I supposed, the idea of blood-pigment being present to my mind, that this was some pigment accidentally introduced. But on repeating the preparation and observation several times, with great care to avoid intrusion of extraneous matter, I still found the colour.

"3. A portion of the calculus was powdered, mixed with an equal portion of dry chloride of sodium, and enough glacial acid to cover it. Heat was applied till ebullition occurred, and the mixture was then allowed to cool. The liquid during boiling assumed a beautiful pure blue colour, and on cooling deposited crystalline material of a coppery lustre. A few hæmin crystals were found among the brown portion of the calculus on examination under the microscope.

"4. A portion of the calculus was digested in a mixture of one part of hydrochloric acid with two of water. This was partly for the purpose of analysis of the earthy constituents. But it is my practice to do this also for the purpose of making examination of the organic matrix of the calculus. The matrix invariably plays a very important part in determining the form and cohesion of the earthy or crystalline constituent of calculi, and much can be learned by its systematic investigation. The residue, insoluble in HCl, was in bulk almost equal to the material before treatment, but was friable so as to be easily reduced to powder between two plates of glass. Under the microscope it was partly brown, partly of intense blue colour, partly purple, but the blue was in great excess of the other constituents. It was seen to be partly crystalline in form, but the exact type of the crystals was not apparent.

"5. The blue colour seen in the foregoing observations being more like that of indigo than anything else, and indigo being already known as a urinary product, a direct test for indigo was applied—the test of sublimation. A small quantity, about one grain, was powdered and placed in a perfectly dry test-tube. On the cautious application of the flame of a spirit-lamp to the tube, a purple vapour, closely resembling that of iodine, was disengaged and filled the lower part of the tube, while the odour of burning indigo was strongly evident. On removal of the heat the vapour instantly condensed, both in the pigments and on the side of the tube. Examination with the microscope showed the deposit to consist of flat prisms, some blue, some black, with much finely granular blue matter.

"Subsequently a permanent microscopical preparation was obtained in the following way:—A tiny heap of powdered calculus was placed on platinum foil, and a glass ring—one of the rings sold for making microscopic cells—was fixed so as to enclose it. On this was placed a clean glass microscopic slide. The vapour emitted on heating the foil was collected on the glass slide, a drop of glycerine added, and on the superposition of a covering-glass a preparation was obtained, which, on comparison with a preparation made in the same way with commercial indigo, presented exactly similar appearances. In both cases there were abundant blue prisms mixed with blue granules. The prisms were oblong with pointed ends, in many cases, however, with the ends truncate or excavated. The tint of colour was exactly the same in both specimens. (The two plates were exhibited together at the Pathological Society.)

"6. A small portion was very finely powdered, and triturated in a mortar with sulphuric acid. At first only a dingy brown colour was produced, but after standing for some days the mixture was found to be of an opaque blue colour. It was taken to Dr. Thudichum, who diluted it with water, filtered it, and obtained a clear blue solution, which, in the spectroscope, gave a marked band in the yellow without stopping the blue or the red rays. This corresponds with indigo, and with no other blue or purple fluid that I know of. Sulphate of copper solution, which has a tint very like that of the sulphate of indigo, gives a band in the extreme red, but none in the yellow. Indigo from urine, in chloroform solution, gives the band in the yellow.

"7. The reduction test for indigo was not made by me, the foregoing evidence being conclusive. The conclusion is that the calculus consisted of some blood-clot, containing crystalline phosphate of lime and a large quantity of indigo, principally as a thick encrustation.

"It remains for me to make some observations upon the relations of the calculus.

"The occurrence of a blue matter like indigo in urine has been occasionally noted. The occurrence of a substance, itself colourless, but, under the influence of acids and oxygen, capable of yielding indigo-blue, as a frequent constituent of urine is now well recognised. But, as far as I know, the presence of indigo in a urinary calculus has never been before observed, much less has a calculus largely composed of that substance been described.

"The observation standing so much alone cannot be regarded as of the greatest importance in reference to the subject of calculi, but it will, at least in my own case, serve to turn attention more strongly to the extent to which indigogenous matter exists in urine, and to the conditions thereof.

"As regards the origin of the indigo in the present case, it is clear that there are at least three possible sources—food, medicine, and pathological conditions.

"1. Although many plants besides woad contain a colourless juice, developing under certain processes of fermentation indigo pigments, there is no reason to believe that, generally speaking, indigo appears in the urine as a consequence of their ingestion.

"2. On the other hand, Jaffé has shown that indigo can be obtained from the urine of animals fed on a diet from which vegetable matter is excluded.

"3. The diet in the present case consisted of soups, broths, and farinaceous foods, none of them likely to include indigo or indigogen.

"3B. Medicines: the patient took creosote for some time before death for the relief of vomiting. It must be borne in mind that the ingestion of creosote and carbolic acid is sometimes followed by a dark discoloration of the urine, and that this has been shown by Dr. Odling to be due to indigo.

"4. The source of indigo in urine cannot be said to be well established. Schunck, finding in indigoferous plants a soluble matter, called by him indican, and decomposed by acids into indigo-blue and indigo-sugar, argues that the same substance furnishes indigo in urine. This theory, which is much disputed by other eminent chemists, in particular by Dr. Thudichum, in this country, does not account for the origin of the indican.

"Jaffé has of late done much to show a definite and more or less constantly present source of indigogen within the system. He suggests that the indigo of urine is derived from indol. This substance, having the formula C_8H_7N, can be obtained from indigo-blue (C_8H_5NO) by a process of deoxidation with hydrogen. It is crystalline, volatile, and soluble in water as well as in alcohol and ether. The same substance is formed when albumen is decomposed by strong alkali, and when peptones are broken up by pancreatic juice, and it is present in the fæces, which are believed to owe much of their peculiar odour to it.

"Jaffé finds indican in the urine of dogs after the subcutaneous injection of indol; also after the ligature of the small intestine, but not after ligature of the large. He finds excess of indican in the urine of persons suffering from fever associated with intestinal affection; no excess in other fevers. He suggests, therefore, that in conditions leading to retention of the products of pancreatic digestion, or to imperfect action of the intestinal juices upon those products, indol gets absorbed from the intestine in larger quantity than normal, and is excreted by the kidneys as indican.

"This argument is certainly supported, as far as it goes, by other observations. In the first place cholera urine has been found by Gubler (1854), and by Hassall, Thudichum, and others since, to yield indigo-blue on exposure and oxydation. The more recent observations of Senator on the occurrence of indican in urine place obstructions and other affections of the intestines among the most frequent associates of its increase.

"5. Indican has been again referred to blood pigment by G. Harley and others.

"On looking over the results of various foregoing observations, and some of my own in addition, I am inclined to believe that, wherever any unusual or rapid breaking down of albuminous matter is proceeding, indican is likely to be found in the urine as a result and evidence. So that, while imperfect gastric or intestinal chemistry may be a cause of one kind, fevers, suppuration, and blood-poisonings may be causes of another kind. Pus, it may be remembered, has a green or bluish-green tint of its own, and has been made by chemists to yield a blue pigment like indigo. The indigo-blue now exhibited on filter-papers was obtained from the urine of a boy having bone disease with free suppuration. And in the present case there are some points which are touched by this relation. The left kidney was a seat of suppuration and disintegration, and an obstacle to the outflow of the pus and *dêbris* existed. It has been suggested to me by Dr. Thudichum that such retention might lead to absorption of indican among other results of disintegration; that the indican would be here formed from indol in presence of alkali, and being carried off by alkaline blood would, at the time of its excretion by the healthy kidney, be deposited as indigo-blue on coming in contact with acid urine. This is, however, nothing more than a suggestion, on which I should not like to argue seriously at present, but which I should just keep in sight for verification or correction during the continued observation to which this discovery will lead me."

CASE II. *Calculus containing Myelin or Cholesterin.*—A soft dark brown sticky mass of the size of a bean was given to me by my friend Dr. Frederic Weber. It looked like some caoutchouc softened by heat; so much so, in fact, that a suspicion had arisen of its being caoutchouc, and question had been made as to the possibility of a caoutchouc instrument having been broken in the bladder. Some of the stuff on being touched with the flame of a match burned with a large smoky flame like camphor or caoutchouc.

When first examined by me, the substance was of a dark brown colour, tenacious, not elastic, and without smell. A portion exposed on platinum put to the flame of a spirit-lamp took fire and burned with a yellow smoky flame, giving off a smell like that of charred flesh or hair, not a resinous odour; the ash fused under the blowpipe flame, and gave afterwards indications of phosphoric acid. The murexide test for uric acid was used with negative results. Under the microscope no structure was found, but part was clear and transparent, part granular and opaque. There were a few crystals of hæmatoidin. The hæmin test with dry chloride of sodium and glacial acetic acid brought out no more crystals; but it was observed that the granular portions became swollen, and that the granules on the surface expanded into spheres and tubes. The tubes thus shot out from the free surface were exactly like the tubes observed by Dr. Montgomery, when myelin was placed in contact with water.

I have lately obtained similar tubes in great beauty from specimens of a highly phosphorised matter extracted from brain substance by Dr. Thudichum—his Kephalin. His "buttery matter," a less purified extractive, rich in cholesterin, yields even more beautiful fibres and processes. And no other substances that I know of give the reaction. Dr. Thudichum's myelin, a sub-crystalline educt of the brain, does not, nor will fresh blood-clots; but there is certainly good reason for believing in the presence of highly phosphorised colloids in blood-corpuscles, both red and white.

On the whole, I was inclined to regard this substance as an old blood-clot long detained in contact with inflamed or ulcerated surface in some part of the urinary passages. I supposed that most of the colouring matter had been washed out or decomposed, leaving the brown tint and the few crystals of hæmatoidin. A clot so placed would be liable to infiltration by amœboid corpuscles; and, if so, these in their turn have probably undergone decomposition, leaving behind only their very stable phosphorised material. For it may be noticed that, whereas lecithin is a very unstable matter, kephalin has been shown by Dr. Thudichum to be remarkably indisposed to decomposition.

The presence of such a phosphorised matter in large quantity would cause combustibility, as well as give rise to the singular microscopical reaction described.

The mass having these characters may be conveniently classed with the rare urinary deposit called urostealith, the nature of which is at present little understood.

Biliary Calculi.—The calculi of which cholesterin forms a predominant part are most interesting. The surface is usually brown in colour and often tuberculated; the section is waxy, and much whiter or only yellow. In a majority of cases the section shows a crystalline formation radiating from the centre to within a half or one-third of the length of a radius; outside this laminæ, very undulating and irregular. In the crystalline part a dark material occupies the interstices of the crystal, which is itself colourless and transparent; in the laminar part the colour is evenly distributed in each lamina, though the different laminæ vary much in intensity of shade. And, occasionally, the calculus is surrounded with a brown paste, which, to the eye, is faintly granular. If, in the first place, the brown paste is examined, it is found to be a mixture of semi-transparent reddish-brown matter, with enormous numbers of minute spherical calculi. Some of the calculi are homogeneous and of a brilliant lustre, as seen by transmitted light; others are deeply tinted with a brown red colour, and are also marked with concentric lines of deeper colour; they are, that is to say, minutely laminated. The lustrous spheres are dissolved at once by ether; the brown laminated spheres become less refractile, but evidently consist, in great part, of a material insoluble in ether. This is shown by the action of nitric acid to be in part bile pigment, and in part it appears to be mucus. Similar forms, with many larger and less regular, are found in the surface of the calculus. If some of this is crushed on a glass slide, they may be readily observed. And if some of this so crushed be treated with ether and warmed, most of the spheres disappear, the brown laminated forms only remaining. If the ether be now allowed to evaporate, cholesterin is redeposited. Where deposited in empty spaces it is in rhomboidal plates; where deposited among the rich brown soft *débris* left after the extraction by ether it takes spherical or rounded columnar, or at least some rounded form. In fact, it can be seen to be modified by the colloid, even when rapidly deposited, an observation of much interest and importance. In the substance of the calculus the cholesterin is in columnar crystals radiating from the centre. These are somewhat rounded at their angles in the outer layers, sharply crystalline in the central part.

From all this the inference is plain that cholesterin, although not soluble in water, behaves like crystalloids soluble in water when it is deposited in colloids; and further, after long deposition, as the mass of the calculus grows, there is a reversion to the crystalline form along lines radiating from and beginning at the centre. A reversion of this kind belongs, in the first place, to colloids generally. It is seen in silica exceedingly well. It is seen in urates deposited from strong saline solutions (see pages 76 *et seq.*) It is seen in the spheres of mixed carbonate and phosphate artificially produced by Mr. Rainey. And it can be seen in cholesterin itself when made the subject of experiment. It is, in fact, a metamorphic condition partly due to the innate tendency of the molecules of the colloid to pass into the crystalline state of rest, and partly to the cessation of the influences which disturb crystalline matters from their proper state of rest. That is to say, the colloids with which the cholesterin is associated are colloids which tend very decidedly to take crystalline form. They belong to the class of colouring matters of which hæmatoidin is the type. And when they do crystallise, the molecules of the cholesterin resume their polarity, first along radial lines in which the forces of ordinary attractive force are most nearly balanced, later on or along lines proper to the substance itself, so that in the centre of the calculus we find actually the rhomboid plates.

In experiment cholesterin can be made to assume spherical form with a readiness which certainly surprised me when I made my first observations.

Pure cholesterin crystallises, as everybody knows, in the form of colourless rhombic plates. It is insoluble in water and most saline solutions, but is supposed to be held in solution in the bile by taurocholic acid or the soda salt of that acid.

Exp. 1.—An ethereal solution of cholesterin is added to fresh egg-albumen in the proportion of one part to two. After good shaking in a test-tube, the mixture becomes gelatinous, and is left for twenty-four hours in the test-tube, or, for any period exceeding half an hour, in an evaporating dish to allow of free escape of the ether. As the ether passes off, the cholesterin is deposited in the substance and on the surface of the albumen. The superficial deposit is partly crystalline, but the deposit in the albumen is entirely spherical or acicular. The crystals on the surface are rarely perfect, and generally have rounded angles (Plate VIII. Figs. 1, 2). The spheres are of all sizes up to $\frac{1}{500}$ inch diameter, and are at first homogeneous and singularly lustrous (Pl. VIII. Fig. 17). But they speedily begin to undergo internal disintegration. Becoming cloudy, they are soon made out to be composed of fine short needles, packed together like very closely cropped hair, brushed in a direction running from one pole to the opposite (Pl. VIII. Figs. 3–11). Subsequently they break up into tufts of hair-like needles, radiating in a brush from the pole of divergence, and these tufts expand and grow till each of them becomes a long curl or ringlet of wavy hair (Pl. VIII. Figs. 10, 11). By the end of a week nearly all the cholesterin has come to this state of long curling fibrils, and the whole process may remind the observer of the growth of minute confervoid filaments from spores.

A new series of phenomena is observed when the albumen, having the cholesterin immersed in it, is treated with glacial acetic acid. But before describing this change, the behaviour of cholesterin in presence of acids may be described.

Exp. 2.—Treated with nitric acid cholesterin loses its crystalline form with some effervescence, and swells out irregularly at its surface, throwing off oily-looking spherules. Finally it is entirely resolved into such spherules.

Exp. 3.—Treated with hydrochloric acid it undergoes little or no change.

Exp. 4.—On the addition of glacial acetic acid to pure cholesterin, the rhombs are seen under the microscope to undergo an instant change of structure. They break up internally into crystalline fibres, usually springing from one of the angles; and they emit radiating tufts of sharp-pointed needles which seem to grow at the expense of the substance of crystals. If, now, the slide be heated till the acid begins to boil, the cholesterin is wholly or in part dissolved; but, as the slide cools, acicular crystals shoot out from any portion of cholesterin that is left undissolved, or from new centres, and rapidly cover the field. These crystals, during their growth, give the impression of their being protruded like spears. They are often as thick as the spicules of fresh water sponge, and as refractile. They are solid. The cholesterin appears in this case to be chemically altered by the acetic acid, combining with it to form a sort of ether.

Exp. 5.—Some pure glycerin being added to such a preparation as is produced in the preceding experiment, during cooling, at any point where the glycerin meets the growing spears it breaks them up wholly or partially into globules, making them look as if they had been put into the fire and fused.

Exp. 6.—If glycerin be mixed in about equal quantities with the acetic acid and cholesterin while still on the slide, and if heat be applied, after the covering glass is in place, till bubbles form rapidly, the slide instantly examined is found covered with spheres, some as large as fat cells and quite regular, others egg-shaped, and others aggregated into masses (Pl. VIII. Fig. 12). The masses are dense and very brilliant. As cooling proceeds all the spheres break up. The large ones contract at their surface, and seem thereby to squeeze out fluid from the interior, which takes at first the form of tubes, afterwards of spheres. An active movement of this kind often results in the formation of a group of small spherules in the place of the large one, looking like a glomerulus of spores (Pl. VIII. Figs. 13, 14). Presently these in turn change each instantaneously into needles, the change proceeding as follows:—a single spherule darts away from the mass; as it goes it leaves a stiff raphis in its course, and it is itself proportionately diminished in size, till its last fragment forms the point of the raphis (Pl. VIII. Figs. 15, 16). The ball is, so to speak, unwound into a stiff thread of glassy substance. Here and there spheres break up, without change of place, into variously shaped tufts of needles.

Exp. 7.—Acetic acid is added to cholesterin and albumen, and the mixture is heated to boiling. Examined now as quickly as possible the mixture presents spheres and tufts of needles rapidly growing in the fluid part of the field; spheres and spheroids and combinations of most fantastic shapes in the transparent albumen. The spheres are at first perfectly homogeneous and circular in outline (Pl. VIII. Figs. 17-26). After a time they become oval and gradually a little pointed at the ends. Then usually a little globular protrusion forms at one end or both;

then a zone of indentation is drawn round the oval, usually at about one-third of the length of the surface from the protrusion; the interior next gives indication of a subdivision of the substance of the ovoid into two, three, or four mutually compressed spheroids; and at last the whole changes, with magical suddenness, into a crystalline mass of obscurely rhombohedral shape. In process of time this mass breaks up yet further into raphides. The great transformation is attended by upheavals and depressions of the surface, causing a general appearance of singularly life-like convulsions and contortions of the mass. All the change is most rapid during cooling, but it continues slowly for hours and days subsequently till every particle of cholesterin has come to the needle form. If solutions of gelatin be used instead of albumen, similar results are observed. In the gelatin spheres are readily formed, and slowly turn into needles. If acetic acid be added and heat applied, the rapid conversion of spheres into needles, attended by active convulsive movements, can be conveniently watched in the cooling mixture; and if glycerin be used as well, a great variety of lively transformations may be witnessed.

This series of observations has, in the first place, some importance as supplying a rapid mode of exhibiting the influence of colloids upon crystalline form. Within a short compass, we are able to see the crystalloid cholesterin assume, when first deposited within the substance of the colloid, perfectly spherical form; we can follow the gradual emancipation of the crystalloid from the control of the colloid and its return to a quasi-crystalline form within the albumen, and to definite crystals within the gelatin or glycerin with acetic acid. We may infer that the crystalloid is not so intensely crystalloid in its tendencies when first deposited as afterwards. We may infer also that the power of the colloid is, under certain circumstances, when coagulation is not produced, intensified by heat; and, in the loss of controlling power experienced by the cooling colloid, we may see a parallel to the loss of power experienced by a degenerating colloid, for instance in the transition from mucous to horny matter. Where the changes are most rapid, as in the heated mixture of cholesterin, acetic acid and glycerin, the transformation is seen to be accompanied by vigorous intestine movements. To review this observation, we have before us in such a mixture, when cooling has only just commenced, perfect lustrous spheres looking like drops of oil. Of a sudden these are affected by peristaltic movements, and, as the surface contracts, the mass is resolved into minute spheres. The heat and the crystallinity have balanced each other for a time, but when the balance has been lost and the process of crystallisation has commenced, the first step has been not the formation of crystals, but of smaller spheres. So long as all was quiet, the large sphere was possible; but when molecular vibrations were set up as the attendants of crystallising separation, the molecules at opposite ends of poles were withdrawn from their power of holding one another in position at such a distance, and the general shaking allowed only of the existence of small spheres, the constituent particles of which were all near enough to each other to allow of each exercising strong enough attractive influence on its fellow to resist the distracting influence of the vibrations set going by the crystallising force. Instead, therefore, of one centre around which, or through which, all attractions were balanced, we have a number of centres with spheres drawn round them proportionate in minuteness to the activity of the perturbing force. The process, in one aspect, may be compared to the whipping of an egg. In another, it may be compared with the cleavage of the ovum after impregnation.

Regarded from another point of view, we see a series of movements resulting from the tendency of matter to come to rest. We see stages which may be compared to the spring of the bow when the drawn string is let go; and, again, to the straightening of the unstrung bow. Or we may see in the chain of movements, beginning with the formation of the sphere and ending in the crystal at rest, a parallel to the chain of force formed when water is raised by the sun to the clouds and hill-tops to descend in rain or rivers to the sea—to rest; or to the chemical chain in which oxygen and carbon, torn asunder by light within vegetables, slowly recompose carbonic acid within animals, and in turn come to rest.

Here, again, the question is suggested to me, how far may the simpler movements of the constituents of animal and vegetable organisms be due (among other things) to the struggle of one group of substances against the grasp of another, to the tendency of each substance to ultimate complete separation from the substances with which it is intermixed, and to the tendency of each separated substance to assume the nearest possible approach to a static condition?

DESCRIPTION OF PLATE VIII.

FIGS. 1–11.—Cholesterin in albumen: 1, 2, on surface; 3–11, successive stages of forms observed in the cholesterin deposited within the substance of the albumen.

FIGS. 12–16.—Cholesterin after being heated with acetic acid and glycerin: 12, sphere first formed; 13, sphere in act of contracting and exuding smaller and tubular processes; 14, mass of globules like mulberry, resulting from subdivision of spheres; 15, 1, 2, 3, 4, diagrammatic representation of transformation of globule into raphis; 16, a mulberry mass in act of transformation into a fan of raphides.

FIGS. 17–26.—Shows three kinds, 17–21, 22 and 23, 24–26, of metamorphic change accompanied by movements undergone by cholesterin after heating with acetic acid and albumen.

FIGS. 27–31.—Spheres of cholesterin mixed with crystalline matter, from the surface of a biliary calculus.

FIGS. 32–36.—Forms seen after solution of a calculus in ether and slow evaporation of the liquid in contact with the pigment. They are transitional from crystal to sphere.

FIG. 37.—Diagrammatic section of Biliary Calculus. 1, outer crust dark-coloured without either concentric or radiating structure; 2, second concentric layer; 3, radiating crystalline layer; 4, centre, pigmentary, structureless.

The metamorphic tendencies of cholesterin acquire much interest when the association of cholesterin with nervous tissue is considered.[1]

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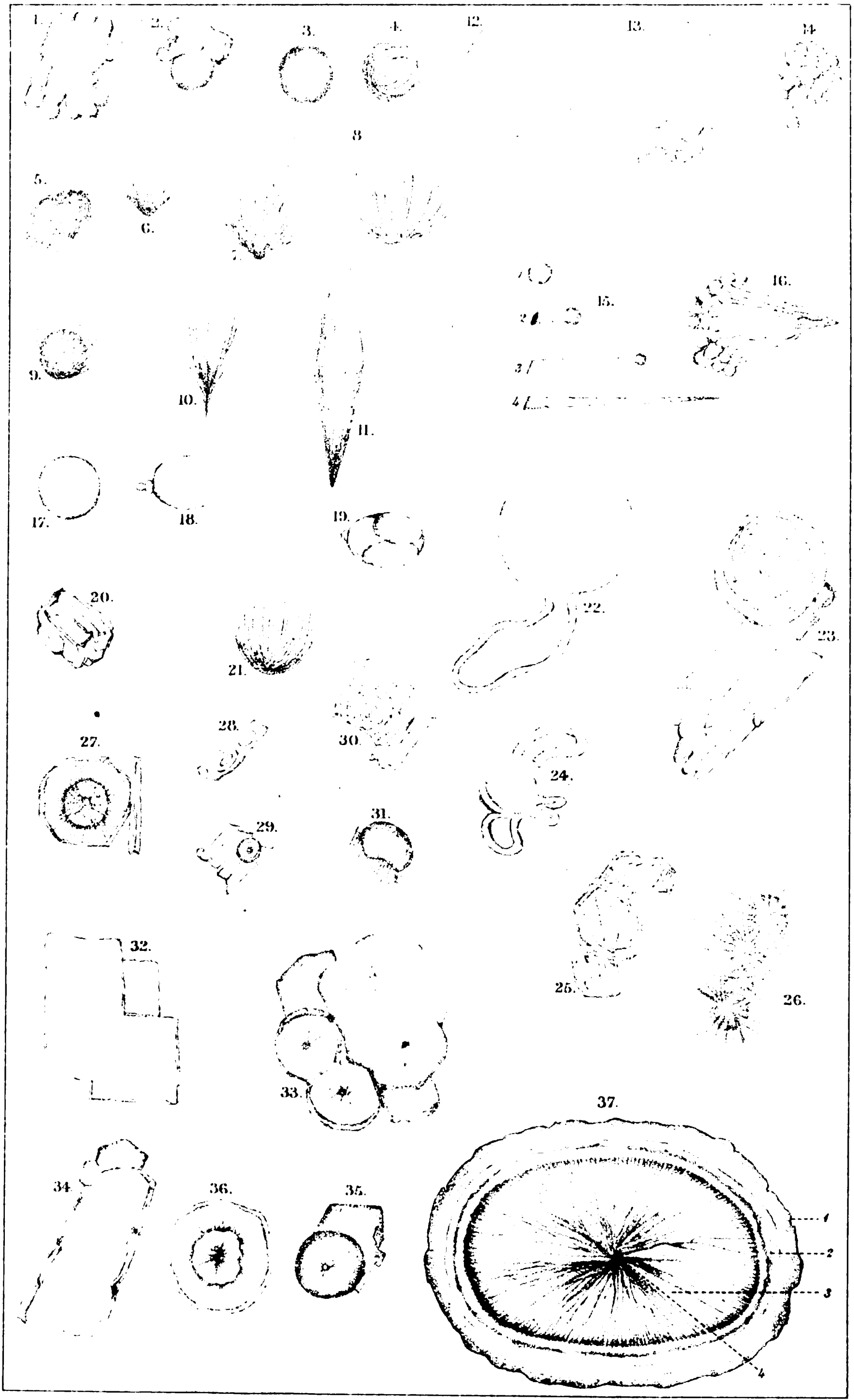
[1] The subject of metamorphisms of cholesterin after deposition in colloids is treated at greater length in a paper of mine in the "Proceedings of the Royal Society," No. 157, 1879, entitled "An account of Experiments on the Influence of Colloids upon Crystalline Form, and on Movements observed in Mixtures of Colloids with Crystalloids."

Plate VIII.



Stanford's Geog! Estab!

OF THE ORGANIC MATRIX OF CALCULI.—After the removal of uric acid and urates by weak alkaline solutions, or of earthy salts by weak acids, some organic matrix is always left. Its appearance varies. It is sometimes a pale yellow soft matter, easily soluble in excess of acid or alkali, and quite structureless. It is sometimes firm and of a deeper yellow or brown colour, and resists reagents of both kinds, having evidently a chemistry allied to that of horny matters. When so firm as this, it retains the form of the earthy matters imbedded in it, but exhibits no structures that might be supposed to be proper to itself. Where the earthy deposit has been spherical, the matrix is vacuolated, or cellular or mottled, with circular area of pale colour. Where the earthy deposit has been lamellar, the matrix is often distinctly lamellated, and sometimes has distinct linear markings at right angles to the lines of the lamellæ.

The horny reaction of the matrix may either be related with its epithelial origin, or may be the result of a reaction between the crystalline and colloid matters. Harting asserts that a change of the kind occurs in albumen when it has been made a matrix for the deposition of earthy matters. The relation of mucin to horny matter being nearer than that of albumen, such a change would be still more likely to occur when mucus should be the matrix.

In examining the matrix of calculi formed of mixed triple phosphate and urates, I have several times found the spores and threads of penicillium glaucum, a further indication of the decomposition that must have been proceeding within the urinary passages at the time of the deposition.

CHAPTER IX.

CONTAINING A SHORT SCHEME FOR THE QUALITATIVE EXAMINATION OF CALCULI.

CONSIDERING how much may be learned from the examination of calculi, and how little it is practised by medical men generally, I venture to append a short scheme for that process, in hope of drawing attention to the simplicity of the means necessary. Every practitioner nowadays has his microscope, and the other apparatus required can be bought for a few shillings. Most of it will be, moreover, useful in the daily examination of urines, a necessity to all, and neither a mystery nor a luxury. The list of things needed includes a spirit-lamp; a Bunsen's burner, with an indiarubber tube for connection with any convenient gas-burner; a small sheet of platinum foil, and a few inches of fine platinum wire; a blow-pipe; iron tongs; a fine saw; a dozen test-tubes; two small funnels, with a set of filter-papers; two or three beakers; two or three four-ounce test-glasses; a porcelain capsule or small evaporating dish; pestle and mortar; test-papers; and the following reagents —pure nitric, sulphuric, hydrochloric, and acetic acids; liquor potassæ, phosphate of soda, chloride of sodium, liquor ammoniæ, oxalate of ammonia, alcohol, distilled water.

First take the calculus in your hands. Feel its consistence, and estimate roughly its specific gravity. Feel if it be hard or soft (cystine); if it be round or angular, smooth or rugged. If round or oval, without faces or angles, the calculus was probably solitary; if facetted, multiple; if more angular, it may be the result of fracture within the bladder. Uric acid and phosphates form smooth or more rarely very slightly tuberculated calculi, oxalate of lime spiked, tuberculated, or rugged calculi. Phosphatic calculi are comparatively light in their specific weight; oxalate and carbonate of lime, heavy; uric acid and urates intermediate.

The next step is to make a section through the calculus—easily done by a fine thread-saw. I usually avail myself, at the cost of a few pence, of the aid of a lapidary, in getting one of the surfaces polished as far as may be.

The section should be carried through the very centre of the calculus. Points to be noted are colour, variety, or uniformity of surface, lamination.

Colour.—Uric acid is usually fawn-coloured; urates fawn-coloured or pink; phosphates and carbonates white, oxalates dark-brown or almost black; cystine pale-green or waxy yellow.

The surface is generally marked with concentric lines, indicating laminæ; if the nucleus differs from the mass, or if the laminæ at one part differ from their neighbours, the several differing strata must be examined separately.

Now break off a piece from the mass, or chip out a piece from the nucleus, or any distinctly-marked stratum, and reduce it to powder in a clean mortar.

A. Place some of the powder upon clean platinum foil, and hold the foil, with the tongs, first over the flame of a spirit lamp, then over the Bunsen flame, and, if necessary, apply the blowpipe.

The substance is either in great part consumed, or remains in great part unconsumed. By this test the matters occurring in calculi are at once divided into two groups, as follows :—

TABLE.

Consumed in great part.	Not consumed.
Uric acid.	Phosphate of lime.
Urate of ammonia.	Triple phosphate.
Urates of soda or lime.	Oxalate of lime.
Xanthin.	Carbonate of lime.
Fibrin.	
Blood.	
Cystin.	
Urostealith.	
Myelin.	
Indigo blue.	

with organic cement,
albuminous,
mucous,
or horny.

The volatile substances usually have some small quantity of earthy matter, and the fixed substances some quantity of organic matrix in combination.

B. The calculus is chiefly combustible or volatile.

Note its behaviour when heat is being applied. It may give off some distinctive odour ; it may simply vanish ; it may blacken ; it may fuse ; it may give off smoke ; it may burn with thick smoke. Hereby the following indications may be obtained :—

(*a*) Uric acid and urate of ammonia blacken and disappear without fusing or giving off any marked smoky vapour or smell.

(*b*) Xanthin fuses, blackens, and is then similarly consumed.

(*c*) Fibrin burns with a smoke like that of burnt feathers, leaving a considerable ash of phosphates.

(*d*) The substances included under the names of "urostealith" and myelin burn like camphor, with a smell like burning fat.

(*e*) Indigo sublimes, the vapour burning with an odour of its own, partly resembling soot, partly burnt feathers.

(*f*) Cystin fuses, blackens, and volatilises, with a faint, sickly, and very persistent odour.

C. In all calculi, whether volatile or not, special search should be made for uric acid. For this the murexide test is used. A small quantity of the powdered calculus is placed in a porcelain capsule with two drops of strong nitric acid. On the application of heat a brisk effervescence ensues, and when this is over, heating is cautiously maintained in such a way as to drive off the acid without charring the residue. The process is aided by moving the capsule so as to distribute the fluid over a large surface, very gently heated. As soon as nitric acid ceases to come off, a drop of liquor ammoniæ is placed in the capsule, and allowed to run into the residue. If uric acid have been present, an intense crimson purple solution (of murexide) is produced. Very often the tint is faintly visible before the addition of the ammonia, either because ammonia was already present, or because the heating process has been carried on too rapidly, and has broken up the oxidation products of uric acid, alloxan and alloxantine, with the result of forming ammonia.

Supposing uric acid to be found in quantity, we have to determine whether it be uncombined, or, if combined, with what. It may be pure, or combined with ammonia, soda, potash, or lime.

(*a*) *For Ammonia.*—Place some of the powder in a small test-tube, add liquor potassæ, and heat gently. Ammonia, if present, may be detected — 1, by its smell; 2, by the white fumes of chloride of ammonium produced when a glass rod dipped in hydrochloric acid is placed at the mouth of the tube; 3, by the blue change produced by the vapour on moist reddened litmus paper placed at the mouth of the tube. Caution must be exercised in not carrying the heating too far. At higher temperatures pure uric acid is broken up by potash, and, among other things, ammonia is evolved.

(*b*) For soda, potash, and lime, the ash left after calcination should be submitted to the blowpipe and the colour of the flame observed—yellow, in the case of soda; purplish blue with potash, reddish purple with lime. If these substances are present together the blowpipe may be supplemented by the spectroscope. For this and like purposes, a pocket spectroscope may be usefully carried. The yellow line of sodium can never be mistaken; with potash the middle of the spectrum is brightly lighted up, and a line appears in the far red and in the purple; with lime, lines appear on each side of the yellow, one in the green, one in the orange red, and a line in the blue is also obtained. The red, yellow, and green lines are the most visible, and their positions are easily made out. The reaction succeeds better if a drop of pure hydrochloric acid be added before incineration.

As is noted on page 92, the microscope gives effective aid in this analysis. If some of the powder be boiled in a little distilled water, and the filtered solution left to crystallise, the forms deposited will differ according to the associations of the uric acid.

If uncombined the acid is deposited in rectangular oblong plates, looking like glass paper weights. If a little ammonia is combined, exceeding large and thin lancet-ended plates will be found; with an equivalent of ammonia or soda fine needles often gathered into radiating tufts; with lime much coarser, thicker, and flattened prisms, gathered into tufts and crosses. The great value of the microscope as an aid to chemical research cannot be too strongly insisted on.

The murexide process incidentally gives information about *cystin*, which after evaporation leaves a dark brown residue, soluble in liquor ammoniæ; and *xanthin*, which, first swelling up, leaves a yellow residue after the action and evaporation of the nitric acid, giving no pink or purple with ammonia; but dissolving in liquor potassæ with a yellowish-red colour, turned to violet-red by heat. The yellow mass is insoluble in solution of carbonate of potash.

D. Guided by the foregoing tests, apply further reactions to the volatile substance.

1. For fibrin apply liquor potassæ, in which that substance dissolves after swelling up a little. The solution is precipitated by acetic acid or by ferrocyanide of potassium with acetic acid.

If the fibrin be combined with blood, the microscope will often detect traces of corpuscles, or, failing this, the presence of blood-pigment may be revealed by the hæmin test (Teichmann's). To some of the powdered calculus some well-dried chloride of sodium is added in about equal proportion. To a grain of this spread upon a microscopic slide, add strong acetic acid, cover with thin glass, and apply heat till ebullition is produced. On cooling, crystals of an elongated rhombic prismatic shape with rounded angles, and of a dull brownish colour, will be found if blood is present. If the acetic acid should have been driven off by the heat, a little glycerine or strong solution of acetate of potash must be run in between the covering glass and the slide. A permanent preparation may thus be made.

For cystin the special tests are — first, liquor ammoniæ, which dissolves the substance, and on evaporation leaves transparent, colourless, six-sided tablets. Neutralisation of the ammonia by acetic acid causes a similar precipitate, but usually in less perfect form. Mineral acids dissolve the substance, a reaction which at once distinguishes it from uric acid.

Under the head of *urostealith* several substances are most probably included; among them — first, a fatty matter, saponified by alkali, and precipitated by subsequent additions of acid; second, a substance of high molecule, containing much phosphorus. Both of these burn, as has been stated, with a large smoky flame. If myelin be present, the addition, under the microscope, of distilled or slightly alkalised water, determines the issue of Montgomery's tubes—a reaction described on page 152.

Last among the volatile substances I have put indigo. This has been as yet found only once, and by myself.

The tests for indigo are:—

1. The presence of black, blue, and coppery pigment in the powdered calculus, when examined under the microscope.

2. The sublimation of the indigo-blue by a gentle heat, and the collection of the characteristic crystals on a clean glass slide. The behaviour of the vapour is very marked. The perfectly dry powder is placed in a perfectly dry test-tube, and very slowly heated over a spirit-lamp. At a heat short of redness, a vapour of a deep violet colour is emitted, rather more purple than iodine vapour. It lies heavily in the tube, and on removal of the heat at once condenses, partly on the tube, partly on the powder. On the tube the microscope shows blue flat prisms.

3. Indigo blue can be dissolved, unchanged, in strong sulphuric acid, yielding a blue solution. This solution is permanent if undiluted. If diluted, it gradually deposits the indigo. The spectroscope shows a band in the yellow, characteristic of indigo, as may be seen on comparing a solution of the calculus with a solution of indigo.

D. The calculus being chiefly or entirely composed of non-volatile matter, further tests are used.

1. The ash left after incineration may be fusible or infusible.

(*a*) Fusible. Soluble in acetic acid; and precipitable from solution by excess of ammonia. *Triple, or ammoniaco-magnesian phosphate.* If the neutralisation be very cautiously performed, crystals of the triple phosphate ("house-tops") will be thrown down, and can be recognised by the microscope.

(*b*) Infusible. Add acetic acid very slightly diluted.

If soluble with effervescence, the substance was, before incineration, either *oxalate or carbonate of lime.* The presence of lime is made evident by a precipitate with solution of oxalate of ammonia. If not soluble in acetic acid, but soluble in hydrochloric acid, add to the solution excess of ammonia. A deposit indicates *phosphate of lime.*

2. The foregoing examination will leave the question of oxalate or carbonate of lime unsettled. Powder some of the calculus, and add acetic acid. If solution with effervescence, *carbonate of lime.* A possible source of error here is the use of glacial acetic acid, which, without dilution, will fail to dissolve carbonate of lime. And in rare cases the presence of organic matter appears to prevent the ready action of the acetic acid. Ammonia added in excess throws down triple phosphate if present. If no solution, add hydrochloric acid. To the solution thus obtained add ammonia in excess with great caution, and examine the precipitate with the microscope. *Oxalate of lime* will be found in octohedra, phosphate in prisms.

By 1 and 2 in conjunction, the presence of carbonate, oxalate, and phosphate of lime, and of triple phosphate may be determined.

3. The action of hydrochloric acid in the preceding stage leaves often an insoluble residue. This may be:—1. "Matrix" or cementing organic material. 2. Uric acid or other insoluble organic matter, such as pigment. 3. Foreign bodies, such as microscopic fungi.

The uric acid is here often found in spherical forms, and is recognised by its solubility in solution of potash. This part of the examination is often of importance in determining the origin and history of the calculus, particularly by showing the form of the matrix, which, under the microscope, often retains the impression of the shapes imbedded in it.

4. It is often convenient, in dealing with complex calculi, to examine the powdered calculus, even though of insoluble kind, mixed with water under the microscope.

(*a*) We can see whether the earthy matter is in the form of crystals, spheres, or molecules.

(*b*) We can detect pigment.

(*c*) We can apply acids and alkalies to the substance and watch their action.

5. Similarly in the case of soluble uric acid or urate calculi, we can add weak solution of potash to the powder under the microscope, and examine for organic forms, particularly of fungi. These are often to be found with mixed urates, and throw light on the state of the urine and urinary organs at the time when the concretion was formed.

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