
*Richard Thomas Daniell.*

# THE URINE

IN

# HEALTH AND DISEASE.

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# HEALTH AND DISEASE:

BEING AN EXPOSITION OF

## THE COMPOSITION OF THE URINE,

AND OF THE

## PATHOLOGY AND TREATMENT OF URINARY AND RENAL DISORDERS.

BY

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TO

THOMAS WATSON, M.D.

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS OF ENGLAND,
ETC. ETC.

This Volume is Dedicated,

BY HIS OBEDIENT AND FAITHFUL SERVANT,

THE AUTHOR.

# PREFACE.

The First Edition of this Work was exhausted within a short period of its publication. This may be accepted as evidence that the idea entertained by the Author, that a work containing a simple exposition of the Composition of the Urine, and of the Treatment of Urinary Disorders, would prove acceptable to the Profession, was based upon a right foundation.

That little Treatise was, however, necessarily imperfect. It did not, moreover, fulfil the desire entertained of producing a more complete work—one, in fact, which should embrace within a moderate compass all, or nearly all, that is known and of value relating to the Composition of the Urine, and the Pathology and Treatment of Urinary and Renal Disorders.

The present, though called a second edition, is really a distinct work. It was preferred, however, to issue it under the old, rather than a new title.

The Author has, nevertheless, in preparing it, adhered to his original purpose of simplicity, by omitting all details which appeared to be unessential, by avoiding repetition, and especially by clearness of arrangement and description.

# LIST OF ENGRAVINGS.

# THE URINE

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## CHAPTER I.

### ON THE FUNCTIONS AND STRUCTURE OF THE KIDNEYS, THE PHYSICAL PROPERTIES AND COMPOSITION OF THE URINE, AND THE ORIGIN OF ITS PRINCIPAL CONSTITUENTS.

Functions of the Kidneys, 1—Their Structure, 3—Quantity of the Urine, 4—Colour, 5—Smell, 6—Reaction, 6—Density, 7—Composition, Qualitative and Quantitative, 8—Origin of Principal Constituents, Normal and Abnormal, 11.

#### ON THE FUNCTIONS OF THE KIDNEYS.

In the living animal organization, two grand processes are in constant operation — the one conservative, that of maintaining and sometimes of adding to its bulk by the deposition of new material; the second destructive, and consisting in the disintegration of the older and worn-out portions of the several tissues and organs, a variety of effete or excrementitious substances of high chemical, physiological, and pathological importance being thereby formed.

Now it is the prime and special office of the kidneys to eliminate these excrementitious substances, some of which are possessed of deleterious properties, so that their retention in the system would speedily be productive of derangement, disease, and sometimes ultimately death.

But the kidneys subserve other important purposes. They not merely constitute channels for the elimination of the excrementitious substances derived from the breaking-down of the tissues, but also for the discharge of those compounds which are formed from the unappropriated parts or constituents of the food consumed.

They likewise assist in removing from the system in a greater or less degree a variety of other substances which may be present in the blood, as is shown by the fact that portions of nearly every poison and medicine prescribed are cast off from the system through the kidneys, and so make their way into the urine.

Again, they co-operate with the skin and lungs in relieving the system of superfluous fluid.

Lastly, and under certain conditions, they perform in part the functions of the skin; indeed, the connexion between these organs is so intimate, that to some extent they often replace each other; thus when the functions of the skin are impaired, the kidneys become increasingly active, and *vice versâ*. In this way a balance or equilibrium necessary to health is maintained; but this compensatory action has its limits, so that the one set of organs cannot wholly or permanently supply the place of the other.

The relation between the kidneys and skin is displayed in a variety of ways.

Thus in hot weather the quantity of urine passed is greatly diminished, in consequence of the activity of the skin, and of the increased amount of fluid which escapes from it in the form of perspiration; while in cold weather the reverse obtains—the fluid eliminated by the kidneys is much increased. The difference of temperature between the atmosphere of crowded theatres and assemblies and that of the external air, is often sufficient to be productive of these effects.

The same relationship is exemplified by the dropsy which so frequently sets in after scarlatina, and the occurrence of which may be thus explained in part:—the epidermis, as a consequence of that disease, dies, and is thrown off by desquamation; during this process the escape of the cutaneous secretion is obstructed; this causes an accumulation of fluid and other products in the system, which the kidneys endeavour to carry off, and successfully for a time; afterwards, however, the extra work thrown upon those organs proving more than they can bear, they become congested and inflamed; in time their eliminative functions are impeded, and the fluids taken into the system not finding ready egress, accumulate therein, giving rise to a temporary form of dropsy. It is probable, however, that these effects are also in a measure due to the irritating action upon the kidneys of the poison of scarlatina in its passage through those organs, giving rise to congestion, albuminuria, and retention of urea.

Again, when the kidneys are extirpated, not only is the amount of fluid which escapes by the skin increased, but it also contains some of the substances proper to the renal excretion; thus proving that the skin does, as stated, under certain circumstances, take upon itself to some extent the eliminative functions of the kidneys.

Lastly, in extreme cases of retention of urine, the perspiratory fluid becomes so impregnated with the constituents of the urine, that it acquires a distinctly urinous smell.

These illustrations sufficiently demonstrate the intimate relations which exist between the kidneys and skin, and they also serve to show the importance of attention to the condition of the cutaneous functions, and the reason of the beneficial effects resulting from the frequent use of the bath.

## ON THE STRUCTURE OF THE KIDNEYS.

We will now proceed to give a general sketch of the minute anatomy of the kidneys. This will serve, first, to show how admirably their structure is adapted to enable them to perform the office of eliminating organs; and second, it will be found most useful in enabling us to understand the nature of those structural changes which occur in them, as a consequence of disease, and their effects in deranging and impeding their action.

On making a vertical section of a kidney, it will be perceived that its substance is divisible into two parts—an outer *cortical* and an inner or *medullary* portion.

The *cortical* portion consists of innumerable exceedingly minute convoluted and tortuous *tubules* lined with *tesselated epithelial* or *secreting cells*, so arranged as to leave a free *central channel* for the passage of the urine. These tubules terminate in *blind extremities*, around each of which a minute plexus or twisted coil of blood-vessels is thrown, forming those remarkable globular bodies named *Malpighian corpuscles*, while the tubes themselves for their whole length are enclosed in a *network* of blood-vessels. According to most authorities, the extremity of each tubule is dilated, and the vessels of the Malpighian tuft pierce the membrane of the tubule, so that the plexus actually lies within its cavity. The membrane of the tubules being structureless, this disposition would appear to be little probable, and indeed scarcely possible.

The Malpighian plexus consists of an *afferent artery*, which breaks up into several branches whose conjoint diameter much exceeds that of the vessel from which they spring; and of an *efferent vein*, which forms a network of capillaries which surround the tubules for their whole length. Now this plexus of vessels embracing the tubules forms, to a great extent, when deprived of blood, the nucleated and fibrous tissue, which has been described as a separate structure, and has been termed the *matrix*.

It follows from the preceding description that the principal part of the blood of the renal artery goes to the Malpighian corpuscles, whose special office it is, as many believe, to separate the more watery parts of blood, the chief urinary constituents being eliminated from the now more concentrated blood of the tubular plexuses, through the agency of the secreting cells of the tubules.

Now it is in the outer portion, principally, that the urine is eliminated from the blood; the inner serves mainly for its direct conveyance to the bladder: it consists of bundles of straight tubules, termed *cones* or *pyramids*, of which there are usually from 10 to 15, the bases being turned outwards towards the cortical division of the kidney and the apices inwards; the *straight tubes* forming these pyramids keep uniting with each other, a greatly reduced number of tubes of larger diameter, but occupying much less space, resulting, and constituting at length the apices, or *mamillæ*, of the cones or pyramids: these apices, on which are seated the apertures of the tubes, varying in number from 10 to 20, terminate in cups, usually one to each cone, and which have received the name of *calyces;* these in turn open into some dozen larger and funnel-shaped channels, *infundibula,* two pyramids sometimes opening into the same channel, and these again into a single large cavity, the *pelvis* of the kidney, from which the urine is discharged into the *ureter*, whereby it is conveyed to the bladder.

A little consideration will show how admirably, indeed marvellously, these arrangements and adaptations are contrived with a view to facilitate the formation and elimination of the urine.

First, the blood from which the urine is secreted is, through the medium of the Malpighian corpuscles and the tubular plexuses, brought into the closest possible relation with the membrane of the tubules, which are lined with the true or secreting epithelial cells: the arrangement of the vessels of the Malpighian corpuscles would appear to be specially designed with a view to retard the flow of blood through them, and so allow time for secretion and the escape of its more watery parts.

Second, by the parcelling out of the substance of the kidneys into innumerable minute tubules, not merely is a great extent of secreting surface obtained, but the tubular arrangement is of course just that which is best adapted to facilitate the escape of the secreted urine—a purpose which is still further promoted by the presence of ciliated epithelium in that part of the tube which may be called the neck of the Malpighian corpuscle, and the office of which is to ensure a constant current of fluid, a purpose effected through the wavelike motion of the cilia.

Lastly, we can now perceive in what way disease of the kidneys—which, for the most part, consists in obstruction and obliteration of blood-vessels and depositions within, and even rupture of the tubules—impedes the elimination, and sometimes altogether puts a stop to the secretion of the urine.

## ON THE QUANTITY AND PHYSICAL PROPERTIES OF THE URINE; AS ITS COLOUR, SMELL, REACTION, AND DENSITY.

The quantity of urine voided even by different healthy persons varies greatly, the difference depending mainly upon the amount of fluid ingested, the degree of activity of the other eliminating organs—as the lungs, skin, and bowels, as influenced by weather and other causes, and the condition of the vascular and nervous systems.

Prout gives an average of 35 ounces in the 24 hours, which is very low; while Böcker makes it as high as 81 ounces: numerous other observers give quantities ranging between these two extremes, the mean of the whole of the observations hitherto made being about 52 ounces.

In the same individual the variations above or below the mean amount may be set down at about one-fourth.

In febrile and inflammatory affections, when diarrhœa or profuse sweating exists, in cases of dropsy from whatever cause, and in obstructive diseases of the kidneys, the quantity is more or less, and usually greatly, decreased; on the other hand, in certain nervous conditions and affections, and especially in diabetes, the amount is frequently much increased.

### *Colour.*

Many useful indications are afforded by attention to the colour of the urine.

The urine of health is usually of a bright *amber* colour.

Sometimes, however, and under certain circumstances, it is of a very pale straw-colour, and may even be nearly as colourless as water; at others it is deeper than natural, being of a more or less deep brownish-red tint. These variations may occur independently of the presence of abnormal colouring matters, which impart to the urine various shades of red, yellow, green, blue, and black, and which will be hereafter more particularly noticed.

Very diluted urine, being also of low specific gravity, is usually of a pale colour; such urine is voided soon after copious imbibition, in most hysterical and nervous affections, in cases of anæmia, in chronic afebrile diseases, and in chronic structural diseases of the kidneys.

On the other hand, concentrated and heavy urine is generally of a high colour, as when but little liquid is drank, or when the water of the system is carried off by other channels, as by the skin or bowels, as occurs in hot weather, after copious sweating from whatever cause, after exercise, or as a consequence of diarrhœa and in acute febrile and inflammatory diseases: it is also usually remarkably high coloured in some organic chronic affections of the heart, liver, and lungs. In some of these cases, of course the increase of colour is due not to concentration, but to an actual augmentation in the amount of colouring-matter, *urohæmatin*, resulting from an increased destruction of the red blood-corpuscles.

Although, as a rule, urine of high specific gravity is deeply coloured, it is not always so, since diabetic urine is often of a very pale colour: this is doubtless owing to the enormous quantity of urine passed, and not to any actual deficiency of colouring matter, for when the quantity of saccharine urine excreted is not large, the colour is frequently deeper than natural.

The abnormal colouring matters by the presence of which the urine is variously coloured, are *hæmatine*, *blood* itself, *uroerythrine*, *uroxanthine* or *indican*, *indigo-red*, *indigo-blue*, *melanine*, and *bile* pigments.

Lastly, the colour of the urine may be affected by the presence of colouring matters derived from certain foods or medicines, as *santonine, gamboge, indigo* (Ranke), *chimaphila* or *winter-green, senna,* and *rhubarb*. These may all be distinguished from *urine pigment* by the action of strong solutions of alkalies and acids, the addition of which to the urine occasions very considerable and unusual alterations of colour, when any of these extraneous pigmentary substances are present. *Creasote,* either taken by the mouth or introduced into the system by the skin, has caused on several occasions the urine to assume a *black* or *blackish colour*. The inunction of *tar* has been known to be followed by the same effect. Both creasote and tar probably give rise to the formation of *carbolic acid,* upon the presence of which in the urine the discoloration may depend.

It has been stated that the colouring matters of *saffron, logwood, madder,* and *alkana* root, all pass into the urine, but Kletzinsky was unable to detect them.

### *Smell.*

The peculiar odour of the urine is due to the presence of certain volatile substances, the nature of which has not yet been precisely determined; but amongst them, according to Staedeler, *phenylic* or *carbolic, taurylic, damaluric,* and *damolic acids* may be enumerated.

This characteristic odour it retains for some time, provided the urine be decidedly acid; but if alkaline, it speedily, in consequence of decomposition, begins to emit an offensive smell; and it may even possess this smell when first voided, especially if the mucous membrane of the bladder be affected; but, independently of its becoming offensive as the result of its more or less decomposed state, it sometimes, as when digestion is much at fault, and in some cases of Bright's disease, emits other odours—in particular, a peculiar fishy smell may not unfrequently be detected.

Again, the odoriferous principles of certain articles of diet, and of some medicines likewise, make their way into the urine—as of *onions* and *garlic, asparagus, oil of turpentine, cubebs, assafœtida, valerian, juniper,* and *saffron.*

### *Reaction.*

The reaction of the urine, except after food, is usually acid, but after meals it is for a time frequently neutral, or even alkaline.

The acids to which the acidity is mainly due, are phosphoric, hippuric, and uric acids; but it may in some cases be occasioned in part by the presence of excess of sulphuric, as also of certain organic acids, to be hereafter noticed.

The acidity is determined by means of a graduated solution of some alkali; but it is frequently expressed as equivalent to so much crystallized oxalic acid, the degree of acidity being more readily apparent when stated in this form, than when contrasted with a certain amount of alkali.

The acidity of course varies greatly even in health, being especially influenced by the nature of the food consumed. Winter, in one case, found the normal acidity to be equal to 36·67 grains of oxalic acid, and in another to 29·70 grains, Kerner to 30 grains, and Vogel to from 30·80 to 61·76 grains.

The whole subject of the acidity and alkalescence of the urine will be found fully considered in a special chapter.

### *Weight, or Specific Gravity.*

The weight of the urine above that of its contained water is of course due to the numerous substances which it holds in solution; and, since the amount of these is constantly varying, depending upon the food consumed and the extent of waste of the tissues of the body, it follows that the weight must be subject to corresponding variations.

Of the several constituents upon which its density depends, the two chief are urea and chloride of sodium or salt. The specific gravity, therefore, of the urine is sometimes but little above that of water, *urina potus;* but after food, and especially after digestion, *urina cibi* and *urina sanguinis,* it is much higher.

In health, the ordinary limits of the specific gravity of the urine may be set down as ranging between 10·12 and 10·30, being sometimes either lower or higher, and the mean as 10·20.

In disease, the variations are still greater. In acute febrile and inflammatory disease and in diabetes, the specific gravity is usually very high, while in most chronic and afebrile affections, and especially in structural diseases of the kidneys, it is usually of reduced gravity.

In order to determine whether the urine has a high or low gravity, we must not be content with taking the weight of a single specimen; but the whole of the urine voided in twenty-four hours should be collected, and the weight of a portion of this determined.

Having thus ascertained the gravity and quantity of the urine of the whole day, by a very simple calculation the amount of solid matter contained in it may be approximately determined. The two last figures of the specific gravity are to be multiplied, in most cases, by two (Trap's formula), and in that of heavy diabetic urine by 2·33 (Christison's formula), which gives the amount in grains for 1000 grains of urine. Thus, the specific gravity being 10·23, the two last figures multiplied by 2·33, give 53·59 grains of solid matter to the 1000 grains of urine.

Taking an ounce of urine, and calculating upon Christison's formula, we shall find that the specific gravity very closely represents the number of grains of solids to the ounce. This is well shown in the following table, calculated by the late Dr. Golding Bird:—

| Sp. gr. | Weight of 1 fluid oz. | Solids in 1 fluid oz. | Sp. gr. | Weight of 1 fluid oz. | Solids in 1 fluid oz. |
|---|---|---|---|---|---|
| 1010 | 441·8 | 10·283 | 1025 | 448·4 | 26·119 |
| 1011 | 442·3 | 11·336 | 1026 | 448·8 | 27·188 |
| 1012 | 442·7 | 12·377 | 1027 | 449·3 | 28·265 |
| 1013 | 443·1 | 13·421 | 1028 | 449·7 | 29·338 |
| 1014 | 443·6 | 14·470 | 1029 | 450·1 | 30·413 |
| 1015 | 444·0 | 15·517 | 1030 | 450·6 | 31·496 |
| 1016 | 444·5 | 16·570 | 1031 | 451·0 | 32·575 |
| 1017 | 444·9 | 17·622 | 1032 | 451·5 | 33·663 |
| 1018 | 445·3 | 18·671 | 1033 | 451·9 | 35·746 |
| 1019 | 445·8 | 19·735 | 1034 | 452·3 | 36·831 |
| 1020 | 446·2 | 20·792 | 1035 | 452·8 | 37·925 |
| 1021 | 446·6 | 21·852 | 1036 | 453·2 | 38·014 |
| 1022 | 447·1 | 22·918 | 1037 | 453·6 | 39·104 |
| 1023 | 447·5 | 23·981 | 1038 | 454·1 | 40·206 |
| 1024 | 448·0 | 24·051 | 1039 | 454·5 | 41·300 |

The only exact method, however, of determining the solids of the urine is by the evaporation of a weighed quantity, first on the water-bath, and subsequently in the vacuum of an air-pump over sulphuric acid.

### THE COMPOSITION, QUALITATIVE AND QUANTITATIVE, OF THE URINE.

The composition of even normal urine is highly complex; the constituents admit of a threefold division.

First, into substances which are formed entirely within the system; — this division includes *urea, creatine, creatinine, uric* and *hippuric acids,* colouring matter or *urine pigment,* and *extractives.*

Second, into those which are partly formed within the body, as *sulphuric* and *phosphoric acids.*

Thirdly, into those which are derived entirely from without—as for example, *chlorine,* and the bases *soda, potash, ammonia* usually, *lime, magnesia,* and minute quantities of *silica* and *iron.*

Of these several constituents, the urea, creatine, and creatinine, and the colouring matter, exist in the free or uncombined state; the hippuric and uric acids for the most part are in combination.

The phosphoric acid is combined in part with the alkalies, usually but not always with soda, and in part with the earths; the sulphuric acid with potash, chiefly, but sometimes with soda and lime. Chlorine is united principally to sodium, but occasionally also in part to potassium and ammonium.

The above include all the principal normal constituents of the urine; but some others occur so frequently, that the question is still undecided whether they ought not also to be regarded as normal constituents: of these *carbonic* and *oxalic acids*, also free *nitrogen* and *oxygen* according to Planer, *xanthine*, *hypoxanthine* (which Scherer believes to be identical with *sarcine*), *xanthoglobulin*, *sugar*, and *indican* may be specially mentioned.

Other compounds in addition to the preceding, included generally in the term "extractives," are Scharling's resinous substances, named *omichmyloxide*, the pigment *resin* of Harley, the *acids* of Marcet, and lastly, unoxidized *sulphur* and *phosphorus*.

Finally, it may here be again mentioned that Staedeler has detected minute quantities of *phenylic*, *taurylic*, *damolic*, and *damoluric* acids, and to the presence of which he attributes the odour of the urine; but little is known, however, respecting any of these acids, and Kopp is even of opinion that they are merely products of the processes employed by Staedeler.

Amongst the principal ABNORMAL substances met with in the urine, may be mentioned *cistine*, *taurine*, *leucine*, several *colouring matters*, the bile acids, *taurocholic* and *glycocholic* acids, *lactic*, and more rarely, other *organic* acids, *albumen*, *blood*, and *semen*.

Having thus obtained an insight into the complex *qualitative* composition of the urine, the mean daily excretion by healthy adult men of its principal constituents may next be stated.

The quantities given are taken from Parkes' elaborate and most valuable work on the urine.

| | | |
|---|---|---|
| Water . . . . . . . | $52\frac{1}{2}$ ounces. | |
| | Grains. | |
| Urea . . . . . . . . | 512·40 | |
| Extractives . . . . . | 154·00 | —Parkes. |
| Uric acid . . . . . | 8·56 | |
| Hippuric acid . . . . | 34·50 | four days mixed food. |
| Oxalic acid . . . . . | 1·42 | |
| Sulphuric acid . . . . | 31·11 | |
| Phosphoric acid . . . | 48·80 | |
| Chlorine . . . . . . . | 126·76 | |
| Total . . . . . | 917·55 | grains in 24 hours. |

Parkes regards the mean of the chlorine above given as much too high, and considers that 108 grains are nearer the true mean: the mean of the hippuric acid is also probably too great, and it may at present be taken at 25 grains, but this acid is sometimes even absent; while the mean of the extractives cannot yet be regarded as satisfactorily determined. With these deductions from the chlorine and hippuric acid, the above total is reduced to 889·29 grains.

The amounts of the several *bases*, which have as yet been determined in comparatively but few cases, are subject to great variation. The mean of the analyses of Neubauer, Böcker, Kerner, Becquerel, Duhemberg, Wagner, and Genth, give of

| | |
|---|---|
| Ammonia . . . . . | 8·58 grains |
| Potash . . . . . . | 58·21 |
| Soda . . . . . . . | 125·37 |
| Lime . . . . . . | 3·55 |
| Magnesia . . . . . | 3·09 |
| Iron . . . . . . . . | undetermined |
| Total . | 198·80 grains |
| Mucus . | 7·00 |

The *potash* has been found to range between 26·36 and 107·77 grains; the *soda* between 79·75 and 171·00 grains; the *lime* between 2·33 and 6·36, and the *magnesia* between 2·53 and 4·21 grains.

It will be perceived that the bases consist in great part of potash and soda. Calculating these from the means of the acids with which they are united, results somewhat different from those above given are obtained. The mean of the sulphuric acid being 31·11 grains, and supposing this to be joined with potash, we obtain 36·55 grains as the amount of that base; and estimating that the mean of the chlorine, 108 grains, is joined to ammonium and sodium; and that the phosphoric acid is combined, in part, with the amounts of lime and magnesia set forth above, and the remainder of that acid with soda ($2\,NaO+PO_5$), it will be found that the total soda amounts to 111·27 grains. Calculated in this way, the bases are reduced to 163·04grains.

No allowance has been made in the preceding calculations for the bases united with uric, hippuric, and oxalic acids.

The preceding numbers—namely, 889·29 and 163·04 grains—furnish a total of 1052·31 grains as the amount of solid matter excreted in 24 hours by the kidneys of healthy men in the middle period of life.

This total is in excess of the mean obtained from the actual evaporation of the urine as calculated by Parkes, from the observations of several inquirers, namely, 945 grains; the lowest individual mean being 610 and the highest 1182 grains. It thus appears that one healthy person may, for a time, excrete twice as much solid matter as another. The range of variation in the same individual is about one-third above or below his mean amount.

Taking 145 lbs. avoirdupois as the mean weight of all the healthy men the analyses of whose urine have furnished the preceding data, and dividing the mean amounts by that number, Parkes has calculated the following table showing the amount of excretion of the several urinary constituents in relation to 1 lb. avoirdupois of body-weight.

| | In 24 hours 1 lb. avoird. excretes in grains |
|---|---|
| Urea . . . . . . . . | 3·530 |
| Uric acid . . . . . | 0·059 |
| Pigment and extractives . | 1·062 |
| Sulphuric acid . . . . | 0·214 |
| Phosphoric acid . . . . | 0·336 |
| Chlorine . . . . . . | 0·875 |

The chlorine Parkes has taken at 108 grains. The determination of the urinary excretion in relation to body-weight, affords, of course, more precise data than the mere estimation of the total daily excretion of each constituent.

## ON THE ORIGIN OF THE PRINCIPAL URINARY CONSTITUENTS, NORMAL AND ABNORMAL.

It will help us to obtain a somewhat clear and comprehensive view of the nature and purposes of the chief constituents of the urine, if some reference be now very briefly made to their origin. For more complete details on this head, the reader is referred to the several chapters in which the urinary constituents are specially treated.

*Urea* is derived from the disintegration of the nitrogenous tissues; it forms indeed the vehicle for the elimination of the nitrogen of about two-thirds of the tissues of the body, the mean daily excretion amounting to no less than 512·4 grains, or considerably more than one ounce. The quantity present in the urine represents, therefore, to a great extent, the measure of the waste of the nitrogenous tissues.

*Creatine* and *creatinine* are also nitrogenous constituents, and are doubtless derived from the disintegration of the muscular tissue, both striped and unstriped.

*Uric acid*, another nitrogenous body, is also a product of retrogressive metamorphosis, but the tissue which furnishes it is unknown; it may possibly be the spleen in a great measure, since it is found largely in that organ.

*Hippuric acid* is doubtless derived in many cases from the *food* consumed, as well as in the herbivora, from the *tissues*, as proved by its occurrence in the urine of fasting animals. Whether in animal feeders it has a tissue-origin is uncertain, since it disappears during fasting; analogy would, however, lead to the inference that in man it is also in part derived from the disintegration of tissue. It has therefore a double origin.

The *colouring matter* or pigmentary substance of the urine is derived from the breaking down of the red blood-corpuscles, and it therefore represents the measure of their metamorphosis.

A great variety of substances are included, as already stated, under the term "*extractives;*" the majority of these have also their origin in the destructive metamorphosis of tissue.

The *Sulphuric acid* is derived to the extent of about one-third from the sulphates of the food; the other two-thirds are due to the oxidation of the sulphur of the albuminous tissues, as well as of that of taurine and cystine.

*Phosphoric acid* is also in part derived from the food, and in part is due to the oxidation of the phosphorus of the body, especially of the muscular, nervous, and osseous tissues.

*Chlorine* is derived entirely from without.

Of the bases, *ammonia* is probably principally derived from without, but in part, in some cases, from the decomposition of urea, and probably of some other bodies, as leucine. *Potash, soda, lime, magnesia, silica,* and *iron,* are of course all introduced into the system through the food and drink consumed. Potash is found particularly in the muscles and in the red blood-corpuscles; soda in the serum of the blood; lime in the bones.

The non-nitrogenous *oxalic acid* ($C_2O_3$) of the urine may be traced to three or four distinct sources. First, to the oxalates contained in articles of food consumed; second, to beverages rich in carbonic and other organic acids; third, to impeded elimination of carbonic acid by the lungs and skin; and fourth, to the metamorphosis of uric acid.

*Leucine* ($C_{12}H_{13}NO_4$) is derived chiefly from the liver, but is found as a normal constituent of the spleen, pancreas, thymus, and other glands.

*Tyrosine* ($C_{18}H_{11}NO_6$) is also derived chiefly from the liver.

*Xanthine* ($C_{10}H_4O_4N_4$) and *hypoxanthine* ($C_{10}H_4N_4O_2$) have most probably the same origin as uric acid, and are found especially in the spleen, liver, and in the muscles.

The large amount of sulphur contained in *cystine* ($C_{12}H_{12}N_2S_4O_8$) and its consequent resemblance to taurine, render it probable that its formation is due to imperfect elimination of sulphur by the liver.

*Taurine* ($C_4H_7NS_2O_6$) is derived from the biliary acids.

The *sugar* ($C_{12}H_{12}O_{12}$) found in the blood and urine may be traced to several origins: to articles of food in which it is present ready formed; to the transformation of the starch of food (the sugar directly introduced by simple absorption into the blood, or which is formed from starch, is usually destroyed within the body, and seldom reaches the urine in any appreciable amount); to the transformation of the glucogenic substance formed in the liver (this is the chief source of the sugar in diabetes); to the decomposition of indican.

*Inosite* ($C_{12}H_{12}O_{12}+4\,HO$) is formed in the muscles, and has also been found in most of the glands. In diabetes it sometimes replaces diabetic sugar.

The *bile pigments,* bile acids, *taurocholic* and *glycocholic* acids, and the *bile* itself, of course proceed from the liver, the biliary pigments being in all probability derived from the blood pigment.

*Uroxanthin, indican,* and its derivatives, *indigo-blue,* or *uroglaucin, indigo-red,* and other urine pigments, as *urrhodin,* appear to have a similar origin from blood pigment.

Lastly, *lactic acid* is considered to be derived from the fermentive transformation of the urinary pigment.

# CHAPTER II.

## UREA.



### *History.*

THE *excrementitial* compound urea was first discovered in the urine, in 1771, by Rouelle le Cadet, but it was MM. Fourcroy and Vauquelin who gave it the name of urea—suggested by the word urine, and bestowed upon it in consequence of its being the most abundant and distinctive of the constituents of that fluid.

Urea exists in the blood of Man, of the Carnivora, and in smaller quantity in that of the Herbivora. In the Carnivorous birds, in Serpents and Insects, uric acid predominates, and in some cases almost entirely replaces urea.

Urea has been met with, not only in the blood and urine, but also in several of the other organic fluids, both normal and pathological, as the aqueous and vitreous humours of the eye, the sweat, the saliva, and *liquor amnii;* occasionally in the vomited matters of persons suffering from retention of urine, or labouring under Bright's disease; in the *egesta* in certain forms of diarrhœa; in the serosity of dropsies resulting from different forms of the same disease, and in the fluid of the ventricles of the brain in cases of albuminuria.

### CHEMISTRY OF UREA.

Urea exists in the urine simply in a state of solution, and usually in the uncombined form. The only definite chemical compounds of urea which have been ascertained to be sometimes formed are those with chloride of sodium, chloride of ammonium, and oxalic acid; oxalate of urea has been found in the urine after taking a large dose of binoxalate of potash; on the other hand, it has been determined that urea will not combine with hippuric, lactic, and uric acids.

It is soluble in nearly every proportion in cold and hot water, in five parts of alcohol of specific gravity 0·816; it is insoluble in anhydrous ether and oil of turpentine; it exerts no action on vegetable colours; has a bitterish cooling taste; it fuses at 248°, and at a few degrees higher it becomes decomposed. It is precipitated by nitrate of silver as a cyanate, and by protonitrate of mercury a nitrate of urea in combination with oxide of mercury is thrown down.

*Composition.*—Urea has the following atomic and percentage compositions:—

| | Atomic Composition. | | Percentage Composition. |
|---|---|---|---|
| Carbon | 2 atoms | . . . . | 20,000 |
| Hydrogen | 4 ,, | . . . . | 6,666 |
| Nitrogen | 2 ,, | . . . . | 46,667 |
| Oxygen | 2 ,, | . . . . | 26,667 |
| | | | 100,000 |

Atomic number, 60.

*Decomposition.*—Urea is decomposed with great facility in a variety of ways—as by heat, acids, alkalies, various salts; by the fermentation of decomposing mucus and other animal matters, yeast, &c. When the temperature is raised much above 248° it becomes resolved into *ammonia, carbonic acid, cyanate of ammonia, cyanuric acid*, and its derivatives.

When treated with nitric acid coloured red with nitrous acid, the urea is decomposed into *carbonic acid, nitrogen*, and *water*.

The nitride of the suboxide of mercury dissolved in nitric acid gives rise to the same decomposition.

Fused with potash or treated with strong sulphuric acid, the urea is converted into *carbonic acid* and *ammonia*.

Caustic lime and magnesia added to hot solutions of urea cause the evolution of *ammonia*.

A solution of chlorinated soda or of hypochlorite of soda causes the decomposition of the urea into *carbonic acid, water*, and *nitrogen:* the two first being absorbed, the urea may be estimated by the bulk of the nitrogen remaining.

When nitrate of silver is added to a solution of urea, and the mixture evaporated, *nitrate of ammonia* and *cyanate of silver* are formed.

Various methods for the quantitative estimation of urea have been based upon these decompositions—one chemist estimating the urea from the *carbonic acid* evolved (Bunsen); another from the *nitrogen* liberated (Davey).

In 1852, when the subject of the decomposition of urea was less understood than at present, the author instituted some investigations for the purpose of ascertaining the circumstances which influenced its transformation while still contained in the urine. The chief results arrived at are included in the following paragraphs:—

1st. "The simple act of boiling an aqueous solution of urea is sufficient to determine the gradual dissolution of that substance, and its conversion into carbonate of ammonia.

2nd. "This conversion of urea takes place, after a time, in distilled water, even without the aid of the spirit-lamp.

3rd. "The decomposition of urea is effected either with or without heat, much more readily in fluids which are alkaline, and especially in those the alkalinity of which arises from the presence of lime in any form.

4th. "The conversion of urea is retarded, and sometimes altogether prevented, by an acid condition of the fluid in which it is present; and this is equally the case whether the solution be subjected to the heat of the lamp or not. The more acid the fluid the more does it prevent the decomposition of the urea.

5th. "Animal or nitrogenous matter, in a state of decomposition, exercises a powerful influence over the transformation of urea; and this it does partly by producing an alkaline condition of the fluid in which the two substances are contained, the alkalinity being produced by the carbonate of ammonia generated during putrefaction."*

*Formation.*—Urea may be artificially prepared in a variety of ways. Thus it may be produced from *uric acid*, by the action of oxidizing agents, as peroxide of lead. It may also be obtained from *creatine* and *alloxan* by the action of alkalies.

Again, it is formed by simply evaporating a solution of cyanate of ammonia, the whole of which is converted into urea.

Or it may be produced by heating dry ferrocyanide of potassium with manganese, extracting with cold water, adding sulphate of ammonia, and removing the sulphate of potash formed by crystallization. The solution must be evaporated, and the urea extracted with alcohol.

It has been affirmed by Béchamp, that urea could be formed from protein compounds by the agency of oxidizing substances, and that he had thus made it by the action of permanganate of potash on albumen. Subsequent experiments have failed to verify this statement. Neither has urea ever been formed from gelatine out of the body, although the belief is entertained by many, that when taken as food it becomes directly converted into urea; the reality of this transformation has not yet been demonstrated, and the investigations of Bischoff are opposed to this view.

*Combinations.*—The chief combinations of urea are with nitric and oxalic acids; these, as also that with protoxide of mercury, will be noticed hereafter.

### *On the Determination of Urea.*

Numerous methods have been devised for the determination of the urea of the urine; some of these are exceedingly ingenious: however, it is not necessary in this place to give a description of the whole of them: those, therefore, only will be described which are the most convenient or interesting, and which are of acknowledged practical utility.

* *Lancet*, June, 1852, and the author's review of Bird's "Urinary Deposits" in *British and Foreign Medico-Chirurgical Review* for July, 1853.

The whole of the processes devised admit of being thus classified.

First, there are several methods based upon the *decomposition of the urea* by the action of reagents; one chemist, Bunsen, selects the resulting *carbonic acid* as the basis of his process; a regulated heat being the decomposing agent and hydrate of baryta being used to fix the carbonic acid. Another, Heintz, calculates the urea from the *ammonia* generated from the urea by the action of sulphuric acid; a sulphate of ammonia is formed, and the ammonia is estimated by precipitation with chloride of potassium, or the amount of carbonic acid evolved is calculated: 44 parts of carbonic acid correspond to 60 of urea. Davy measures the *nitrogen* given off by its decomposition. A measured quantity of urine is poured into a graduated tube partly filled with mercury; an excess of hypochlorite of soda is added, and the tube inverted: decomposition of the urea shortly ensues; the carbonic acid is absorbed by the hypochlorite, while the nitrogen collects in the upper part of the tube.

In other processes the urea is made to combine with certain acids, as the nitric, oxalic, and tartaric, forming salts which in water or urine are but little soluble, and from which the urea may either be calculated or obtained in the separate form.

*Nitrate of Urea.*—This combination may be thus obtained. A certain quantity of the urine by weight is taken, 500 grains being in most cases sufficient. The urine should be concentrated by gentle evaporation to about one-third or one-half its bulk, and then pure nitric acid added, in the proportion of about one-half of the urine, which still remains. Usually, on the addition of the nitric acid, some amount of effervescence takes place; this arises from the decomposition of the chlorides effected by the nitric acid, and also from the escape of carbonic acid gas, should any carbonates be present.

If the quantity of urea present be very great, crystals of the nitrate will immediately appear, the whole of the urine being apparently converted into a solid mass. If the amount be less, the crystals will appear only after the urine has undergone still further, but spontaneous, evaporation; and if the amount be very small, they will not be formed until the greater part of the urine has become dissipated.

That the crystalline substance formed in urine on the addition of nitric acid consists of *nitrate of urea* is sufficiently shown by the characters of the crystals, which have the form of flat six-sided plates, as seen under the microscope.

The nitrate of urea thus obtained is not pure, but is stained with the colouring matter of the urine; the crystals should, therefore, be collected, washed with a little ice-cold water, dried with blotting paper, redissolved in water, and purified by recrystallization. One hundred parts of the nitrate correspond to nearly forty-eight parts of pure urea.

The fluid remaining after the first crop of crystals has been removed, may be set aside in order to ascertain whether any fresh formation of nitrate of urea will occur, as sometimes happens.

A very good general idea of the *quantity* of urea present in any urine may be obtained by adding a little nitric acid to a few drops of the urine on a slip of glass, when a crust, more or less dense and thick, according to the amount of urea present, will be left on evaporation, and the crystals under the microscope will be found to possess all the characters of those of nitrate of urea. (Fig. 5.)

*Oxalate of urea.*—Oxalic acid may be employed in place of nitric acid, and an *oxalate of urea* formed. The urine should be evaporated to one-fourth, or even sometimes one-eighth of its bulk, filtered through coarse filtering paper, or muslin, in order to separate the phosphates and urates which have become deposited during the gradual evaporation, and then about an equal bulk of a strong solution of oxalic acid in hot water is to be added. The mixture soon deposits an abundant crop of crystals of oxalate of urea, the characters of which, as seen under the microscope, are very different from those of the nitrate of urea. The oxalate of urea thus formed, like the nitrate, is usually stained with colouring matter, and is to be decolorized in the same manner as the nitrate. (Fig. 6.)

*Separation.*—The urea may be obtained *in a separate state* from the oxalate in the following manner: — The oxalate of urea is to be dissolved in hot water, and the solution treated with carbonate of lime so long as any effervescence continues; the oxalate is decomposed, the urea remaining in solution, while the oxalate of lime formed, together with any excess of carbonate of lime which may have been employed, are precipitated. Or carbonate of baryta may be used in place of the lime salt. The urea may also be obtained from the nitrate by means of the same reagents. Crystals of nitrate of baryta soon separate from the filtered fluid, which must be evaporated and the residue extracted with ether.

Dr. Marcet separates the urea from the dry extract of the urine by means of *alcohol*. The steps of the process are as follow :—

The urine is evaporated to dryness, first on the water-bath and afterwards over sulphuric acid. When the residue has become hard and brittle, it is treated with several successive portions of boiling absolute alcohol, decanting it after each operation. An alcoholic extract of urine is thus obtained, containing all the urea, a little salt, and showing a marked acid reaction. There is then to be added to this liquid a small quantity of sulphuric ether, allowing it to descend along the side of the vessel, so as to avoid the mixture of the two fluids. At first a cloud-like precipitate is produced at the point of contact of the liquids; this extends gradually above and below. Five or six hours afterwards the precipitate has disappeared, and the bottom and sides of the vessel are then found covered with fine crystals of urea. It is necessary to add the ether until no further precipitate is occasioned. A little salt is often found amongst the crystals, which may be separated by a new crystallization in water. This operation is necessary, as otherwise the urea in this state is very deliquescent.

This process of extraction will be found useful when the urine is albuminous, or in the analysis of the blood for urea. The sulphuric and phosphoric acids should be first removed by means of a solution of baryta, and the filtrate neutralized with nitric acid previous to evaporation.

It will seldom be found necessary in practice to have recourse to the processes of Bunsen, Heintz, or Davy, neither will it be requisite frequently to estimate the urea either from the nitrate or oxalate. The process which, on account of the facility of its application, has nearly superseded all others, and by which most of the determinations of urea are now made, is the *volumetric* method devised by Liebig, and which will next be described as concisely as possible.

*Liebig's process* is based upon the following chemical facts:—Nitrate of protoxide of mercury precipitates urea from its aqueous solution, forming with it a compound insoluble in water. If the solution contain chloride of sodium (and this salt is present in most urines) as well as urea, then no precipitate occurs until sufficient of the solution of the nitrate has been added to decompose the whole of the chloride of sodium; bichloride of mercury, or corrosive sublimate, being formed. The moment the salt is decomposed, the compound of urea and mercury is formed, just as though no chloride of sodium had been present. Thus, by adding to a given quantity of urine a known amount of a solution of nitrate of protoxide of mercury, of ascertained strength, we arrive at two important results in the analysis of the urine: first, the quantity of chlorine in the urine is ascertained, by noting the quantity of the mercurial solution used previous to the appearance of a precipitate; and, second, the amount of urea. The precipitate contains four equivalents of protoxide of mercury to one of urea.

The main steps of the process, as applied to the urine, and as described by Lehmann, are as follow:—

The first step necessary is the removal of the *phosphates* and *sulphates*: this is effected by means of what is called the *Baryta test-solution*. A definite quantity of urine is mixed with half its volume of a mixture formed of one part of a saturated solution of nitrate of baryta and two parts of a saturated solution of caustic baryta. We then take 15 cc. of the filtered fluid, which is of course alkaline, and which contains, for every three volumes, two volumes of urine; and, without neutralizing it, we add from a burette a solution of protoxide of mercury, of known strength, *the mercurial test-solution*, so long as any precipitate is formed. The mixture must be well stirred during the process. The precipitate is the compound of urea and protoxide of mercury: U+4 Hy. O.

In order to ascertain whether sufficient of the mercurial solution has been used or not, a drop of the turbid fluid is placed in a watch-glass, and one drop of a solution of carbonate of soda is added, the mixture soon becomes yellow when an excess of the solution of mercury has been used; but it remains white when the solution added is insufficient to precipitate all the urea.

The *Test-solutions.*—It is scarcely needful to enter into any lengthened description of the steps by which the test-solutions of baryta and mercury are prepared, since they, as well as the required apparatus, are now regularly made and supplied by most of the manufacturing and philosophic chemists. Before using the mercurial test, its strength ought always to be ascertained by the operator: this may be effected either by means of sulphuretted hydrogen, by potash, or a standard solution of chloride of sodium and phosphate of soda.

Perhaps the best means of determining the strength of the solution is by means of potash, by which the protoxide is precipitated, when it may be collected and weighed; or the mercury may be precipitated as a sulphide: a solution of sulphate of soda is added, nitrate of soda is formed, and sulphate of protoxide of mercury is precipitated, which is decomposed by sulphuretted hydrogen.

The *rationale* of the chloride-of-sodium process is as follows:—When phosphate of soda is added to a solution of nitrate of mercury, phosphate of protoxide of mercury is precipitated; but this is prevented by the addition of chloride of sodium, owing to the formation of bichloride of mercury, which is not thrown down by the phosphate. From the amount, therefore, of the standard solution required to redissolve the precipitated phosphate of protoxide of mercury, the amount of protoxide in a given bulk of the liquid is determined.

As the first few drops of the test-liquid do not, owing to the presence of chloride of sodium, produce any precipitate of urea, it is necessary to make a deduction on this account. It is found that for all practical purposes it is sufficiently accurate to subtract 2cc. from the whole volume of the test-solution used.

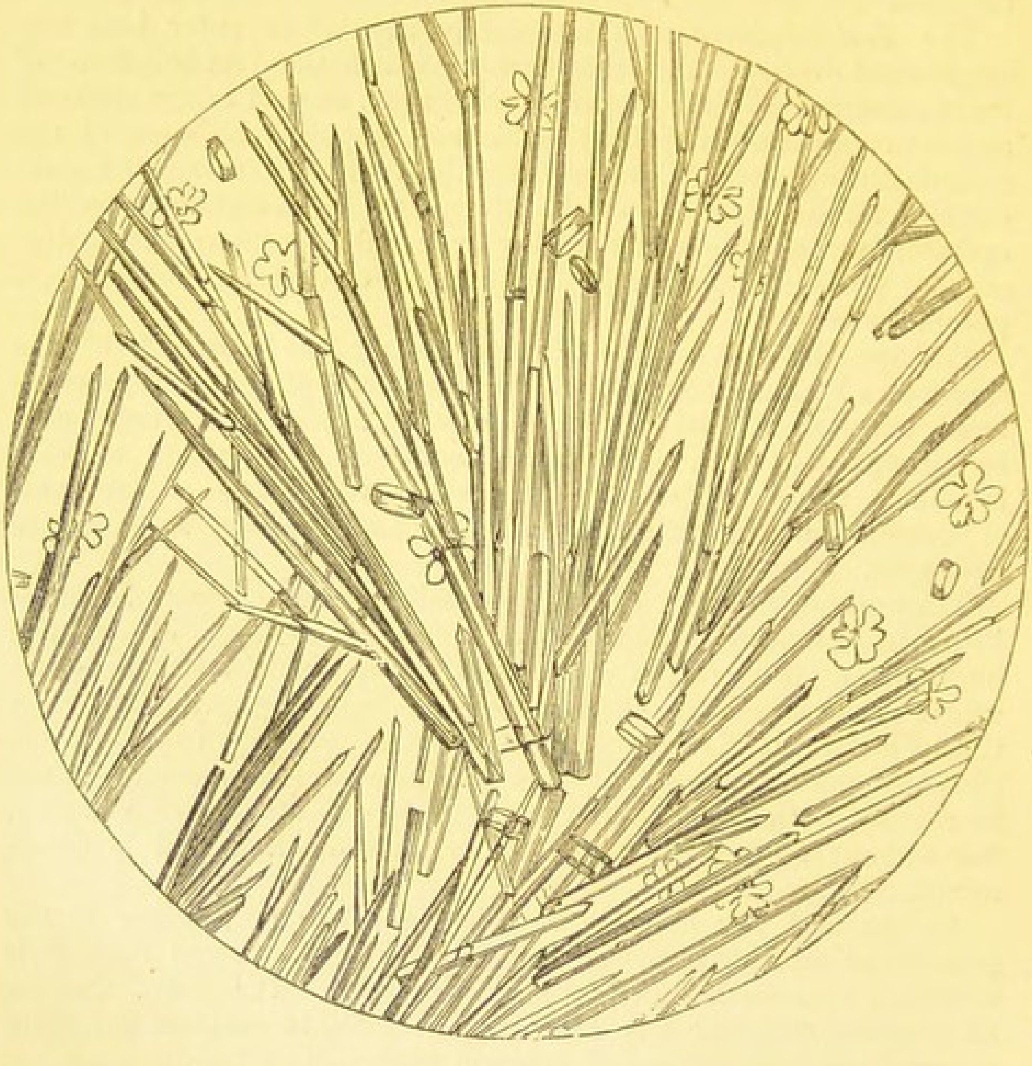
The usual strength of the solution is 11·92 grains of peroxide in 10 cc. or 154·40 grains of the solution; 1 cc.=15·44 grs. indicating 0·01 gr.=0·154 gr. of urea.

It should always be ascertained whether the baryta solution added has been sufficient to precipitate all the phosphates and sulphates.

## MICROSCOPICAL CHARACTERS OF UREA.

Some years since, the author showed that when a drop of any urine containing urea in any considerable amount is evaporated on a slip of glass, a glistening crystalline crust is left, formed of needle-like crystals of urea, arranged in more or less of a radiate or arborescent form, as exhibited in Fig 1.

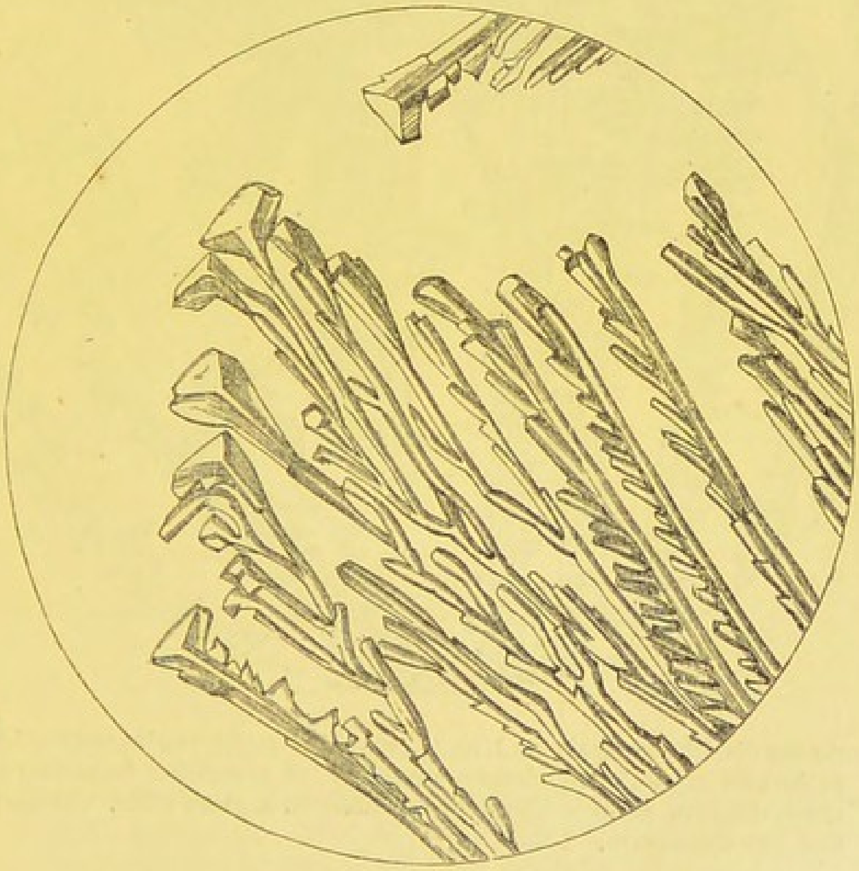
Fig. 1.



Urea from a drop of *Human Urine* spontaneously evaporated on a glass slide. Magnified 90 diameters. 1850.

If these crystals be closely examined, a prominent ridge will be observed running down many of them. In some cases the distal extremities of the needles assume the shapes exhibited in Fig. 2, showing a tendency to take on a regular and defined crystalline form. Again, when pure urea is evaporated on a slip of glass, the needle-like crystals forming the edge of the crust frequently break up into short crystals, of irregular form, but some of which appear of a wedge shape. Crystals, more perfectly shaped, are sometimes met with in the evaporated extracts of urines. Indeed, under certain circumstances, especially when slowly evaporated, urea does crystallize in a definite form, that of the rectangular or right rhomboidal prism. The regularly-formed crystals are usually met with in the shape of flat four-sided prisms, often full of cavities and appearing to be formed of numerous parallel crystalline lamellæ, the prisms being terminated at the ends by one or two oblique surfaces. According to C. Schmidt, these forms do not pertain to the monoclinometric system, but rather to the hemihedral form belonging to the rhombic system, and bounded by parallel surfaces. In the engraving, (Fig. 4,)

FIG. 2.

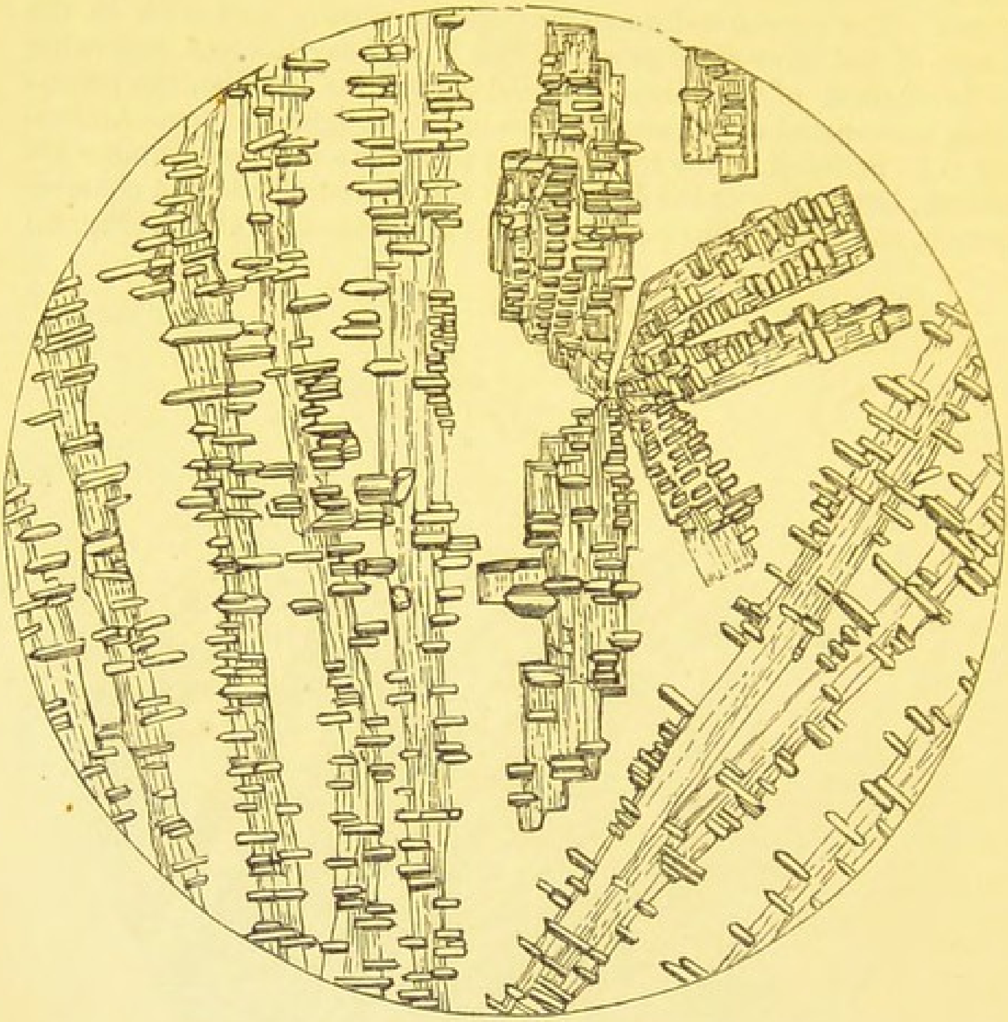


UREA from a drop of *Human Urine* evaporated on a glass slide. Magnified 100 diameters. 1850.

the various forms are delineated assumed by the crystals of urea, as observed by myself and others.

Not unfrequently, the needle-shaped crystals forming a crust of urea after the evaporation of a drop or two of urine on a slip of glass, are themselves beset in a very curious manner with other crystals, probably of creatine, and regularly placed at right angles, as though they had become formed and deposited under some electric agency. (Fig. 3.)

Fig. 3.



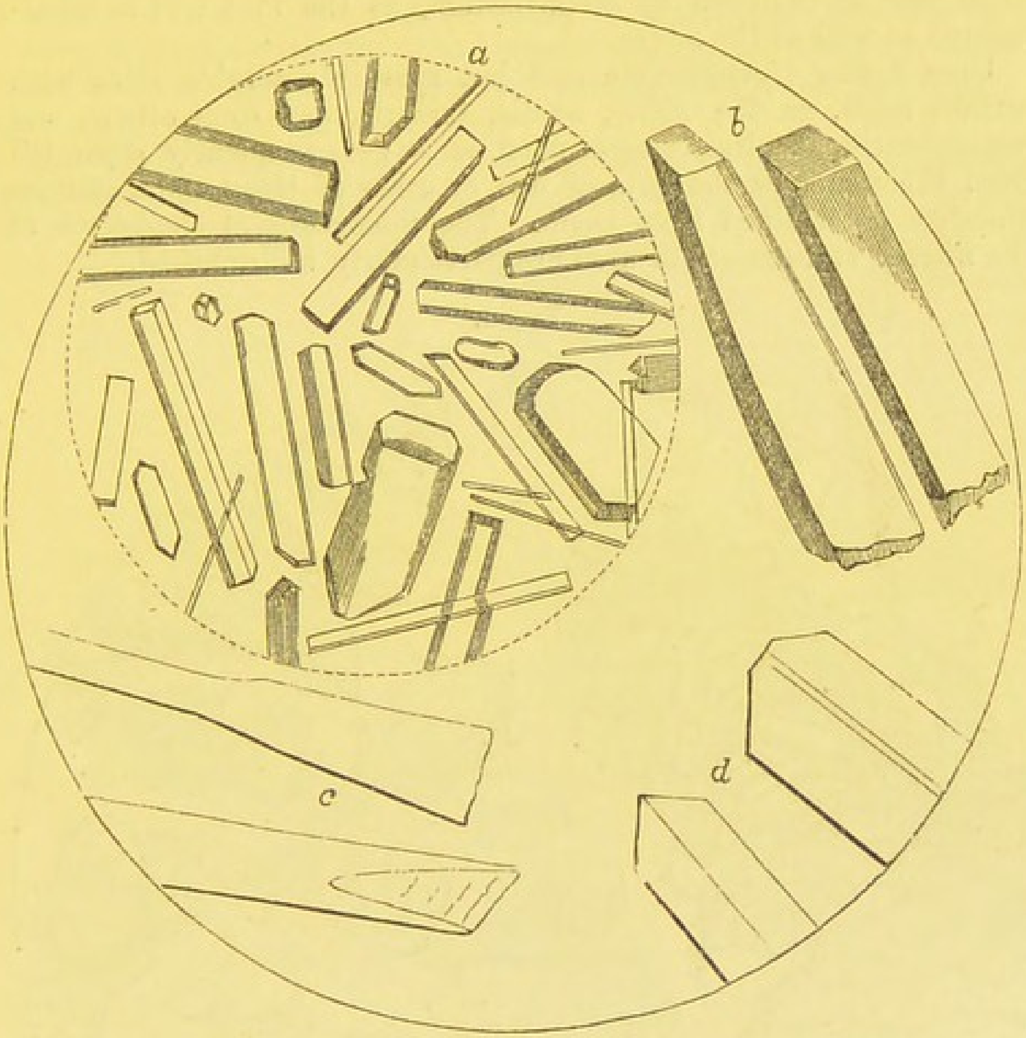
Long needle-like crystals of Urea, crossed at right angles with other prismatic crystals, consisting, probably, of *creatine:* from two or three drops of *Human Urine* evaporated on a glass slide. Magnified 100 diameters. 1850.

Crystals of urea when not pure, and mixed with chloride of sodium, readily deliquesce, and therefore easily lose their form.

The evaporation of one or two drops of urine on a slip of glass affords one of the readiest means of determining whether urea is present in excess or not in any urine.

The presence of urea modifies the form of the crystals of chlorides of sodium and ammonium: thus the former salt is said to crystallize in octohedra instead of cubes, and the latter in cubes and not in octohedra. We have not found this to be the case; but the crystals of the compound of urea and salt have been in the form of four-sided prisms and plates more or less broad and long, variously truncated and mostly united together, so that usually one extremity of each crystal only is perfect. (Fig. 4, *d.*)

FIG. 4.



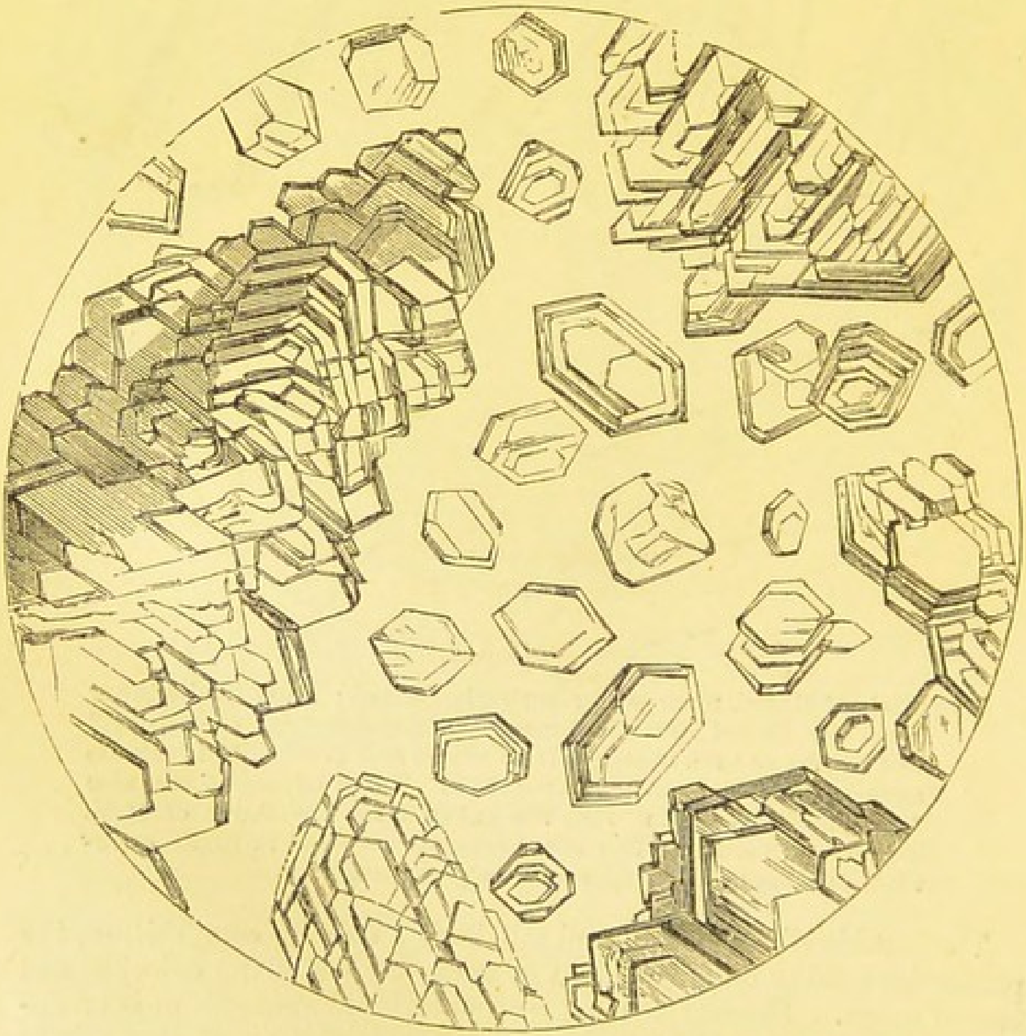
Crystals of UREA, more or less perfectly formed; those in the inner circle are copied from Lehmann's "Physiological Chemistry," and consist of urea obtained from urine, and crystallized from its aqueous solution by slow evaporation. Those lettered *b* are also from aqueous solution, and are taken from the Atlas of M.M. Robin and Verdeil. The other crystals occurred in small quantities of *Human Urine* spontaneously evaporated.

The combinations of urea and salt have a definite composition, the proportions being one equivalent of urea for one of the chloride and two of water. The combination with chloride of ammonium is analogous. The crystals of urea and salt differ from those of pure salt in not, like the latter, polarizing light; they may be formed artificially, as by adding salt to the urine; they are soluble to a considerable extent in alcohol and ether.

There are some substances occasionally present in the urine which interfere considerably with the crystallization of urea, and the removal of which is therefore rendered necessary; one of these is albumen, which may be removed by boiling. If sugar be present, it must not be removed by fermentation, as the urea will be transformed as well as the sugar.

Urea forms crystallizable and but sparingly soluble salts with certain acids, as the nitric, oxalic, tartaric, and some others, and consequently, as already mentioned, it is very frequently separated from the urine in the form of one or other of these salts, and its quantity determined from them. The microscopical characters of the nitrate and oxalate of urea are particularly well-marked.

FIG. 5.

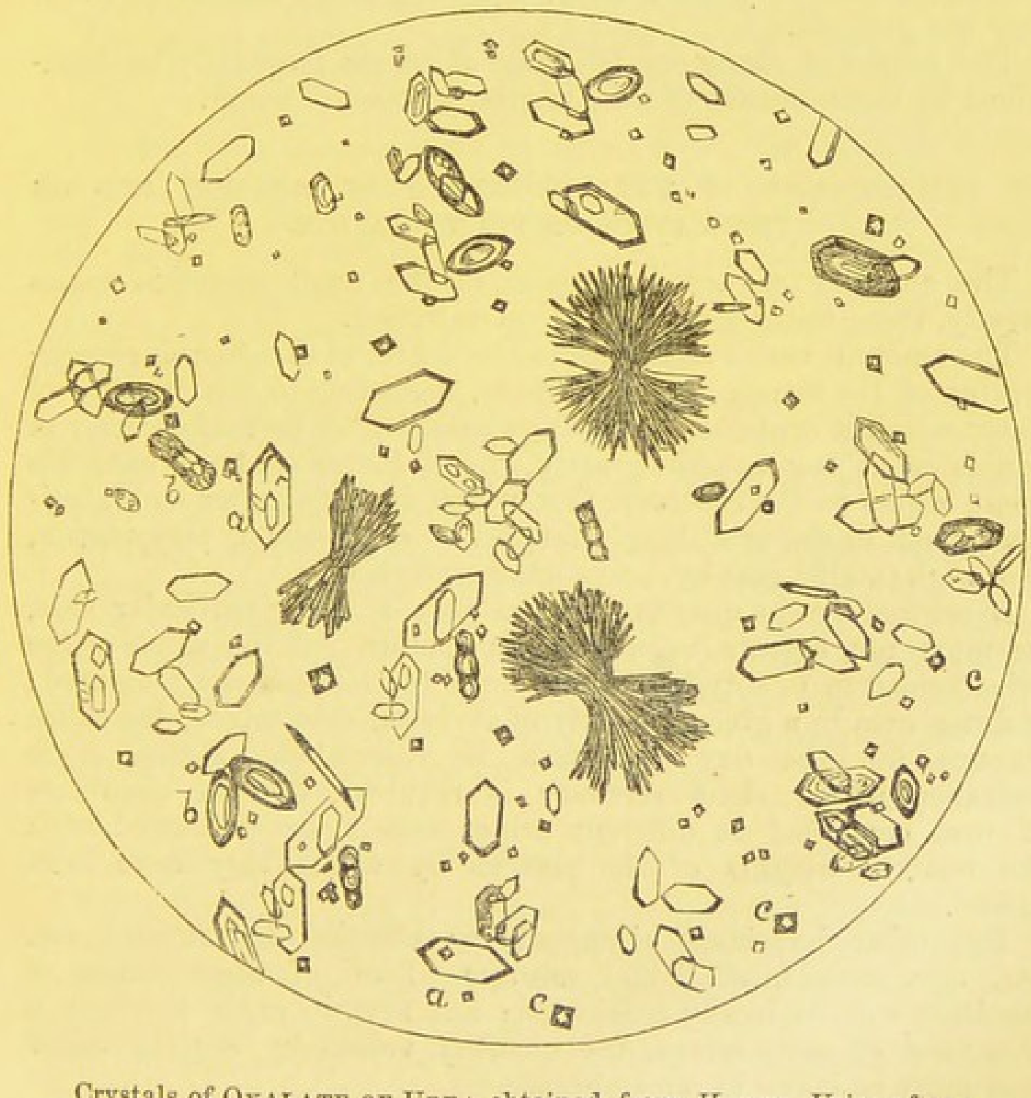


Crystals of NITRATE OF UREA. Magnified 100 diameters.

The treatment of the urine necessary for the formation of *nitrate of urea* has already been explained, but the nitrate may be formed on a small scale for observation with the microscope. Thus, a single drop of urine may be placed upon a glass slide, and part of a drop of nitric acid added, when, if urea be present in anything like considerable amount, crystals of the nitrate will speedily appear. The crystals occur in flat rhomboidal or rectangular plates, often six-sided and generally longer than broad, the angles being variously truncated, and the crystals frequently being compound and aggregated into masses. (Fig. 5.)

*Oxalate of urea* may not only be prepared artificially, but it may occur ready formed in the urine. The engraving (Fig. 6) represents

FIG. 6.



Crystals of OXALATE OF UREA obtained from *Human Urine* after a dose of *binoxalate of potash*. Octohedral and scaphoid crystals of *oxalate* of *lime* also occurred, and are represented in the engraving. Magnified 100 diameters. 1851.

crystals of oxalate of urea found in the urine after a large dose of binoxalate of potash. The mode of crystallization of this salt is sufficiently remarkable to allow easily of its discrimination from the nitrate.

The forms assumed by the crystals of oxalate of urea are all derived from the rectangular and right rhomboidal prisms. Like the other oxalates, the crystals very often assume a dumb-bell shape. (Fig. 6.)

For a full description of the various modifications presented by the crystals of oxalate of urea, see "Traité de Chimie Anatomique et Physiologique," par MM. Robin and Verdeil, as well as the Atlas to the same work.

The crystals of urea and of its nitrate and oxalate all colour polarized light, often very remarkably, according to the manner in which they are grouped.

The nature of many crystals may of course frequently be determined by measurement of their angles, in cases of doubt.

## ON THE AMOUNT OF UREA EXCRETED IN HEALTH, AND ON THE CAUSES OF ITS VARIATION.

The quantity of urea contained in the renal excretion varies greatly, there being several causes of variation.

The amount varies according to the degree of *dilution* or *concentration* of the urine; in other words, according to the quantity of water which it contains. The urine passed after partaking freely of liquids is of low specific gravity, and of course contains but little urea; while, on the contrary, that which is voided after long abstinence from fluids, or at long intervals, or after copious perspiration, is of high specific gravity, and contains much urea.

In estimating the quantity of urea passed in any particular case, we must not operate upon a single sample, but the whole of the urine voided in twenty-four hours must be collected and measured; and the urea in a given quantity of it being determined, the entire amount for the day may then be calculated. Again, it is desirable, where strict accuracy is required, that the quantities of urea contained in different urines should be contrasted with the relative weights of the persons by whom they have been passed.

But other important circumstances affecting its amount are, *sex, age, weight, diet,* and *exercise.* Each of these causes of variation will be briefly considered; but first, in order to obtain a *standard of comparison,* the quantity voided by *healthy adult men* must be borne in remembrance.

It appears from the calculations of Dr. Parkes, based upon several days' observations, carried on by 24 different observers, that the mean daily amount of urea voided by healthy men between the ages of 20 and 40, ranged from 286·1 grains to 688·4 grains; the mean of the whole being 512·4 grains, or 21·3 grains per hour.

The maximum and minimum amounts passed by any individual in one day are usually about one-fifth above or below his mean daily excretion, supposing the individual not to be under any unusual physiological condition.

In men between 20 and 40 years of age, for every pound of body-weight the mean amount of urea excreted is 3·53 grains.

### *Influence of Sex.*

It appears that *women* excrete less urea than men.

Dr. Parkes gives the mean of numerous analyses by six observers, in twenty adult women between 16 and 40 years of age, at 390 grains.

The mean amount of urea in different women may vary from 185·28 to 463·20 grains, but it is usually from 247·04 to 432·32 grains.

As far as can at present be ascertained, the amount of urea excreted to each pound avoirdupois weight of the body is 2·96 grains. It is therefore probable, though not finally determined, that women excrete, according to weight, a little less urea than men: 1 kilogramme of body-weight in women furnishes 0·414 gramme, or 6·39 grains; and in men, say 0·459, or 0·500 gramme =7·72 grains.

The range of urea in different women appears to be quite as great in the 24 hours as in men, from 0·600 to 0·320 gramme, equal to 9·26 and 4·94 grains respectively per kilogramme of 2 pounds 3 ounces and 5 drachms avoirdupois.

The deviation in women, states Dr. Parkes, from the mean amount is also as great as in men; many women excrete on an average only 12, 14, or 18 grammes of urea daily, equal to 185·28, 216·16, and 277·92 grains respectively; others 28 to 30, equal to 432·32 and 463·20 grains. The usual individual range appears to be about 3 or 4 grammes, equal to 46·32 and 61·76 grains respectively, above and below the mean amount proper to the person.

### *Influence of Age.*

The amount of urea eliminated varies in a very marked degree with *age*. Children and young growing persons excrete relatively to their weight much more urea than adults; during the periods of adult and middle life the quantity is comparatively stationary, while from the end of middle life to old age it continues to decrease, the amount being greatly reduced as the more advanced periods of life are attained. These particulars are now all thoroughly established.

The explanation of them it is obvious, on reflection, is to be found in the rate of nutrition of the body. In children and young persons nutrition and growth, and, as a consequence, disintegration of tissue, are rapid and considerable; in middle age these proceed at a more uniform rate; while from middle life to old age nutrition is slower, and there is a less active destruction of the tissues of the body.

From the calculations of Parkes, based upon the researches of Scherer, Rummel, Bischoff, and Lecanu, it appears that, in children of both sexes, the mean of whose age was four years and ten months, the urea excreted in twenty-four hours was for every pound weight of body, 5·77 grains.

The following figures show approximately the relative amounts of urea excreted by children of both sexes between the ages of three and seven, and adults, in twenty-four hours:—

| | Per Kilogramme=2 lb. 3 oz. 5 drachms. | | | |
|---|---|---|---|---|
| In children . . . | 0·973 grammes, or | 15·02 grs. | | |
| In male adults . . | 0·500 | ,, | 7·72 ,, | |
| Excess in children . | 0·473 | ,, | 7·30 ,, | nearly double. |

After eight years of age the analyses made appear to show that the excess diminishes, till at about sixteen and eighteen years of age it nearly reaches the excretion of adults.

With respect to the diminution of urea from forty to sixty years of age, Parkes estimates provisionally the decrease to be for the first ten years five per cent., and for the second, ten per cent.

In an analysis by Rummel of the urine of a man aged sixty-five the urea was only 19·17 grammes, or 295·98 grains; so that one pound weight excreted only 0·184 gramme of urea, or 2·84 grains.

Lecanu, in men from eighty-four to eighty-six years of age, found the urea greatly lessened—it amounted on an average to only 125 grains in twenty-four hours.

## *Influence of Weight.*

All other things being equal, as the age, food, &c., it is found, as might have been anticipated, that there is a relation between the weight of the body and the amount of urea excreted, and that, as a rule, the greater the weight the larger the quantity of urea; and this applies not alone to this constituent, but to other solids of the urine.

Dr. Parkes gives the following table, compiled from his own observations and those of Beneke and Kerner, in proof of this relation. The author has merely converted the French into English weights.

*Ureal Excretion in Adult Males.*

| Weight in kilogrammes of 2 lb. 3 oz. 5 drachms each. | Age. | Urea in 24 hours. | 1 kilogramme excreted of urea in 24 hours. |
|---|---|---|---|
| | | grains. | grains. |
| 51·8 | 30 | 346·62 | 6·68 |
| 53·2 | 22 | 370·56 | 6·96 |
| 62·5 | 35 | 441·58 | 7·06 |
| 65·5 | 25 | 489·44 | 7·46 |
| 71·5 | 23 | 529·74 | 7·41 |
| 72·0 | 23 | 588·26 | 8·17 |
| 76·0 | 24 | 526·50 | 6·93 |

As might also have been expected from *à priori* reasoning, the rate of increase is by no means regular. The weight of one person may be increased by an undue proportion of bone, that of another by fat. Now the metamorphosis of bone is slow, and it furnishes but little urea, while that of fat gives rise to the formation of water and carbonic acid. It is from the nitrogenous tissues solely that urea is produced.

*Influence of Diet.*

Another circumstance which exercises a very marked effect on the amount of urea formed is diet, the quantity and kind of food consumed. This effect evidently bears a close relation to the nitrogen contained in the food; the greater the amount of this, the larger the formation and elimination of urea.

Lehmann, from experiments on himself, found that on a purely animal diet, or on food very rich in nitrogen, there were often two-fifths more urea excreted than on a mixed diet; whilst on a mixed diet there was almost one-third more than on a purely vegetable diet; and, lastly, on a non-nitrogenous diet the amount of urea was less than half the quantity excreted during an ordinary mixed diet. "On a well-regulated mixed diet," states Lehmann, "I discharged in twenty-four hours 32·5 grammes of urea (I give the mean of fifteen observations); on a purely animal diet, 53·2 grammes (the mean of twelve observations); on a vegetable diet, 22·5 grammes (the mean of twelve observations); and on a non-nitrogenous diet, 15·4 grammes (the mean of three observations)."

These results will be better appreciated as exhibited in the following table, in which the grammes are reduced to grains:—

| | Animal diet. | Vegetable. | Mixed. | Non-nitrogenized. |
|---|---|---|---|---|
| Urea, in grains, in urine of 24 hours | 819·2 | 346·5 | 500·5 | 237·1 |

"It is especially worthy of remark that the augmentation of the urea in the urine occurs very soon after the use of highly nitrogenous food, and that in such cases often five-sixths of the nitrogen taken in the food, in twenty-four hours, are eliminated as urea by the kidneys.

"When I took thirty-two boiled hen's-eggs daily, I consumed in them about 30·16 grammes of nitrogen; but in the above-mentioned quantity of urea, I discharged only about twenty-five grammes in twenty-four hours. On the morning following the day on which I had taken only flesh or eggs, the urine was so rich in urea that immediately on the addition of nitric acid it yielded a copious precipitate of nitrate of urea."

"Notwithstanding the considerable influence which the nature of the food exerts on the quantity of urea excreted by the kidneys, there is as much urea after prolonged abstinence from all food (after a rigid fast of twenty-four hours), as after the use of perfectly non-nitrogenous food.

"Lassaigne found urea in the urine of a madman, who had taken no food for fourteen days; and we observe something similar almost daily in patients with typhus fever and other diseases, who for fourteen days or more have taken nothing but an oily emulsion or an emollient decoction, and yet always pass urine containing urea, and often rich in it. After living for three days on a perfectly non-nitrogenous diet, I still found in the morning urine more than $1\frac{2}{0}$ of urea."*

The researches of Lehmann as to the effects of food on the urea are fully confirmed by Bischoff and others; indeed Bischoff shows that they are even greater than had been previously supposed. Thus, for instance, one of the dogs on which he experimented, when taking 4000 grammes of beef (freed from fat and bone) discharged 190 grammes of urea daily, equal to 2933 grains; and when fed on 500 grammes of potatoes and 250 grammes of fat, excreted not more than from six to eight grammes, equal to 92·64 and 123·52 grains.

Böcker† experimented with pure albumen, and found that when 100 grammes of that substance were given, the urea in six hours was increased from 5·7 to 7·6 grammes—that is, from 88·00 to 117·34 grains.

*Gelatine*, like other nitrogenous substances, greatly augments the urea of the urine, it is generally supposed from direct oxygenation in the blood; but Bischoff questions whether gelatine does not enter into the composition of the tissues.‡

"In either case," observes Dr. Parkes, "the practice of giving strong jellies in fever, and in cases in which it is wished to arrest

* Translation, by Dr. Day. American Edition, p. 151.

† "Archiv des Vereins," von Wiss Heilh. Band 2, p. 281.

‡ "Laws of Nutrition in Flesh Feeders," p. 215.

metamorphosis, is sound; for either gelatine is a true aliment, or, if not, it is an absorber of oxygen, and thus limits metamorphosis."

From the effects of articles of food containing nitrogen, in augmenting the formation of urea, it is rendered probable that the administration of non-nitrogenous substances—such as *fat*, *sugar*, and *starch*—would be followed by a decrease of urea; and this, by experiment, has actually been proved to be the case. This diminution depends not entirely upon the subtraction of the nitrogen, but also on the appropriation, by the non-nitrogenous food, of the oxygen which would otherwise assist in the metamorphosis of the nitrogenous tissues.

Passing from solids to liquids, it has been ascertained that *water* taken in large quantity, the diet being the usual one, greatly increases the urea eliminated; and this not simply by acting as a diluent, by washing the urea out of the tissues, and so promoting its elimination by the kidneys, but by favouring disintegration of tissue.

According to Genth, the mean daily increase with large quantities of water was 216 grains over the amount passed when no excess of water was taken. According to Böcker, the increase was but 46 grains daily.

The facts which tend to prove that this increase of urea is, in part, derived from metamorphosis of tissue, are that the increased elimination is long continued; that it is accompanied by an augmentation in other urinary constituents; and, above all, that considerable wasting and loss of weight quickly ensue. Accompanying the loss of weight, there is usually, in the healthy, an increase of appetite; and, if the powers of digestion and nutrition be vigorous, the increased waste is quickly repaired. The effect of water in increasing disintegration is greatest in persons of weak habit and in children; in all cases, it is promoted by a high temperature, whether of the air or the water itself.

The action of water in increasing disintegration is of the utmost importance, considered practically: it throws great light upon the effects of habitual water-drinking and the so-called water-cure. It shows us how far and in what cases these systems may prove beneficial; and it likewise teaches us that they are equally potent for evil when pursued in the wrong cases.

The light, white, German wine, *Nierstein*, according to Böcker, augments the urea slightly.

On the other hand, *alcohol* lessens the urea, and this to a very great extent, and when added to a regulated diet. In Böcker's experiments the decrease per day was no less than 206·2 grains; while, according to those of Hammond, the decrease was 87 grains.

Now, this decrease must result from diminished disintegration, since the urea was not merely retained, as no subsequent discharge occurred. This conclusion is still further strengthened by the effects produced by alcohol on the other urinary constituents, and by the diminished amount of carbonic acid expired under its influence by the lungs.

The effects of *strong wines* and *spirits* generally have not as yet been determined by experiment; but it is probable that they also, from the alcohol contained in them, diminish the formation of urea. *Strong beer, tea,* and *coffee* certainly do so, as has been satisfactorily ascertained: tea lessens the urea slightly, coffee much more than tea, and in some cases to a remarkable extent. In these instances, the diminution likewise appears to be attributable to lessened formation, as shown by the effects on the other excretions.

Again, variations in the amount of urea excreted are occasioned by certain *salts* and *chemical substances.*

With the increase in the amount of urea, the *extractives,* the *urine pigment,* the *sulphates,* the *alkaline phosphates,* and often the *uric acid,* are also augmented; but this part of the subject will fall under consideration hereafter.

### *Influence of Exercise.*

The last influence to which we shall at present advert, as affecting the formation of urea, is *exercise.*

Strong exercise increases greatly the general waste of the body, and not alone of its nitrogenous, but of its non-nitrogenous constituents, as the hydrocarbons.

The nitrogen escapes from the body chiefly in the form of urea, and by the kidneys usually; but in those cases in which the lungs and skin are inordinately active, by those channels as well. Thus, after exercise, as a rule, an increase of urea is present in the urine.

The hydrocarbons are eliminated from the lungs and skin, principally in the form of carbonic acid.

The amount of increase in the urea varies from 10 to 25 per cent.

Lehmann ascertained, from numerous observations, that during his ordinary habits of life, he discharged about 32 grammes in twenty-four hours; but he found that, after strong bodily exercise, he, on one occasion, passed 36 grammes, and on another 37·4 grammes, in twenty-four hours.

These experiments of Lehmann have been fully confirmed by the researches of other inquirers. Hammond* determined the amount of urea in his own urine on three consecutive days, the food and drink consumed being the same each day. The first day he took his ordinary exercise; the second he walked briskly eight and a half miles over a hilly country, rode ten miles on horseback, and pitched quoits for two hours and a half; while on the third day he rested continuously on a sofa for twenty-four hours. The results were as follow:—

* "American Journal of Science."

| | Urea. | Uric acid. |
|---|---|---|
| Moderate exercise . . . . | 682·1 grs. . . | 13·7 grs. |
| Increased exercise . . . . | 865·0 „ . . | 8·2 „ |
| No exercise . . . . . . . | 487·0 „ . . | 24·9 „ |

The following experiments of Beigel illustrate the effect of both food and exercise on the excretion of urea. Beigel found that the mean excretion of urea of healthy men, living on a scanty diet and taking no exercise whatever, was 491·91 grains, and that with strong exercise it reached 514·46 grains; on a superabundant animal diet and no exercise, it rose to 708·78 grains, and with strong exercise to 806·89 grains.

The increase in the urea takes place not alone during exertion, but for some hours afterwards; gradually the urea lessens to even below the mean amount, so that the elimination for the twenty-four hours is less than even the normal excretion.

According to Hammond, the urea is increased by *mental exertion*. and Mr. Haughton has arrived at a similar conclusion. Prout was also of opinion that *mental anxiety* increased the urea.

Lastly, the amount of urea varies in different pathological states or conditions, and in different diseases, as will be shown hereafter.

## ON THE SOURCE OR ORIGIN OF UREA.

It is impossible that we can possess any correct knowledge of the pathology of urea, or indeed, of any of the other constituents of the urine, normal or abnormal, until the source or sources from which they proceed have been ascertained.

One source of urea is undoubtedly in the nitrogenized tissues of the body; and from the large proportion which the nitrogen of the urea excreted bears to the total quantity of nitrogen introduced into the system with the food, it would appear that all the nitrogenous tissues contribute by their disintegration to its formation. In some animals, as dogs and cats, and probably in all flesh-feeders, the whole of the nitrogen contained in the food is recovered in the urea of the urine, while in man the proportion of nitrogen in the urea amounts to about two-thirds or four-fifths of that consumed with the food.

The reason of this diminution in the quantity is that, in man, part of the nitrogen escapes from the body in other forms, as in the uric and hippuric acids; in the creatine, creatinine, and ammonia of the urine; in the ammonia of the breath; in the urea, and other nitrogenized compounds of the cutaneous secretion.

Of the several tissues, it is probable that the muscular furnishes the largest amount of urea, but from its absence in that tissue it appears certain that it is not formed there, but from some other substance, as possibly creatine, after it has quitted that situation, and probably in the blood; urea may also be formed in the liver and other glandular organs.

In fasting animals it is obvious that the urea excreted cannot come from the food, but must proceed from the disintegration of the tissues, or else from the nitrogenous constituents of the blood.

But Bischoff's* latest experiments seem to prove that the albumen, hæmatoglobulin, and fibrine of the blood do not become transformed under the influence of oxygen into urea; certainly these elements of the blood of fasting animals are not thus transformed, as shown by the small quantity of urea then excreted; neither is it possible to transform them by treatment out of the body into urea. What Bechamp actually succeeded in producing artificially from albumen, was not, as first stated, urea, but benzoic acid.

According, then, to Bischoff—and this view seems specially confirmed by the fact that in cats and dogs the whole of the nitrogen is recovered in the urea of the urine,—the urea excreted is an exact measure of the extent of the destruction and waste of tissue. This is a point of the highest practical importance, and if Bischoff's opinion is correct, then the views of Bidder, Schmidt, Frerichs, and Lehmann, concerning which so much controversy has arisen, are incorrect.

These distinguished observers maintained that part of the urea was formed from surplus albuminous matters of the food; that is, those not required or appropriated by the system. They considered that the rapid increase in the amount of urea after partaking of nitrogenous food was a sufficient proof of the correctness of this doctrine. But if the nitrogenous constituents proper to the blood itself are not, as proved by the case of the fasting animals, converted into urea, what reason is there why the albumen of the food should be thus converted?

Altogether this much disputed point may be considered as not yet quite settled, although the evidence is much in favour of Bischoff's view. The opinion entertained by Liebig, as to the formation of urea, may here be adverted to: he believes that uric acid is first formed from the nitrogenous tissues, and that the urea proceeds from its transformation under the action of oxygen and water during respiration. Certain objections present themselves to this view, which will be discussed when uric acid comes to be considered.

## ON THE PATHOLOGY OF UREA.

In most well-marked diseases urea is either *in excess* in the urine, or is present *in diminished amount*.

In nearly all disorders accompanied by *pyrexia*, it is in excess,

* "Die Gesetze der Ernährung des Fleischfrasser." 1860.

as in fevers in their active stages, and in *inflammatory* diseases. The acute and active diseases of the kidney form an apparent exception to the rule of increased formation of urea; since in these cases it occurs in the urine in less than the normal quantity: but this exception is apparent only, since an excess of urea is really formed, as in other acute diseases, but owing to the impaction of the tubules with fibrinous casts, its elimination is impeded.

It has been determined that as a rule the amount of urea found in the renal excretion stands in close relation with *the intensity of the fever*, and also specially with *temperature*.

Although the rule in active diseases is that during the stage of febrile action the urea is increased, yet there are cases, as will be shown presently, in which, independent of fever or temperature, the ureal excretion is augmented. These exceptional cases admit usually of being readily explained.

Again, in some fevers the temperature is high, and the urea formed not great, and there are chronic diseases with augmented heat, in which the urea is not increased and may even be diminished. The deficiency of urea may in some cases of febrile diseases be accounted for by increased action of the skin and bowels, and in certain non-febrile or chronic disorders, the increase may arise from a previous retention, being followed by increased elimination.

Now, as during most acute maladies but little food is taken, this increased elimination can proceed only from disintegration of the nitrogenous tissues; and in the increase of urea under such circumstances, we are furnished with an additional argument against the notion that urea, when excreted in such large quantities, is derived directly from the nitrogenous elements of the food.

It may be here just noticed, that it is not alone the urea which is increased in febrile and inflammatory disorders, but also several of the other urinary constituents, especially uric acid; but this part of the subject will be treated in another place.

On the subsidence of the febrile action, the urea falls even below the average amount of health.

To descend to particulars, the urea is increased during the fit of an attack of *ague;* but taking the total amount excreted by a person suffering from ague, according to the testimony of several observers, it is less than in health. The increase suddenly commences with the fit, lasts through the cold and hot stages, and sinks through the sweating stage, until the amount falls below the average of health. The amount of increase is generally considerable, being about three times that excreted on a fever free day. In Mr. Ringer's case, the particulars of which are given by Dr. Parkes, the connexion between heightened temperature and the amount of urea is clearly shown.

In *typhoid fever*, during the febrile period, the urea is increased, and this in proportion to the extent of the elevation of temperature, but subsequently it falls below the normal standard. Alfred Vogel found in one case as much as 1200 grains in the twenty-four hours, and Parkes 880 grains. In most of his cases the latter found the average increase to be about one-fifth.

In *typhus* fever there is likewise an increase of urea to the extent of one-fifth.

In *small-pox, measles,* and *scarlatina,* the urea is also increased.

In *meningitis* the urea is considerably augmented.

In the *acute pneumonia* of adults during the height of the disease, from the second to the eighth or tenth day the urea is largely increased; and it has been found from various observations to range from 516 grains to 1321 grains (Parkes) in the twenty-four hours. It may be again observed that this large excretion of urea has no connexion with food, for in most of the cases in which observations have been made, the patients were on low, almost starving diet. The increase is greater before than during resolution, although it is considerable during this last period. "During resolution," writes Parkes, "when the temperature may be as low as in health, and yet the urea may be still in large amount, the urea may arise either from absorption and metamorphosis of the exudation, or it may have formed some time before, but been retained until a later period."

Some exceptional cases of pneumonia have been noticed, in which there has been diminution of urea, uric acid, &c. It is most probable that in such cases the urea has been formed, but has been from some cause retained. This is a very important practical point, since it has been ascertained that such cases do not recover so well as those in which the elimination is greater. It serves also to indicate the direction which the treatment should take.

In *acute pleurisy,* uncomplicated with pneumonia, the increase in the urea is but slight, and this although the temperature may be considerably heightened.

In *acute capillary bronchitis,* and where aëration is greatly impeded, the urea, as in pneumonia, is much increased, but cases not unfrequently occur in which the urea and other urinary constituents are retained. Two such cases have fallen under the observation of Parkes, in one of which the urea excreted amounted for two days to only 176 grains per day. In a case recorded by Moos, that of a girl, only 139 grains of urea per day were passed during the height of the disease. It does not appear that the state of the kidneys had anything to do with the retention, as the urine was not albuminous, nor were any symptoms of uræmia present. During convalescence the urea was increased, which appears to prove that there really was retention in these cases.

In *acute phthisis* there is considerable increase of urea.

In *acute hepatitis,* an affection rarely met with in this country, the ureal excretion is increased.

In *rheumatic fever* the urea is very considerably augmented, the quantities met with in several cases ranging in the twenty-four hours between 600 and 872 grains.

In a few exceptional cases of acute rheumatism there is retention of urea: this in some instances may be explained by the profuse sweating which frequently occurs in this disease, as well as by the occurrence of local congestions and inflammations. It has been noticed by Parkes, however, that in some of the cases attended by inordinate sweating, the quantity of urine passed has been large, and the elimination of urea considerable.

*Before* the paroxysm of *acute gout* the urea is very deficient; during the paroxysm, from the analyses hitherto made, it would appear to be about or even below the normal standard. In a man aged 57, Garrod ascertained the mean to be 320 grains; while Parkes, in a man aged 49, small and emaciated, found it to be 322·3 grains. The amount of urea excreted *after* the paroxysm has not been determined.

But little has yet been accomplished in the determination of the effect of *skin diseases* upon the urine. In a case of *acute eczema*, recorded by Beneke, in which the ingesta amounted to 3660 grammes, the urinary elimination was 2023 grammes, and there was a small excess of urea during the acute stage of the affection.

In all the active diseases hitherto enumerated, there is an increase of urea. We come now to notice a disease in which there is a remarkable deficiency—namely, *acute yellow atrophy* of the liver accompanied by jaundice, and in which the hepatic structure is much destroyed. Frerichs, in a case of this kind, found the urea to be absent; in a second case recorded by the same observer, a small quantity of urea was present. These results are in the main corroborated by other observers.

We pass now from acute to *chronic* diseases. Hitherto an excess of urea has for the most part been met in the urine. In many of the diseases about to be enumerated, we shall find that there is a *deficiency* of urea.

In *epilepsy* there is a considerable diminution of urea. From Parkes' calculations, based on the figures of Scherer, the proportions of urea per kilogramme of body-weight in five cases were, men, 0·190, 0·269 and 0·367 gramme, equal to 2·93, 4·15, and 5·66 grains; women, 0·319 and 0·315 gramme, equal to 4·92 and 4·86 grains respectively: the mean excretion of urea in healthy men in the middle period of life being 0·500 or 7·72 grains; and in women 0·414, or 6·39 grains per kilogramme.

In *Phthisis* so long as the disease progresses gradually and equally, the appetite being good, the urea remains at about the normal standard, but when fever, and especially hectic, supervenes, there is augmentation of the urea, as might be expected. During hectic, it appears from Sidney Ringer's observations, that, as in ague, it falls just before the rigors set in, and then rises rapidly and goes on increasing till near the sweating stage. In one case the urea rose from 17½ to 24 grains in the hour. Of course where vomiting or diarrhœa exists, the excretion of urea by the kidneys is greatly influenced.

In *spasmodic asthma*, Ringer has shown that immediately succeeding the fit there is a considerable diminution of urea.

In *non-febrile icterus*, arising from obstruction, there would appear to be a diminution of urea.

In the majority of cases of *diabetes* there is an increase of urea; this is, no doubt, mainly due to diet, but it appears, especially from the investigations of Sidney Ringer, that the increase is beyond what can be explained in this way. The inaction of the skin, the great water drinking, and the non-oxidation of the sugar, also tend to explain the excess of the ureal excretion.

In eleven cases occurring in adults, the urea excreted in the 24 hours ranged between 545 and 1411 grains, corresponding in body-weight per pound to 3·91 grains the lowest, and 11·19 grains the highest amount.

There appears to be a definite relation between the amounts of urea and sugar excreted, especially during fasting hours; in a case made the subject of special investigation by Ringer, the urea was to the sugar as 1 to 2·35. In this case the mean hourly discharge of urea during fasting was 30·88 grains as compared to 67·93 grains of sugar. Others of Ringer's cases confirm these results. The large amount of urea excreted in fasting hours proves that in diabetes, wholly independent of food, there is a very considerable disintegration of tissue and resulting waste of the body.

In other cases in which nitrogenous food only was given, Ringer observed the same relation between the urea and sugar during fasting hours. When food containing starch was given this relation was of course destroyed. Thus while during inanition hours in one case, it was as 1 to 2·35, in nitrogenous food hours it was as 1 to 1·9. These numbers were in the main confirmed by experiments on two distinct cases. During the food hours, therefore, the urea is in slight relative excess to the sugar.

It would appear probable, though as yet scarcely established, that the urea in some cases of diabetes is deficient; but further investigation on this point is required. In such cases, if they occur, it should be determined whether the urea escapes from the body either by the skin or bowels.

In several cases of Polydipsia or *diabetes insipidus* in which analyses of the urine have been made, the urea has in general been found very deficient, showing an absence of any excess of tissue metamorphosis.

In other cases, on the other hand, in which the thirst has been less excessive, and consequently less water drank, the urea has been increased. In such cases there is of course excess of tissue change, followed by emaciation more or less rapid.

The explanation of the deficiency of urea in certain cases of so-called diabetes insipidus has yet to be given. It has already been stated that when much water is drank, even in health, the urea is increased, but in the disease under consideration accompanied by extreme thirst no such increase takes place.

In the *diuresis* which often supervenes on dropsy, whether renal, hepatic, splenic, or cardiac, a considerable excess of urea is found in the urine; much of this urea has no doubt been retained in the system, both in the blood and in the dropsical effusion itself. In a case of cardiac dropsy, after digitalis the urea amounted to 755 grains. In another case in which the urine was increased by digitalis, the urea found was 696 grains. In a case of splenic dropsy during diuresis the urea amounted to 622 grains. (J. Vogel.)

Prout described a disease to which Willis afterwards gave the name *azoturia*, characterized by a great excess of urea, but without an increased formation of urine; this disease does not appear to have been recognised since the time of Dr. Prout, except the case observed by Ringer is an instance of it.

It was the case of a middle-aged man weighing 109 lbs.; he was not febrile, and appeared weak only.

When on full hospital diet, he passed as the mean of twelve days the large amount of 1130 grains of urea, or 10·36 grains to each pound of body-weight. It should be observed, however, that the urine voided in this case, as the mean of twelve days, was 2739 c.c., or 96 ozs. 3½ drachms, and also that it contained a trace of sugar.

The affection, according to Prout, is rare, and he enumerates as amongst its causes dyspepsia from inattention to diet, intemperance, mental anxiety, sexual excess, and mercurial irritation; and it is particularly worthy of remark in connexion with Ringer's case, that Prout entertained the opinion that such cases may pass into diabetes melitus.

The effect of *disease of the kidneys* upon the excretion of urea may next be considered.

In *acute nephritis*, at its onset and during the existence of fever, the urea is sometimes augmented, but in other cases it is much diminished, this arising from mechanical impediment in the kidneys to its elimination, and not depending upon any deficiency in its formation.

If this deficiency continues, uræmic symptoms supervene. In a case of extreme uræmia, Mosler found the urea reduced to 55·5 grains in twenty-four hours.

The urea is also still further diminished when dropsical effusion sets in, and on the other hand it is increased when diuresis occurs.

In *chronic nephritis* there is also, as the rule, diminished elimination of urea. The average of seventeen analyses by Frerichs makes the urea to vary from 0·97 gramme to 16·98 grammes, equal to 149 and 262·17 grains in twenty-four hours, the mean of the whole being 99 grains.

Rosenstein's analyses give a nearly similar mean result—namely, 112 grains; his lowest amount was 1·04 grammes, or 16·04 grains.

In some exceptional cases, however, of chronic Bright's disease there is either no great diminution of urea, or there may even be an excess.

In a case recorded by Schottin, with uræmia and only seven days before death, 267 grains of albumen were excreted and 305 grains of urea.

In Mosler's case of renal disease, followed by anasarca and occasioned by cold, the mean of three days' observation was 620 grains of urea. The temperature was only 93·3° F.

This increase of the urea may be explained in one of three ways—it may be produced by febrile action, by absorption of dropsical effusion, or simply by increased elimination. The nature of the diet, also, is not without its influence.

There is good reason to believe that in chronic Bright's disease, there is not only as a rule diminished elimination, but also lessened *formation* of urea; this belief is supported by the fact that although the urea of the urine is in some cases diminished for a long period, yet no symptoms of uræmia occur, which could hardly be the case were the urea formed in anything approaching the normal amount and at the same time retained.

## ON THE TREATMENT OF EXCESS AND DEFICIENCY OF UREA IN THE URINE.

In the facts which have already been detailed, first, as to the origin of urea, and second, as to its pathology, some highly important data are furnished of a practical character, upon which the treatment of excess or deficiency of urea in the urine should be based.

In regard to its origin, there are two important particulars which must ever be held in view; the first, there is much reason for believing, is that the true and only source of urea is in the waste or disintegration of the nitrogenous tissues, no less than two-thirds or four-fifths of the whole amount of nitrogen consumed in the food being discharged from the body in the form of urea.

The second particular is, that if the nitrogenous elements of the food be not, as maintained by many, an independent source of urea, yet that their administration is followed by a rapid and very considerable increase in the amount of urea excreted.

In respect to the pathology of urea, there are likewise certain particulars which should constantly be remembered.

One of these is, that, as the rule, in all diseases of an active, febrile, or inflammatory character and independent of diet, there is a greater or less increase of urea.

Another is, that in diseases of an opposite character—that is, in non-febrile or chronic diseases—there is, as the rule, a deficiency of urea.

The third particular is, that urea may be abundantly formed, and yet not make its appearance in the urine, through being retained in the system: the causes of this retention are various; but they should always be carefully sought, and in a large proportion of cases it will be found that it arises either from temporary, or, as in the case of chronic Bright's disease, from permanent renal obstruction.

Other causes of retention or diminution which may be mentioned, are dropsical effusions, vomiting and inordinate action of the skin and bowels.

The marked effect of *strong muscular exercise* in increasing the urea must likewise not be forgotten.

One of the first points to be determined is whether the urea is in excess or not. The nature of the disease will usually, as already pointed out, furnish the required information on this point; but since there are many exceptions to even the general rules laid down with regard to urea, we should not rest satisfied with anything short of an absolute examination of the urine and determination of the urea: this, as has already been pointed out, is by no means difficult or laborious. The necessity of this is sufficiently shown by the circumstance, that in some instances in which there is a directly increased formation of urea, there is diminished elimination, and which but for analysis we should not have been led to suspect.

It has been already shown that the extent of the formation and elimination of urea, are dependent as a rule upon the extent and intensity of the fever or inflammation, and especially on temperature. In this fact we are clearly furnished with the clue to treatment, and are directed to resort to all those remedies which are known to lessen fever, abate inflammation, and lower temperature. The precise nature of these remedies must depend upon the character of the disease.

In the influence of food on the urea, we also perceive how important in all such cases is a judicious and appropriate regulation of the diet.

In the second class of cases—namely, those of an afebrile or chronic character,—where there is deficiency of urea, the treatment required is of a very different character. In many of such cases tonics and stimulants must be administered, and the diet prescribed must be, according to circumstances, more or less generous and rich in nitrogen.

In regard to diet, *gelatine* seems to require a few special remarks. Where nitrogenous food of a light and mild kind is required, this is one of the best forms in which it can be given, as it is less strong than albuminous compounds, replacing albumen, according to Bischoff, to the extent of one-fourth.

From the marked increase in the urea which follows its use, two theories have been started: first, that this large increase affords a proof of the derivation of urea from the destruction of the gelatinous tissues; and second, that the appearance of the urea in the urine is so rapid and the quantity so considerable that it must proceed not from any metamorphosis of tissue, but from the direct transformation of the gelatine, and hence that substance has come to be ranked very low in the scale of nutritious substances.

The answer to the first theory is, that the normal amount of urea furnished independent of gelatinous food is too considerable to be derived from the gelatinous tissues alone.

If gelatine—and the point can hardly be considered as determined as yet—be not appropriated, but is converted at once in the blood into urea, a view opposed by Bischoff,* this conversion takes place by the appropriation of oxygen, and the gelatine thus saves waste of tissue by lessening oxidation.

Again, in the third class of cases, where there is lessened elimination of urea from impediment to its escape, arising from the condition of the kidneys, a totally different treatment is demanded. In these cases, although there is great deficiency of urea in the urine, there is excess of it in the blood, its accumulation there giving rise to certain constitutional symptoms. Here while the treatment adopted must have reference, in the first place, to the disease of the kidney, in the second, it must have regard to the effects produced by the urea accumulated in the blood. Every means must be adopted by which the amount of urea may be lessened in the blood and increased in the urine. One obvious means of lessening the quantity in the blood would be by cutting off part of the supply of nitrogen in the food. This means in the case of certain active or acute structural diseases of the kidneys, it would be proper to adopt; while in those having a constitutional origin, it would, for the most part, be a highly improper method of treatment to pursue, as tending still further to reduce the already impaired constitutional powers. In these last cases the excess of urea must be got rid of, first by endeavouring to increase the eliminative powers of the kidneys; and second, by promoting the escape of urea through other emunctory channels, as the skin and bowels. The first indication is fulfilled by improving the constitutional powers, by relieving congestion of the kidneys, and by the use of mild and appropriate diuretics. The second indication requires the employment of diaphoretics, gentle aperients, the warm bath, friction, and moderate exercise.

* "Laws of Nutrition in Flesh-Feeders."

The following passage from Parkes' invaluable work on the urine, will form an appropriate conclusion to the chapter on urea:—

"The great uses of the examination of the urine are for *prognosis* and *treatment*. The amount of metamorphosis is a good indication of the severity of the disease, and may indicate the necessity of restraining it; or if exudations are to be got rid of, a copious excretion may show us that the chemical alterations, ending in elimination, are proceeding satisfactorily without aid. On the other hand, we may detect, by the urine, insufficient elimination in a disease in which the thermometer indicates a good metamorphosis; and measures may be taken to augment such elimination."

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# CHAPTER III.

## CREATINE AND CREATININE.



THESE two alkaloids resemble each other so closely in their composition, mutual convertibility, and origin, that it is more consistent with a natural arrangement to treat of them in the same rather than in different chapters.

Schottin finds that their presence in the urine in health as well as in many diseases is very inconstant, that their amounts vary greatly, and that frequently the quantities are so minute as to be only microscopic: further, he inclines to the belief that normally they are transformed into urea. Creatinine is usually, and probably always, derived from creatine; whether the reverse ever obtains has not, we believe, been determined.

### CREATINE.

#### *History.*

This principle was originally discovered by M. Chevreul in 1835, in the broth of meat. In 1844, Heintz and Pettenkofer detected it contemporaneously, combined with *creatinine*, in the urine, and in 1847, Liebig made known the results of his elaborate researches on this substance. He traced it through all the Invertebrata, demonstrated the constancy of its occurrence in the juices of *muscle*, both striped and unstriped, and he also found it frequently in the *urine*; indeed, so constantly has it been met with in the renal excretion, that it is now regarded as a normal constituent. Creatine has likewise been discovered in the *blood* and in the fluid of the *amnion.*

*Quantity.*

In the muscular tissues its presence is constant, and the quantity found there is considerable. The heart, the most active muscle in the body, in particular contains much creatine; but the largest amount hitherto met with occurs in the muscles of birds, as the *martin* and *fowl*. As a rule, the quantity would appear to increase in proportion to the activity of the muscles. Liebig found the creatine doubled in the muscles of a hunted fox.

But little has, however, been hitherto done to determine the quantity occurring normally in the urine. Thudichum gives 4·7 grains as the average amount excreted in 24 hours, but this is probably too high.

The following quantities have been met with in different kinds of muscular tissue :—

| | | | |
|---|---|---|---|
| Heart of Ox, 100 parts, | . | 0·1375 | Gregory. |
| Ditto | " | 0·1418 | Ditto. |
| Pigeon | " | 0·0825 | Ditto. |
| Skate | " | 0·0607 | Ditto. |
| Cod | " | 0·0935 | Ditto. |
| Horse | . . . . . . . . | 0·072 0/0 | Liebig. |
| Human | . . . . . . . | 0·067 0/0 | Schlossberger. |
| Fowl | . . . . . . . . | 0·32 0/0 | Liebig. |

### ORIGIN OF CREATINE.

Creatine, like *urea*, is doubtless to be regarded as a strictly *excrementitial* substance. This view is opposed to that first enunciated by Liebig, who regarded it as a nutritious principle; but its constant presence in the urine and its relations to creatinine and urea are conclusive. Its excrementitial character was first advocated by Heintz, whose opinion has since been generally adopted.

The invariable occurrence of creatine in connexion with the muscular tissue, its excrementitial character, and the variations in the amount found in the urine in certain diseases, prove conclusively that it is formed during the disintegration of that tissue.

### CHEMICAL CHARACTERS OF CREATINE.

Anhydrous creatine has the following elementary composition :—

| | | |
|---|---|---|
| Carbon | 8 | 36·64 |
| Hydrogen | 9 | 6·87 |
| Nitrogen | 3 | 32·06 |
| Oxygen | 4 | 24·43 |
| | | 100·00 |

It is a nitrogenous crystallizable substance, neutral to test-paper, and not forming combinations with any of the other constituents of the urine, being in fact, a chemical indifferent substance, not playing the part of either an acid or a base.

It has a rough, bitter, pungent taste, extending to the fauces, which it irritates, is inodorous, and unalterable in the air: it is soluble in 74·4 parts of cold water; in boiling water it is very soluble; it dissolves only with difficulty in alcohol, requiring 9410 parts for its solution, while in ether it is insoluble; at 110 Fah. it loses its two atoms of water of crystallization, and is decomposed at a higher temperature: boiled with baryta water, it is transformed into *urea*, which is in its turn decomposed into *ammonia* and *carbonic acid*, which unite with the baryta, and also into *sarcocine*: it is dissolved without alteration in the weak acids, but in the strong acids, aided by heat, it is changed, by the loss of two atoms of water, into creatinine; this, in the act of separating from its combination with chloride of zinc, takes up water and is re-converted, according to Heintz, into creatine.

Creatine is regarded by Liebig as ammonia, plus two atoms of *glycocoll*, or *sugar of gelatine*.

In stale urine creatine becomes converted into creatinine.

Liebig noticed, that in a solution of creatine not quite pure, which stood for several months in a cupboard, the creatine became gradually changed into creatinine, which was deposited in a single fine large crystal; a slight mouldiness also appeared.

"The readiness with which creatine becomes decomposed into creatinine, into urea, and sarcocine, which is isomeric with lactimide, all of which are undoubtedly products of excretion, proves beyond a doubt, that creatine approximates more nearly to these substances than to albumen and fibrin, and indicates the great probability of creatine being decomposed, even in the living body, into these and other similar substances."*

## PHYSICAL AND MICROSCOPICAL CHARACTERS OF CREATINE.

A knowledge of the forms and characters of the crystals of creatine, as they occur in the urine, is very necessary. With this knowledge, and with the aid of the microscope, this substance may frequently be recognised in single drops of the urine, evaporated on a slip of glass, and always, if it be present in the urine, in the evaporated syrupy extract.

The crystals of creatine are transparent, brilliant, and nacreous, and they contain two atoms of water of crystallization; they belong to the clinorhombic system, and crystallize in the form of the right rectangular or right rhomboidal prism; the right rectangular prism is the most frequent form.

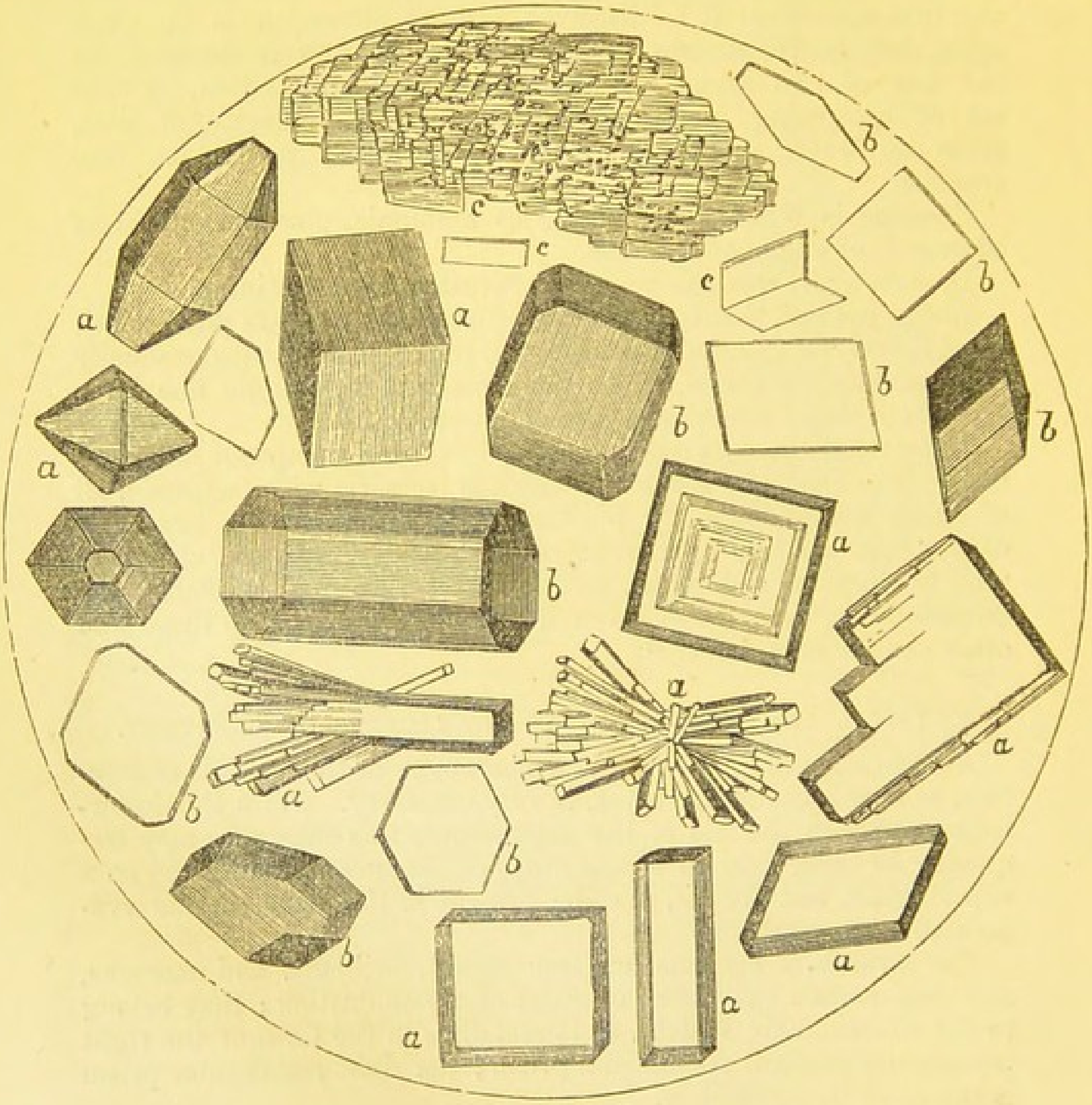
The prisms may be either long or short, narrow or broad, thick

* Lehmann, "Phys. Chem." p. 131.

or thin; when both broad and thin, they constitute plates or lamellæ; the extremities of the crystals are usually square, but sometimes oblique, the angles being either entire or cut off in various degrees.

When the crystals are very thick and short, the angles being at the same time entire, they form cubes; but the angles of these may also be removed. Again, when the crystals are thick and long, the angles may be cut off lengthways, prisms with eight sides resulting.

FIG. 7.




Crystals of CREATINE: *a*, from the juice of *Flesh*; *b*, from *Human Urine*; *c*, from the same hastily crystallized.—From Atlas of MM. Robin and Verdeil.

When very thin and broad, the lamellæ may be either square, or oblique and rhomboidal, and the angles either entire or removed.

Illustrations of these several modifications of the crystals of creatine are given in Fig. 7.

Not unfrequently the crystals, in place of being single, occur united together more or less; the thick long rectangular crystals are often thus united, but it is the thin lamellæ which the most frequently occur in this compound form.

Lastly, single crystals occasionally split up into several other crystals, and so present a compound character. (Fig. 7.)

Some other curious modifications of the crystals of creatine obtained from the juice of muscles, will be found delineated in the Atlas of MM. Robin and Verdeil, and the chief of which are shown in Fig. 7.

The author has himself met with crystals of creatine in the urine in several forms.

First, they have occurred to him in long, thick, rectangular, or rhomboidal prisms, intermixed with shorter, broader, and thinner plates or lamellæ. These sometimes exhibit a curious tendency to unite at acute angles in twos and threes, when they frequently resemble open books and boxes. (Fig. 7, *c*). This form the author first met with in urine some years since, and described it in the *British and Foreign Medico-Chirurgical Review* for 1853.

Another form in which they have occurred to him is that of short rectangular prisms or cubes. (Fig. 8.)

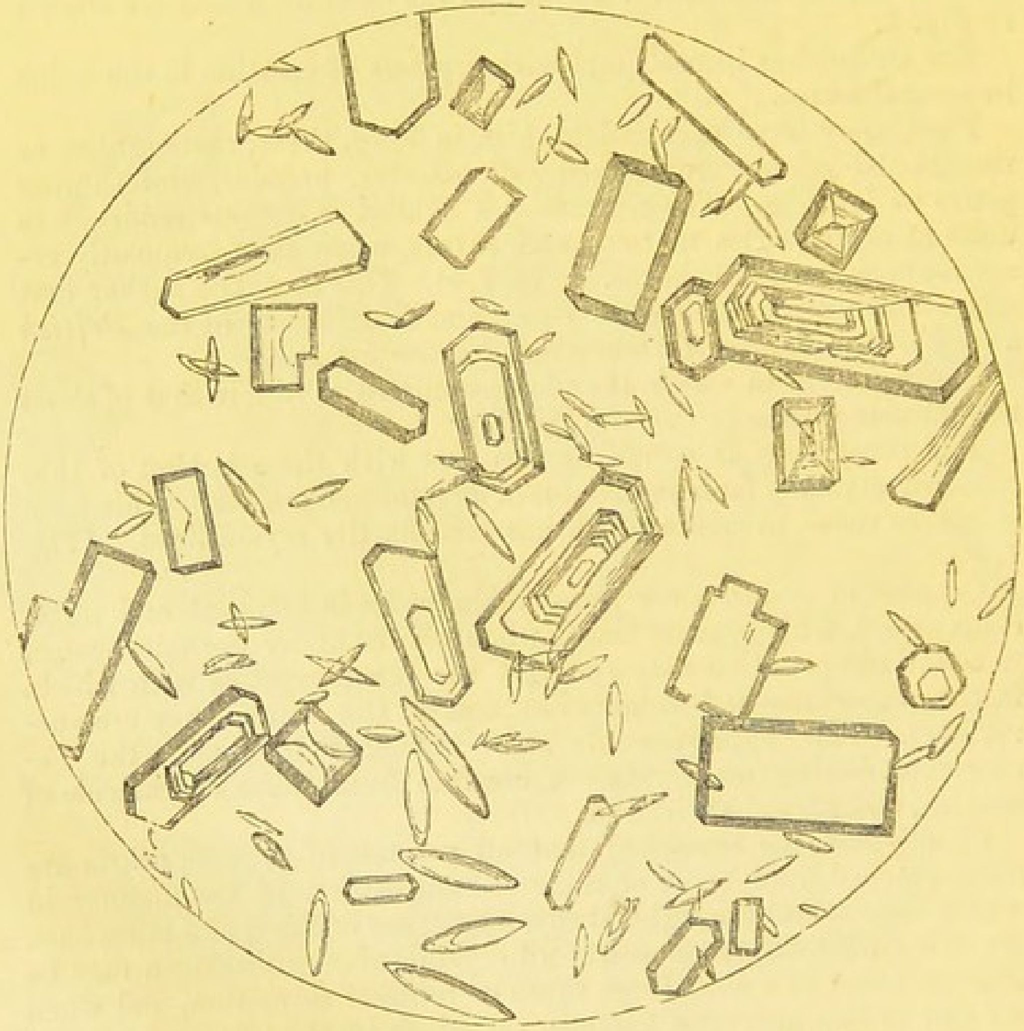
The third form in which he has met with them is that of thin cohering crystals, forming confused crystalline masses. This form is apt to occur in urine which has been hastily crystallized. (Fig. 7, *c*.)

Crystals of creatine are remarkable for their brilliant and micacious aspect, which causes them, when viewed under the microscope, to stand out conspicuously amongst the other crystals with which, in the evaporated and coloured extract of the urine, they are surrounded. This appearance is alone sufficient to enable the observer to distinguish crystals of creatine from those of chloride of sodium, and phosphate of lime.

It may here be remarked that all crystals of organic origin are distinguished from those of mineral composition by the manner in which they reflect the light, always appearing brilliant and micacious. By this single difference nearly all crystals of organic origin may be discriminated as a class from those of mineral formation, and when we add to this general difference, variations in the type and form of the crystals, the discrimination, by means of the microscope, of the crystals of various salts and substances becomes a matter of absolute certainty.

The chief salt present in the urine with which creatine is apt to be confounded is chloride of sodium; for this, like creatine, sometimes crystallizes in the extract of the urine in quadrangular prisms and cubes. The two substances may, however, be readily distinguished, for, independently of the differences already referred to in their general aspect, the crystals exhibit very different appearances under the polariscope; thus while crystals of creatine, viewed by polarized light, appear vividly coloured, those of the marine salt are uncoloured. The discrimination of the crystals of chloride of sodium, as well as of the phosphates from those of creatine, may, however, always be effected in a very ready and satisfactory manner by means of a solution of nitrate of silver.

FIG. 8.



Crystals of CREATINE. Magnified 100 diameters. April, 1849.

For the detection of the crystals of creatine in the evaporated extract of the urine, it is requisite that this should be examined within a short time of its evaporation, for it soon attracts water from the atmosphere, which acts upon and dissolves the crystals to a greater or less extent.

By the aid of solution of alcohol creatinine may be dissolved out of the concentrated extract, and afterwards procured in a crystalline state by the evaporation of the alcoholic solution.

It appears, therefore, that creatine is distinguished by well-marked chemical, but especially microscopical, peculiarities; so distinct are the appearances presented by its crystals as they occur in the urine, that no difficulty need be experienced in identifying this substance when present in that liquid.

### *Extraction and Determination of Creatine.*

The following is the method given by Liebig for obtaining creatine from urine:—

The acidity of the urine, which should be perfectly fresh—for in stale urine the creatine is converted into creatinine—is first removed by the addition of a little lime-water or milk of lime; chloride of calcium is then added, until no further precipitate of phosphate of lime takes place; the filtered urine is then evaporated to the consistence of syrup, and the greater part of the inorganic salts which have become crystallized are removed: the clear liquid is then heated with about one twenty-fourth part of a saturated solution of neutral chloride of zinc. After three or four days, roundish crystalline masses, or granules, of a yellowish colour, will have formed, and will be found adhering to the bottom and sides of the vessel. These granules are a mixture of creatine, and a combination of creatinine and chloride of zinc; they are then separated from the liquid, washed with cold water, dissolved in boiling water, and treated with recently precipitated hydrated oxide of lead, until the fluid becomes alkaline; the liquid is kept boiling until it coagulates into a light-yellow magma; the salt of creatinine and zinc is decomposed; the creatinine and creatine are set free, a chloride of lead is formed, which, as well as the oxide of zinc, are precipitated; the filtered liquor is evaporated to dryness, and to the crystalline residue, boiling alcohol is added; this dissolves out the creatinine, creatine alone remaining. The creatine may be redissolved, decolorized with animal charcoal, and recrystallized.

The above process is open to one source of fallacy; creatine and creatinine are both very readily crystallizable substances, and hence they may unintentionally be removed from the urine, together with the other crystallized salts formed during the evaporation, and so escape detection altogether. This is no doubt one reason why observers so often fail to detect these substances in the urine by the process above described; however, in some instances the failure is attributable to the small quantity of them present in the urine, or even to their entire absence. In order, therefore, to avoid this source of failure, the evaporation of the urine should not be allowed to proceed too far, and the extract should be poured off the deposit of inorganic salts while still hot.

In connexion with the chemical examination of the urine for creatine and creatinine, the microscope may be so applied as to afford valuable aid. Before proceeding further with the analysis, the deposit from the evaporated urine should be examined microscopically, in order to ascertain whether it contains crystals of creatine or creatinine; if so, the evaporation has been carried too far. Again, a small portion of the urine to be analysed may be partially evaporated, and when cold this may be examined with the microscope for crystals of creatine and creatinine; if none are present then, it is useless to proceed further with the analysis. Indeed, a tedious and fruitless chemical examination of the urine will often be avoided by simply allowing a drop or two of the fresh urine, just as it has been voided, to evaporate spontaneously on a slip of glass, and then examining the crystals that remain; if creatine or creatinine be present in appreciable quantities, crystals of those substances will generally be seen. Lastly it is not advisable to operate for creatine, creatinine, or urea, upon urines of very low specific gravity.

## PATHOLOGY OF CREATINE.

Sound pathology must always rest upon, and be consistent with physiology. Two important facts have been determined in respect to creatine,—first, that it is formed in connexion with the muscular tissue; and second, that it is an excrementitious substance. If derived from the disintegration of the muscles,—and of the correctness of this view there is but litttle room for doubt—then we should expect to meet with the largest proportion of creatine primarily in the muscular tissue, and secondarily in the urine, in all cases in which the muscles are exercised greatly, or where, from disease, they undergo marked wasting.

The direct observations which have hitherto been made support this view; thus much creatine has been found in the muscles of the more active birds, amongst mammalia in the heart, a never-resting muscle, and in hunted animals.

But few observations have as yet been made as to the quantity of creatine in the muscles and urine in cases of wasting of the muscular tissue from disease, as in marasmus or active inflammatory and hectic fevers, but as far as these have extended, they fully support the opinions here expressed.

These general views and statements are borne out by the elaborate researches of Schottin, of which a very clear abstract is given by Parkes in his work on the urine.

Schottin's investigations confirm those of other inquirers, in respect to the origin of creatine and creatinine from muscular fibre.

The diseases in which he found these alkaloids in relatively large quantities were referable to two groups.

In the first he attributes their appearance in the urine to their transformation into a higher oxidized body—most probably urea—being impeded, there being no increase of formation.

In the second there is increased formation, resulting from augmented muscular degeneration or wasting.

To the first group, cases of *Bright's disease*, especially accompanied by symptoms of *uræmia*, are to be referred; the increase in the amount of creatine being greatest in those cases in which the uræmia is most marked.

The amount of creatine in twenty-three different cases excreted in twenty-four hours, ranged from 0·3 to 1·10 gramme, equal to 4·63 and 16·98 grains, the creatine being found in the blood, and also in the dropsical fluids where these were present.

Schottin attributes the reduction in the amount of urea in the urine in cases of Bright's disease, not merely to diminished elimination, but he expresses a decided belief that it consists also "certainly in a want of transformation of lower oxidized substances into urea," and of which he conjectures that creatinine may be one. He thinks that so powerful a base may well act as a poison, and produce decomposition of ammoniacal compounds in the blood, such as occur in typhus and uræmia, as indicated by the ammonia of the urine.

In the second group there is, as already noticed, increased formation of creatine and creatinine, resulting from augmented disintegration of the muscular tissue. This Schottin noticed particularly in *typhoid fever*. In twenty-two cases the increase of creatinine began in the second week, and reached its highest amount between the third and fourth weeks; and in some cases the increased elimination continued during convalescence to the sixth and even seventh weeks. The amount varied from 0·2 to 0·34 gramme, equal to, in round numbers, from 3 to 5 grains. Schottin likewise proves that the formation of creatine is actually increased in the muscular tissue in typhoid fever.

In a case of *pulmonary emphysema with catarrh*, Schottin found 0·3 gramme, and in one of *cancer of the stomach* 0·52 gramme of creatinine, equal to 4·63 and 8·02 grains respectively. In both cases there was slight albuminuria, but no disease of the kidneys.

In three cases of *phthisis*, one of *granular liver*, one of *pneumonia*, one of *Bright's disease* without *uræmia*, one of "*ataxie locomotive progressive*," one of *lead poisoning*, one of *spinal paralysis*, and one of *chlorosis*, neither creatine nor creatinine were present in the urine.

Further observations are evidently much required to determine the range of variation in the amounts of creatine and creatinine excreted within physiological limits. The researches of Schottin point to the inference that the averages given by Thudichum, namely, 4·7 grains of creatine and 7 grains of creatinine, are much too high.

## TREATMENT OF CREATINE.

Incomplete as is our knowledge at present in regard to the occurrence of creatine and creatinine in the urine, the views and facts set forth in the preceding paragraphs furnish important data upon which the treatment of such cases should be based.

In the case of *Bright's disease* with uræmia, the indications to fulfil, are to have recourse, first, to all those suitable and appropriate means by which increased *oxidation* may be effected, as especially by attention to the action of all the decarbonizing organs; and second, to resort to such remedies as are calculated to augment *elimination.*

In *typhoid fever*, and other cases of rapid muscular wasting, this, as far as may be in our power, should be retarded. We are scarcely sufficiently advanced as yet in our knowledge of the pathology of this subject to lay down any precise details of treatment, but so far as the facts hitherto made known go, these appear to be the principles upon which the rational treatment should be founded.

## CREATININE.

### *History.*

Creatinine is present, together with creatine, in the fluid surrounding the muscular fibre; it has likewise been found in the blood, in the water of the amnion, and it is very frequently contained in the urine.

MM. Robin and Verdeil state that they have found it in the urine of the horse, and particularly in that of the pig and sheep; it has very often been detected in the urine of man.

While in the muscles the amount of creatinine is smaller than that of creatine, in the urine the proportions are reversed. It exists in the urine generally in a free state.

### *Quantity of Creatinine.*

Thudichum gives 7 grains as the average amount present in the urine of 24 hours in health; the quantity is, however, very variable, and is usually much less than that above named.

## CHEMICAL CHARACTERS OF CREATININE.

It dissolves in 11·5 parts of water of an ordinary temperature, more readily in hot and boiling water. 100 parts of ordinary cold alcohol dissolve about one part of creatinine; in boiling alcohol it dissolves in such quantity that the solution, on cooling, becomes crystalline: it is tolerably freely soluble in ether; it possesses a caustic taste, and a strong alkaline reaction, turning reddened litmus blue, and turmeric paper brown, its expels ammonia from its ammoniacal salts; it forms crystallizable salts with hydrochloric and sulphuric acids. A moderately concentrated solution of nitrate of silver added to a solution of creatinine, causes a congelation into a network of acicular crystals; a solution of corrosive sublimate yields a curdy precipitate, which soon becomes crystalline; with chloride of zinc it likewise forms a crystalline granular precipitate. Bichloride of platinum yields no precipitate when the solution is somewhat dilute; hydrochlorate of creatinine forms with this salt a compound which crystallizes in crimson prisms, while with all the salts of copper, creatinine forms crystallizable salts of a blue colour. It has the following *composition* :—

| | | |
|---|---|---|
| Carbon . . . | 8 atoms . . . | 42·48 |
| Hydrogen . . | 7 ,, . . . | 6·19 |
| Nitrogen . . . | 3 ,, . . . | 37·17 |
| Oxygen . . . | 2 ,, . . . | 14·16 |
| | | 100·000 |

The hypothesis of Berzelius respecting its theoretical composition is most probably correct—namely, that it is ammonia conjugated with a highly nitrogenous body, containing one atom less hydrogen than caffeine: a comparison of the formulæ shows that creatinine contains two atoms less water than anhydrous creatine, and the same amounts of nitrogen and carbon.

### MICROSCOPICAL CHARACTERS OF CREATININE.

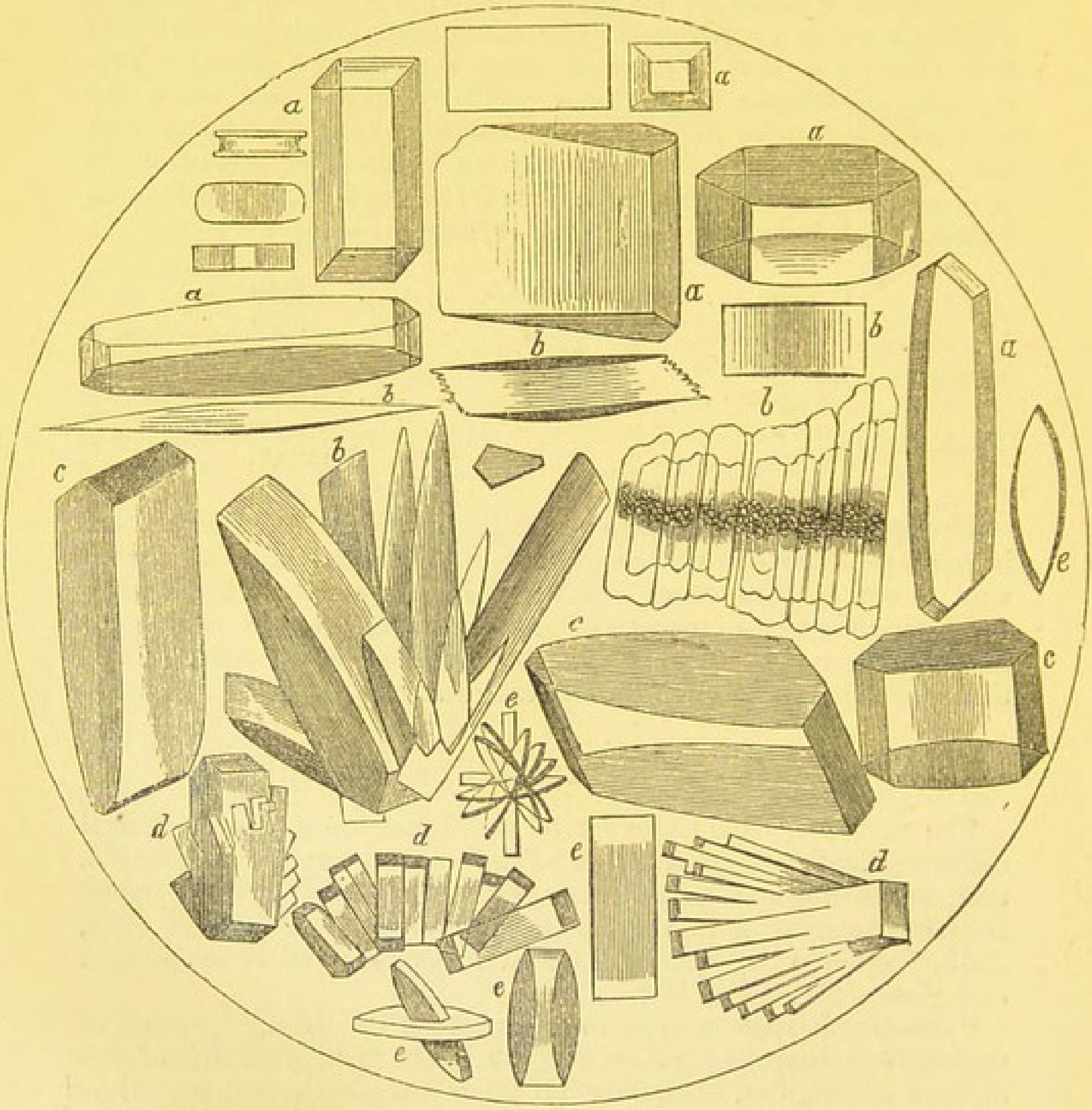
The microscopical characters of creatinine are particularly well marked; the form and grouping of the crystals are so distinctive, that, as the author showed in his critique on Dr. Bird's "Urinary Deposits," published in the *Medico-Chirurgical Review* for July, 1853, they may be readily detected in drops of urine evaporated on a glass slide. (Fig. 10.)

"Creatinine appears to us to crystallize in the third type, that of the *right rectangular prism*, and not in the fifth type, that of the oblique rectangular, or rhomboidal prism (monoklinometric of German authors). It is, consequently, the same type as creatine, but in place of presenting, like creatine, forms approximating either to the system of prisms with a rhomboidal base, or to the system of prisms with a rectangular base with different groupings, creatinine never departs from the system of prisms with a rectangular base. The only inclines (*décroissements*) which it exhibits, have the form of diamonds (*briseaux*) upon the two great ridges of the base;

the groupings are much less numerous, and altogether different from those of creatine." (MM. Robin and Verdeil.)

The crystals of creatinine thus possess, for the most part, a bi-convex or navicular shape, which is most distinctive.

FIG. 9.

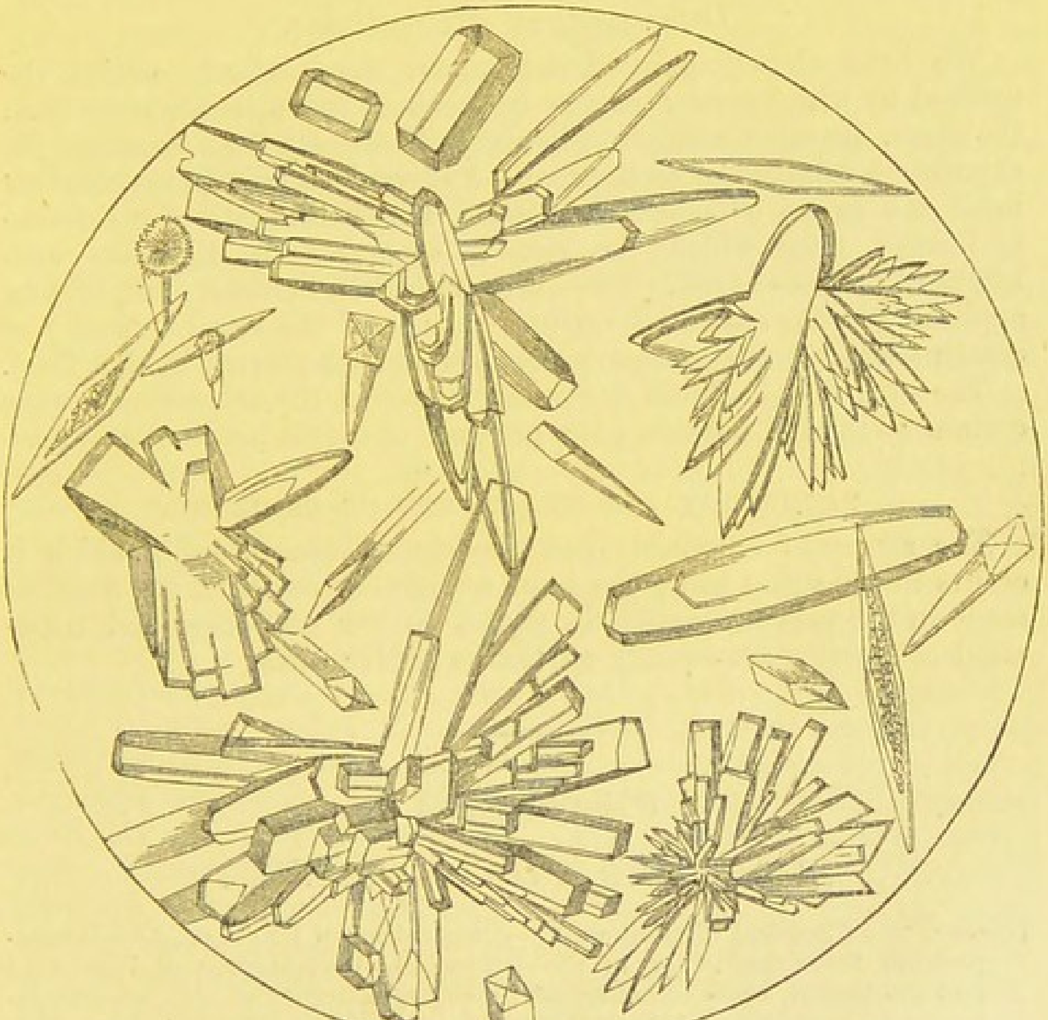



Crystals of CREATININE : *a*, deposited from *Aqueous* solution ; *b*, from Alcoholic solution ; *c*, from the very acid *Urine of the Pig*, evaporated ; *d*, from the *Flesh of the Horse* ; *e*, from that of the *Ox*.—Robin and Verdeil.

In the above engraving the chief modifications in the form of the crystals of creatinine are exhibited ; the crystals, some of them reduced in size, are selected from the admirable figures of creatinine, contained in the Atlas of MM. Robin and Verdeil.

The great transparence of the crystals of creatinine, and the absence of that brilliant nacreous tint observed on those of creatine, prevent our confounding these two substances, even when the forms of the crystals are at all similar.

FIG. 10.



Crystals of CREATININE from a few drops of *Human Urine*, evaporated on a glass slide. Magnified 220 diameters. May, 1853.

" In those cases in which all the lamellæ are square, and the crystals are rectangular prisms, which are rare, it is sufficient to take a drop of liquid, to place it upon a plate of glass, and to allow the water to evaporate. There then form irregular groups of crystals, which stand out upon the glass; and amongst the crystalline varieties which one meets with, there exists always a certain quantity of *navicular* forms, or lamellæ, more or less abundant, which are fusiform. They represent exactly the form of a bi-convex lens. This fact is altogether special to creatinine." (Robin and Verdeil.)

The last particular respecting the crystals of creatinine which requires to be noticed, is their colour. When viewed by reflected light the crystals are white and brilliant, but when seen as transparent objects, they are of a brownish tint. By this character, therefore, they are further distinguished from creatine.

### *Determination of Creatinine.*

We have already pointed out, under the head of creatine, the method by which creatinine may be procured in a separate state from the urine. Another method is to obtain it directly from creatine. By exposing a mixture of creatine and hydrochloric acid to evaporation until the excess of acid is volatilized, a hydrochlorate of creatinine is formed, from which the base is separated by digestion with hydrated oxide of lead. This last method is, however, but seldom applicable in the case of the urine, because of the small quantity of creatine which, under ordinary circumstances, is present in that fluid.

The microscope affords the readiest and at the same time a very certain method of detecting the presence of creatinine in the urine.

### PATHOLOGY AND TREATMENT OF CREATINE.

The source of creatinine and the circumstances under which it occurs in the urine being the same as those of creatine, the remarks made in the previous article in regard to the pathology and treatment of creatine are equally applicable to creatinine.

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# CHAPTER IV.

## URIC ACID AND THE URATES.



### URIC ACID.

### *History.*

Uric acid is one of the normal *nitrogenous* and *excrementitious* constituents of the urine.

It was called lithic acid by its discoverer, Scheele, from *lithos*, a stone, he having first detected it as a constituent of a urinary calculus or stone; but it received its present name from *Fourcroy*.

It occurs in the *urine* of man, of the *carnivora*, of the *omnivora*, and very sparingly in that of the *herbivora*.

It exists in the *blood*, in the combined state, and it is found, as a urate, in the juice of the *spleen*, in the *liver*, *lungs*, and *brain*.

The urine of birds, both carnivorous and granivorous, and of serpents, which, as is well known, is generally discharged with the solid excrement, although in snakes it is often unmixed with the latter, consists almost entirely of *urates*. The red excrement of butterflies consists wholly of alkaline urates, and the same are present in the biliary vessels and excrements of many larvæ and beetles. It has been found by Garrod in pericardial and peritoneal effusions, and in the serum of a blister.

## CHEMICAL CHARACTERISTICS OF URIC ACID AND THE URATES.

*Properties.*—Heated in the urine, *uric acid* deposits do not dissolve, but usually become more clear from the solution of the urates with which they are frequently more or less mixed. Uric acid readily burns, evolving an odour resembling bitter almonds, and leaving a small quantity of a white ash, consisting generally of phosphate of soda or lime, or both. It is soluble with the aid of heat in solution of potash, a urate of potash being formed, from which the uric acids may be again obtained by precipitation with acetic acid. It also dissolves readily in the alkaline carbonates, borates, phosphates, lactates, and acetates, abstracting some of the alkali from these salts. It is precipitated from its solution in the urine, whether it be free or combined, by hydrochloric, nitric, acetic, and most other acids. It readily dissolves in nitric acid, furnishing a delicate and characteristic test. When a drop or two of strong nitric acid are added to uric acid in a state of powder, it slowly dissolves with effervescence, carbonic acid gas and nitrogen being evolved, and a mixture of alloxan, alloxantine, and some other compounds, being left behind. On the evaporation of the acid to dryness, and the application of a gentle heat, a red residue is left, which, when cold and moistened with a drop or two of ammonia, or exposed to its fumes, developes a beautiful purple colour. This pigment is the *purpurate of ammonia* of Prout, and the *murexide* of Liebig.

*The urates* are distinguished from all other urinary deposits by becoming dissolved when the urine containing them is heated, and by being again deposited as it becomes cold; the deep-coloured urates require a somewhat higher temperature for their solution than the paler varieties; either liquor potassæ or ammonia immediately dissolves these deposits, while acetic and hydrochloric acids cause the separation of the uric acid, which becomes visible under the microscope in the form of crystals.

*Composition.*—The following formulæ represent its ultimate or atomic and per-centage composition :—

| | Basic. | Bibasic Acid. | | Basic Acid. |
|---|---|---|---|---|
| Carbon . | 5 | . . 10 | Carbon . | 35·72 |
| Hydrogen | 1 | . . 2 | Hydrogen. | 2·38 |
| Nitrogen. | 2 | . . 4 | Nitrogen . | 33·33 |
| Oxygen . | 2+HO | . . 4+HO | Oxygen . | 28·57 |
| Atomic number: basic acid 84, bibasic acid 168. | | | | 100·00 |

*Decomposition.*—Submitted to *dry distillation* uric acid is converted into cyanuric acid, *urea,* carbonate of ammonia, cyanide of ammonium, and hydrocyanic acid, a brownish-black substance, rich in nitrogen, remaining.

On boiling uric acid with twenty parts of water, and adding *peroxide of lead* as long as the brown colour of the oxide continues to disappear, there are formed *oxalate* of lead, carbonic acid, which is evolved, *urea,* and *allantoin,* which is deposited in crystals as the liquid becomes cold.

Treated with *dilute nitric acid* it dissolves, and *alloxantin* is obtained, which, with ammonia, forms *murexide* or *purpurate* of *ammonia.*

By *concentrated nitric acid* carbonic acid and nitrogen are evolved and *alloxan* formed, which may be obtained in octohedral crystals.

It appears, from the recent experiments of Wöhler and Frerichs, that the introduction of about forty grains of uric acid, or urate of potassa, into the stomach or the veins is followed by a considerable increase in the urea of the urine, and the appearance of oxalate of lime; none of the uric acid administered being found in the urine. The result of this and other experiments proves that uric acid undergoes, in many cases, in the organism a decomposition, by oxidation, into urea, oxalic acid, and probably other compounds, similar to that artificially produced out of the body by peroxide of lead and other reagents. Liebig, for other reasons, is of opinion that the whole of the urea excreted, even in health, is derived from the uric acid by a process of oxidation.

The experiments of Neubauer prove very clearly the transformation of uric acid into urea: the amount of urea excreted by a rabbit being determined, the large amount of 20 grammes, = 308·8 grains, of uric acid was given, and which was capable of furnishing 17·13 grammes, = 264·5 grains, of urea. The rabbit excreted

15·95 grammes, = 246·3 grains, of urea over the normal excretion previously determined, thus proving that nearly the whole of the uric acid given was transformed into urea and carbonic acid. There was no allantoin or huppuric acid in the urine, nor was the oxalic acid perceptibly increased.

### *Chemical Composition of the Urates.*

Until within a very recent period the opinion was entertained, by even the highest chemical and practical authorities on the urine, that the base with which the uric acid was combined was almost invariably, *ammonia*. Amongst those who held this opinion in this country may be mentioned Prout, Bence Jones, and Bird.

Prout thought that two lithates of ammonia existed normally in the urine; one of them he termed the acid lithate, attributing to it the acidity of the urine.

Lehmann first pointed out that this statement as to the composition of the urates was erroneous; he and Heintz believing it to consist of urate of soda mixed with very small quantities of urate of lime and magnesia. Even this view of the composition of the urates is too limited, as will now appear.

The error pointed out regarding the composition of the urates pervades all the writings and reasonings of Prout, Bird, and Bence Jones. The author first exposed it in his review of the fourth edition of Bird's "Urinary Deposits," to which reference has already been more than once made.

He there published the results of the quantitative analysis of five samples of urates:—

| | Composition. 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Biurate of Lime | 61 | 70 | 18·37 | 20·0 |
| „ Potash | Traces | None | 57·12 | 42·0 |
| „ Ammonia | 13 | 9 | 10·06 | 19·5 |
| Moisture | 19 | 16 | 11·74 | 10·0 |
| Colouring matter | 7 | 5 | 2·71 | 8·5 |
| | 100· | 100· | 100· | 100· |

*Colour*:—1. Bright rose-red. 2. Rose-red, changing to yellowish or grey-red. 3. Light rose-pink, changing to green. 4. Deep pink.

The fifth specimen was of a dull pink; it consisted, in great part, of *urate of soda*, a small quantity of urate of lime, and probably also of urate of ammonia.

It may be questioned whether the ammonia in the above analyses was not, in part at least, derived from the decomposition of the urea, of which it is not easy altogether to free the urates.

The following analyses were published by Scherer, in 1849:—

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Uric Acid | 82·89 | 80·02 | 81·31 | 82·89 |
| Ammonia | 2·30 | 8·29 | 7·09 | 2·23 |
| Potash | 2·04 | 1·38 | 2·80 | 2·04 |
| Soda | 0·55 | 2·05 | 0·17 | 0·55 |
| Lime | 0·56 | 0·34 | 0·26 | 0·55 |
| Phosphate of Lime | 0·37 | 2·72 | —— | —— |
| Oxalate of Lime | 0·33 | | | |
| Colouring matter and loss | 11·03 | 5·20 | 7·66 | 11·74 |
| | 100·00 | 100·00 | 100·00 | 100·00 |

From the preceding analyses it appears that uric acid is present in the urates in tolerably uniform amount, and that it is considerably in excess of the combining proportions of the bases, owing probably to its forming acid urates. It is somewhat strange that in none of the analyses was urate of magnesia discovered.

Hitherto the urates have been treated collectively; they will now be described separately, and a little more in detail. The urates which have been detected in the urine are the neutral urate of soda, acid urate of soda, urate of potassa, urate of ammonia, urate of lime, and urate of magnesia.

Potash and soda, according to Lehmann, are the only bases with which uric acid forms *neutral* salts; with ammonia and all other bases it forms acid salts.

### *Neutral Urate of Soda.*

This urate is very frequently encountered in the urine. It occurs in calculi, and in the pulverulent deposits of the urine, also in the peri-articular concretions of the gouty. It likewise occurs in great abundance in the urine of persons subjected to treatment with alkaline waters containing soda, or who have taken much carbonate of soda. It is this salt which is said to be so abundant in the blood of those labouring under attacks of gout.

It is met with usually in the urine in a granular or pulverulent state, but sometimes also in the form of minute and compact spherules, mostly single, but sometimes united; or it forms "round yellowish or white opaque masses provided with projecting, generally curved processes, forming a very remarkable figure. Varieties of this more confused crystalline are less unfrequent." (Bird.)

### *Acid or Biurate of Soda.*

This acid urate sometimes, though not frequently, occurs in a crystalline state in the ordinary pulverulent deposit of the mixed urates.

While the neutral urate forms only minute shot-like grains or spherules, the needle-like crystals of this urate are arranged so as to form glomeruli very much larger than those of the neutral urate. These glomeruli, according to the description of MM. Robin and Verdeil, are opaque, black, or a little transparent, and then somewhat yellow. Their periphery is sometimes defined; the needles which form the little sphere are visible in its substance, as striæ radiated around a centre; but ordinarily, some needles extend beyond the periphery. The most common disposition is that in which the surface of each sphere is rendered rough by the little points of the crystals which exceed more or less the circumference of the sphere. Sometimes this circumference is visible between the extremities of the needles as a defined border; at other times the margin is vague and diffused by reason of the number of points which issue from it. The authors above named consider this mode of crystallization to be very characteristic of this salt.

*Biurate of Potassa*

Has been found in the urine when potash has been largely administered; it has also been met with as a constituent of calculi and in the concretions of gout.

The author has observed it to occur in the urine as an amorphous powder, and in the form of globular shot-like spherules, resembling those of urate of soda, but more deliquescent and coherent. When artificially prepared, urate of potassa likewise crystallizes in little globular masses. Lehmann describes two urates of potash, the neutral and the acid or biurate.

*Biurate of Ammonia.*

Urate of ammonia is only occasionally present in the urine, and generally in small amount; but instances are recorded of the occurrence of urate composed in part, or even entirely, of urate of ammonia. This urate, pure and unmixed, and as deposited from boiling water, crystallizes in long, delicate, colourless, needle-shaped crystals; but Heintz has shown that when mixed with other alkaline urates it does not crystallize at all, but, like the other mixed urates, excepting only the acid urate of soda, it assumes the granular or pulverulent state. An excellent figure of this urate is given by MM. Robin and Verdeil in their Atlas, Table 18, Fig. 1.

*Biurate of Lime.*

Another urate which is frequently met with, entering largely into the composition of urinary deposits, is urate of lime. It has been found, though somewhat rarely and in small quantity, in certain urinary calculi, especially the phosphatic; more frequently it has been detected in phosphatic deposits. M. Leroy (d'Etiolles) has found that it exists frequently with carbonate of lime and urate of soda in calculi which form in persons subjected to treatment with alkaline waters.

When pure, it crystallizes in little round yellow grains, with well-marked borders or margins. Herapath found as much as 14 parts in 100 of this urate in a gouty concretion.

### *Biurate of Magnesia.*

The last urate found in the urine is urate of magnesia.

In calculi it has been found combined with either uric acid, ammonio-magnesian phosphate, phosphate of lime, or urate of ammonia. In one case a calculus has been met with formed entirely of urate of magnesia.

When urate of magnesia is dissolved in hot water, it becomes precipitated from its solution in a crystallized form as the water becomes cold. These crystals are very distinct; they belong to the right rectangular system. It is rare to obtain them in their typical forms, although M. Samuel Bigelow has succeeded in procuring them in that condition. They are then always of a large size, and usually present two terminal facettes, are colourless, and effloresce in the air.

Ordinarily urate of magnesia crystallizes in rectangular crystals, which are usually long and sometimes so narrow as to become needle-shaped; these crystals do not interlace with each other, but lie side by side, frequently forming stellæ; they polarize light.

The preceding description of the crystals of urate of magnesia is taken in great part from the Treatise of MM. Robin and Verdeil. Excellent figures of this salt are given in the Atlas of these authors, Tables 21 and 22.

## ON THE PRECIPITATION OF URIC ACID AND THE URATES.

The precipitation of uric acid and the urates in the urine is not necessarily indicative of their being in excess; in fact, they may be present in but minute amount, and yet be deposited.

There are several causes which contribute to this precipitation. One is the composition of the urine.

Another is its reaction; in acid urines the uric acid is quickly liberated from its weak combinations and thrown down.

A third cause is temperature: the colder the urine the more quickly and completely do the urates become precipitated.

The fourth reason is diminished amount of urine; the urates are only sparingly soluble, so that the smaller the quantity of urine the less of them it can hold dissolved.

Uric acid, even when in excess in any urine, does not always become deposited as soon as the urine is cold; but as many as twenty-four, and even forty-eight hours or more, are required in some cases for its precipitation. Moreover, its separation even then, unless an acid be added, is seldom complete. This deposition, a day or two after the urine has been voided, is attributed to the acid fermentation which many urines undergo at that period.

Even when hydrochloric acid is added to urine in considerable amount, some hours are necessary for the separation of all the uric acid.

When the urine is alkaline a considerable time is required for the subsidence of the acid.

The first situation in which uric acid may be deposited from the urine is in the *tubules* of the kidney. The crystals may be washed away from this situation by the urine; or, as frequently happens in cholera, they may be formed in the renal tubules in connexion with the escape of albumen, and be thrown off impacted in the albuminous casts or, lastly, the uric acid crystals may accumulate in the tubules to such an extent as to form *renal* calculi.

The second situation in which uric acid may be deposited is in the bladder. After its precipitation in this viscus, it may be voided wholly or in part, as a sand-like deposit. When not entirely discharged, it is apt to accumulate, giving rise to *vesical* calculi.

Lastly, the uric acid may not become deposited until after the urine has been voided, as, indeed, is the case generally; and it is frequently held in solution for many days.

### CHARACTERS OF URINE DEPOSITING FREE URIC ACID.

Urines depositing uric acid are frequently, but by no means constantly, somewhat high-coloured, possessing a deeper amber tint than natural, and being sometimes of a reddish-brown colour; they are of considerable specific gravity, are always acid, and frequently contain such an excess of urea that, on the addition of nitric acid to a little of the urine in a watch-glass, crystallization obvious to the naked eye ensues, resulting from the formation of nitrate of urea.

### MICROSCOPICAL CHARACTERS OF FREE URIC ACID.

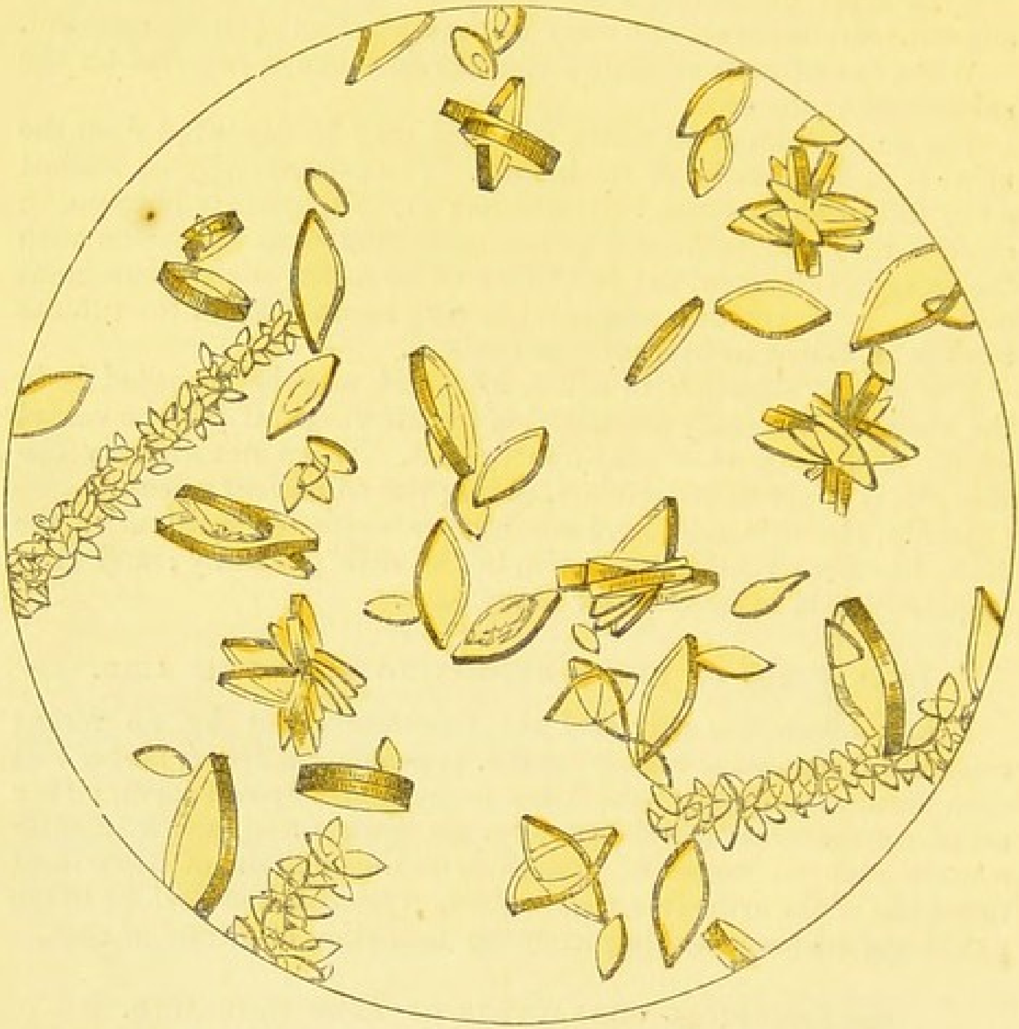
Free uric acid occurs in the urine chiefly as a deposit, and this is always crystalline. The crystals form a sand-like sediment, more or less fine or coarse, and more or less coloured; in general, the higher the colour of the urine the deeper that of the crystals.

Uric acid crystals vary greatly in colour; they may be pale-fawn, yellow, deep amber, orange, red, and even of a reddish-brown or black colour, like burnt sienna. This last colour is observed particularly when the uric acid has been precipitated artificially by means of hydrochloric or nitric acid. According to their colour are deposits of uric acid likened to either *yellow* or *red* sand.

The normal or typical form of the crystals of uric acid is the *rhombic prism*. (Fig. 11.)

This form is subject to every possible and conceivable variety of outline, the variations being rendered the more striking in consequence of great differences in the size and thickness of the crystals.

FIG. 11.



*Rhomboidal* Crystals of URIC ACID. Magnified 100 diameters.

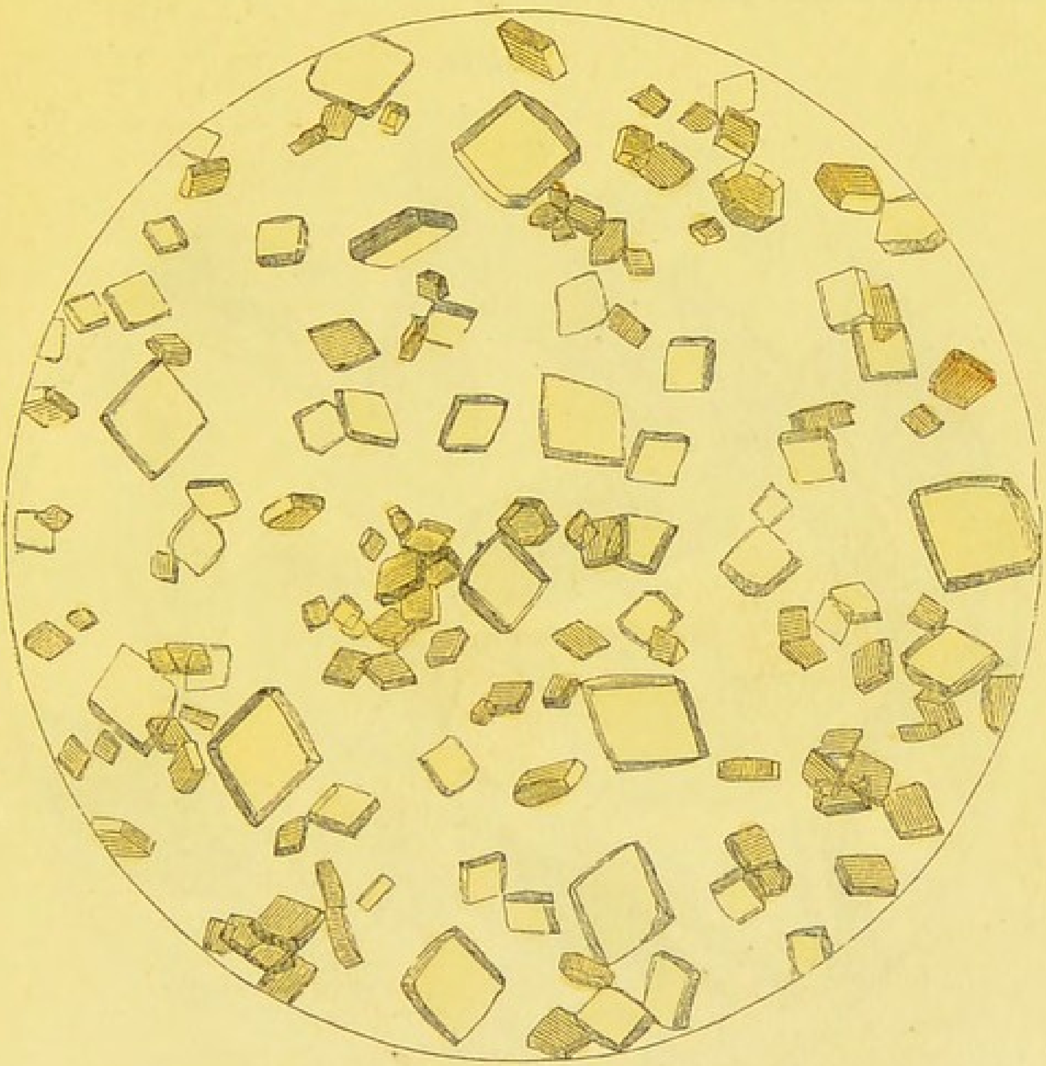
Occasionally the crystals appear *nucleated*, more rarely one crystal appears to *include another;* occasionally they are *double.* (Figs. 13 and 29.)

Sometimes the crystals are nearly *square* (Fig. 12); at others, *diamond-shaped.*

The following interesting observation respecting the *square* crystals occurs in Dr. Golding Bird's "Urinary Deposits." It is there stated, that "when the deposit has been of long continuance, especially in cases of calculous disease, the rhomboidal outline of the crystal is replaced by a square one." The deposit is then generally high-coloured, and the crystals thick.

A very curious modification is that in which the crystals are elongated, two angles being rounded and two pointed; they then

FIG. 12.



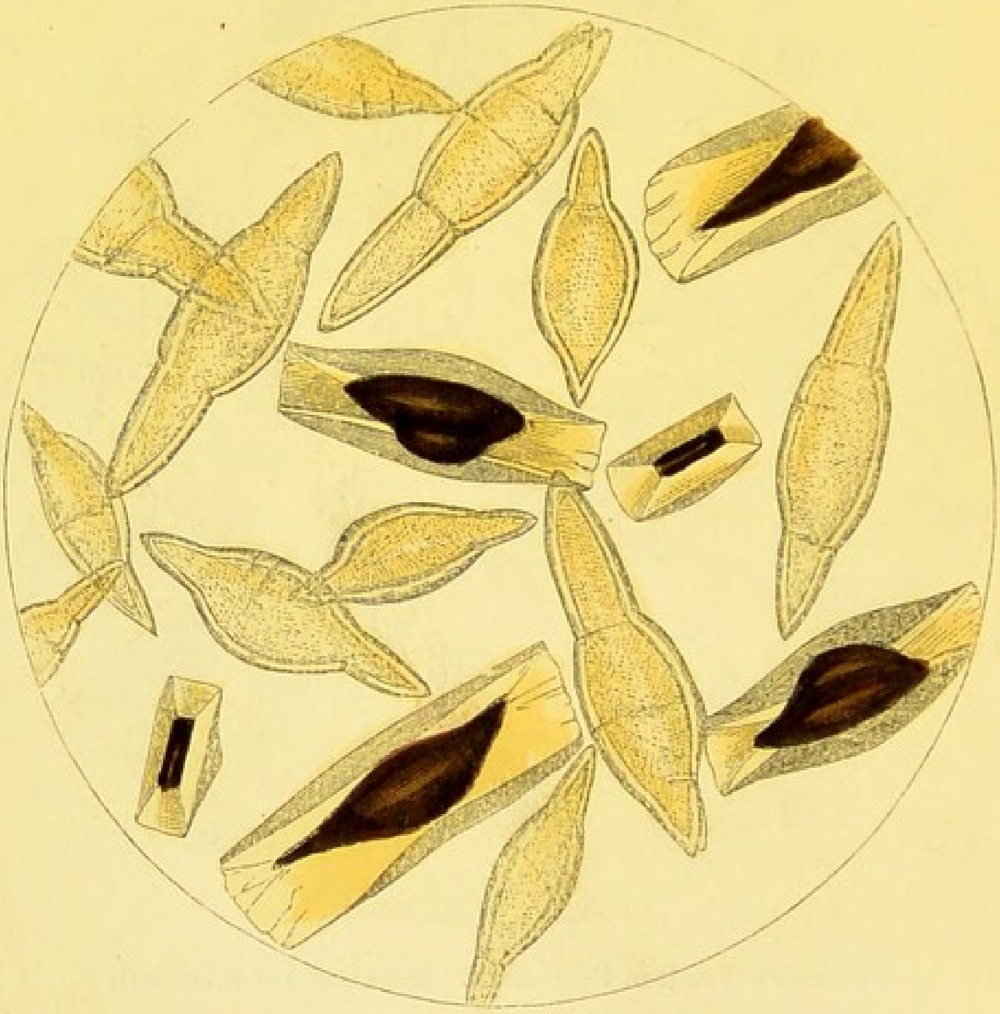
*Quadrate* Crystals of URIC ACID. Magnified 100 diameters.

appear *spindle-shaped.* (Fig. 13.) Sometimes all the angles are pointed; they then have an outline somewhat resembling a cross.

An interesting variety is that in which the crystals are of an *hexagonal* form: this occurs chiefly in the urine of young children. (Fig. 14.)

It has already been remarked, that one source of difference in the crystals is occasioned by their variable thickness; sometimes they are thin and transparent; at others they are much thicker, and occasionally the prism is so much prolonged that the crystals lie upon their sides in place of their faces; they then appear *tubular,* resembling flattened cylinders, slightly excavated at the sides. When an end view of these crystals is obtained, which by agitation may be readily effected, their lozenge-shape or rhomboidal form becomes apparent. Dr. Bird states that this variety often occurs mixed with urate and oxalate of lime. (Fig. 15.)

FIG. 13.



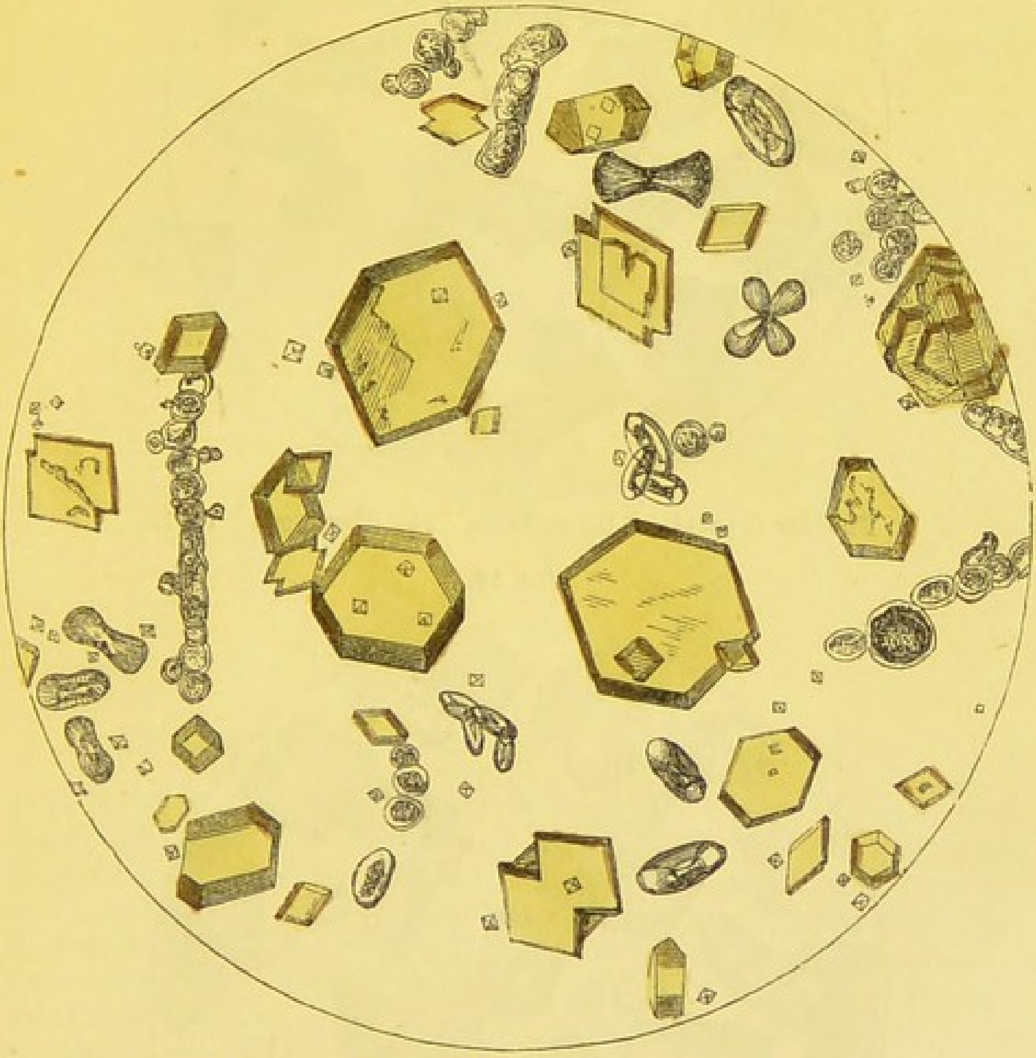
*Spindle-shaped* Crystals of URIC ACID. Drawing made from specimen lent the author, many years since, by Dr. Griffith. 100 diameters. 1850.

There is another modification of rather frequent occurrence resembling somewhat the preceding, in this the crystals, although thick, are shorter, being square rather than tubular, their peculiarity consisting in their *obliquity*. (Fig. 16.)

A tendency which the crystals of uric acid very frequently exhibit is to attach themselves to any hairs or threads with which they may happen to come in contact, just as sugar-candy crystallizes on a string. Dr. Garrod has availed himself of this circumstance in order to separate uric acid from the serum of the blood. (Fig. 11.)

Not uncommonly the crystals unite together so as to form *compound crystals* or masses; the crystals lie across each other more or

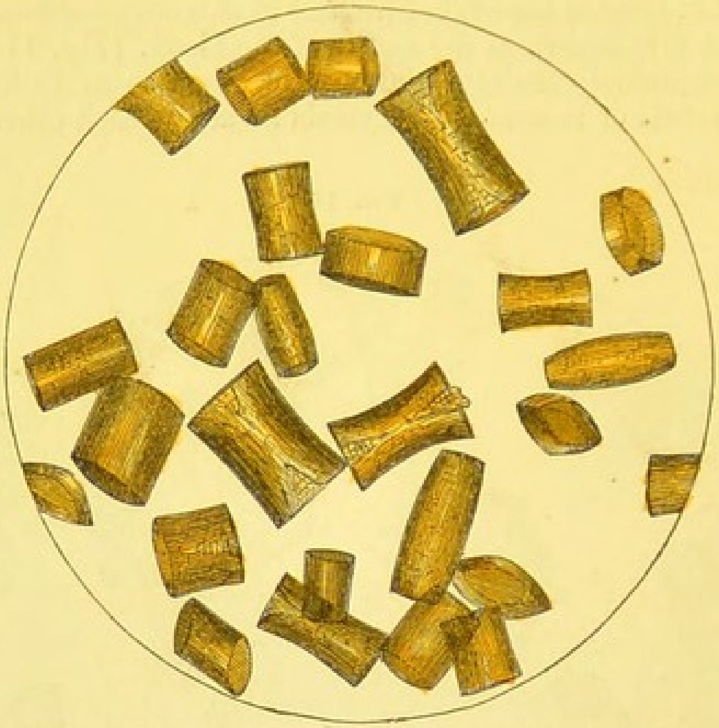
FIG. 14.



*Hexagonal* Crystals of URIC ACID, with *Oxalate of Lime* in *dumb-bells* and *octohedra;* also with *sporules* and *thallus* of the *Sugar Fungus.* From a case of Diabetes. 220 diameters.

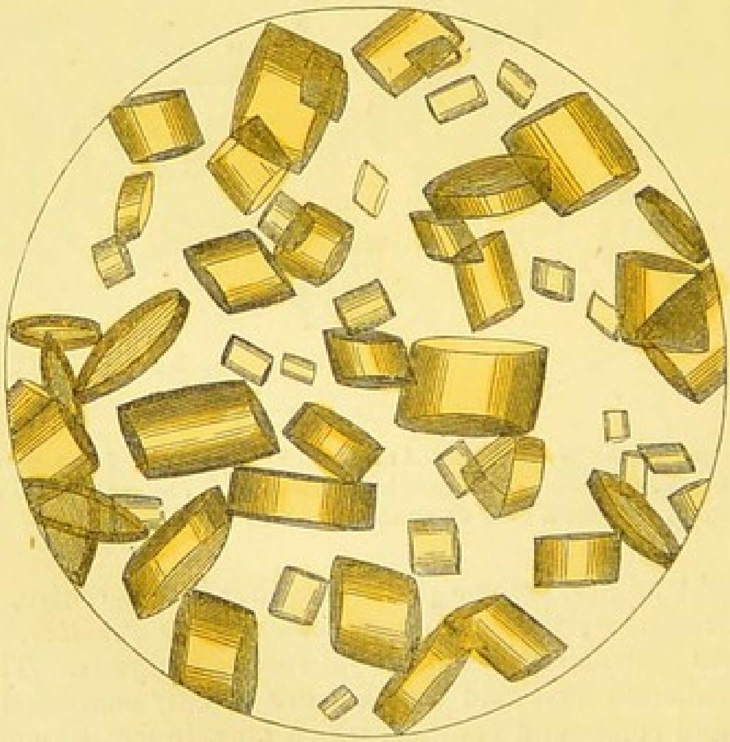
less at right angles, become joined together in the centre, and free at the extremities; thus forming *glomeruli* or *rosettes,* many of which form extremely beautiful microscopic objects. The coarse and deep-coloured uric acid deposits are usually composed of these cohering and compound crystals, which may, in fact, be compared to minute calculi. (Figs. 17, 18, and 19.)

Fig. 15.



*Tubular* Crystals of Uric Acid. 100 diameters. 1851.

Fig. 16.



*Oblique tubular* Crystals of Uric Acid. 100 diameters. 1850.

Another curious modification of uric acid crystals is that in which they present a *striated* appearance, as though each was com-

FIG. 17.

Slender *Glomeruli* of URIC ACID. 100 diameters. 1852.

pounded of numerous small linear crystals. These crystals occur occasionally, though rarely, as a natural deposit; but they are more frequently produced by adding nitric or hydrochloric acid to about an ounce of urine, when, after a few hours, they become deposited. Not unfrequently these striated crystals present a peculiar *hour-glass formation* in the centre, the nature of which has given rise to a good deal of discussion. This hour-glass appearance is only visible in the central non-striated part of the crystal, and, according to Bird, is most clearly seen after the crystals have been dried and preserved in Canada balsam. Dr. Burton regards these striated crystals as being formed of two rhomboidal crystals placed end to end, and then covered up with an aggregation of acicular crystals. This explanation does not appear to be altogether sufficient, nor does it explain the nature of those crystals, not unfrequently met with, which are simply striated, and which do not present any hour-glass formation. These striated crystals are, in many cases, simple rhomboidal crystals, exhibiting a tendency to split up into fibres and the fibres again into granules or molecules. (Fig. 24.)

To the compound varieties of the crystals of uric acid ought to be referred the "*pisiform*" concretions of Golding Bird, in regard to which we find these observations at page 142 of Dr. Birkett's edition of Bird's "Urinary Deposits:"—

"Another variety of uric acid deposit is exceedingly common in gouty persons. It occurs in little spherical masses of a pale-yellow colour, varying in size from that of small millet-seeds to that of a large pea, which ought, indeed, to be referred to the class of calculi rather than of deposits.

FIG. 18.

*Glomeruli* of URIC ACID. 100 diameters. 1854.

"This pisiform deposit is remarkable for its persistence often during many years; it frequently vanishes for many months, and then reappears. I have generally observed the patient to remain free from gout during the presence of this deposit, and often to suffer from a severe paroxysm on its sudden disappearance. It is really remarkable what an enormous number of these minute calculi are frequently passed. I have met with cases in which upwards of two hundred, the size and colour of small mustard-seeds, have been passed in two days.

"These pisiform concretions, after a few minutes' digestion in weak nitric acid, undergo a curious change, their crystalline structure becoming visible, presenting the appearance of numerous acute rhomboids, diverging from a common centre. It is evident that they, at their first formation, possess this form, the rounded smooth surface being subsequently produced by the deposition of minute crystals of uric acid, or the urates, between the projecting angles."

Sometimes the angles of the crystals of uric acid are more or less produced, or rounded, a variety of figures resulting, and some of which are represented in the engravings illustrating this Chapter.

FIG. 19.

*Glomeruli* of Crystals of URIC ACID mixed with octohedral crystals of *Oxalate of Lime*, and cells of *Vesical Epithelium*. 100 diameters.

*Dumb-bell* crystals of uric acid have been described by Dr. Wilson and others; they are rarely met with in human urine as a natural deposit, but they may be produced artificially by pouring a warm solution of urate of potassa or ammonia into a warm dilute solution of hydrochloric acid.

Lastly, crystals of uric acid, formed by adding acetic acid to a urate placed on a slip of glass, are sometimes seen to be imperfect—that is, *one-half* of each crystal only is formed.

When viewed by *polarized light*, thin transparent crystals of uric acid exhibit a series of coloured bands, equalled in brilliancy of tint only by the scales of the diamond beetle.

The circumstances which modify the form and arrangement of the crystals of uric acid are the temperature of the urine, acidity, and alkalinity, its specific gravity, and its varying composition. The exact effects of these several modifying causes and conditions have not as yet been fully and accurately determined.

It is very probable that a knowledge of the several circumstances which modify the form, size, and arrangement of the crystals of uric acid might lead to some useful practical results, and might possibly serve to indicate particular pathological conditions of the urine.

It is, however, certain, that many of the modifications of uric acid crystals, as well as those of other salts, are determined by very trivial causes. This is shown by the fact that several different forms of the crystals of the same substance or salt may frequently be obtained by the evaporation of a single drop of the solution containing it on a slip of glass. Again, Dr. Smidt has shown that variations in the rapidity and manner of the precipitation of the uric acid greatly modify the result. Thus by the precipitation of uric acid from solutions of urate of potassa by means of acetic acid, more or less rapidly, the solutions being more or less heated, crystals of uric acid may be obtained, some of which are oval, some diamond-shaped, some hexagonal, others in rectangular columns and tables, and others in rhombic prisms.

We now pass on from uric acid to treat of the

## URATES.

### *Characters of Urine depositing Urates.*

The variations in the colour of the urates deposited correspond with certain descriptions of urine.

The urine depositing the nearly *white* urates is pale and of low specific gravity, usually from about 1010 to 1014. Moreover, these urates do not readily subside, but remain suspended like clouds in the fluid, presenting in some cases, as remarked by Golding Bird, the appearance of muco-pus, for which indeed not unfrequently they have been mistaken.

The urine depositing the *fawn*-coloured urates is usually of an amber colour and of higher specific gravity, namely, about 1018. This deposit is a frequent attendant upon colds, in which the action of the skin has been impeded.

The urine from which the red, lateritious, or *brick-dust* sediment is thrown down, is of a still deeper colour and higher specific gravity.

Lastly, the urine from which the brilliant purple and bright-pink sediments are precipitated is always highly coloured and of considerable density, it being sometimes of a deep purple verging on crimson, and conveying the impression of blood being present.

These purple deposits occur especially where great obstruction exists to the elimination of carbon from the system, as in organic diseases of the liver and spleen, and where extensive suppuration is going on.

As is the case with uric acid, the quantity of urate spontaneously deposited from any urine does not always indicate the whole amount contained in that urine. If the urine be decidedly acid, an abundant deposit of urate will occur, even when the quantity present is not considerable; but if the urine be but little acid or alkaline, then much of the urate will be held dissolved.

### *Physical and Microscopical Characters of the Urates.*

Deposits of urates, like those of uric acid, vary greatly in colour, as already stated, being sometimes nearly colourless, or *white*, at others pale *fawn*, *pink*, *red*, and even *purple*. The tints of these deposits are best seen after the urine has been separated from them, and when they are collected on a filter.

Deposits of urates seldom occur in a crystalline form, but usually as *granular amorphous* powders. Dr. Golding Bird has described these powders as consisting "of myriads of excessively minute globules adhering together, forming little linear masses." It is but very rarely that the granules present the linear disposition described by Dr. Bird; almost constantly they are separate and scattered without order or arrangement.

Although the urates, especially when mixed, do not often occur in a crystallized condition, yet they are sometimes met with in that state, as previously pointed out under the descriptions given of the several urates discovered in the urine.

Thus, the *acid*, or *biurate of soda*, has been detected in the form of needle-shaped crystals, arranged often in tufts or spherules. (See description.)

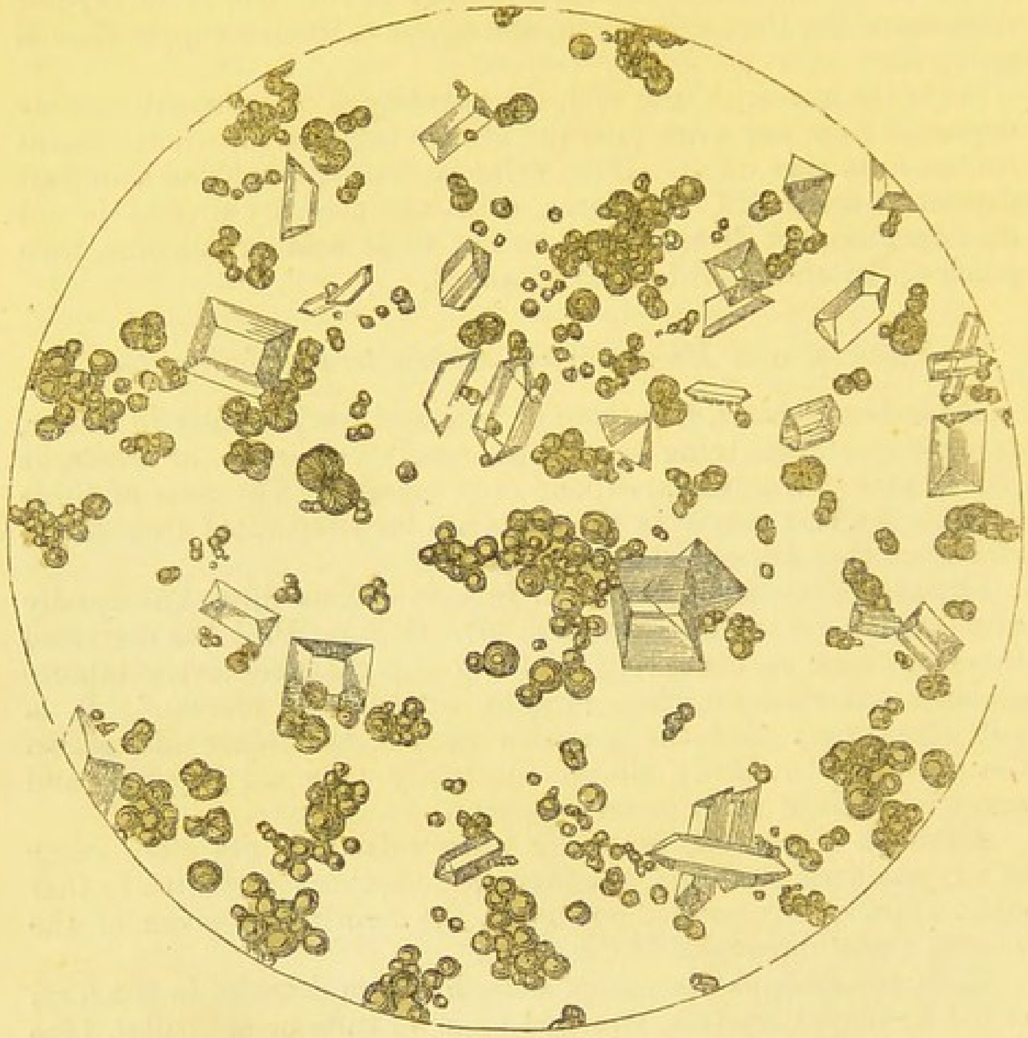
The *neutral urate of soda* is frequently encountered in urine, especially when alkaline, in the form of minute shot-like solid *spherules*, resembling *mustard-seeds*.

The *urate of potassa* is met with in the same globular state, the globules being more deliquescent than those of the soda salt.

*Biurate of magnesia*, when pure and unmixed, also crystallizes in a very characteristic manner. (See description.) It has not, however, been detected in the urine of man in the state of crystals.

The globular shot-like masses of the urates of soda and potassa, although usually separate, sometimes coalesce in masses; when carefully examined with the one-eighth inch object-glass, they are occasionally seen to exhibit a radiated or stellar character, it being obvious that the spherules consist of numerous needle-like crystals. In some rare cases I have noticed the globules to unite in twos, forming *dumb-bells.* (Fig. 20.)

FIG. 20.



*Globular* and *dumb-bell* Crystals of URATE, with Crystals of the *Neutral Phosphate* of Ammonia and Magnesia. 100 diameters.

These globules occur in large quantities in urines which have been kept for some weeks, and which have thus become alkaline. If a urine containing a large amount of amorphous urate be put aside for a time, and be then examined, the urate will frequently be found to have passed into the globular form.

Occasionally the globules become deposited upon the thallus of the fungus, *Penicilium glaucum.* (Fig. 21.)

Very rarely spherules of urate have been observed penetrated by crystals of uric acid. This form has been particularly described by

FIG. 21.

*Globular* URATE attached to thallus of the fungus *Penicilium glaucum.* 220 diameters.

Dr. Bird. It is in albuminous urine chiefly, occurring in dropsy after scarlet fever, that it is occasionally detected. (Fig. 22.)

Another modification has been noticed by Dr. Bird and others, which somewhat resembles that previously described; it occurs in round yellowish-white opaque masses, provided with projecting and generally curved processes. (Fig. 23.) These crystalline formations, there is little doubt, consist of urate of soda; they occur occasionally in gout, but Dr. Bird states that he has more generally met with them in the urine of persons labouring under fever, who have had carbonate of soda administered to them.

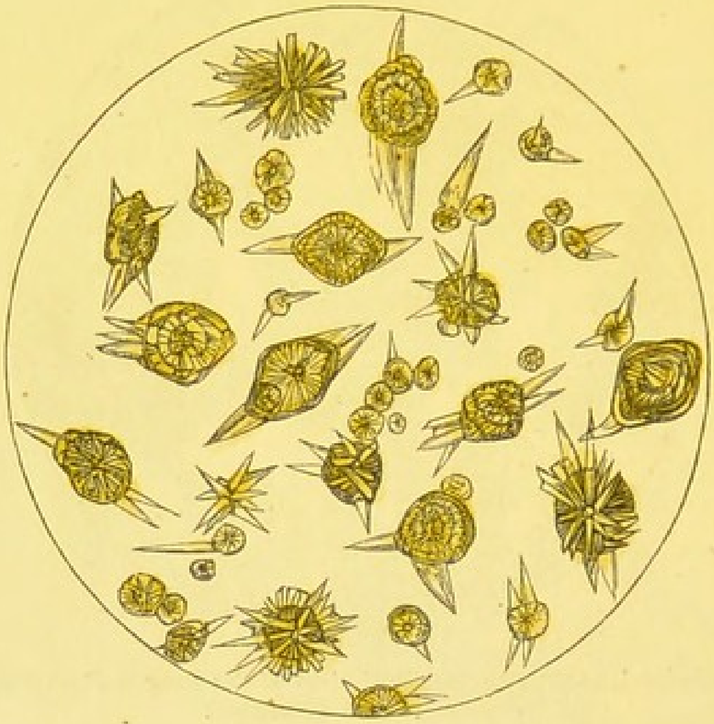
No satisfactory instance of the occurrence in human urine of a crystalline deposit, consisting wholly of urate of ammonia, has been observed, although it is met with in abundance in the urinary excretions of birds and reptiles, forming roundish bodies presenting a radiated arrangement, each globule being composed of numerous cohering needle-like crystals.

### *Determination of Uric Acid and Analysis of the Urates.*

*Uric acid* is usually determined by precipitation by means of a mineral acid; the deposit being collected, is washed, dried, and weighed.

To 1000 grains of the urine of twenty-four hours, about one drachm of strong hydrochloric acid should be added, and the mixture set aside for a day and night, when the uric acid will have all become deposited.

FIG. 22.

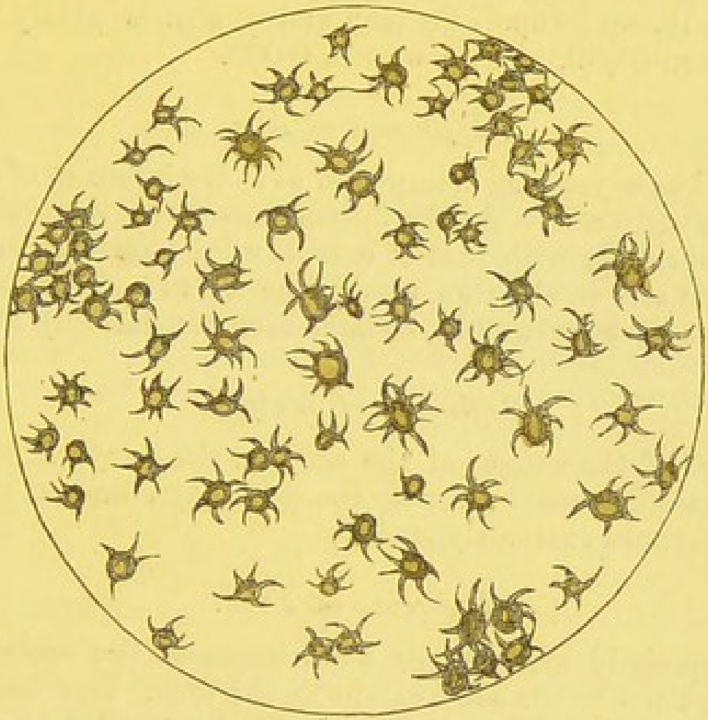


*Globular* URATE with spicula of URIC ACID; from Albuminous Urine after Scarlatina. Drawing made from specimen furnished the author by the late Dr. Golding Bird. 100 diameters.

A rough approximate analysis of the *urates* may be readily accomplished. The uric acid should be determined in a weighed portion of the dried urate by means of dilute hydrochloric acid, while another portion of the urate should be incinerated, and after washing the ash, a portion of it should be tested with the blow-pipe. If the base in any case consists of ammonia, a very small quantity of ash only will remain. In those cases in which a full analysis of the urates is required, they should be previously examined with the microscope, in order to ascertain whether they are free from phosphate of lime or magnesia, or oxalate of lime.

Uric acid may be detected in the *blood* by the following process:—The serum must be dried, treated with alcohol, the residue drenched with four or five portions of hot water successively; the aqueous infusions are then to be evaporated to the consistence of an extract. A portion of this extract treated with nitric acid, and exposed to the vapour of ammonia, gives the characteristic red tint of murexide; the remainder of the extract treated with hydrochloric acid furnishes crystals of uric acid. But if the serum of the blood be simply acidulated with acetic acid, and a few threads of tow or silk placed in it, crystals of uric acid will, in a short time, as first shown by Dr. Garrod, become deposited upon the threads.

Fig. 23.



Urate of Soda, from Urine of Fever patient treated with Carbonate of Soda. Drawing made from preparation lent the author by the late Dr. Golding Bird. 100 diameters.

## ON THE AMOUNT OF URIC ACID EXCRETED IN HEALTH, AND ON THE CAUSES OF ITS VARIATION.

The mean amount of uric acid excreted by numerous adult men varies, according to Parkes' calculations, based on the investigations of fourteen different observers, from 4·32 to 14·49 grains in the 24 hours, the mean of the whole being 8·569 grains.

The variation in different adult men is even greater than that of the urea, as one man may excrete three times as much uric acid as another. The excretion also varies from day to day even in the same person, but usually not to any great extent.

From present investigations it would appear that the variation in the same individual, taking the average of several days, is from 20 to 30 per cent. or from one-fifth to a third of the mean amount.

In proportion to the urea, the uric acid is usually as 1 to 50 or 60, but it may range in health from 1 to 40 or from 1 to 80.

The amount of uric acid in relation to *weight* is very variable. Parkes calculates it at 0·059 of a grain per lb. only.

### *Influence of Sex.*

Numerous analyses of the urine of 20 adult women between the ages of sixteen and forty, give the mean amount of uric acid per day at 7·3 grains, which is less than in men, in whom the mean is 8·56 grains.

But when the quantity is calculated according to weight, the amount per lb. avoirdupois for men and women is nearly the same, being for men 0·059, and for women 0·060.

### *Influence of Age.*

Nothing has as yet been determined as to the influence of age on the excretion of uric acid. As the fluctuations in the quantities of this acid vary so closely with that of urea, it might have been anticipated that the uric acid in children would, like the urea, have been found, in proportion to body-weight, to have been considerably augmented.

### *Influence of Weight.*

The effect of the weight of the body on the excretion of uric acid appears but little marked, and the quantity eliminated by heavy men is sometimes extremely small.

### *Influence of Food.*

*Food*, especially *nitrogenous* food, increases the amount of uric acid, though not to the same extent as the urea. This has been conclusively shown by the experiments of Lehmann, which have since been confirmed by numerous other observers.

Taking the normal amount of uric acid at 1 gramme, = 15·44 grains, animal diet increased it to 1·27 gramme, or 21·61 grains; while, according to Ranke, the increase is as 1 to 1·4.

Jones has also proved that a few hours after food, whether vegetable or animal, the amount of uric acid is increased, but that long after all food it is diminished.

| | 1000 grains of urine. |
|---|---|
| After animal food, highest amount . . . | 1·022 grain. |
| After vegetable food „ . . . | 1·010 „ |
| Before animal food, lowest amount . . . | 0·049 „ |
| Before vegetable food „ . . . | 0·049 „ |

On *non-nitrogenous* food, the uric acid is diminished nearly one-half: thus assuming the normal amount to be 1 gramme, it becomes reduced, according to Lehmann, to 0·63 gramme, or 9·72 grains.

When *sugar* is added in large excess to ordinary diet, the uric acid, according to Böcker, is lessened.

When *vegetable food* alone is taken for some time, the uric acid is diminished, as appears from Lehmann's experiments, from 1 gramme to 0·887 gramme, or from 15·44 to 13·69 grains. In Ranke's experiments the mean amount of several days was, on vegetable diet, 0·650 gramme, or 10·03 grains; and on flesh diet, 0·880 gramme, or 13·58 grains.

There is some reason to believe that when large quantities of *water* are drunk fasting, the uric acid is lessened, and, according to Böcker, it even disappears from the urine. When with ordinary diet much water is drunk, both Mosler and Genth have found the uric acid to be diminished.

The effect of *alcohol* on uric acid is to slightly lessen the amount only; this is very different from its influence upon the urea, which is greatly lessened.

According to Liebig, *wine* increases the uric acid; and from Böcker's experiments it would appear that *strong beer* has the same effect.

By tea, uric acid is diminished as much as two grains per day, according to Böcker; and this considerable decrease is confirmed by the experiments of Hammond. It would further appear that the diminution is not from retention, but from lessened formation.

Böcker found that *coffee* slightly diminished the uric acid, but in Hammond's experiments the reduction was considerable.

Roberts has proved that the urine rendered alkaline by food is rich in *uric acid*, the hourly quantity, as calculated for 1000 grains, was nearly three times greater than during the period when the acidity was restored, and more than three times greater than during sleep. The differences are not so great, when the per-centage of uric acid in the solid residue is calculated, although here also the alkaline urine gives notably the highest figure. These particulars are shown in the subjoined table.

| Time. | Uric Acid per 1000 grs. of Urine. | Uric Acid per hour. | Uric Acid per 100 grs. of Solid Urine. |
|---|---|---|---|
| 4—7 p.m. alkaline tide . | 0·40 | 0·36 | 0·83 |
| 9—11 Acidity restored . | 0·18 | 0·13 | 0·34 |
| 1—7 Urine of sleep . . | 0·39 | 0·10 | 0·60 |

These observations serve to prove that increased alkalescence of the blood is favourable to the elimination of uric acid.

*Influence of Exercise.*

The evidence as to the effect of exercise on the formation or excretion of uric acid is conflicting, but it is on the whole in favour of an increase, especially after strong exercise.

*Influence of Mental Exertion.*

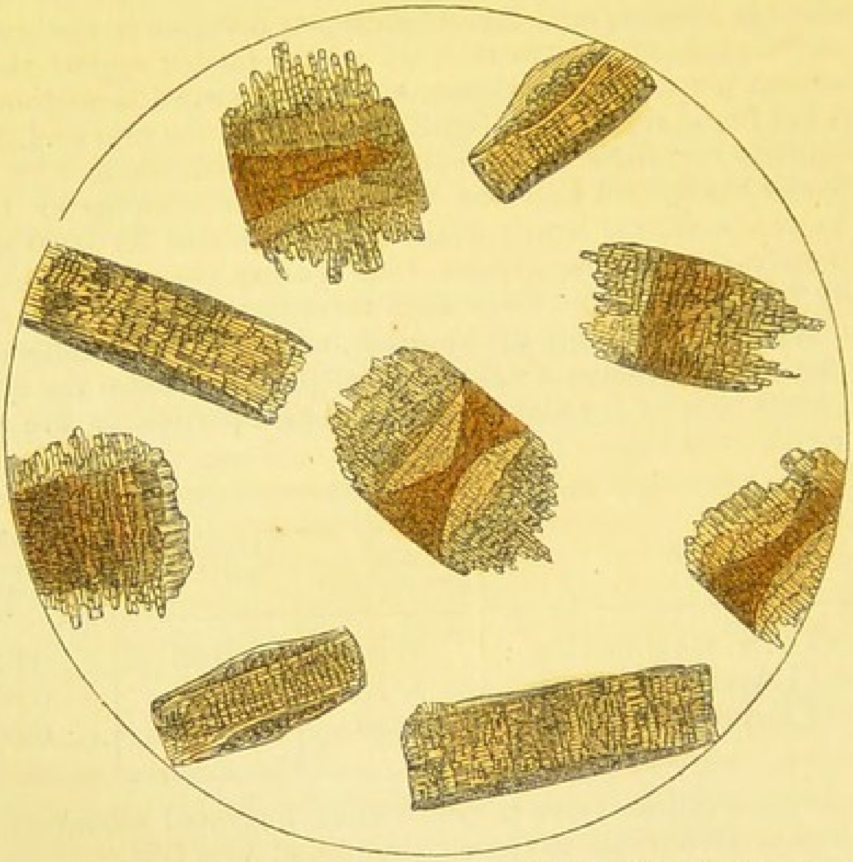
Hammond has found the uric acid to be lessened by mental anxiety.

ON THE ORIGIN OF URIC ACID.

Uric acid is an excrementitious nitrogenous substance, derived unquestionably from the metamorphosis of tissue. Whether all the tissues contribute to its formation, or whether some one only of them, is at present undetermined; and consequently, we are considerably in the dark as to its true pathological relations.

From the ready conversion of uric acid, both in and out of the body, into urea, it has been conjectured that the latter is derived from uric acid by oxidation in the system: this is Liebig's theory; but its correctness has never yet been established, while there are some circumstances which tend to throw a doubt upon it.

FIG. 24.



Crystals of URIC ACID formed after the addition of hydrochloric acid to *Human Urine*, exhibiting a *molecular* and *fibrous* composition, and also the *hour-glass formation*; seen sideways the *rhomboidal* character of the crystals becomes apparent. 100 diameters. 1850.

It is certainly true that in very many cases where there is excess of urea, the uric acid is increased; but if the former were derived from the latter, we should rather look for a diminished amount of uric acid, in those cases in which the urea was in excess. Moreover, in many cases the uric acid is increased where the urea is diminished. Add to this the fact, that no constant or definite relation of any kind can be traced between the excretion of the two bodies. Again, if urea is derived from the decomposition of uric acid, we should expect that cases would occur in which this transformation was hindered to such an extent, as that it would be found in the urine in amounts approaching those in which the urea is met with. But to this view it might be objected, that owing to the comparative insolubility of the salts of uric acid, the urates, it is physically impossible that they should pass the kidney in any very great quantity. It is clear that we know infinitely more of the urine than the blood: when this latter fluid comes to be studied with the same care as the urine, many of the difficulties with which the subject of urinary pathology is now beset will undoubtedly be removed.

Lastly, since the whole of the uric acid injected into the blood is destroyed, and appears in the urine as urea, how comes it that any portion of the uric acid formed naturally in the system escapes this transformation, and finds its way into the urine unchanged? To this question no satisfactory reply has yet been given, possibly the uric acid may exist in some form of combination which prevents, the transformation.

If Liebig's theory of the formation of urea were correct, much light would be thrown upon the pathology of uric acid, and that acid, free or combined, would be found in the urine, in all cases in which there was deficient or impeded oxygenation; and sometimes this is really so, as in certain diseases of the respiratory organs, including pneumonia.

With regard to the place of formation of uric acid, nothing definite is known. It is found in large quantity in the *spleen*, and in some amount in the *lungs*, *liver* and *brain*. No doubt can be entertained, from the various pathological observations that have been made, that some intimate relation between uric acid and the spleen exists. It is present not alone in the spleen in health, but in still larger quantity in most of the affections, including ague, in which that organ is more particularly affected.

As in the case of urea, it has been supposed that uric acid is sometimes derived immediately from the nitrogenous elements of the food. In proof of this, however, there is no evidence whatever; and if, as Bischoff now believes, the urea always results from tissue metamorphosis, the uric acid must be supposed to follow the same rule. The increase of uric acid after food, especially after full, heavy, and indigestible meals, affords no proof whatever of its direct formation from the nitrogenous constituents of the food.

Another particular which tends to disprove the notion of the origin of uric acid from the food in any case, is that out of the body that acid has never been formed from albuminous materials.

## ON THE PATHOLOGY OF URIC ACID.

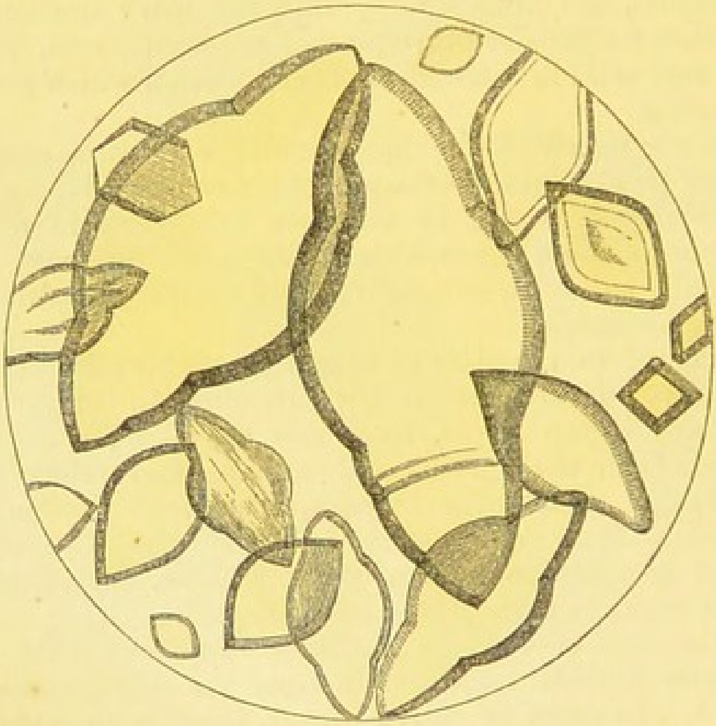
Like the other constituents of the urine, uric acid may in disease be either in excess, or it may be deficient; that is, it may either be above or below the standard of health.

For the most part it follows the same rule as urea, and is increased when the amount of that substance is augmented; but to this there are certain exceptions: the rule being that uric acid is *increased in most active febrile and inflammatory diseases, and diminished in those of a contrary type and character.*

Uric acid is greatly increased in *intermittent* fever, or *ague,* during the fit.

Ranke did not find that there was any great difference during the cold and hot stages; but the amount was much increased some hours after the paroxysm, when the urates are often spontaneously deposited.

FIG. 25.



Various forms of Crystals of URIC ACID, including square, hexagonal, and spindle-shaped Crystals, from *Human Urine.* Drawing made from specimen lent the author many years since, by Dr. Griffith. 100 diameters.

It is also over the normal amount, according to Ranke, on the days succeeding the paroxysm.

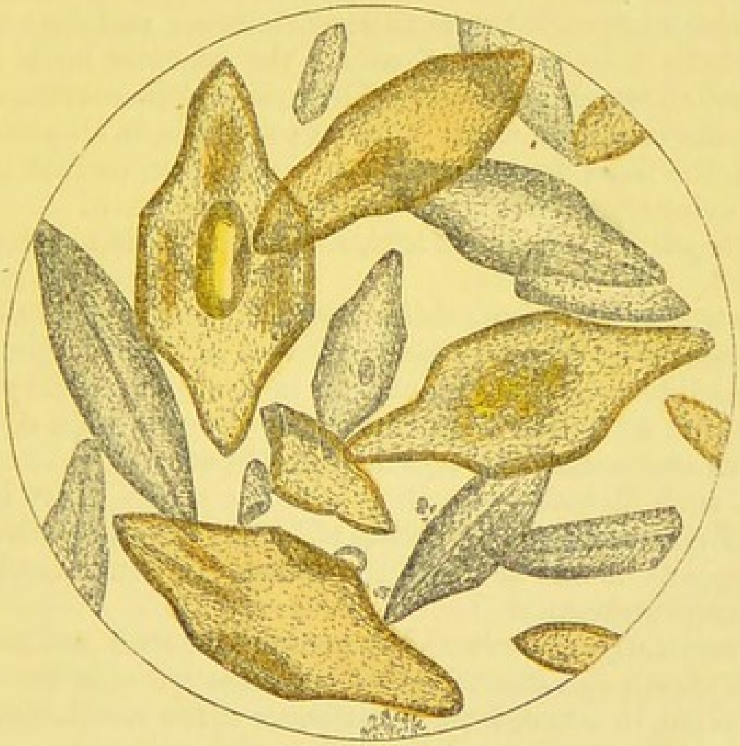
In *typhoid fever, typhus abdominalis,* there is constantly a very marked increase in the uric acid, greater relatively than that of the urea, it being often more than double the normal amount. Zimmerman states that the increase continues to the fourteenth day, when the quantity is usually double; that it then diminishes, until it falls during convalescence below the healthy standard.

In some cases of *typhoid fever* there is retention of uric acid, and of the other constituents of the urine, giving rise to more or less uræmia and symptoms of blood-poisoning.

This retention may arise from the condition of the kidneys, from local congestions and inflammations, as well as from some other causes.

The free elimination of uric acid, urea, and other organic extractive matters, is, in this, as in so many other diseases, a favourable symptom.

FIG. 26.



Remarkable modification of Crystals of URIC ACID. Drawing made from preparation of the late Dr. Golding Bird, lent the author many years since. 100 diameters.

In a case of *typhus*, in which the urine was specially examined by Parkes, the uric acid was "in large amount and spontaneously, or on the addition of an acid, deposited." During convalescence it was below the normal amount.

In *small-pox* and *scarlatina* the uric acid is increased, and sediments of urates occur, or uric acid is thrown down on the addition of an acid.

In *pneumonia* there is generally a very large increase of uric acid; it ranges usually from 12 to 20 grains, and in a case recorded by Zimmerman, 29½ grains were excreted in the 24 hours: it is towards convalescence that the largest amount is voided, and that the most copious deposits of urates occur. In a patient of Dr. Parkes, Ranke found on the fifth and sixth days 0·468 and 0·480 grammes, equal to 7·22 and 7·41 grains, while on the tenth day, when resolution was going on, the uric acid amounted to 1·210 gramme, or 18½ grains. During convalescence it was only 0·209 gramme, or 3 grains per day.

This increase is doubtless due mainly to augmented elimination; uric acid, owing to its comparative insolubility, is very readily retained, much more so than the highly soluble urea.

Sediments of urates and uric acid most frequently occur in pneumonia from the seventh to the thirteenth days; and their occurrence is undoubtedly favourable; of course the converse holds good, and their retention is unfavourable. The uric acid is sometimes retained owing to the condition of the kidneys; and this, in all acute diseases, is one of the most frequent causes of retention, so that in all such cases the urine should be specially tested for albumen.

In *acute pleurisy* the uric acid, like the urea, is not considerably augmented.

In *acute capillary bronchitis* there is most probably a considerable increase, the urine resembling that of acute pneumonia.

There is likewise an augmentation in *acute pulmonary phthisis.*

In *cardiac affections* the urine is usually very high coloured, and deposits of urates are both copious and frequent.

In all such diseases, as well as in many others, there is of course *disturbed circulation;* and on the effect of such a condition in giving rise to deposits of uric acid and the urates, the remarks of Lehmann are of much interest.

"We especially observe the formation of such sediments, when from any reason the due interchange of the gases in the lungs does not take place, or when, from disturbance of the circulation, the blood does not really permeate the pulmonary vessels. . . . . . In fully developed *emphysema,* or even when only a part of a lung has lost some of its elasticity, a sedimentary urine is one of the most common symptoms. *Heart disease,* enlargement of the *liver,* &c., are associated with disturbance of the circulation, and hence give rise to sedimentary urine. Large masses of secreted urate of soda are found in no disease except in true granular liver, which obviously can never exist without considerable disturbance of the circulation. In *fever* also, the due relation between respiration and circulation is no longer maintained, and hence there is augmentation of the uric acid in the urine." All these instances of uric acid deposits, Lehmann attributes, as Liebig would do, to defective oxygenation; and he regards uric acid as one degree higher in the scale of descending metamorphosis than urea, from which also he concurs with Liebig in considering it to be derived.

In *rheumatic fever* the uric acid is considerably increased. In two cases noted by Parkes, "The mean in twenty-four hours was 9·445 grains on the fourth, fifth, and sixth days, in one case; and 12·694 grains from the fifth to the tenth day in a second case. In both instances, however, liquor potassæ was given, and some influence may perhaps be ascribed to it. The largest amount I have ever noted in rheumatic fever was 17 grains. The man was taking liquor potassæ; but when he was well, and took liquor potassæ as an experiment, the largest amount of uric acid passed was 9·8 grains; so that the former large quantity must be attributed to the disease."

Precipitates of urates and uric acid are frequent and abundant, especially as soon as the fever and other symptoms begin to abate.

In the period between the paroxysms of *acute gout* there is diminution of most of the solids of the urine, especially the urea and uric acid, while immediately before the paroxysm it may even be absent.

During the paroxysm the excretion of uric acid is also lessened. The mean amounts in seven cases recorded by Dr. Garrod, were 5·95, 2·05, 2·58, 3·76, 4·46, 3·28, and 3·28 grains; the mean of the whole being 3·62 grains, as compared with 8·569 grains, the mean standard of health.

As uric acid in cases of acute gout is so abundant in the blood, it is obvious that it is not its formation but its elimination which is impeded.

When the fit is passing off, and just after the paroxysm, the uric acid is considerably increased.

In *subacute* and *chronic* gout the deficiency of uric acid, according to Garrod, is still greater, and sometimes it is even absent. Lehmann and Ranke, as well as Garrod, have found uric acid absent in cases of chronic gout with tophaceous deposit.

In a case of *acute eczema impetiginodes* made the subject of investigation by Dr. Beneke, the uric acid was increased; as the disease improved it decreased.

The condition of the uric acid in CHRONIC DISEASES may next be considered. In the majority of chronic affections there is lessened metamorphosis, and consequently diminished excretion by the kidneys; the urea, pigment, sulphuric acid, and chloride of sodium are in particular reduced in amount; but this rule does not hold good so generally as respects the uric acid and the earthy phosphates: these may either be diminished in normal amount, or even be increased.

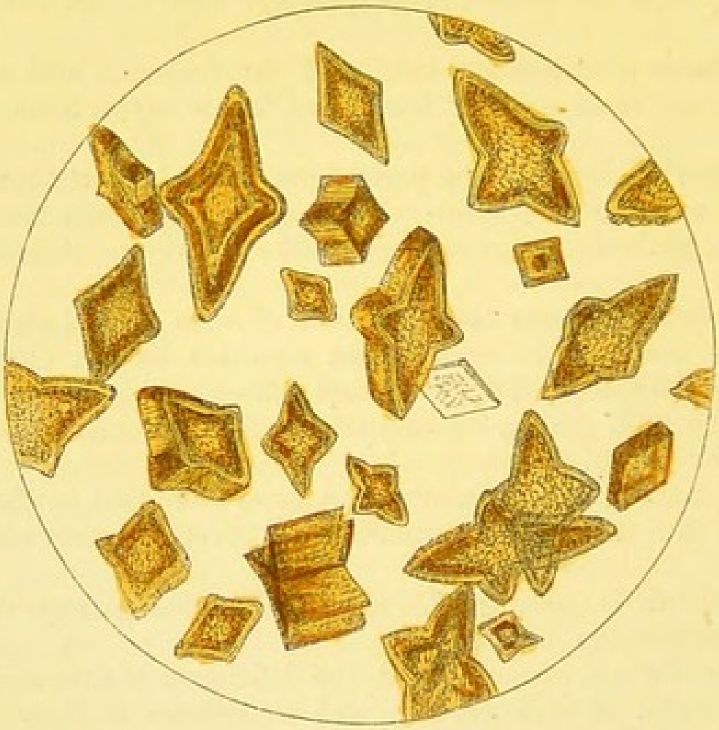
When the paroxysms of *epilepsy* occur, uric acid and the urates are usually deposited, but whether they are augmented in amount in this disease has not been determined.

Neither has it been ascertained whether uric acid is in excess in *phthisis*. Copious deposits of urates are very common in this disease; but these may often be traced to diminished water, resulting from sweating and diarrhœa.

In *Emphysema pulmonum*, apart from hepatic, bronchial, or cardiac complications, Dr. Parkes states that he has not found any increase in the uric acid.

When considerable *bronchitis* is combined with *emphysema*, uric acid is in large amount.

FIG. 27.



Remarkable *Crucial* Crystals of URIC ACID, from *Human Urine*. 100 diameters. 1850.

In *cirrhosis* of the liver, the uric acid would appear to be generally in large amount.

In simple *icterus*, or *jaundice* from obstruction, there is also a considerable augmentation in the uric acid, as much as 17 grains having been found. Kühne has also observed the increase.

In *chronic enlargement of the spleen* it is believed that the uric acid is increased.

In a case of *Leucocythemia* in which the urine of 24 hours was analysed by Parkes, he found no less than 31·5 grains of uric acid;

the urea amounted to 427·5 grains, about the normal quantity; the extractives and salts were also greatly augmented.

In a case in which the urine was analysed by Ranke, the uric acid was much increased—0·915 gramme, equal to 14·27 grains; the urea was not increased, and the other solids were present in small amount.

In *Leucocythemia* there is then a remarkable increase in the uric acid, connected probably in some way with the enlargement of the spleen. *Hypoxanthine* is also found in the blood and urine in these cases, proving the implication of the spleen.

FIG. 28.

*Spindle-shaped* Crystals of URIC ACID, from *Human Urine.*
100 diameters. 1854.

In cases of *anæmia,* as in *chlorosis,* the uric acid is diminished.

In *indigestion* and *chronic diseases* of the *stomach,* deposits of uric acid and the urates are frequent, especially in the *urina cibi;* it is not proved, however, whether they are in excess or not, although Lehmann states they are so. Their appearance in some cases would appear to depend upon the nature of the food.

In *diabetes* the uric acid is usually diminished, and is not unfrequently absent: on the other hand, it appears sometimes to be present in normal amount. When fermentation sets in, or the urine is more than usually acid, it is frequently precipitated in diabetes.

Except when there is retention, the uric acid is increased, in *acute nephritis*, and the urates are often precipitated in consequence of deficiency of water. In *chronic nephritis* it is diminished, and the urates are seldom deposited.

## ON THE TREATMENT OF URIC ACID DEPOSITS.

The physician is more frequently called upon to treat affections connected with the presence of uric acid in the urine than any other urinary deposit, and this for several reasons: one of these is, that deposits of uric acid, either free or combined, are readily recognised, even by the patient himself; and a second reason is, that they frequently give rise, mechanically, to considerable irritation and pain in the kidneys, ureters, bladder, and urethra, causing the patient to seek for relief.

The treatment admits of division into two kinds, the curative and and the palliative: too frequently the treatment adopted is of the latter character only.

For the *curative* treatment it is necessary that we should ascertain the cause of the excess of uric acid.

Excess of uric acid, it has been shown, occurs in nearly all disorders accompanied by pyrexia, in which also the urea is still more considerably increased. In such cases the treatment must be that which is specially suited to the particular nature of the complaint—the fever must be restrained.

This excess has been likewise noticed in connexion with affections of the spleen. Other causes of either the excess or the precipitation of uric acid in the urine are, indulgence in animal food, its malassimilation, and defective cutaneous excretion.

The *palliative* treatment has for its object the solution of the uric acid deposit, whether this occurs in the kidney or the bladder, the distressing mechanical effects being thereby obviated, or in the urine subsequent to its emission.

Sometimes the only treatment required is the palliative, the excess of uric acid being due to temporary causes only, and treatment being needed solely on account of the irritation produced by the deposit.

At others, treatment is needed for uric acid deposit even where there is no excess of it in the urine, the precipitate formed being due not to excess, but to over-acidity of the urine.

Again, there may be excess of uric acid in the blood, producing constitutional derangement, with a deficiency of the acid in the urine, as in gout in some stages, and in structural diseases of the kidneys: here elimination of the acid must be promoted.

If the excess of uric acid be due to fever and waste of tissue, this must be moderated. The waste may arise, as already described, from inflammatory disorders, active fevers, &c. In such cases we must lessen undue action, and regulate the circulation and secretions. When the liver is at fault, special attention must be paid to that organ.

If it be caused by over-indulgence in animal food, the obvious indication is to reduce the amount of this within proper limits.

If it be attributable to mal-assimilation, the diet must be regulated carefully, and the digestive organs improved and strengthened.

Lastly, if the excess be traceable to defective cutaneous elimination, the first indication to be fulfilled is to restore the skin to a more perfect performance of its functions.

In general, however, it is not advisable to confine our attention exclusively to the cause of the excess: in our treatment of these affections generally, we must have regard at once to the diet, the state of the digestive organs, of the skin, &c.

Attention to *diet* is most important. This comprises the regulation of the quality and quantity of the ingesta: too much nitrogenous food must be avoided, as also all such articles as tend to the production of undue acidity.

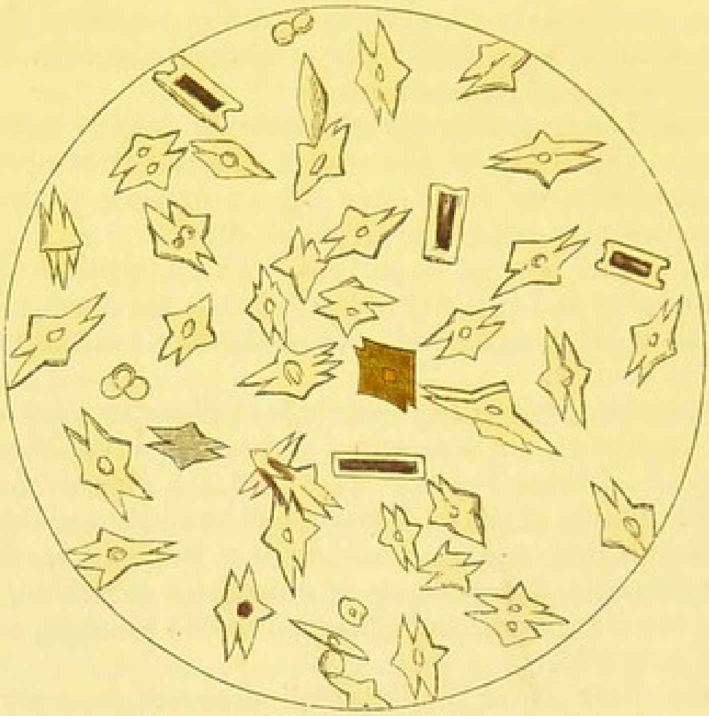
For the improvement of the functions of digestion, not only must the diet be regulated, but alteratives and tonics administered. The administration of these has for its object the improvement of the primary assimilation of the food, whereby the entrance into the blood of crude nitrogenized and acid materials is prevented. The acids, the lactic and acetic, the products of unhealthy digestion, being absorbed into the circulation and conveyed to the kidneys, act as precipitants of uric acid.

When the liver is at fault, small doses of mercury must be administered; and if the digestion is weak, vegetable bitters, such as cinchona, gentian, calumba, and serpentary; the latter remedy is in some cases to be preferred, on account of its action on the skin. When gastrodynia exists, benefit will frequently be derived from the use of the trisnitrate of bismuth, or oxide of silver, combined with hyoscyamus or hydrocyanic acid. The gastric symptoms being relieved, a very marked improvement frequently takes place in the character of the urine.

Some of the milder preparations of iron, as the ammonio-citrate or the citrate of quinine and iron, will be found of great service, especially when, connected with mal-assimilation, an anæmic or chlorotic state exists. From three to five grains of either of the above-named preparations may be given twice or thrice daily in a wine-glass of water or beer, either with or directly after food. Taken with the food, these preparations are more readily absorbed, and agree better.

When there is reason to suspect that the deposit is kept up by a gouty or rheumatic tendency, in addition to a careful regulation of the diet, *colchicum* will often be found to lessen in a very obvious manner the amount of uric acid deposited. The colchicum may be administered in combination with some of the solvent remedies presently to be described, and a bitter vegetable infusion, or the acetous extract of colchicum may be used, combined or not, as may be necessary, with small doses of blue pill.

FIG. 29.



Peculiar *Double* Crystals of URIC ACID, from *Human Urine.*
100 diameters. 1851.

Scarcely less important than careful regulation of the diet is attention to *air*, *exercise*, and particularly to the action of the *skin*.

Air and exercise increase oxidation, tend greatly to the improvement of all the bodily functions, and especially promote the healthy performance of digestion. Moderate exercise, by increasing the waste of the tissues, likewise calls the digestive organs into greater activity.

The action of the *skin* is promoted by warm clothing, by cold and warm bathing, friction, and sometimes by diaphoretics. In some cases persistence in the use of the cold bath and friction by horse-hair gloves will be sufficient; in others, the warm, or, better still, the vapour-bath, may be required, and in others James's powder. It has already been noticed that serpentary exerts a diaphoretic action on the skin; benzoic acid, about which we shall have to speak presently, is also diaphoretic.

A great variety of solvent remedies are employed in the treatment of uric acid deposits; the chief of these are *alkalies;* but *water*, especially soft and distilled water, is a solvent, and the diuretics, by increasing the quantity of water in the urine, likewise act indirectly as solvents.

It should be clearly understood that alkaline remedies, though commonly described as solvents, are so only indirectly—that is, their bases combine with the uric acid, compounds resulting which are much more soluble than the uncombined acid.

The chief alkaline remedies resorted to are liquor potassæ, carbonate of potassa, carbonate of soda, salts of the vegetable-acids, as the acetates, citrates, and tartrates of soda and potassa, borates of potassa and soda, phosphates of soda and ammonia.

### *Liquor Potassæ.*

The liquor potassæ of the Pharmacopœia contains only about one grain of potash in ten minims of the solution: hence, when this remedy is administered, it should not be given in less than scruple or half-drachm doses, three times a day. It may be administered in some bland vehicle, or in a mixture, in combination with other remedies. Brandish's alkaline solution is much stronger than the ordinary solution, and hence its greater efficacy. The flavour of solution of potash is caustic and disagreeable, and the remedy is probably not so efficacious as the carbonates of potassa and soda.

### *Carbonate of Potassa.*

The dose of this remedy which should be given is from one scruple to half a drachm, thrice daily. To render it more agreeable, it may be taken in combination with about half its weight of citric acid; this causes slight effervescence. The administration of alkaline remedies should be accompanied by the free use of diluents, of which the best is pure water—if *distilled*, so much the better.

A popular remedy in the treatment of uric acid gravel, in some parts of the country, is a quack nostrum which has received the absurd appellation of "Constitution Water." The empirical employment of this remedy was brought prominently under the notice of the profession, by the author, in his review of the fourth edition of Bird's "Urinary Deposits," published in the *Medico-Chirurgical Review*. It owes its efficacy to *carbonate of potassa.* From an analysis of a sample, it was found to contain about 3·2 per cent. of impure carbonate of potash or pearl-ash. The following remarks respecting this water are from the Review mentioned: "The dose of constitution-water is the eighth part of a bottle the size of a wine-bottle, four doses to be taken daily, this being about 184 grains or upwards of three drachms of carbonate of potassa. The price is 62*s.* per dozen; its actual cost, exclusive of bottles, is not nearly as many farthings.

"Furnished with the above recipe or analysis, the admirers of 'constitution-water' may supply themselves with it at a very much cheaper rate than 5*s.* 2*d.* per bottle. The remedy is indiscriminately recommended in all cases of 'strangury, gravel, and stone.' The only cases to which it is really applicable are those of uric acid diathesis. In some forms of urinary deposit and stone, it would be productive of incalculable mischief, and therefore it should on no account be taken excepting under medical advice. Persons are too apt to imagine that there is some hidden charm in these secret and empirical remedies. For the removal of this delusion, no method is so effectual as the publication of their actual composition."

### *Carbonate of Soda.*

The dose of this salt is about the same as that of carbonate of potash. A remedy which has acquired some celebrity in the treatment of uric acid is "Vichy water," the chief constituent of which is *bicarbonate of soda.* Some years since, the author employed Dr. Letheby to make an analysis of the artificial Vichy water of the German Spa at Brighton; this was published in the review of Dr. Bird's "Urinary Deposits," already mentioned. It was as follows:—

*Artificial Vichy Water.*—2000 grains of the water were evaporated, and they yielded 9·88 grains of a saline residue, which had the following composition:—

| | |
|---|---|
| Bicarbonate of soda . . . | 10·14 |
| „ magnesia . | ·58 |
| „ lime . . . | ·26 |
| Sulphate of lime . . . . | ·58 |
| „ soda. . . . | — |
| Chloride of sodium . . . | 1·16 |
| Silicate of alumina . . . | ·12 |
| | 12·84 |

From this analysis, it appears that the artificial water very closely resembles in its composition the natural water from the wells of Vichy, and which was analysed by Henry in 1847. It also resembles the water of the springs of Cusset and Hauterine, in France.

The dose of Vichy water is a small tumblerful two or three times a day, amounting to about a pint, and containing 35·5 grains of bicarbonate of soda.

With a little dry sherry, such as Montilla, the artificial Vichy water forms an agreeable after-dinner beverage for persons whose urine contains an excess of uric acid.

### *Salts of the Vegetable Acids, as the Acetates, Citrates, and Bitartrates of Soda and Potassa.*

These salts are very efficacious when given in sufficient doses; they may be administered in combination, or the acids may be added separately to the carbonated salts, the mixture being sweetened with syrup of orange-peel, and drank in a state of effervescence.

The immunity of the inhabitants of wine-producing countries from calculous affections is supposed to be in a great measure attributable to the large quantity of bitartrate of potash, or wine-stone, contained in the wine.

These salts, in passing through the system, are usually converted into carbonates; but when the digestive organs are weak the decomposition is more or less incomplete.

Not unfrequently the continued use of the carbonates of potash and soda disorders digestion greatly; in such cases the salts of the vegetable acids become very valuable, and of these, on account of the tendency of the tartrate to affect the bowels, the best preparations are the acetates and citrates. The dose of all these salts is about half a drachm, three times daily.

### *Borates of Soda and Potassa.*

The biborate of soda is a very active solvent of uric acid, more so than the alkaline carbonates; and hence it has been advantageously employed in some cases of uric acid gravel. Its administration to women is not advisable, since it exerts a stimulant action on the uterus; and Dr. Bird met with two cases in which it produced abortion.

Borate of potassa is a still more active solvent for uric acid than biborate of soda. It should be largely diluted; indeed this remark applies to all the alkalies.

The following prescription for uric acid gravel is by M. Bouchardat:—

℞ Potassæ bitartratis, ʒi.<br>
„ boratis,<br>
„ bicarbon. *aa.* grs. xv. M.

Fiat pulvis.

### *Phosphates of Soda and Ammonia.*

These salts are also excellent solvents of uric acid. Golding Bird has stated that he administered *phosphate of soda* in several chronic cases of uric-acid gravel, with the effect of rapidly causing a disappearance of the deposit.

*Phosphate of ammonia* has been particularly recommended by

Dr. Buckler, of Baltimore, even in cases in which the uric acid is deposited as a calculus, or around the joints, combined with soda, as in gout. At page 176 of the fifth edition of Bird's "Urinary Deposits," the following remarks respecting this salt occur:—"I have given it a fair trial in hospital practice, and have no hesitation in saying that it has always succeeded in keeping uric acid in solution in the urine, and in this respect it has appeared to be at least equal, if not superior, to borax and phosphate of soda; but I certainly have never seen it diminish the tophaceous deposits in chronic gout. In more recent effusion into the joints of sub-acute forms of rheumatic gout, it has certainly been of service."

The dose of phosphate of soda is from one scruple to half a drachm, and of phosphate of ammonia about ten or fifteen grains, much diluted.

We have now completed the description of the chief solvent remedies employed in the treatment of uric acid deposits. It will be perceived that the number of these is great, and that the effect of many of them is considerable. *We must never, however, lose sight of the fact, that these remedies do not go to the root of the mischief, but are merely palliative.* In all cases it behoves us to search out the cause of the excess of uric acid, and it is to this that the more important part of our treatment must be directed.

### *Benzoic and Cinnamic Acids.*

Another remedy resorted to in cases of uric acid deposits is benzoic acid. Its chemical action is very peculiar: while the salts already described act upon the uric acid *after* it has been formed, these are said to *prevent its formation.* Benzoic acid, itself destitute of nitrogen, combines with nitrogen derived from some nitrogenous substance contained in the blood, and which it is believed would otherwise go to form urea and uric acid, and is itself converted into hippuric acid, a substance rich in nitrogen.

It has been stated that under the use of benzoic acid uric acid sometimes altogether disappears. This is questionable. It has been shown by Dr. Garrod that the hippuric acid is formed at the expense of the urea, but probably not entirely, as it is certain that uric acid is also in some cases greatly diminished.

The body with which benzoic acid combines is probably sugar of gelatine or glycocoll, one atom of each of these forming one atom of hippuric acid. *Cinnamic acid* undergoes a similar change to benzoic acid, and is likewise converted into hippuric acid. *Benzoate of ammonia* has been particularly recommended as an efficient remedy by Dr. Holland. Benzoic acid possesses the additional advantage over many other remedies of exciting diaphoresis, thus fulfilling an important indication in the treatment of uric acid deposits. The dose of this acid is about ten grains taken in syrup three times a day.

We are sometimes called upon to treat deposits of urates apart from those of uric acid. The nature of the curative treatment required of course depends upon the cause of the deposit, according as this is connected with fever, cold, over-indulgence, mal-assimilation, gout, &c.

It may be stated generally that urine containing urates is less acid than that depositing uric acid, and that the urates are much more readily dissolved than the uncombined acid; hence solvent and antacid remedies are not so much required in these cases, and it will usually be sufficient that the quantity of urine be increased, as by means of diluents and small doses of diuretics, such as the nitrate and acetate of potash.

# CHAPTER V.

## HIPPURIC ACID.



### *History.*

Hippuric acid is found in the urine of the herbivorous mammalia, in that of the omnivorous, but not of the carnivorous mammalia: the animals in which it has been specially studied are the horse, cow, pig, and camel; it has likewise been detected in guano and in the excreta of the tortoise and butterflies. Like all the other constituents of the urine, it is present in the blood.

According to Liebig, hippuric acid is always contained in the urine of man, and that chemist therefore regards it as a normal constituent. Liebig's statement was mainly founded on the circumstance that he detected benzoic acid in every stale urine tested by himself for a period of three months. This conclusion has, however, been negatived, to some extent, by the researches of Duchek and Hoefle: it is certain, however, that hippuric acid is very generally present in the urine of man.

It occurs usually in the combined state; the bases with which it has been ascertained to be united are those of lime, soda, or potash. Brande and Bouchardat treat of a hippurate of urea. The hippurates are more soluble than the free acid.

#### CHEMICAL CHARACTERS.

It is devoid of smell, and has a slightly bitter taste; its aqueous solution reddens litmus; it is very soluble in hot, and but sparingly so in cold water; it is also very soluble in alcohol, but much less so in ether. It dissolves without decomposition in hot hydrochloric and warm nitric acids; but when the boiling is prolonged, it is decomposed into *benzoic acid*, the nitric acid solution containing *glycine, glycocoll*, or *sugar of gelatine*. It is deposited from its solution in hydrochloric or nitric acid, as this becomes cold, and also on evaporation. The same decomposition into benzoic acid and glycocoll occurs when hippuric acid is boiled with either caustic soda or potash, and also by the action of yeast or other azotized substances in a state of decomposition: this fact explains the transformation of hippuric into benzoic acid in putrid urine. By oxide of lead the boiling aqueous solution is converted into benzoic acid, or benzamide, carbonic acid, and water. When heated, hippuric acid first melts and is then decomposed into benzoic acid, which sublimes and is recognisable by its odour, and into ammonia; at the same time an oily liquid is formed which evolves the aroma of the Tonquin bean; exposed to a rapid and strong heat, hydrocyanic acid is evolved and a porous carbonaceous residue remains.

*Composition.*—Hippuric acid has the following atomic and percentage composition:—

| | | |
|---|---|---|
| Carbon | 18 | 59·76 |
| Hydrogen | 9 | 5·09 |
| Nitrogen | 1 | 7·79 |
| Oxygen | 6 | 27·36 |
| Atomic number | 179 | 100·00 |

*Formation.*—Dissacgne has shown that hippuric acid may, under certain circumstances, be artificially formed by the mutual action of chloride of benzoyl and the compound of oxide of zinc and glycine.

Guckelberger has further shown that benzoic acid may be artificially produced from nitrogenous tissues by oxidation with nitric acid, benzoic acid, and hydruret of benzoyl, or oil of bitter almonds, being produced. (Day.)

*Combinations.*—The combinations formed by hippuric acid in the urine have already been very briefly alluded to. Those which have been actually detected, either in the urine of man or certain animals, are the *hippurates of lime, soda*, and *potash*, while by some writers an *hippurate of urea* is mentioned. It would appear, however, that there is no such compound, as shown by the fact that when solutions of hippuric acid and urea are mixed together, no matter in what proportions, these salts crystallize separately, the crystals of each preserving their typical characters. The hippuric acid crystallizes much sooner than the urea.

*Hippurate of lime* is commonly met with in the urine of the horse: it is soluble in boiling alcohol and assumes the crystalline form as the solution evaporates. In order to obtain it, the fresh urine of the horse should be evaporated to a considerable extent. The salt crystallizes on the surface and also occurs as a deposit; after separation it should be dissolved in hot alcohol and the alcoholic solution evaporated.

This hippurate is very crystallizable; the crystals form four-sided prisms, having oblique terminal facettes, which are very characteristic. The typical form and its chief modifications are exhibited in Fig. 36. The crystals are coloured by polarized light.

*Hippurate of potash*, like most other salts of that base, is very deliquescent, and, therefore, when a drop or two of a solution containing this hippurate is evaporated on a glass slide, no regular crystals are obtained if the air be at all damp; but if dry, a silky crust is formed consisting of needle-like and branched crystals. It readily crystallizes in urine with chloride of sodium, in the form of crosslets and daggers, either single or variously united.

*Hippurate of soda*, on the contrary, is an efflorescent salt: it crystallizes from its aqueous solution, forming a silky crust composed of needle-shaped crystals arranged in a stellar manner, the different stars usually touching each other at their circumferences: sometimes the crystals are disposed in the form of dumb-bells. In combination with chloride of sodium, nearly the same forms result as from the union of the chloride with hippurate of potash.

The *benzoic acid* formed in stale urines at the expense of the hippuric acid may be either free or combined, forming benzoates.

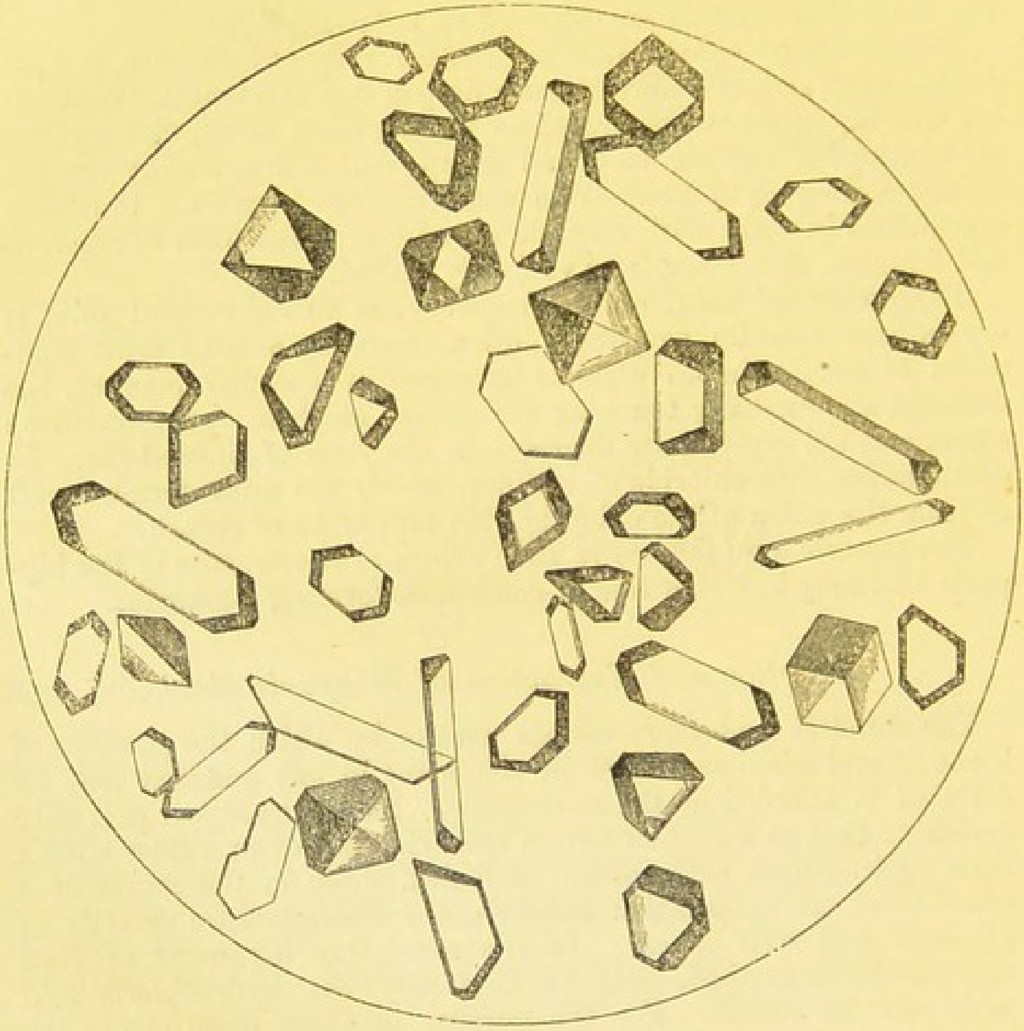
### *Detection and Extraction of Hippuric Acid.*

The simplest and most certain means by which the presence of hippuric acid when contained in the urine in any quantity may be detected is afforded by the microscope. For this purpose it is only necessary that to a drop or two of the urine placed on a glass slide a little hydrochloric acid should be added, when in the course of a short time, as evaporation proceeds, the characteristic crystals of hippuric acid will appear. In the same way hippurate of lime may be distinguished, only in this case the hydrochloric acid must not be added. For the purpose of these experiments the urine must of course be fresh, as the hippuric acid, in the course of a few days, changes into benzoic acid; but the microscope also supplies the means of detecting this acid, either in a few drops of the urine evaporated without the use of any reagent, or, still better, after the addition of a minute quantity of hydrochloric acid. (See Figs. 31, 32, and 33.)

When the hippuric acid is free, and occurs as a deposit, which it but rarely does, it may be extracted by agitating the urine in a flask with ether; this will dissolve out the acid, which on the evaporation of the ethereal solution will become deposited in the crystalline form. Or if the quantity of hippuric acid be not very considerable, the urine may be evaporated in a water-bath to the consistence of an extract, previous to the addition of the ether.

When combined with bases, the following method may be pursued, —the urine is to be concentrated by evaporation, and while hot

FIG. 30.

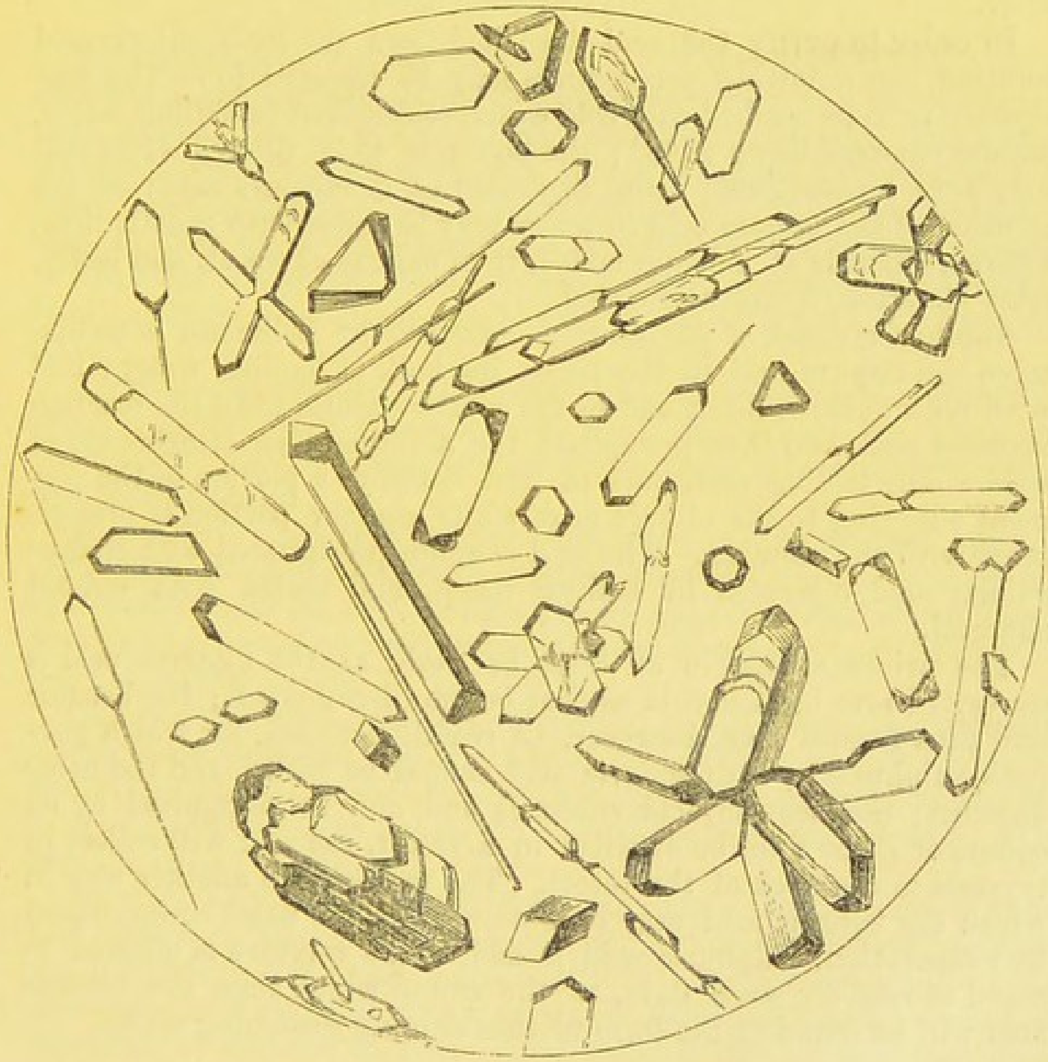


Crystals of HIPPURIC ACID, formed on the evaporation of a drop or two of the aqueous solution. 200 diameters.

treated with hydrochloric acid: as the mixture becomes cold, the hippuric acid will be thrown down in the crystalline condition.

The preceding methods of extraction are applicable chiefly in cases where the hippuric acid is abundant, as in the urine of the horse; when the quantity is but small, as in normal human urine, we must proceed as follows:—When the urine, after neutralization with lime, has been sufficiently concentrated by evaporation, it is placed in a flask and hydrochloric acid is added, which decomposes the hippurate of lime previously formed; ether is then introduced in large quantity, the flask is closed and agitated from time to time; the ethereal solution which floats on the top is decanted, washed with a

Fig. 31.



Crystals of Hippuric Acid, from a drop of *Human Urine*, to which a little hydrochloric acid had been added, after a dose of benzoic acid. 200 diameters.

little water to remove the traces of hydrochloric acid, and afterwards evaporated. As in some cases the ether will not separate readily from the mixture, a very small quantity of alcohol may be added, which facilitates the separation: the water added removes the alcohol together with any urea which may have become dissolved, as well as the hydrochloric acid.

Lehmann recommends that the urine should be evaporated almost to the consistence of a syrup, and the acid extracted with alcohol, sp. gr. 0·830. A little oxalic acid must be added to the alcoholic extract during its evaporation to a syrupy consistence; the residue is then to be acted upon with ether containing one-sixth of its volume of alcohol. This extract must now be evaporated, treated with warm water, and the solution passed through a moistened filter.

In order to purify the acid deposited from the hydrochloric acid solution, the following proceedings may be resorted to:—The precipitate is to be washed with cold water, redissolved in boiling water, animal charcoal being added; the liquid is to be filtered while still hot, pure hippuric acid being deposited as it becomes cold: or the solution of the impure acid in water may be boiled with caustic lime, filtered, chloride of calcium added, then animal charcoal, and lastly, after filtration, hydrochloric acid.

Another method of purification described by Lehmann is to dissolve the impure acid in ten times its bulk of boiling water; boil with milk of lime, filter, add to the solution alum, until the reaction becomes acid, and then precipitate the alumina with bicarbonate of soda. The boiling with milk of lime destroys a portion of the pigment adhering to the impure acid, while another portion is precipitated with the alumina. The acid is again precipitated with hydrochloric acid dissolved in boiling water, and boiled with animal charcoal.

The urines should in all cases be fresh, as the hippuric acid is converted into benzoic acid as they become decomposed; the benzoic acid thus formed may, however, be readily detected, for which purpose sulphuric or hydrochloric acid should be added, and the urine distilled; the benzoic acid sublimes and may be recognised by its odour, or if the fluid be distilled in a retort, the acid will collect in crystals in the neck of the retort. The following is another way in which the benzoic acid may be obtained: to the urine concentrated by evaporation, sulphuric acid is added, the mixture is allowed to stand at rest for some days, at the end of which time the benzoic acid will be found in the form of thin shining glistening scales.

## MICROSCOPICAL CHARACTERS OF HIPPURIC ACID.

The crystals of hippuric acid belong to the type of the oblique rhomboidal prism. When crystallized from their solution in boiling water, crystals of the typical form are often obtained; but at the same time various modifications of that form occur, as shown in Fig. 30.

Crystals closely resembling the preceding may be obtained from the urine after a dose of benzoic acid, by simply allowing two or three drops to evaporate spontaneously on a slip of glass, a little hydrochloric acid having been added. (Fig. 31.)

From similar urine, by simple evaporation and without the addition of any reagent, crystals of either hippuric acid or an hippurate, probably *hippurate of soda*, may also be obtained. (Fig. 32.)

From the same, after it has been kept for a day or two, *benzoic acid* in the crystalline state may likewise be procured. (Fig. 33.)

## ON THE AMOUNT OF HIPPURIC ACID IN HEALTH, AND ON THE CAUSES OF ITS VARIATION.

Weissmann found in his own case that on four days' mixed food he excreted a mean of 34½ grains of hippuric acid per day, and on three days' animal food 17 grains, or just one half. Wreden (Canstatt's *Jahresb.* 1860) found that it even exceeded the phosphoric acid, the mean daily excretion of which is 48·80 grains. These results show that, in some cases, even in health, a considerable amount of hippuric acid is eliminated; that its formation is greatly increased by vegetable food; and also that it may be produced independently of vegetable food.

According to body-*weight*, Parkes calculates the mean of hippuric acid per pound excreted in 24 hours at 0·237 of a grain: however, the analyses hitherto made are too few to allow of even an approach to a correct mean.

*Animal food* not only causes a reduction in the amount of hippuric acid, but it is asserted by some observers that it sometimes disappears under its use; neither Weissmann nor Hallwachs found this to be the case, as both excreted about a gramme, or 15 grains, per day on a meat diet.

On *vegetable food*, although no benzoic acid or benzoyle compound be contained in it, the hippuric acid is much increased. Weissmann shows that the increase is not owing to vegetable albumen, or starch, and he attributes it to the lignin. Hallwachs considers that it is not due to the chlorophyll.

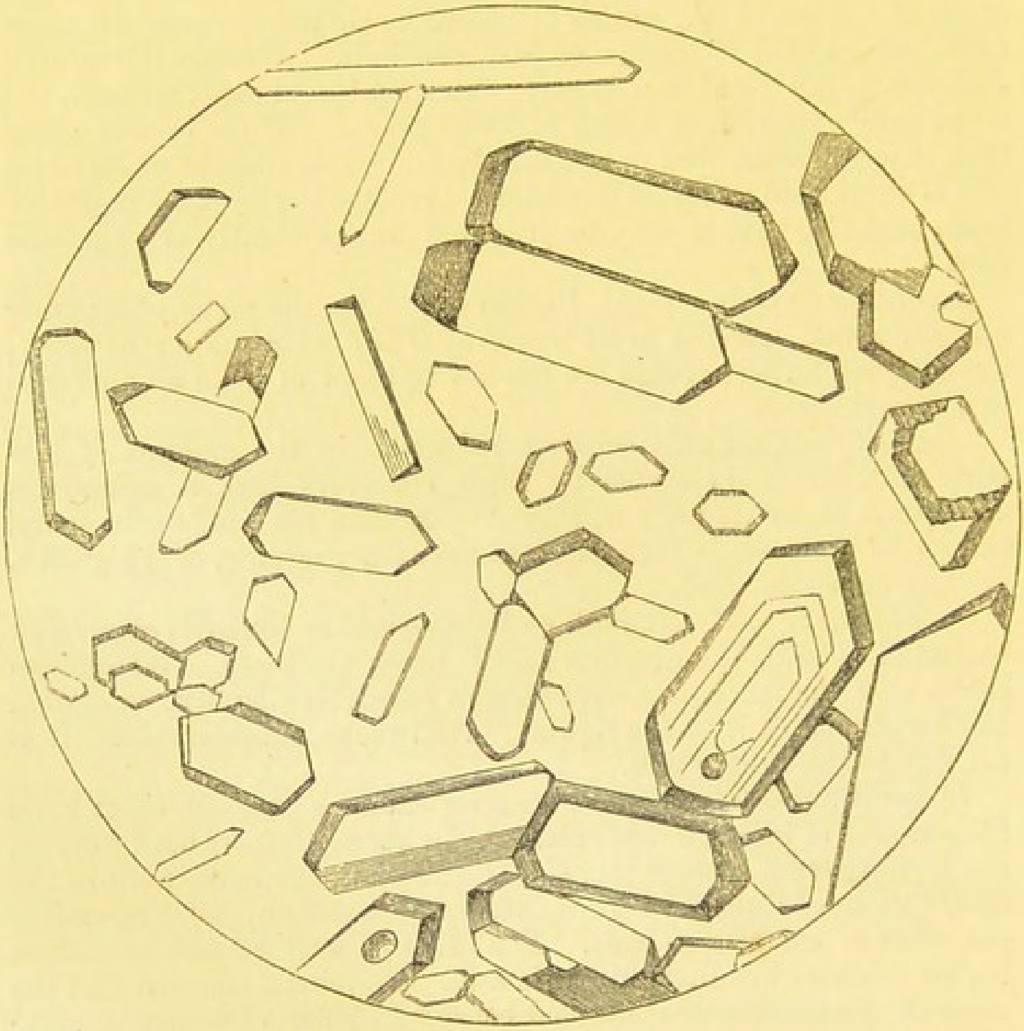
In some animals, as horses, *exercise* exerts a marked effect upon the amount of hippuric acid excreted. In horses that are hard worked, the hippuric acid is much increased; this is the general result of the observations of Roussin, Hallwachs, and Weissmann, and it resembles the effect of exercise on urea. The urine of well-fed and unworked horses contains but little hippuric acid. Marchand affirmed that the urine of plough-horses contained benzoic in place of hippuric acid: this is an error; but Hallwachs has found a small quantity of benzoic acid in such cases, which Parkes suggests may have been derived from decomposition of the hippuric acid in the bladder.

ON THE ORIGIN OF HIPPURIC ACID.

The hippuric acid found in the urine may be derived from three different sources.

*First*, it may proceed from certain benzoyle compounds, as benzoic, nitro-benzoic, and cinnamic acids, or any substance containing benzoyle, oil of bitter almonds, or balsam of tolu, either taken separately or consumed in articles of food. Thus, when benzoic or nitro-benzoic acids are administered by the mouth, they make their appearance in the urine in the form of hippuric acid.

FIG. 32.



HIPPURATE OF SODA (?), from a drop of *Human Urine*, evaporated after a dose of benzoic acid. 100 diameters.

It would appear that only a limited amount of hippuric acid can be formed at one time in the body after a dose of benzoic acid: thus Duchek found in the urine :—

| | Hippuric Acid. | Benzoic Acid. |
|---|---|---|
| When 1 gramme of benzoic acid was taken | 0·714 | 0·000 |
| „ 2 „ „ „ | 1·857 | 0·420 |
| „ 4 „ „ „ | 1·714 | 2·500 |

Fig. 33.


Benzoic Acid, from a few drops of *Human Urine*, evaporated after a dose of benzoic acid—*a*, after simple evaporation; *b*, after the addition of hydrochloric acid. 50 diameters.

Protrowsky's experiments give a different result: he found that nearly all the benzoic acid appeared in the urine in the state of hippuric acid. This difference may arise, as Parkes suggests, from one system being rich and another poor in *glycine*.

Hippuric acid, as already stated, is formed whenever articles of food are consumed which contain benzoic acid, or some benzoyle compound: amongst such articles, grass, hay, greengages, and plums have been mentioned. Hallwachs states, however, that neither grass nor hay contains benzoic acid or any member of the benzoyle series which could produce benzoic acid in the system.

Hippuric acid is therefore formed whenever any benzoyle compound comes in contact in the system with *glycine*, which is a constituent of glycocholic acid, one of the bile acids.

It appears established from the researches of Kühne and Hallwachs that the union of benzoic acid and glycine takes place usually in the liver and not in the general circulation, unless glycocholic acid or glycine be present therein.

*Second*, the hippuric acid may be derived from food, especially vegetable food, not containing benzoic acid or analogous compounds: this is proved by the fact that the hippuric acid of the urine is always greatly increased by the use of vegetable food of all kinds; it also continues to appear, although in diminished amount, when *animal food* only is taken.

When vegetable food is taken, Weissmann attributes, as previously noticed, the increase to the lignin constituent of the food.

*Third*, it is in some cases derived from the disintegration of some of the nitrogenous tissues. In the herbivora much of the hippuric acid found in the urine proceeds from this source, as proved by the circumstance that the urine of fasting herbivorous animals still furnishes hippuric acid; indeed, in the herbivora that acid replaces urea to a considerable extent. Since, however, in man fasting causes the total disappearance of the hippuric acid, it is clear that in such cases it cannot have a tissue origin, but must be derived from the food.

Nevertheless, it is highly probable that in the human subject, in some cases, it results, as in the herbivora, from disintegration of tissue; and wherever the quantity found is large and persistent, and there is no peculiarity of diet serving to explain its occurrence, we should be apt to suspect such an origin.

The hippuric acid found in the urine after animal food may possibly in some cases be due to the formation of benzoic acid, by oxidation, out of the nitrogenous constituents of the food. Guckelberger, Staedeler, and Hallwachs have all shown experimentally that benzoic acid may be formed from such substances out of the body by artificial oxidation.

It appears that hippuric acid cannot be formed in the system from all nitrogenous substances. "From experiments on rabbits, Weissmann has concluded that protein matters do not give it. In men also, he thinks vegetable albumen is wholly indifferent. As might be anticipated, starch, neither in men nor rabbits causes it; nor, according to Hallwachs, does chlorophyll. In rabbits, Weissmann thinks (without, it seems to me, any convincing evidence) that it is the 'encrusting substance' (lignin?) which forms benzoic acid and then hippuric acid." (Parkes.)

Von Maack has pointed out a possible source of hippuric acid from *tyrosine* by oxidation, this substance differing only from hippuric acid in its atomic composition, it containing two atoms more hydrogen.

## *Characters of Urine containing Hippuric Acid.*

In Lehmann's cases in which the hippuric acid occurred in persons attacked with fever, the urine was very acid : in Bouchardat's cases it was only feebly so : in that recorded by MM. Robin and Verdeil, the urine was also only slightly acid, and it deposited much urate of soda and a little ammonio-magnesian phosphate; the urine passed after excitants, such as wine, coffee, and liqueurs, was very acid, and furnished an abundant deposit of oxalate of lime and of hippuric acid ; it possessed the ordinary odour, and its colour approached that of the urine of fever.

## PATHOLOGY OF HIPPURIC ACID.

In all cases of the occurrence of hippuric acid in the urine in abnormal quantities, we must consider, first, its origin, and determine whether it proceeds from the medicine or food taken ; or whether its occurrence is independent of these, and is due to the disintegration of tissue.

The presence of hippuric acid in the urine in the free state in pathological quantities has been observed especially by Lehmann, Bouchardat, and Bird, in the human subject.

Lehmann obtained it from the urine of patients attacked with *fever*, and he attributes the acidity of the urine in these cases to the presence of an excess of the acid. According to Weissmann, there is less that the normal amount of hippuric acid in "*typhus*" patients.

M. Bouchardat detected it in the urine of a woman aged 53, who in consequence of an affection of the *liver* was subjected to a milk diet for 9 years, and whose health became gradually deteriorated; this patient drank from 3 to 5 litres of liquid per day, the quantity of urine being proportionate.

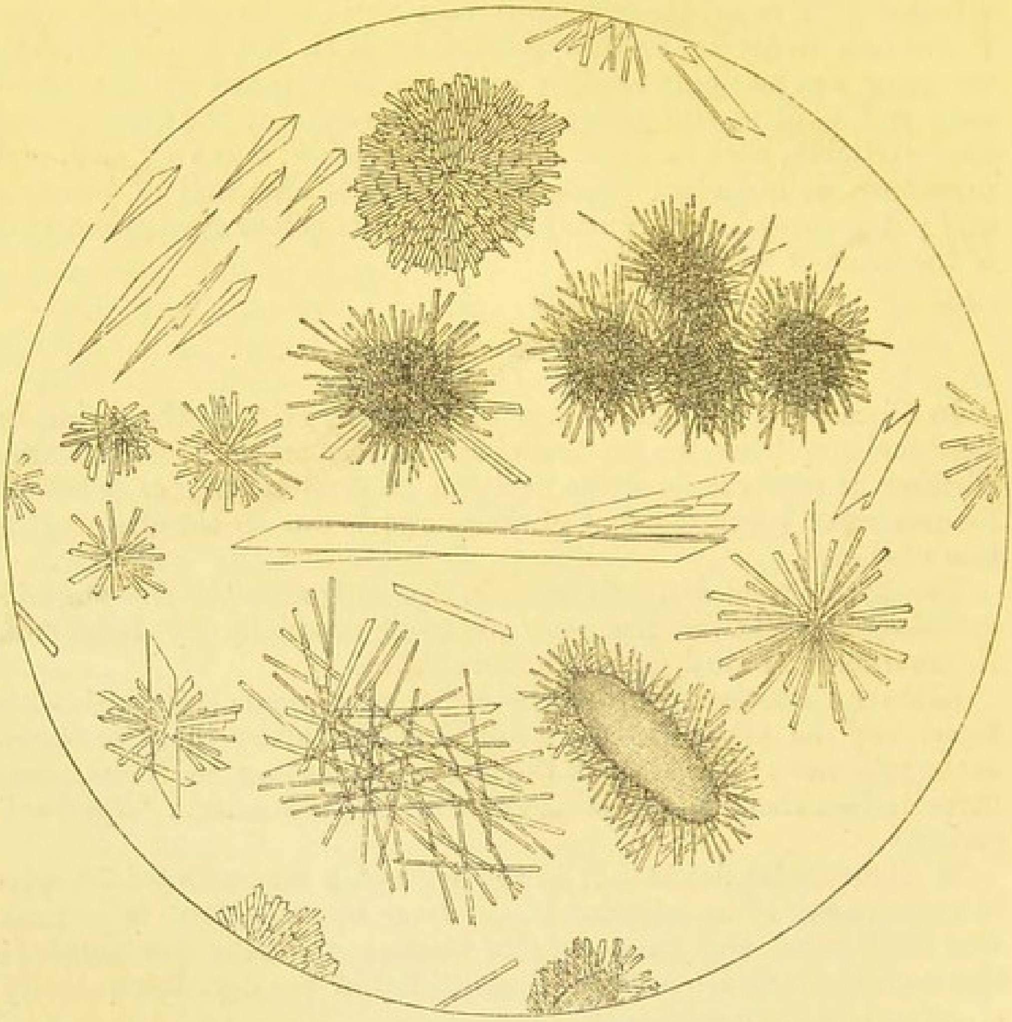
Golding Bird likewise found hippuric acid in large amount in the urine of a drunkard with *contracted liver*.

Lehmann, Ambrosiani, Duchek, Hunefeld, and other observers, have found hippuric acid in the urine in *diabetes mellitus*, while Bouchardat detected it in a case of *diabetes insipidus*.

"On the other hand, Bouchardat could not find it, nor Stockvis either, with certainty in diabetes. In the case already quoted from Gorup-Besanez it was also absent. Garrod in no case 'noticed an augmentation;' and the latest observer, Weissmann, found it lessened in three cases, he believes from the meat diet." (Parkes.)

Pettenkofer found much hippuric acid in the urine of a young girl, aged 13 years, labouring under *chorea*. The girl was fed upon bread and apples, and the acid disappeared as soon as she took meat. It has likewise been found by other observers in large amounts in the urine in other cases of chorea.

FIG. 34.



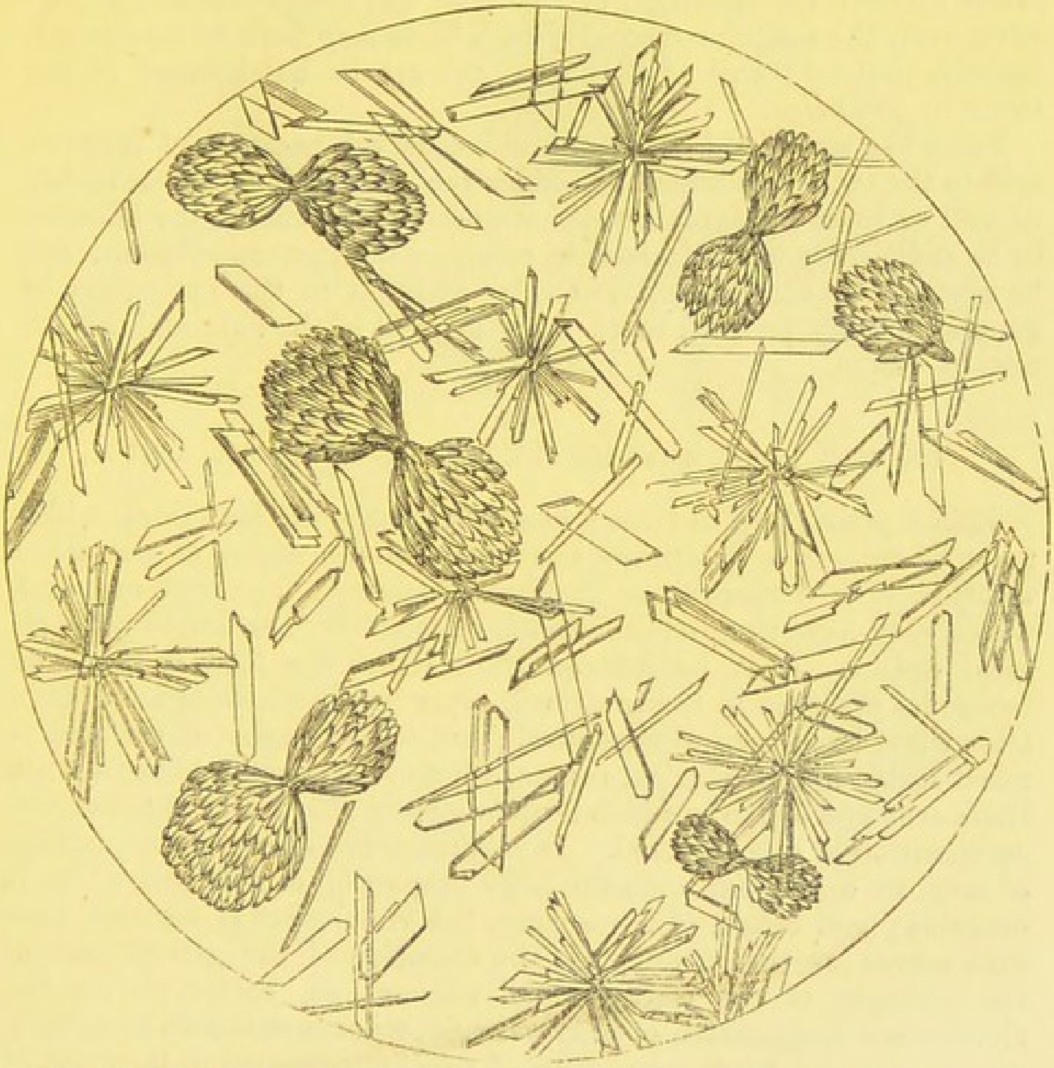
Crystals of HIPPURIC ACID, deposited naturally from *Human Urine*. From Atlas of MM. Robin and Verdeil.

Dr. Garrod's case was that of a young man aged 23. He was suffering from atonic *dyspepsia*, with pain in the loins. The hippuric acid was found in the urine for several days, half a pint furnishing as much as 40 grains; gradually it disappeared. There was no peculiarity in the diet in this case to explain the occurrence of the acid.

In one case this acid has been discovered in the scales of *Ichthyosis*.

Messrs. Robin and Verdeil state that they met with a deposit of hippuric acid in the urine of a vigorous man 30 years of age, who taking but little exercise, yet consumed highly nitrogenous food.

FIG. 35.



Crystals of HIPPURIC ACID, from *Urine of the Horse*, after the addition of hydrochloric acid. 200 diameters.

According to Weissman, hippuric acid is diminished in *pneumonia*, but the statement requires confirmation.

It is often present in the urine of *cholera*.

Its occurrence in connexion with *diseased liver*, as in the cases of Bouchardat and Bird, is worthy of note. In reference to this point Parkes makes the following observation :

" The production of hippuric acid is a subject of great interest :

it may indicate a mal-action of the liver; for it must be supposed that glycine is either produced in excess, or that the elements which should form it do not do so in consequence of the stronger attraction of some body which acts upon them, as benzoic acid will do when taken into the system. So, is it possible to suppose that there is in pyrexia an increased production both of benzoic acid and glycine?"

As tending still further to show that in some cases a connexion exists between the condition of the liver and the production of hippuric acid, the singular discovery of Kühne may here be mentioned, namely, that no traces of hippuric acid are to be detected in the urine in *jaundice*.

From the considerable amount and constant presence of hippuric acid in the two cases which fell under the observation of Bouchardat, as well as from the symptoms, that observer considered the affection to be sufficiently characteristic to receive a distinct appellation, and he proposed to call it *hippuria*. In addition to the symptoms of general debility present, there were dryness of the skin and feebleness of vision.

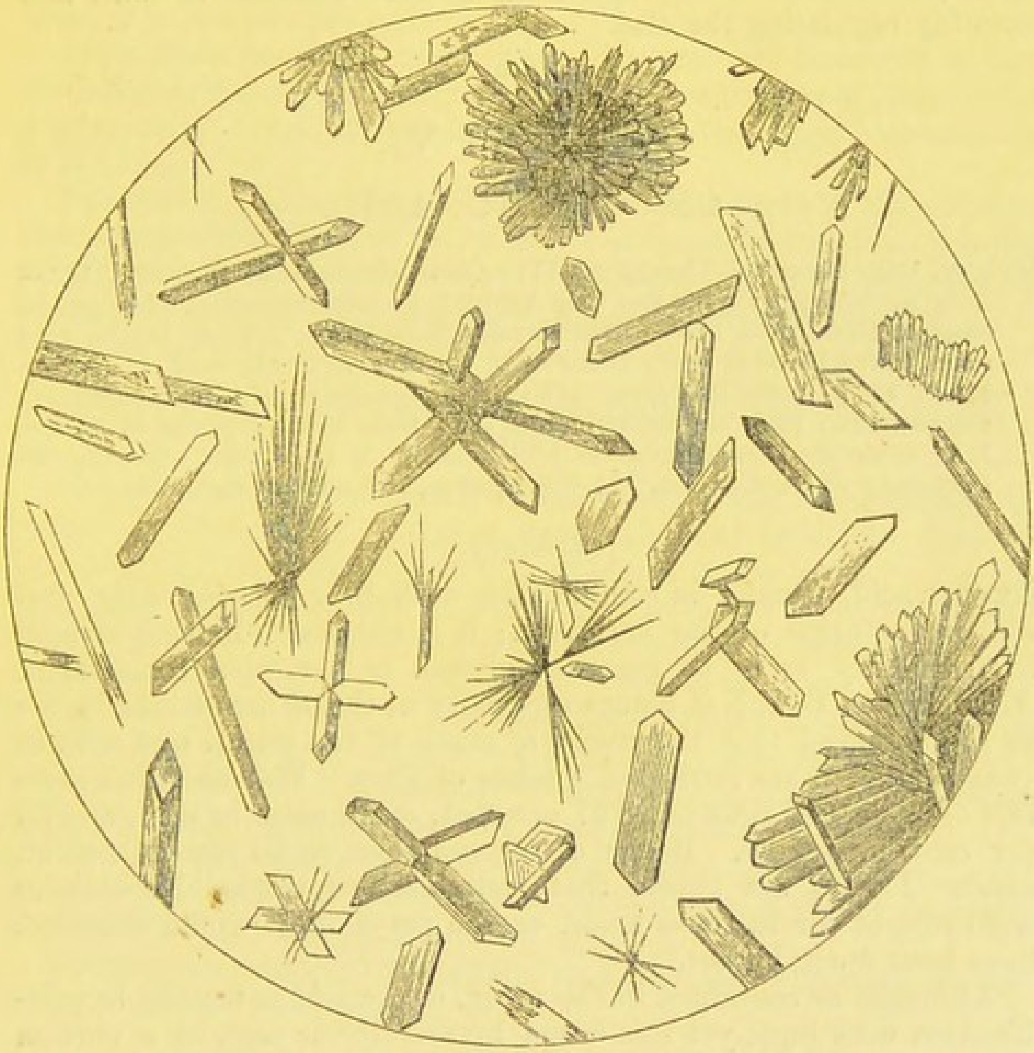
## ON THE TREATMENT OF EXCESS OF HIPPURIC ACID.

Before proceeding to treat a case of hippuria, the first thing which must be done is to determine the source of the excess of the acid: whether it is derived from the food consumed, from any medicine which may have been administered, or whether it is due to pathological causes. If it be derived from either the food or medicine taken, its presence in the urine will cease in the course of a few days after these have been discontinued; but if the excess of the acid is attributable to pathological causes, we must endeavour to learn what these are; and a clue to which is undoubtedly afforded by the chemical composition of hippuric acid. In regarding the ultimate composition of urea, we are struck with the large proportion of *nitrogen* which it contains; and hence, in a measure, the conclusion is derived, that urea serves as the medium for the excretion of the greater part of the nitrogen of the disintegrated tissues: so, contemplating the elementary composition of hippuric acid, we cannot fail to be equally struck with the large proportion of *carbon* contained in it, whereby it manifests a relation to bile and especially urine pigment. This affinity is shown in the following analyses :—

| | Hippuric Acid. | Bile. | Urine Pigment. |
|---|---|---|---|
| Carbon | 59·76 | 68·40 | 58·43 |
| Hydrogen | 5·09 | 10·13 | 5·16 |
| Nitrogen | 7·79 | 3·44 | 8·83 |
| Oxygen | 27·36 | 18·03 | 27·58 |
| | 100·00 | 100·00 | 100·00 |

The composition of hippuric acid and its relation to bile and urine pigment, point unmistakeably to the conclusion that it is a vehicle for the elimination of an excess of carbon from the system.

FIG. 36.



Crystals of HIPPURATE OF LIME, from *Urine of the Horse.* 50 diameters.

Now this excess of carbon may be due to two causes,—either to the free or continued use of food rich in carbon, or to defective action of one or more of the great decarbonizing organs. The occurrence of hippuric acid in the urine of the herbivora and in that of infants at the breast, may possibly to be due to the first-named cause, while its presence in connexion with liver disease would be referrible to the second cause.

These views are not only in accordance with the chemical composition of hippuric acid, but they agree with those expressed by the late Dr. Golding Bird.

"From what little I have observed," he remarks, "I feel inclined to believe that when an excess of hippuric acid exists, it may always be regarded as traceable to and pathognomonic of the deficient functions of the liver, lungs, or skin, the great emunctories of carbon; or to the use of food deficient in nitrogen. It hence follows that our treatment will consist in appealing to the functions at fault and careuflly regulating the diet."

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## CHAPTER VI.

## ON OXALIC ACID.



### *History.*

OXALIC acid, usually in combination with lime, is constantly present in the urine of the herbivora; it is also found in that of man so frequently as to be regarded almost as a normal constituent. According to Donnè, it occurs especially in the urine of infants, for he has observed that the nuclei of many of the calculi met with in young children are formed of oxalate of lime. Walshe found crystals of oxalate of lime in 28·57 per cent. of all cases in men, and 33 per cent. in women. Roche discovered them in 36 per cent. of all cases. It does not appear that oxalic acid or the soluble oxalates were sought for in these cases, or the per-centage would doubtless have been much higher.

Although as contained in the urine, oxalic acid is usually in combination with lime, yet this is not invariably the case, as a portion of it may exist either in the free state or in combination with potash or soda as a soluble oxalate. This has been proved by the observations of Bird and the more exact experiments first of Wöhler and afterwards of Buckheim. Free oxalic acid, or a soluble oxalate, as oxalate of urea, is also sometimes found in the urine after taking repeated doses of oxalic acid or oxalate of potash.

"Some of the specimens of oxalic urine," according to Bird, "gave a precipitate with salts of lime insoluble in acetic acid and consisting of oxalate of lime. This, in some instances at least, depended on the presence of oxalate of ammonia, or some other soluble salt of the acid."

When oxalic acid or the soluble oxalates are introduced into the stomach, part only appears in the urine in the form in which it was administered, and part invariably as oxalate of lime, the greater portion being lost in the system. Buckheim obtained from 8·23 to 14·52 per cent. of the oxalic acid taken; the acid disappeared equally when given in the form of a soluble oxalate. When oxalate of lime itself is taken, the proportion of the salt recovered in the urine is under two per cent.

From these results of experiments the practical observation may be deduced, that the quantity of oxalic acid or oxalate of lime in the urine rarely, if ever, represents anything like the amount circulating in the blood.

The reason that oxalic acid is usually encountered in the urine in combination with lime, is found in the circumstance of the chemical affinity which exists between those two bodies, and which is so strong that oxalic acid will separate lime from all other combinations.

### CHEMICAL CHARACTERS OF OXALIC ACID AND OXALATE OF LIME.

*Oxalic acid* crystallizes in combination with three atoms of water: it effloresces on exposure to the air, and loses the whole of its water of crystallization, crumbling into a white powder; heated, it becomes decomposed into *carbonic oxide* and *carbonic acid, formic acid*, and water: it dissolves much more readily in hot than in cold water, and is soluble in four parts of spirits of wine. On boiling oxalic acid with a solution of oxide of gold, carbonic acid is evolved and the gold precipitated as a black powder: treated with concentrated sulphuric acid it is decomposed into carbonic oxide and carbonic acid; by oxidizing agents, as nitric acid, peroxide of lead, or permanganate of potash, it is also transformed into carbonic acid. It combines with alkalies in three proportions, forming oxalates, none of which are soluble in alcohol.

*Composition.*—Anhydrous oxalic acid has the following atomic and per-centage compositions:—

| | | |
|---|---|---|
| Carbon . . . | 2 . . . . . . | 33·33 |
| Oxygen . . . | 3 . . . . . . | 66·67 |
| Atomic number . | 36 | 100·00 |

Crystallized oxalic acid contains 3 atoms of water of crystallization, and its atomic number is therefore 63.

Sugar, by the oxidizing action of nitric acid, is readily converted into oxalic acid.

*Oxalate of lime* is a white, tasteless, and, as it occurs in the urine, a crystalline and glistening powder, containing two atoms of water of crystallization, and having, therefore, the following atomic constitution:—$C_2O_3 + CaO + 2\,HO$. Atomic number, 82. At 212° F.

it loses one atom of water: at 500° F. it becomes anhydrous. Exposed to the air it loses half its water of crystallization: it is insoluble in boiling water, boiling urine, and ammonia; it is scarcely acted upon by oxalic or acetic acid, but is dissolved by nitric and hydrochloric acids: in strong hot hydrochloric acid, it is in part decomposed into chloride of calcium and free oxalic acid. It becomes changed, when burned, into carbonate of lime.

### *On the Amount of Oxalic Acid in the Urine in Health.*

Scarcely anything has hitherto been done to determine the normal amount of oxalic acid or oxalate of lime occurring in the urine. Until this branch of the subject has been investigated, our knowledge of the pathology of this acid will necessarily be very incomplete.

Böcker found that in his own case, he being in good health, the average amount of oxalic excreted in twenty-four hours was 1·42 grains; but of course this quantity is greatly exceeded in disease.

### *On the Relation subsisting between Oxalic and Uric Acids.*

A variety of circumstances prove the intimate relation which exists between *oxalic and uric acid*, a relation which, on the ground simply of their chemical composition, would never have been suspected, the one of these acids being a nitrogenous and the other a non-nitrogenous compound. We should rather have been led to expect that the stronger evidence would have been in favour of a connexion between oxalic acid and sugar in the urine; but this is not so, however.

Many years since, Dr. Prout observed the relationship between oxalic and uric acids. From an analysis of twelve cases of oxalic calculus, he states we are authorized to draw the conclusion, "That from the dissection of calculi formerly mentioned, it appears that the oxalate of lime diathesis is preceded and followed by the lithic acid diathesis, a circumstance which seems to be peculiar to these two forms of deposit, and when taken in connexion with the other circumstances already related, appears to show that they are of the same general nature."

Dr. Bird has likewise remarked, that these two deposits occur so frequently together as to indicate some intimate connexion between them. Out of 85 specimens of urine,

| | |
|---|---|
| Oxalate was present, unmixed, in . . . . . | 43 cases |
| Mixed with urates . . . . . . . . . . | 15 „ |
| Mixed with uric acid . . . . . . . . . | 15 „ |
| Mixed with triple phosphate . . . . . | 4 „ |
| Phosphate deposited by heat . . . . . | 8 „ |
| | 85 „ |

But a variety of other facts and observations prove what, looking at the constitution of the two acids, would hardly have been anticipated.

Thus, when uric acid is subjected to the action of oxidizing agents out of the body, as was first more particularly shown by Liebig, it is converted into a variety of compounds. If the supply of oxygen be but limited, it is changed into *alloxan* and *urea;* if larger, the alloxan is transformed into either *oxalic acid* and *urea*, or into *oxaluric* and *parabanic* acids; and if it be still greater, into *carbonic acid* and *urea*. The conversion of uric acid into urea and oxalic acid, Liebig regards as the normal process occurring within the body.

The researches of Dr. Aldridge confirm the fact, that oxalic acid is one of the products of the decomposition of uric acid. He has shown that by the addition of the elements of water, in different proportions, uric acid may be theoretically converted into oxalate and carbonate of ammonia, hydrocyanic and formic acids; and that simply by heating urine, and in some cases evaporating it, it may be made to furnish oxalate of lime as well as evidences of the presence of hydrocyanic and formic acids.

Again, Wöhler and Frerichs found that when urate of ammonia was injected into the stomach of a dog, crystals of oxalate of lime appeared with but very little urate; a deposit of oxalate of lime likewise occurred in the urine of a man after taking urate of ammonia. At the same time it was proved that more *urea* was eliminated than under ordinary conditions.

Dr. Ranke has informed Dr. Parkes, that fermentation in the presence of an alkali will give rise to the production of oxalic acid from uric acid; and in this way, in some cases, it may be formed in the urine after emission.

In the treatise of Dr. G. O. Rees on Calculous Disease, the following remarks occur on the conversion of the urates into oxalic acid, by simply boiling the urine:—

"If urine loaded with the lateritious sediment (urate of ammonia) be gently heated, the whole deposit, as is well known, will disappear. On allowing the specimen to cool, the sediment is generally again observed; but if we compare microscopically the sediments as seen both in the urine after excretion and as re-deposited after solution by heat, we shall, in many cases, find a quantity of crystals of oxalate of lime in the last. So complete sometimes is the change effected, that the original deposit never appears again, while we find, on allowing the urine to stand a few hours, that oxalate of lime is present in abundance. These facts will show how impossible it is to determine whether or not oxalic acid or its compounds really exist in the blood, by a method of analysis requiring the application of continued heat."

Lastly, it has been ascertained that the urate of ammonia contained in recent samples of guano becomes after a time converted into oxalate of ammonia. This change sometimes occurs in the course of the homeward voyage.

It should here be stated, that Parkes and Racle found that when they boiled the urates in water, no conversion into oxalic acid occurred: indeed, Parkes never succeeded in transforming uric into oxalic acid, unless with the aid of oxidizing agents. Again, Neubauer denies that uric acid is ever transformed in the urine into oxalic acid by the action of the mucus, or in any other way.

The facts adduced are, at all events, sufficient to establish a very close connexion between oxalic and uric acids, and they render it highly probable that the latter acid is sometimes converted in the system into, amongst other products, oxalic acid; but it may, we think, still be considered as extremely doubtful whether, under any natural or ordinary combination of circumstances, uric acid, by its decomposition in the urine subsequent to its emission, yields oxalic acid.

These transformations of uric into oxalic acid, whatever be the precise circumstances which determine them in the animal economy, are, as will be shown hereafter, of great practical importance.

### *Determination of Oxalic Acid and Oxalate of Lime.*

It is usually sufficient for practical purposes to determine that oxalate of lime is persistently present in the urine in considerable amount, and it is but seldom that a quantitative analysis will be required.

When requisite, however, we should adopt such a process as will furnish us with the whole amount of the oxalic acid contained in the urine of twenty-four hours, and which may be present in one or more of its three forms or states—free, combined with the alkalies forming soluble oxalates, or with lime: part of the oxalate of lime may be in solution and part precipitated.

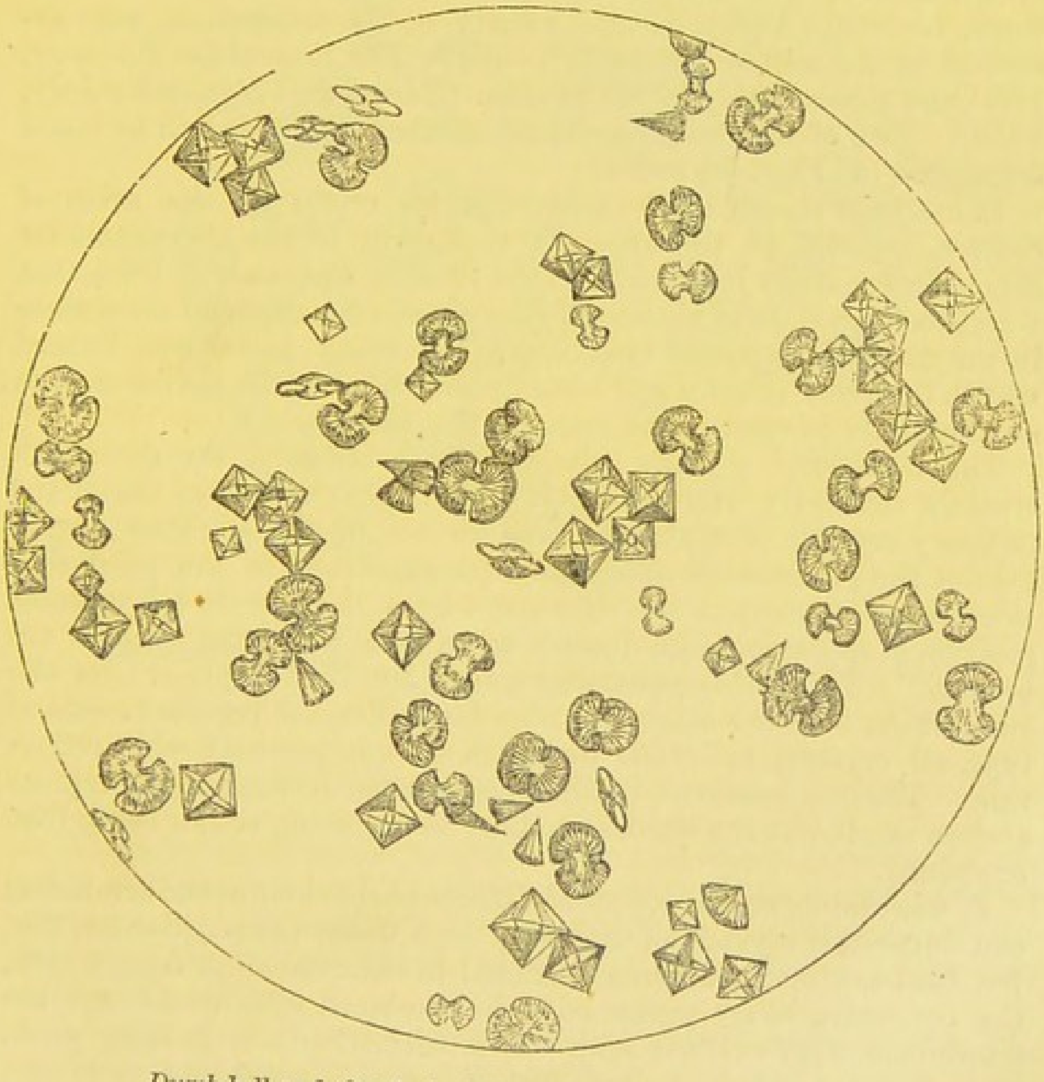
The following process may be adopted. The urine should be evaporated to about one-fourth its bulk, neutralized with ammonia, be strongly acidulated with acetic acid to keep the phosphates dissolved, and then a solution of chloride of calcium added. The oxalate of lime formed must be separated by filtration, dried, converted into either the carbonate or the sulphate in the usual manner, weighed, and the oxalic acid calculated from the resulting carbonate or sulphate. If there is any reason to suppose that the oxalate is mixed with uric acid, we must proceed as follows:—Dissolve in hydrochloric acid, filter, neutralize with ammonia, and again acidulate with acetic acid.

Should any oxalate of lime have become deposited before commencing the analysis, this may either be separated or redissolved.

## MICROSCOPICAL CHARACTERS OF OXALATE OF LIME.

Whenever oxalate of lime is present in the urine in any quantity, it forms a crystalline deposit. The subsidence of this deposit is usually very gradual and occupies some hours. In some cases the oxalate of lime is not separated from the urine for two or even three days after its emission, a fact which has been noticed by several observers, and which has been variously explained. Neither when it

Fig. 37.



*Dumb-bell* and *Octohedral* Crystals of Oxalate of Lime. Magnified 220 diameters.

has subsided does it form a compact deposit like that of uric acid or the earthy phosphates, but the crystals, intermixed with the mucus and epithelium of the urine, form a cloud-like deposit.

For the detection of these crystals, nothing further is required than that, after subsidence, a few drops of the urine at the bottom of the bottle or glass containing it, should be examined under the microscope: they may be completely separated from the urine by filtration.

The crystals are not wholly composed of oxalate of lime; this is shown by the action of either dilute hydrochloric or nitric acid; these dissolve out the calcareous salt, but leave a matrix of fibrinous matter, which still retains the original form of the crystals.

Oxalate of lime crystallizes in the urine in two principal forms, the octohedron and the dumb-bell, each of which presents several modifications (Figs. 37 and 38). Some of the more remarkable of these, including the prismatic variety of the octohedron, were described by the author for the first time in *The Lancet* for February, 1850, and subsequently in the *Medico-Chirurgical Review* for July, 1853. Two of the more important of these varieties will be found delineated in Figs. 40 and 41.

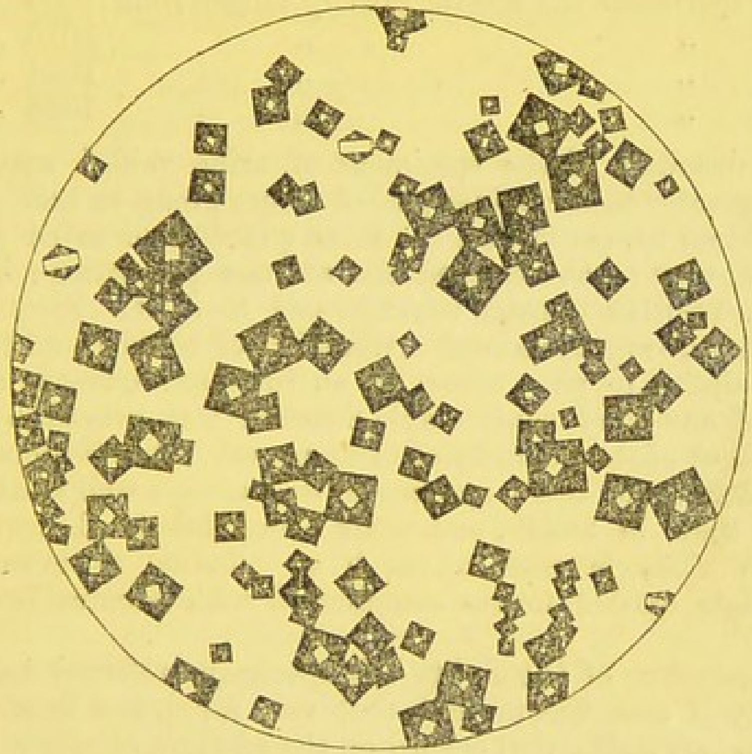
It has been shown by the author, in his report on the urine of cholera, printed in the appendix to Report of the Committee for Scientific Inquiries in relation to the Cholera Epidemic of 1854, that dumb-bell crystals of oxalate of lime are of very common occurrence in the first urines passed in cholera, they being sometimes formed within the renal tubules and actually imbedded in the fibrinous casts so commonly present in the urine in that disease.

The octohedral crystals polarize light feebly only, the dumb-bell crystals decidedly and strongly. Dr. Bird has stated that "the ordinary crystals of oxalate of lime do not in the slightest degree exhibit the phenomena of colour when examined in the polarizing microscope; merely in the slightest degree, if lying in a favourable position; appearing illuminated when the polarizing prisms are crossed." This feeble polarizing action, Dr. Bird explained on the supposition that the octohedra were formed on the regular or cubical type, all crystals referrible to which do not possess double refraction. The fact, however, is, that they are not formed on the regular system at all, but the quadratic, their decomposing action being thus explained.

It was mainly on the supposed different behaviour of the octohedral and dumb-bell crystals of oxalate of lime under the polariscope, that Dr. Bird assumed a difference existed in their chemical composition, the octohedra being presumed to be combined with oxalic and the dumb-bells with oxaluric acid. The distinction not holding good, there does not remain a single fact, chemical or optical, to prove that they are not of the same composition.

It appears that urines which furnish a deposit of oxalate of lime usually contain an excess of epithelium. "One very constant phenomenon," states Dr. Bird, "is observed in the microscopic examination of oxalic urine—viz., the presence of a very large quantity of epithelial cells: it is indeed the exception to the general rule to meet with this form of urine free from such an admixture. So constantly has it been found, that a white deposit of epithelium has repeatedly attracted my attention, and led to the suspicion of the probable presence of oxalate of lime."

FIG. 38.



*Octohedral* Crystals of OXALATE of LIME, viewed in the dry state. Magnified 100 diameters.

### *Characters of Urine depositing Oxalate of Lime.*

We have not been able to connect the presence of oxalate of lime with any constant and peculiar characters of the urine. On the contrary, we have met with it in urines of almost every class and variety. We will, therefore, under this head, simply quote from Dr. Bird's work.

"In the great majority of cases the urine is of a fine amber hue, often darker than in health, but never presenting to my view any approach to the greenish tint which has been described as characteristic of this secretion during the presence of the oxalic diathesis, unless the colouring matter of blood be present. In a few cases the urine was paler than natural, and this was always of lower specific gravity. This, however, was in most instances but a transient alteration, depending upon accidental causes; the odour was generally natural, rarely aromatic, like mignonette. In many instances a deposit of urates, occasionally tinted pink by purpurine, fell during cooling. . . The specific gravity of oxalic urine varies extremely; in rather more than half the specimens being, however, between 1015 and 1025. In eighty-five different specimens, of which I preserved notes, the ratio of the densities was as follows :—

| | | | | |
|---|---|---|---|---|
| "In 9 | specimens | the specific gravity ranged from | 1000 to | 1015 |
| " 27 | " | " | 1016 " | 1020 |
| " 23 | " | " | 1021 " | 1025 |
| " 26 | " | " | 1025 " | 1030 |

"The densities of the specimens of urine voided were, on the average, greater in the urines passed before going to bed.

"It seldom happened that the total quantity of urine passed in these cases very much exceeded the average proportion; in a very few only, positive diuresis could be said to exist. Frequently the patients have, from occasional irritability of bladder, mistaken the frequent desire to pass urine for an increased quantity; but the absence of any very considerable increase was proved by positive measurement of the quantity of urine passed in twenty-four hours.

"The acidity of these specimens was always well marked, often more so than in health, and never being absent. I have not yet met with a single case in which an alkaline or even positive neutral state existed, unless complicated with calculus or diseased bladder."

In twenty-four of the eighty-five specimens referred to, so large a quantity of urea was present, that very rapid, and in some almost immediate, crystallization ensued on the addition of nitric acid. In general, in cases where the greatest excess of urea was present, the largest and most abundant crystals of the oxalate were detected.

Lastly, Mr. Stallard, of Leicester, has observed that the indeterminate organic matters are greatly increased, sometimes doubled, in oxalic urine.

A singular gelatinization of the urine has been noticed in some cases by Dr. Bird, in reference to which we find the following remark :—"During the application of heat, the urine underwent a remarkable change. It did not become opaque or coagulate, but assumed a gelatinous consistence, retaining its transparency. It then required violent agitation to diffuse it through water. This effect, at the time new to me, I have since repeatedly observed, and it seems to chiefly arise from the urates combining with the water, thus forming a gelatinous hydrate."

### *Is Oxalic Acid formed in the Blood or in the Urine?*

This is a very important question, and one which has already been considered to some extent. Is the oxalic acid formed in the blood or in the urine in those cases in which its presence in the renal excretion cannot be traced to the food or other articles consumed?

The fact that oxalic acid and the soluble oxalates, whether given separately or contained in articles of food or medicine, are absorbed into the blood and other fluids of the system, and appear again in the urine, proves that this acid, either free or combined, is capable of passing through the system unchanged. This circumstance alone shows that no chemical reason exists why oxalic acid should not be formed in the blood.

But Dr. Garrod, by the following plan of proceeding, succeeded in detecting oxalic acid in combination with lime in the blood. The serum of the blood was evaporated to dryness and digested in alcohol, the insoluble residue was repeatedly treated with boiling water, the solution evaporated, and mixed with acetic acid for the purpose of detecting uric acid. Instead of crystals of this acid, a white deposit of oxalate of lime, in the form of octohedral crystals, appeared.

To this experiment Dr. Owen Rees has objected that, since the uric acid of the urates of the urine is often converted into oxalic acid by the simple operation of boiling that secretion, the oxalic acid discovered in the blood probably did not exist in it originally, but was formed in it under the action of the heat employed in the process followed by Dr. Garrod. In reply to this objection, it may be urged that, according to Parkes and Racle, boiling with hot water will not convert the uric acid of the urates into oxalic acid.

Again, it has been stated, on the authority of Mr. Rose, that when certain articles of consumption are partaken of, as turnips, which do not contain oxalic acid in any form, yet that acid, in combination with lime, very generally makes its appearance in the urine.

Lastly, oxalate of lime, as already noticed, is frequently met with in the crystalline form in the renal tubes in cases of cholera.

There is no question, therefore, but that oxalic acid is in some cases formed *in the blood.*

The facts urged in favour of the view advocated by Dr. Rees, that the oxalic acid is always formed *in the urine,* either in the urinary organs or after it has been voided, are:—

First, that uric acid and the urates are, out of the body, by various agencies, readily converted into oxalic acid, and even by simply boiling the urine. Dr. Aldridge has arrived at the same conclusion: nevertheless, the point is still open to doubt. Parkes and Racle, as already stated, found that simply boiling the urates in water was not sufficient to occasion the formation of oxalic acid, while, as before mentioned, Neubauer denies that it is ever formed in any way from uric acid in the urine.

Second, that oxalate of lime in some cases makes its appearance, after the lapse of one or more days, in urines in which at first it was not present; also, that when the oxalate of lime already formed has been completely separated from any urine by filtration, a second quantity of the oxalate often appears in the same urine. These facts have been repeatedly observed, but they are by no means conclusive, and are susceptible of a wholly different interpretation.

The appearance of oxalate of lime in the urine some time after being voided, admits of two explanations, independent of its derivation from uric acid or the urates.

First, oxalic acid, free or in the form of soluble oxalates, might be excreted by the kidneys, and the acid subsequently and gradually only become united to the lime, forming an oxalate of lime, the base being abstracted from the phosphate of lime always present in the urine.

Or the oxalate of lime may be excreted from the blood as such, and be held in solution by some means not as yet fully determined, for a time only, subsequent to its being voided.

Thus Dr. Schmidt has assumed that there exists in the animal economy a tendency to the formation of a soluble compound of oxalic acid, lime, and albumen, the oxalate of lime being set free, and crystallizing, after its passage through the mucous membrane of the urinary passages, either by the decomposition of the albumen or by the action of an acid. In this way, Dr. Bird seemed disposed to explain the precipitation of the oxalate of lime from the blood on the addition of acetic acid, in Dr. Garrod's experiment. Two or three facts may be cited in favour of this view. Thus when crystals are dissolved under the microscope by the action of hydrochloric acid, an animal matrix, composed most probably of fibrin and presenting the form of the crystals, is left, as previously noticed. Again, crystals of oxalate of lime have been observed deposited in the cavities of cells, both in vegetables and animals; indeed, this is their ordinary situation in vegetables: they have even been noticed in the cells of decomposing yeast.

As relating to the views of Dr. Schmidt, the remarks of Lehmann may be quoted:—" That oxalate of lime is at first actually held in solution in filtered urine, and that it does not, as Schmidt supposes, proceed from the mucus of the bladder, is a view which is supported by the experiment which I have often repeated—that in urine which, after thoroughly cooling, was freed from its mucus and urate of soda by filtration, the most distinct crystals of oxalate of lime might, after a time, be recognised; while no traces of them could either previously be detected in the mucus of the fresh urine, or be found after the residue on the filter had been for some time in contact with water.

" We may very easily convince ourselves that oxalate of lime is present in a state of solution, by extracting the solid residue of filtered urine with not too concentrated spirit, and agitating the spirituous extract with ether: after the extraction with ether, there may be observed in the alcoholic extract a sediment insoluble in water, which consists of the most beautiful crystals of this salt. While in the acid urinary fermentation the separation of the oxalate of lime increases with the augmentation of the free acid of the urine, in the latter case the salt is separated by the removal of the free acid."

It is nevertheless a fact, confirmed by many observers, that oxalate of lime is often deposited upon the surface of mucous membrane. This has been noticed to be the case especially with the mucous membrane of the *gall-bladder* and *uterus*.

Scherer also refers the precipitation of the oxalate of lime to the acid urinary fermentation.

## ON THE SOURCES OF OXALIC ACID.

The oxalic acid found in the urine may be traced to several distinct sources.

### *To certain Articles of Food.*

There are several articles of consumption which contain oxalic acid, usually in the form of oxalates, the use of which is always followed by the appearance in the urine of oxalate of lime. Amongst these the following may be named—rhubarb, sorrel, onions, and tomato.

Gallois makes the curious statement, that if sorrel be taken for some time, oxalate of lime, although at first abundant, soon ceases to appear in the urine.

Onions contain oxalate of lime; but since this is scarcely acted upon by the stomach, they do not, under ordinary circumstances, give rise to the presence of that substance, but do so in certain deranged conditions of digestion.

There are also certain articles of food not containing oxalic acid, the use of which, especially when digestion is deranged, is followed by the formation of oxalate of lime and its presence in the renal excretion.

Thus Dr. Prout has stated, that he has known the use of sugar in excess in cases of dyspepsia to give rise to the formation of oxalate of lime, and ultimately to lead to oxalic calculus.

According to MM. Robin and Verdeil, frothy or sparkling wines, and beers which are rich in carbonic acid, also give rise to the appearance of oxalate of lime in the urine.

Again, Mr. Rose, of Swaffham, has shown by careful researches, that many articles of ordinary diet, as turnips, parsnips, and carrots, occasion, especially in certain states of health, "a temporary oxaluria."

Cauliflowers and asparagus likewise occasion the appearance of a few crystals of oxalate of lime in the urine.

Dr. Bird, as shown by the following remarks, arrived at a similar conclusion. "That some very slight disturbing causes influencing the assimilating functions will give rise to the presence of oxalate in the urine is perfectly true, even when the food taken does not contain oxalic acid ready formed; but this is generally a temporary change, and soon disappears on the removal of the exciting cause."

*To certain Medicinal Substances.*

According to MM. Robin and Verdeil, the alkaline bicarbonates and the other alkaline salts with a vegetable acid augment the quantity of oxalate of lime in the urine.

Again, when essence of bitter almonds, deprived of hydrocyanic acid, or any urate, is injected into the stomach, oxalate of lime is met with in the urine.

*To Disorders of the Respiratory Organs, impeding their Functions.*

Whenever the decarbonizing functions of the lungs are impaired, an excess of carbonic acid is contained in the blood, leading to the formation of oxalic acid. Such, at least, is the opinion of Lehmann, as will be apparent on a perusal of the following remarks :—" In all the well-marked cases to which I have alluded, the increase of the oxalate of lime seemed to be combined with disturbance of the respiratory process. Thus it may easily be understood, why, after the use of drinks rich in carbonic acid, of alkaline bicarbonates, or vegetable salts, oxalic acid is increased in the urine; superfluous carbonic acid, which has entered the blood, or been generated there from the salts of organic acids, must obstruct the absorption of oxygen and the perfect oxidation of certain substances in the blood; hence also the quantity of oxalate of lime has been found to be increased by the partially impeded exchange of oxygen and carbonic acid in the lungs, consequent on emphysema, pulmonary compression during pregnancy, &c. We might in such cases assume, according to a formerly prevalent belief, that the kidneys in some degree acted vicariously for the lungs, since under the form of oxalic acid they remove from the organism the carbon which the latter organs would have excreted as carbonic acid."

This view is also entertained by Schmidt of Dorpat, and Pavy has recorded the occurrence of much oxalate of lime in the urine of animals whose respiration, while under experiment, was greatly impeded.

*To Mal-assimilation.*

The fact has already been referred to, that certain articles of food not containing oxalic acid yet give rise to the formation of oxalate of lime and its presence in the urine, owing to some defect or derangement of digestion; in other words, to mal-assimilation. Under this head some further remarks by Bird may be quoted :—

" From the symptoms presented in cases of this disease, there is no difficulty in proving to a demonstration the positive and constant existence of serious functional derangement of the digestive organs, especially the stomach, duodenum, and liver; and further, that the quantity of oxalic acid generated is, to a very considerable extent, under the control of diet; some articles of food quite free from oxalic acid at once causing the excretion of this substance in very large quantities, whilst others appear to have the effect of nearly totally checking it. These circumstances alone, together with the emaciation so generally present in the disease under consideration, at once prove, that whatever be the immediate agent which causes the kidneys to secrete the oxalic acid from the blood, the primary cause must, as Dr. Prout has well and satisfactorily shown, be referred to an unhealthy condition of the digestive and assimilative functions."

Again, the same author has remarked: "It may, however, be asked, from whence are the nitrogenized matters derived, whose metamorphic changes give rise to the formation of oxalic acid? Are they derived from the tissues of the body, like healthy urea and uric acid? Of course, it is quite possible that such may be their origin; but as the quantity of oxalate of lime deposited from the urine is always greatest after a full meal, and often absent in the *urina sanguinis*, or that passed on rising in the morning, frequently disappearing under the influence of a carefully regulated diet, and reappearing on returning to the use of unwholesome food, it is highly probable that this salt is, in the majority of cases, primarily derived from the mal-assimilated elements of food, and not, like uric acid, generally, a product of metamorphosed tissues."

### *To Metamorphosis of Tissue.*

Another source to which the oxalic acid of the oxalate of lime of the urine may be traced is the metamorphosis of tissue, it in some cases being the immediate result of the metamorphosis, but more frequently its formation being indirect, it being derived either from the uric acid or more rarely the urea first formed.

It would appear that there are good reasons for believing that the oxalic acid may proceed from the metamorphosis of either the *non-nitrogenous* or the *nitrogenous* tissues.

Amongst the former is included fat and some other hydrocarbons, the metamorphosis of which may be arrested at the stage of oxalic acid, and not go on, as is ordinarily the case, to the formation of carbonic acid.

According to Lehmann, when oxalic acid occurs in large amount in the urine, lactic acid is also met with, and this results from the decomposition of the hydrocarbons.

Out of the body and by means of oxidizing agents, a variety of substances, both nitrogenous and non-nitrogenous, in addition to uric acid may be made to yield oxalic acid, as creatine, guanine, leucine, and tyrosine, fat, starch, sugar, lactic, tartaric, malic, citric, butyric, and metacetonic acid. To what extent any of these compounds undergo this decomposition in the body is undetermined, although, as already mentioned, Wöhler and Frerichs found that when uric acid or the urates were taken, not only was the urea increased, but sediments of oxalate of lime occurred.

In reference to the origin of oxalic acid in the disintegration of tissue we meet with the following remarks in Dr. Bird's "Urinary Deposits:"—

"Indeed, I am convinced that traces of this salt in the minutest microscopic crystals are to be detected in the urine of persons who are free from any apparent disease. Hence oxalate of lime must be regarded as one of the common results of the metamorphosis of tissue; but the existence of the traces of the substance (which indeed may be regarded as a physiological condition) is a very different thing from its presence in large crystals and considerable quantities, and which can be only deemed as existing under a state of system strictly pathological."

In another place Dr. Bird has thus expressed himself:—"I am inclined to the opinion, though not as yet furnished with sufficient evidence to assert it confidently, that whenever the crystals of oxalate of lime are not to be found in the morning urine, *i.e.* in the *urina sanguinis*, the case is more one of ordinary dyspepsia, the deposit being the result of changes in the nitrogenized food, and may generally be relieved by the usual treatment; but that if not so relieved, it passes on to the stage of confirmed oxaluria, when the deposit is due to the abnormal destructive assimilation of effete tissues."

*To the Transformation of Uric Acid in the Urine.*

A last source of oxalic acid may possibly be found, as already shown, in the transformation of the uric acid of the urine subsequent to emission: of the reality of this mode of origin, however probable, exact proofs still appear to be wanting.

The statement, already noticed, of Ranke, that uric acid is decomposed and oxalic acid produced, by fermentation in the presence of an alkali, suggests the probability of such a conversion in alkaline and stale urine.

On the other hand, the statements of Owen Rees and Aldridge, that uric acid and the urates furnish oxalic acid when the urine containing them is simply heated or boiled, is questioned by several observers, as Parkes, Racle, and Neubauer.

Altogether, it does not appear proved that the conversion of uric acid after emission is a source of oxalic acid.

The fact that in some cases much of the oxalate of lime of the urine is not always precipitated immediately, but is held in solution for one or more days, is obviously no proof of such conversion, since it may be more naturally explained on the supposition that the precipitation is determined by changes in some of the other constituents of the urine to which its solution is due.

In those cases in which the oxalate of lime makes its appearance quickly and in perfectly fresh urines, there is but little probability of its being derived from uric acid either in the bladder or in the urine after emission, although, probably, it may in some cases result from the transformation of uric acid in the blood.

No evidence has hitherto been adduced to show that oxalic acid is ever produced in the blood or urine from the decomposition of urea.

## ON THE PATHOLOGY OF OXALIC ACID AND OXALATE OF LIME IN THE URINE.

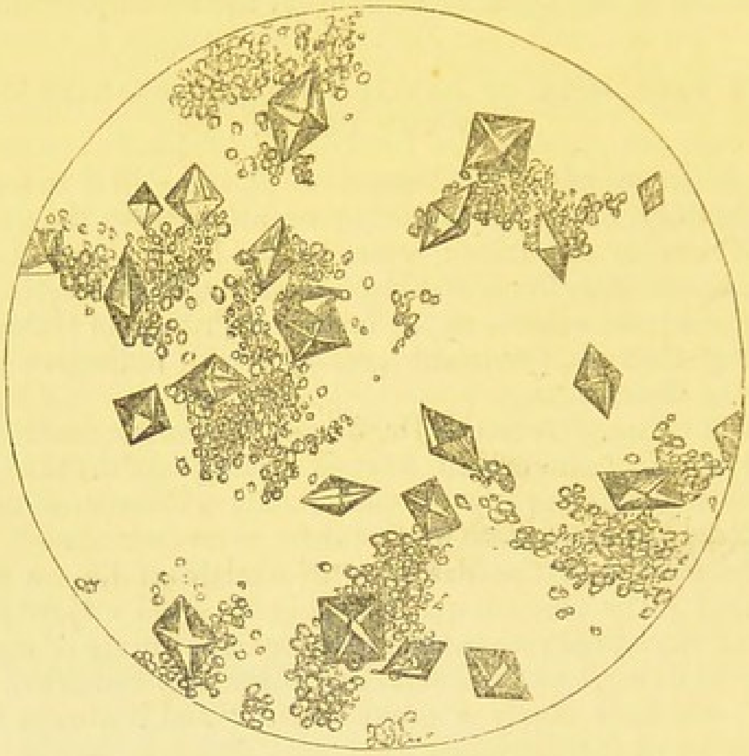
Much difference of opinion has prevailed, and still does so, respecting the signification which ought to be attached to the presence of oxalate of lime in the urine: some, as Dr. Bence Jones, Lehmann, and, in a less degree, Dr. Owen Rees, regarding its occurrence of but little moment; and others, as the late Drs. Prout and Golding Bird, considering that its persistent presence was indicative of grave pathological disturbance.

"Oxalate of lime," remarks Dr. Jones, "is so frequently found in the urine of those who are in a good state of health, that I do not consider it as indicating any disease, but only a disorder of no serious moment." In another place we find these observations:—"You will be inclined to ask, Is the detection of oxalate of lime a matter of importance? The true answer is, that in the great majority of cases it is not of more importance than the deposit of urate of ammonia." "It may, however," he somewhat contradictorily remarks, "form a calculus," which is surely a grave result, "and it always indicates some disorder of the digestion."

Dr. Jones cites Lehmann in confirmation of his views. Lehmann certainly dissents from some of the statements of Bird; but still he does not deny the pathological importance of the presence of this salt in the urine. "In reference to the occurrence of oxalate of lime in certain morbid conditions, Prout, Bird, and others make very different statements, none of which are yet fully established." And, again, he remarks: "In the dyspeptic conditions in which Prout and Bird have found sediments of oxalate of lime, I have failed in discovering anything of the sort. On the contrary, I have generally found the sediments in the urine of such patients to be free from these crystals." Lehmann, however, as will be mentioned presently, has detected the presence of deposits of oxalate of lime in a variety of affections, and his chemical views of its relation go to prove that its occurrence in the renal excretion is pathologically of high importance.

Dr. Owen Rees writes, "I have, in fact, entirely failed to detect the peculiar pathological conditions which have been said to connect themselves with the oxalic acid diathesis, and am every day more confirmed in my opinion, that it must be regarded, as I have before suggested, as an accidental and unimportant modification of that most significant variation from health which consists in the excretion of uric acid or its compounds in abnormally increased proportion." A few lines further on he observes: "This last proposition involves

FIG. 39.



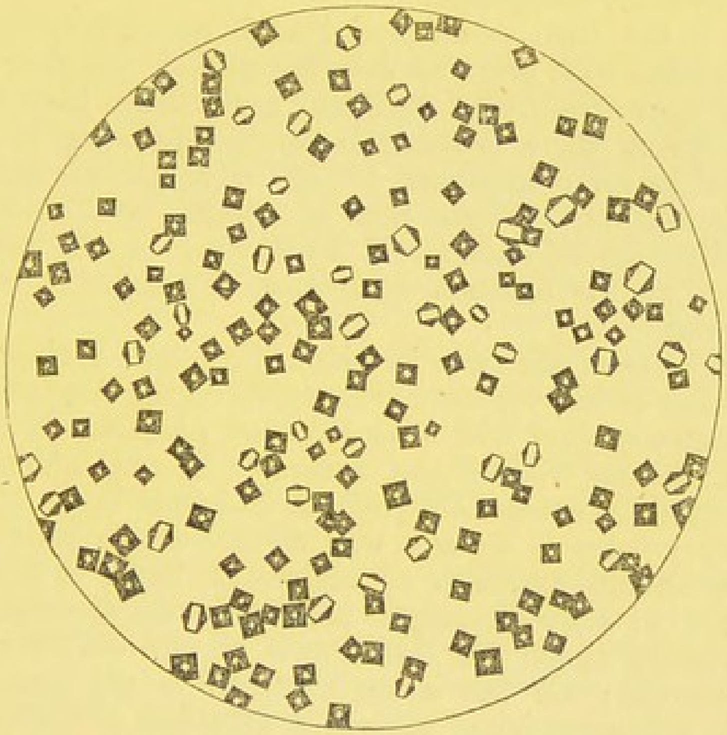
Crystals of OXALATE of LIME having the appearance of *elongated octohedra*, arising from the oblique position in which they are viewed. From Saccharine Urine. Magnified 220 diameters. 1852.

the necessity of proving that the gouty diathesis is present where oxalate of lime prevails." Again observes Dr. Rees: "The chemical reasoning which shows how unlikely it is that oxalate of lime should exist in the blood, is quite borne out by the pathological bearing of the case; and the conclusion appears to my mind quite inevitable, that, whenever oxalate of lime is found in the urine, it should be regarded as *produced* after *excretion*, and that there is no such thing existing as an oxalic diathesis."

These remarks, so far from proving that deposits of oxalate of lime are of but little moment, it appears to the author, just prove the very contrary. The fact of placing oxalic acid in intimate relation—chemically, physiologically, and pathologically—with uric acid, is alone a sufficient acknowledgment of its importance.

The discrepancy in the views quoted above admits, in a measure, of explanation, on the ground that those writers who attach but little significance to the presence of oxalate of lime in the urine, have not sufficiently considered the varying circumstances attending its appearance and occurrence. When derived from the food or medicine consumed, and which previously contained it, it is, of course, of but little moment; but when due to either mal-assimilation, to the transformation of tissue, or even the decomposition of uric acid, it is certainly of not less consequence than deposits of uric acid or the urates.

FIG. 40.



Octohedral Crystals of OXALATE of LIME, with intervening *prism*. Drawing made from preparation lent the author many years since by the late Dr. Golding Bird. Magnified 220 diameters.

To say that oxalate of lime sometimes occurs in the urine without its presence being accompanied by any appreciable symptoms, and that hence it is of little moment, is by no means conclusive reasoning; for the same remark is frequently applicable to deposits of uric acid and the urates, and it is not even asserted by any that such deposits are without importance.

Further, since oxalate of lime is not uncommonly deposited in the bladder so continuously and in such quantity as to give rise to one of the worst forms of calculus; for this reason alone, if for no other—and there are others of great weight—we can arrive only at the conclusion that under certain circumstances deposits of this oxalate are eminently pathological, and their treatment therefore becomes of extreme importance.

We will now proceed to enumerate the diseases in which deposits of oxalate of lime have been particularly noticed.

According to Walsh and Beneke, oxalate of lime is of common occurrence during *convalescence from severe diseases*, as typhus.

It is met with in the urine in many *chronic diseases*, owing, it is supposed, to lessened oxidation.

It has been observed to occur especially in connexion with *dyspepsia*. This is one important class of cases in which its presence has been specially recognised.

Again, it has been determined that it occurs frequently in the urine associated with uric acid and the urates: this fact, as well as the ready convertibility of uric into oxalic acid, have led to the inference, which there is much reason for believing to be correct, that it is in some instances to be regarded as indicative of the *gouty diathesis*. This view is rendered still more probable by the detection of oxalic acid by Garrod in the blood of the gouty, and by the common occurrence of oxalate of lime in the urine in gout.

Another class of affections in which it has been noticed to be present are those of the respiratory organs, including *emphysema*, particularly when combined with *bronchitis* and *phthisis*. It is Lehmann especially who has noticed the connexion between affections of the lungs and the occurrence of deposits of oxalate of lime. " When the respiratory process is in any way disturbed, we most frequently observe a copious excretion of oxalate of lime: it is most common either in fully developed pulmonary emphysema, or when the pulmonary tissue has lost much of its elasticity after repeated catarrhs; on the other hand, it is not present nearly so often in inflammatory or tubercular affections of the lungs."

In *cirrhosis*, a disease involving another highly important decarbonizing organ, oxalate of lime is frequently met with mixed up with sediments of the urates; it occurs also in *jaundice*.

In *chronic Bright's disease*, while sediments of urates are rare, oxalate of lime is not uncommon.

In the urine passed on recovery from *cholera*, it is almost constantly present, both in the dumb-bell and octohedral forms, the crystals being frequently deposited in the fibrinous casts themselves; likewise so generally present in the urine of cholera.

It is of frequent occurrence in the urine of *scrofulous* and *rickety* children, according to Lehmann.

In *diabetes*, deposits of oxalate of lime, though sometimes met with, are by no means so frequently present as might have been anticipated.

Lehmann states, " I have only met with actually pure sediments of this salt in three persons, who sometimes (at somewhat considerable intervals) suffered from *epileptic attacks*."

It is met with in the urine of *pregnant women*, according to Hofle.

In *seminal losses*, according to Donnè, MM. Robin and Verdeil, and others, it is almost constantly present. The explanation of the occurrence of this salt in these cases is, we believe, to be found in the fact that the fluid itself contains the oxalate.

Many *calculi* are composed, either wholly or in part, of oxalate of lime; it often occurs, as already stated, in the urine together with uric acid and the urates, and it is found in calculi mixed up with these, or with phosphate and carbonate of lime, silica, and oxalate of magnesia.

We have now to notice certain other particulars connected with the pathology of oxalate of lime in the urine. One of these is the increase in the quantity of *urea*, which often accompanies the excretion of the oxalate. This increase has been noticed particularly by Bird, Stallard, and Frick, an American writer.

Dr. Bird states, that in twenty-four out of eighty-five specimens of urine examined, so large a quantity of urea was present, that in some samples very rapid, and in others almost immediate crystallization ensued on the addition of nitric acid; indeed, he regarded the presence of excess of urea almost as characteristic of the morbid state of the urine as the oxalate of lime itself.

Frick states, that not only is the urea increased, but the *phosphates;* and, on the other hand, that uric acid is diminished, it reappearing when the oxalate is absent.

Beneke likewise affirms from very numerous approximate determinations, that the earthy phosphates are in excess.

Mr. Stallard finds that the *indeterminate organic matters* are also greatly increased, often reaching to nearly double the average proportion excreted in twenty-four hours.

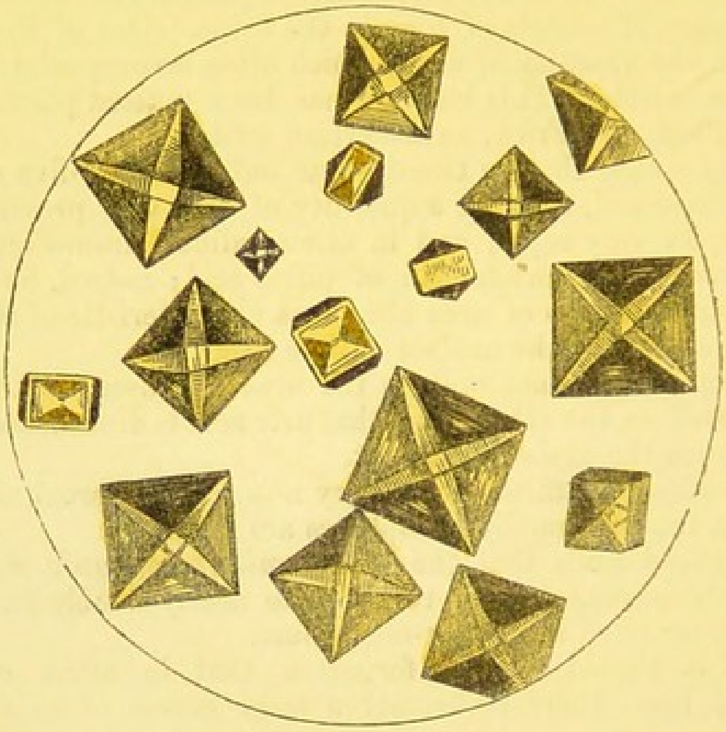
Again, it should not be forgotten that in urine containing oxalate of lime, there is usually a large excess of *epithelium*, a proof that the mucous membrane of the urinary passages is in a state of irritation.

Lastly, contrary to what from chemical reasoning might have been anticipated, it does not appear that any special connexion or relation exists between the presence of oxalic acid and sugar in the urine.

It follows from these particulars that the constitutional effects accompanying the persistent presence of oxalate of lime in the urine are not wholly to be referred to that salt, but are in part due to the excess of urea and phosphates which usually, in true cases (to adopt for once the term used by Dr. Bird) of oxaluria, accompany the oxalate.

One or two remarks may here be appended in regard to the relation of oxalate of lime to the other urinary concretions. It is found that this oxalate forms the nucleus of calculi in the proportion of about 1 to 4; the proportion of oxalic calculi is as 1 to 15: the ratio in which deposition of oxalic acid in alternating calculi succeeds to uric acid is 1 to $15\frac{2}{3}$. On the contrary, the ratio in which uric acid succeeds to oxalate of lime is 1 to $13\frac{5}{23}$; hence the alternation is nearly equal. Oxalate of lime succeeds to the urates in the proportion of 1 to $9\frac{5}{8}$; but the urates succeed to the oxalate only in the proportion of 1 to 38. Oxalate of lime very rarely succeeds to the phosphates; but the phosphates follow the calcareous oxalate in the proportion of 1 to $7\frac{1}{2}$. (Thudichum.)

FIG. 41.



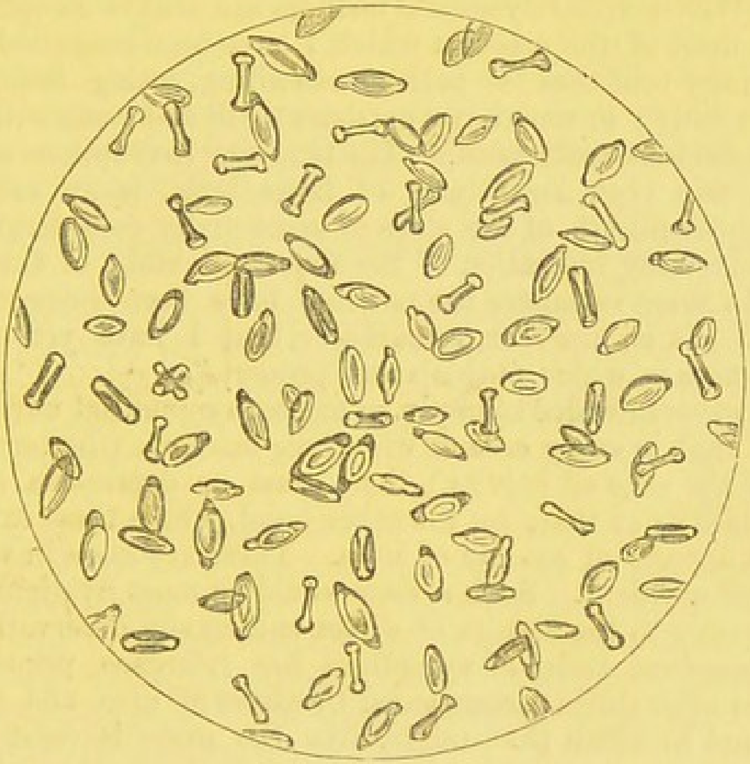
Large *Octohedral* Crystals of OXALATE of LIME, from the *Urine of the Horse*, presenting, in some cases, an intervening *prism*. Magnified 100 diameters. 1849.

### *Symptoms of Oxaluria.*

When we consider how different are the sources from which the oxalic acid of the oxalate of lime of the urine is derived, it is obvious that it would be irrational to expect that its presence would be characterized by a constant and peculiar set of symptoms, or that in certain cases there should be any constitutional disturbance at all. The absence of any well-marked train of symptoms has been urged by various writers in proof of the little importance of deposits of oxalate of lime. This mode of reasoning carries but little weight;

and it might be applied to almost every other deposit and substance occurring in the urine. The fact that the same symptoms are not invariably present in all cases, was fully recognised by Bird: who, however, grouped together certain symptoms as being ordinarily associated with true oxaluria.

FIG. 42.



*Modified Dumb-bell* or *Navicular* Crystals of OXALATE of LIME. Magnified 160 diameters. 1850.

"Persons affected with the form of the disease referrible to this class, are generally remarkably depressed in spirits, and their melancholy aspect has often enabled me to suspect the presence of oxalic acid in the urine. Sometimes a peculiar lurid, greenish hue of the surface has been observed; but more generally the face has the dark and dingy aspect so common in some forms of dyspepsia in which the functions of the liver are deranged. They are generally much emaciated, excepting in slight cases; extremely nervous, and painfully susceptible to external impressions; often hypochondriacal to an intense degree; and in very many cases labour under the impression that they are about to fall victims to consumption. They complain bitterly of incapability of exerting themselves, the slightest exertion bringing on fatigue. Some feverish excitement, with the palms of the hands and soles of the feet dry and parched, especially in the evening, is often present in severe cases. In temper they are irritable and excitable. In men the sensual power is generally deficient and often absent—an effect probably owing to the exhaustion produced by the excessive secretion of urea so common in this affection. A severe and constant pain, or sense of weight, across the loins is generally a constant symptom, with often some amount of irritability of the bladder. The mental faculties are generally but slightly affected, loss of memory being sometimes more or less present. Well-marked dyspeptic feelings are always complained of; indeed, in most of the cases in which I have been consulted, I have been generally told that the patient was ailing, losing flesh, health, and spirits daily; or remaining persistently ill and weak without any definite or demonstrable cause. The tendency to eruptions of minute furunculi, and even sometimes of large boils, is an exceedingly frequent concomitant of the state of urine under consideration, and becomes a striking indication of the depressed state of the general health. In some instances the patients have been suspected to be phthisical. It is, however, remarkable, that I have yet met with very few cases in which phthisis was present."

Dr. Bird never intended to imply, as has been somewhat unreasonably supposed, that in every case of even true oxaluria (the term is used merely for the sake of brevity), there must be depression of spirits and irritability; or that, on the other hand, where these exist, there must be a deposit of oxalate of lime. There are cases in which the two are independent. Such a view would be most irrational, and of course opposed to the results of direct and careful observation.

The preceding train of symptoms has reference principally to those cases of oxaluria accompanied by excess of urea and extractive matters, and in which the oxalate, like the urea, is most probably derived from increased destruction of tissue. In those cases in which there is little or no excess of urea, the oxalate of lime is frequently referrible to derangements of the assimilative functions, and in such cases many of the symptoms previously described may be wanting: in some of them the presence of the oxalate is merely temporary.

There is reason for believing that oxalate of lime acts as an irritant to the mucous membrane of the bladder. In reference to this subject, the following remarks occur in Bird's "Urinary Deposits:" "Among chronic diseases, especially in certain forms of chronic dyspepsia attended by gastralgia, oxalate of lime often abounds in the urine, and seems to act as a local irritant. This is exceedingly frequent amongst persons whose nervous systems become much excited by anxiety and the pressure of important business. It has occurred to me repeatedly to notice this state of things in barristers and solicitors, especially when hard worked. The irritability of bladder, so common an ailment among many members of the legal profession, has been, in so many cases which have fallen under my notice, accompanied by the abundant excretion of crystals of oxalate of lime, and has disappeared on the removal of this deposit, that I cannot avoid regarding this substance as playing the part of a local irritant."

Concretions of oxalate of lime of about the size of hemp-seed, and hence called *hemp-seed calculi*, not unfrequently form in the calyces of the kidneys: they are often numerous; they occasion pain in the region of one or both kidneys, sometimes bloody urine; occasionally they become dislodged and are discharged through the urethra. It has been observed, especially by Prout, that these concretions occur very much more frequently after the prevalence of cholera, a circumstance which is doubtless to be explained by the fact, that the tubules of the kidneys often become, on recovery from an attack of that disease, much obstructed by the deposition within them of oxalate of lime in the crystalline state.

## ON THE TREATMENT OF DEPOSITS OF OXALATE OF LIME.

The first thing to be done before commencing the treatment of a deposit of oxalate of lime, is to determine the source from which it proceeds. We must ascertain whether it is derived :—1. From articles of food or medicine containing oxalic acid, either free or combined. 2. From beverages or other articles rich in carbonic acid. 3. From articles of diet which do not contain oxalic acid, as arrowroot, &c.—that is, from mal-assimilation. 4. Whether from excess of carbonic acid in the blood, resulting from disease of the respiratory or other decarbonizing organs. 5. Whether from abnormal destruction of tissue. 6, and lastly, whether it occurs together with uric acid and the urates, and in connexion with the gouty diathesis.

The source or cause of the deposit being ascertained, the principles of treatment at once become obvious.

When the presence of the oxalate can be traced to the use of articles either containing oxalic acid, or which not containing that acid have yet been found from experience to give rise to its formation, all that is necessary is their discontinuance.

When it is traceable to or associated with mal-assimilation, as indicated by symptoms of disordered digestion, the treatment must be directed to the improvement of the digestive organs.

In those cases in which the deposit is connected with abnormal or excessive metamorphosis of tissue, this condition we must endeavour to rectify.

When the oxalate occurs in connexion with uric acid deposits and is associated with the *gouty* diathesis, our treatment must be specially directed to the primary disease.

Lastly, where it is due to defective action of the lungs, the liver, or other decarbonizing organs, our chief efforts must be directed to the restoration of the functions of those organs.

In the discrimination of the important point, whether the formation of the oxalate of lime is connected with abnormal or undue waste of tissue, we shall be much aided by the characters of the urine. If, the quantity being normal, it be of low or moderate specific gravity, there is reason obviously to conclude that there is no excessive waste of tissue in progress; if, on the other hand, it be of high gravity, this is due to excess of urea and of extractive matters, indicative of increased metamorphosis. This distinction has been well pointed out by Bird, as appears from the following quotation:—

"It may, however, often assist in our diagnosis to recollect that the great acidity, the high specific gravity, and the excess of urea generally present in true oxaluria, will often at once distinguish between a deposit the result of diseased action and one of accidental origin."

In the treatment of all cases of persistent deposit of oxalate of lime, we should not limit our attention too much to any one particular: we must have regard to the nature of the ingesta, the state of the digestive organs, and especially to the right and healthy performance of the functions of the great decarbonizing organs, the lungs, liver, and skin. It should ever be borne in mind there is good reason for believing that the appearance of oxalate of lime in the urine, when not traceable to the ingesta, is connected with defective oxidation.

It is unnecessary to dwell upon the precise means by which these various objects may be accomplished: their character must vary somewhat with the details and peculiarities of each case.

Amongst the particular or special remedies which have been found useful in cases of oxaluria are the mineral acids, especially nitro-hydrochloric acid, mixed in the proportions (and this is a point of some importance) to form *aqua regia*, which consists of one part nitric and two of hydrochloric acid.

It has been noticed by several observers, by Dr. Prout in the first instance, that, under the treatment by the mineral acids, in proportion as the oxalate of lime disappears, uric acid becomes deposited. This has been regarded as a favourable symptom. Whether this really is so has not been proved; it may, however, be suspected that the precipitation of the uric acid is due mostly to the increased acidity of the urine occasioned by the mineral acids.

When any connexion is ascertained or suspected to exist between the oxalic acid deposit and gout, colchicum will frequently be found useful.

When oxalate of lime, uric acid, and the urates are deposited together, we are apparently involved in a contradiction as regards treatment. While the one deposit is often treated with advantage by alkalies, the other requires the mineral acids. In such cases, supposing the deposit of oxalate to be considerable and persistent, the best course appears to be to treat the oxalate of lime in the first instance. In those cases in which the uric acid deposits are constant and in large quantity, alkalies and acids may sometimes be administered with advantage alternately. Suitable tonics, where debility exists, will often be found most serviceable, no matter what may be the nature of the deposit.

When much depression exists ammonia may be prescribed; and in cases attended by anæmia, some of the milder preparations of iron may be given.

When the oxalate of lime acts as a local irritant, as shown by increased discharge of mucus and epithelium, the bladder symptoms will require treatment with demulcents and anodynes.

The presence of blood-globules mixed with the crystals of oxalate of lime renders it probable that a calculus exists either in the kidney or bladder.

Waters containing much lime are specially to be avoided, and distilled water substituted.

The opinion of Dr. Prout may here be again adverted to, that "the oxalate of lime diathesis" and "the lithic acid diathesis are of the same general nature; or, in other words, that the oxalic acid merely takes the place, as it were, of the lithic acid;" and, applying this connexion practically, Dr. Prout held "that the diathesis being of a similar nature, the principles of treatment adopted for counteracting the original tendency to it must be also similar."

In regard to treatment, Dr. Rees remarks, "Perhaps the most important secret in mild cases consists in emptying the intestinal canal, which will sometimes be sufficient to remove the whole mischief."

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# CHAPTER VII.

## ON DIABETIC SUGAR OR GLUCOSE, AND ON DIABETES.



### *History.*

Grape-sugar, or glucose, belongs to the class of chemical compounds termed carbohydrates— that is, of bodies which consist of carbon as a basis, in union with oxygen and hydrogen in the proportion to form water, the number of atoms of carbon and of water differing with different substances, but the carbon always being in multiples of six: this view of the composition of the carbohydrates is extremely simple, and affords the key to the explanation of many of the properties and reactions of bodies of this class.

In the animal economy glucose is formed normally from a substance generated in the *liver*, and which has received the name of *glucogen* or the glucogenic substance.

The sugar thus formed in the healthy animal organism, according to the theory of Bernard, is destroyed by oxidation, principally in the lungs, and hence it does not and cannot make its appearance in the urine; in disease, however, and especially in diabetes, this normal destruction of sugar is arrested, and hence its presence in the renal excretion.

Glucose occurs normally in the *chyle* and in the *blood*. According to Bernard and others, it is either absent from the blood of the *portal* veins or traces only are found, while that of the *hepatic* veins is rich in sugar. In the vessels near the heart it gradually diminishes, and but very little is to be found in arterial blood.

Bernard has found sugar in the fluids of the *amnion* and *allantois* in the calf, lamb, and pig.

The same observer has found it in the *urine* of the *fœtus* of the *cow* between the fifth and seventh months, and in that of the *sheep* at two months. It is doubtful whether it is a normal constituent of human urine; but it is very frequently found there in minute amount; and its presence may be always occasioned by certain injuries to the cerebro-spinal and sympathetic nerves, and even, in some cases, by excess of sugar introduced into the stomach.

Bernard first, and subsequently many other observers, have found sugar in the liver, where they believe it to be, as already mentioned, formed normally.

### CHEMICAL CHARACTERS OF GLUCOSE.

Glucose is only half as soluble as cane-sugar, and not nearly so sweet; it is but slightly soluble in alcohol and not at all so in ether; its aqueous solution turns the plane of polarization of a ray of light to the right.

It melts at 212° F. with the loss of its two atoms of water of crystallization, and at 284° F. it is converted into caramel.

In contact with decomposing animal substances, especially caseine, it undergoes, first the *lactic*, and subsequently the *butyric* fermentation, and with yeast the *vinous* fermentation.

Lactic acid has the same elementary composition as grape-sugar, and this acid may be also transformed into butyric acid.

Digested with nitric acid it is converted into oxalic and saccharic acids; by the action of concentrated sulphuric acid it is partially converted into charcoal; its solution boiled with potash turns of a deep rich reddish-brown colour; lastly, when boiled with a salt of copper and caustic potash, the yellowish suboxide of copper is thrown down. With chloride of sodium it forms a definite crystalline compound, containing 13·3% of the chloride.

| | | | |
|---|---|---|---|
| Glucose consists of | Carbon | 12 | 40·000 |
| | Hydrogen | 12 | 6·666 |
| | Oxygen | 12 | 53·334 |
| $+HO_2$. | | | 100·000 |

The sugar produced by irritation of the base of the brain of animals and liver-sugar are stated by several observers to differ from true diabetic sugar in being more easily decomposed.

The sugar of diabetic urine, if set aside for some time in a stoppered bottle, is sometimes transformed into *mannite* and a viscid gum-like substance.

There is no such variety of grape-sugar as that which used formerly to be called "insipid;" the nearest approach to it is *inosite*, or muscle sugar.

## EXTRACTION OF GLUCOSE.

Glucose may be obtained from diabetic urine by the following process:—The urine is treated with basic acetate of lead, and the excess of lead, after filtration, is removed by means of sulphuretted hydrogen; the liquid is then evaporated and the sugar extracted with alcohol. Lehmann recommends that the urine should be evaporated to the consistence of a syrup: this is to be extracted after a time, first with absolute alcohol and subsequently with hot spirit. The sugar dissolved in the latter is removed, after it has crystallized, by filtration; the spirit is submitted to évaporation and then treated with a little water, whereby a second crop of crystals of sugar is obtained. Glucose may be procured in a state of chemical purity from the compound of sugar and chloride of sodium, by the removal of the salt with sulphate of silver.

## TESTS FOR GLUCOSE.

A whole volume might be written on the subject of the tests for sugar and the fallacies of some of them. It is not proposed to discuss this question at any length, but in as brief and concise a manner as possible to point out the best methods of proceeding for the detection of glucose. When the amount of this in the urine is at all considerable nothing is more easy than to discover its presence, either by the potash or copper tests: it is only when the quantity is small that any difficulty arises.

The principal tests of which it is necessary to treat at all fully are the potash, the copper, and the fermentation tests.

*The Potash Test,*

Termed also More's test.—Two parts of the suspected urine and one of a solution of potash are to be boiled together, when, if glucose be present, the mixture will turn, immediately that the boiling-point has been reached, of a sherry or even molasses brown, more or less deep according to the quantity of glucose, the change of colour depending upon the conversion of the glucose into molassic or saccharic acid. The objection to this test is, that very many, indeed most urines, are deepened one or more shades in colour when boiled with solution of potash; so that this test cannot be relied upon for the detection of a very minute quantity of glucose, since it often gives indications of sugar when none is really present, as shown by the author in a paper published in the *Lancet*, in 1851. When the amount of glucose is at all considerable, it is, however, highly satisfactory.

*Garrod's Glucometer.*—An ingenious application of this test has been made by Dr. Garrod: the principle depends upon the degree of colour produced by boiling diabetic urine and carbonate of potassa together.

The apparatus consists of a standard solution exhibiting the tint produced by half a grain of sugar to the ounce of fluid; a tube of the same diameter as that which holds the standard solution of the potash solution, and an accurate minim measure.

The necessary apparatus and solutions may be procured of Mr. Coxeter.

*The Copper Test,*

Called sometimes *Trommer's* test.—When a solution of caustic potash and a few drops of a dilute solution of sulphate of copper are added to diabetic urine, the mixture becomes of an azure-blue colour, if sugar be present; a precipitate of oxide of copper takes place, which, however, on agitation of the liquid, disappears.

On allowing this mixture to stand at rest for some hours, the suboxide of copper, by the reducing power of the sugar, becomes deposited, it being of a more or less yellow or red tint. If, however, the mixture be at once boiled in a test-tube, the suboxide is immediately thrown down.

The addition of an excess of solution of potash is of no consequence; but if the quantity of sugar present be very small, but little of the solution of copper must be added.

*Fallacies of the Copper test.*—This test, in true diabetic urine, is invariably successful: like the potash test, it is only when the amount of glucose is small that it is liable to mislead. Certain of the fallacies of this test are occasioned by the circumstance that there are other bodies as well as glucose which occasion, under the same circumstances, a precipitation of the suboxide. Amongst these uric acid, the urates, allantoine, creatine, creatinine, and albumen have been enumerated; though this last only does so after prolonged boiling. But, on the other hand, sugar may even be present in the urine, and yet not be detected by this test, as was pointed out by the author some years since.

Several papers were published by the author in the *Lancet*, on the tests for sugar in the urine. Those of the following dates—April 12th, 1851; June 12th, 1852; and January 1st, 1853—had reference exclusively to the copper test. In these communications, especially the last, numerous sources of fallacy were described, affecting more particularly the indications of the copper test.

In the paper published in the *Lancet* of April 12th, 1851, these remarks occur:—

"The next point to determine was, whether small quantities of sugar may be discovered in urine with ease and certainty.

"Two grains of grape-sugar were added to separate ounces of forty-two different urines: in twenty cases only was the test applied in the ordinary manner successful *to any extent;* in the remaining twenty-two it utterly failed.

"We have thus arrived at the fact, as important as unexpected, that sugar may exist in considerable quantities in urine, and yet escape detection by the copper test.

"In order to ascertain, therefore, the cause of failure, I experimented with all the known and ordinary constituents of the urine.

"And first, with urea. From a solution containing one grain of urea and the eighth of a grain of diabetic sugar to the drachm of water, the red oxide, on the application of heat, was thrown down. It is therefore evident that *urea,* as such, does not interfere with the action of this test.

"But urea is convertible into *carbonate of ammonia.* I therefore next tried a solution containing half a grain of that salt and the eighth of a grain of sugar to the drachm of water. The precipitate which was thrown down in this case was of a light reddish-brown colour, probably a mixture of the black and red oxides of copper; with the same quantity of the carbonate and half the sugar, the precipitate was still darker.

"Now, it is stated by some that the simple act of boiling the urine is sufficient to convert the urea into carbonate of ammonia; and if so, the quantity of urea contained in the urine being considerable, it is possible that, in some cases, the conversion of this may occasion the failure of the test.

"It becomes, then, of importance to ascertain, as far as possible, the circumstances under which this transformation of urea into carbonate of ammonia takes place."

The remainder of this paper is occupied with the details of numerous experiments demonstrating the different circumstances under which the urea of the urine is converted into the ammoniacal carbonate. The results arrived at have already been enumerated under the head of UREA.

The second paper on the copper test was not published till 12th of June, 1852; and it commences with the following remark:—"The present and following articles have been prepared and written for upwards of a year; their publication has been delayed to this time in consequence of numerous pressing engagements."

This paper is chiefly occupied with further details respecting the decomposition of urea; and near the conclusion it is observed: "It appears then that, in slightly acid, neutral, or alkaline urine, carbonate of ammonia is developed from the decomposition of the urea during the application of the heat ordinarily employed in making trial of Trommer's test, and, as will be seen presently, to such an extent as to interfere possibly, in some slight degree, with the proper action of the test. We will now go, *seriatim*, through the remaining salts and substances of the urine."

A further delay occurred in the publication of the third paper, which appeared in the *Lancet* of January 1st, 1853.

It is therein remarked:—"I showed, contrary to what had been previously stated, that potash, when boiled with non-saccharine urine, almost always deepened the colour; and hence I inferred that this test cannot be relied upon for the detection of small quantities of sugar in the urine.

"I showed likewise that diabetic sugar, in quantities by no means inconsiderable, might be introduced into many urines, and yet not afterwards be detected by the most careful application of the copper test; further, I began the attempt to trace out to what causes this very frequent failure was to be attributed.

I proved that the carbonate of ammonia derived from the decomposition of the urea interfered with the action of the test. With reference to the other salts and substances experimented with, the results were:—

"With one-fourth of a grain of *urate of ammonia*, dissolved in half a drachm of distilled water, holding one-eighth of a grain of sugar in solution, the test failed; with the eighth of a grain it succeeded imperfectly only, but with the sixteenth it was successful.

"With *carbonate of lime*, dissolved in excess of carbonic acid, the test was found to answer satisfactorily with the thirty-second of a grain of diabetic sugar.

"With one grain of *phosphate of lime* to half a drachm of a solution slightly acidified with dilute phosphoric acid, containing one-eighth of a grain of sugar, no precipitate formed on the application of the test; with half a grain of the phosphate a brownish modification of the black oxide appeared; with a quarter of a grain, the precipitate was of a lighter brown; with one-eighth, it was of a reddish-brown; with one-sixteenth, of a very light brown; and it was only with the thirty-second of a grain of phosphate of lime that the precipitate became of a dirty and dull yellow, sufficiently characteristic, however, of the presence of sugar.

"In similar quantities of saccharine solutions, of the same strength as in the previous case, containing respectively the eighth, sixteenth, thirty-second, and sixty-fourth of a grain of *phosphate of magnesia*, no precipitate appeared; and with the one hundred and twenty-eighth of a grain, a cherry-red or brownish precipitate was thrown down.

"With one grain of *phosphate of ammonia* the precipitate was of a decided brown; with half a grain, of a light brown; with one-fourth, of a yellowish-brown; and with the one-eighth, the test was successful.

"With one grain of *phosphate of soda*, the precipitate was brown; with half a grain, the same; with one-fourth, it was of a brick-red colour; with one-eighth, of a light red; and with the one-sixteenth, the test was successful.

"The conclusions to be deduced from these experiments will be considered hereafter.

"The results of the experiments with the *sulphates* were as follow:

"In a solution containing two grains of *sulphate of potash* and one-sixteenth of a grain of sugar, the precipitate was dark yellow, and characteristic of the presence of sugar.

"With one grain of *sulphate of magnesia* and the thirty-second of a grain of sugar, the precipitate was of a red or lake colour, and the same with twice the quantity of sugar; with one-eighth of a grain of sugar, the test succeeded.

"With the *oxalates* the following results were obtained:—

"In a solution containing the one hundred and twenty-eighth of a grain of *oxalate of ammonia*, the test succeeded imperfectly only.

"With one grain of *binoxalate of potash*, the precipitate was grey, with half a grain pinkish, and with one-fourth bright yellow.

"In a solution with one grain of *oxalate of lime* dissolved in dilute hydrochloric acid, the red oxide was copiously precipitated.

"The *chlorides* gave the following results:—

"In a solution containing two grains of *chloride of sodium*, the test was perfectly successful. It was equally so in a solution of *chloride of calcium*, of the same strength.

"The results with the *acids* were as follow:—

"The test answered very well in solutions containing one and two grains of *tartaric acid* to the half-drachm of fluid, and the sixteenth and thirty-second of a grain of sugar.

"With one grain of *citric acid* and one-sixteenth of a grain of sugar the test succeeded equally well; but failed when the acid was increased to two grains.

"With one grain of *oxalic acid* and the one-sixteenth of a grain of sugar, a rich golden-yellow precipitate subsided; but with the thirty-second of a grain the precipitate inclined to green, and could not be distinguished with certainty as a modification of the red oxide.

" With five drops of *dilute phosphoric acid*, the test was likewise completely successful.

"Animal matter, mucus, epithelium, and particularly *albumen*, have been said to interfere greatly with Trommer's test. It succeeded, however, completely, in the ordinary saccharine solution to which half a drop of white of egg was added.

" We have now to consider whether it appears, from the foregoing experiments, that any of the other constituents of the urine, in addition to the carbonate of ammonia, are ever present in quantity sufficient to occasion the failure of Trommer's test.

" The chlorides, sulphates, the acids, and albumen, do not require to be further noticed, as they do not appear to affect the test in any sensible degree; there remains, then, for consideration only the urate of ammonia, the phosphates, and the oxalates.

" Urate of ammonia (and probably all the other urates), which is often present in the urine in such large quantity, exerts a very marked effect over the action of the test, which is successful only in solutions which do not contain more than one grain of the urate to the ounce of fluid holding dissolved two grains of sugar.

" The phosphates, as appears from the experiments, affect to a considerable extent the successful action of the test, but particularly the earthy phosphates, and especially phosphate of magnesia. Thus the test will not succeed in solutions containing two grains of sugar and more than two grains of phosphate of ammonia, one grain of phosphate of soda, half a grain of phosphate of lime, and one-eighth of a grain of phosphate of magnesia, to the ounce.

" The oxalates likewise affect very greatly the copper test, especially oxalate of ammonia; but the affinity of the oxalic acid is so strong for lime, which is always present in the urine, that oxalate of ammonia is contained in that fluid probably only very rarely, and in ordinary cases, therefore, it has little or nothing to do with the non-success of the test.

" It is, then, evident that several of the constituents of the urine, even when separated from each other, do affect the success of the copper test; and there is no doubt but that, in many cases, acting in combination, they are the causes of its failure.

" The same conclusion is proved in another way—viz. by the results of the evaporation of different urines.

" Four grains of diabetic sugar were dissolved in two ounces of several different urines; these, after having been first tested for sugar, were carefully evaporated to the consistence of syrup; a portion of the residue of each was re-dissolved in distilled water, and again tested.

" It was found, as the result of this proceeding, that the test succeeded much more frequently after than before evaporation, although it still frequently failed.

"On referring to my notes, I observed that in those cases in which the test was most successful, the urines were of low specific gravity, and were but slightly acid or even alkaline; while, on the other hand, the urines in which it failed were of high specific gravity, and usually strongly acid.

"It therefore occurred to me, that the condition of the urine as to acidity was at least one of the causes of the failure of the test. Acting on this idea, I rendered the urine alkaline previous to the addition of the copper, and subsequently added the alkali in very large excess. Since I have adopted this plan, I have less frequently failed to detect a very small quantity of sugar, even when purposely introduced into the urine.

"In testing urine, therefore, for sugar, if acid, as it almost invariably is when that substance is present, it should be first rendered alkaline, and after the addition of the copper, a large excess of potash should be employed."

In January, 1853, that is, at the time of the publication of my third paper on the copper test, a communication appeared in the "Medico-Chirurgical Review," by Dr. Beale, on the tests for sugar.

The principal conclusions arrived at were:—

"That if the urine contain chloride of ammonium (even in very minute quantity), urate of ammonia, or other ammoniacal salts, the suboxide of copper would not be precipitated if only a small quantity of sugar were present."

These results, as far as they go, accord with my own experiments, which, however, prove that various other urinary constituents, in addition to those above specified, interfere with the action of the copper test.

The author has been induced to enter thus at length into the sources of failure of the copper test, mainly on account of their practical value and interest; but also, in a less degree, because his own observations and experiments on this subject appear to have been very generally overlooked. Dr. Beale makes no mention of them even in his latest publications, and the writers who quote Beale's observations omit to refer to the author's—doubtless from their having been over looked.

Several modifications of the copper test have been suggested, having for their object to render it more certain and delicate, and to adapt it to the quantitative estimation of the sugar, the amount of the sub-oxide precipitated being proportionate to the quantity of sugar present.

Of these modifications the most important are those of *Barreswil* and *Fehling*.

Fehling's test-liquor is prepared as follows:—

Dissolve 69 grains of pure crystallized sulphate of copper in five times their weight of distilled water, and to this add, first, 276 grains of a saturated solution of tartrate of potash, and then 80 grains of hydrate of soda dissolved in an ounce of distilled water: shake all well together, and introduce the mixture into a vessel capable of holding 2000 grains, graduated in 100 equal parts, and fill up with distilled water. Every 200 grains or 100 parts of this test-liquor are sufficient to decompose one grain of glucose.

The sugar may be determined in either of two ways: an excess test-solution may be used, and the sugar calculated from the weight of the precipitated suboxide; or the solution may be gradually and cautiously added so long as the suboxide is thrown down —that is, volumetrically. The former is the easier, although the latter has the advantage of being the quicker method.

When employed volumetrically, the test-liquor may be heated to near the boiling-point, and the measured quantity of the previously diluted urine may be added gradually until the mixture from being at first blue becomes colourless, and the addition of the urine ceases to produce any further precipitate of suboxide. Near the end of the process the urine must be added very cautiously, and even drop by drop, to avoid using an excess, which of course would vitiate the result.

When excess of the test-liquor has been added with a view to weigh the precipitate, the mixture must be gently heated on a sand-bath till the whole of the suboxide has become deposited: this should be collected by decantation, washed with boiling water, dried, and weighed. 100 parts of anhydrous grape-sugar correspond to 198·2, or, according to Neubauer, 201·62, of suboxide of copper.

Fehling's solution should be kept in a dark place, and if it has been made for any time before being used, it should be boiled with water, in the proportion of one part of the test to four of water; if this operation causes the separation of even the smallest quantity of suboxide, the solution is of course spoiled.

The sugar solution should be very dilute, and not hold dissolved more than one per cent. of sugar; therefore the urine, if it contain much sugar, should be diluted with from ten to twenty times the amount of water.

It must be remembered that the separated suboxide of copper will gradually dissolve as oxide in the supernatant liquor, as soon as this becomes cold, into which it is converted; and hence the necessity of washing the precipitate with boiling water.

The following is the formula for the preparation of the *Barreswil* solution:—

| | |
|---|---|
| Bitartrate of potash . . . . . | 96 grains. |
| Crystallized carbonate of soda . . | 96 „ |
| Sulphateof copper . . . . . | 32 „ |
| Hydrate of potash . . . . . | 64 „ |
| Water . . . . . . . . . . | 2 ounces. |

*Treatment of Urine or other Fluid containing but little Sugar.*—If glucose be present only in small amount, and no distinct indications are obtained by the copper test employed in the ordinary manner, we must proceed as follows :—

The urine or other fluid must be evaporated to a syrupy consistence, the solid residue extracted with alcohol, the alcoholic solution diluted with water, and the copper test then applied.

If the quantity of sugar be very minute, and albumen be present either in the urine, blood, serum, or chyle, previous to evaporation, dilute acetic acid must be added to neutralization, as the albuminate of soda, which would otherwise be formed, is soluble in alcohol. If now the test fail to act properly, and we still suspect the presence of sugar, an alcoholic solution of potash must be added to the alcoholic solution of the extract; the sugar is precipitated in combination with the potash, the compound is dissolved in water, and the test again applied.

Or the urine may be treated with excess of acetate of lead, and after filtration concentrated by evaporation, treated with potash, filtered, and then tested for sugar with the copper test. The excess of lead added may be removed, previous to evaporation, by sulphuretted hydrogen, or by means of either chloride of sodium or carbonate of soda.

It is rarely necessary for clinical purposes to carry the investigation to this extent; and unless the quantity of sugar be excessively minute, it is always readily detected in the diluted alcoholic solution.

## *The Fermentation Test.*

There are four ways of determining the presence and amount of sugar by means of this test :—by the diminution of specific gravity, resulting from the destruction of the sugar by fermentation; by the alcohol generated; by the carbonic acid formed; and lastly, by the characters of the yeast fungus developed during fermentation as seen under the microscope. Of these methods, the first two are by no means accurate, and are now seldom employed.

The carbonic acid evolved is sometimes determined by volume, or more usually and more accurately in combination with potash.

If by *volume*, a tube graduated into cubic inches is filled with the urine, warmed to a temperature of about 80° F., a little yeast is added, the tube carefully inverted so as not to allow the entrance of air, and placed in a shallow dish containing mercury. The apparatus is then removed to some warm place, and kept there for about 48 hours, until fermentation is completed, which is shown by the cessation of the liberation of the carbonic acid: one cubic inch of this gas corresponds to about one grain of glucose.

If the sugar is determined by the *weight* of the carbonic acid, 500 grains of the urine, with a little yeast, are put into a small flask, attached to which is a bent drying tube, containing chloride of calcium or pumice-stone moistened with sulphuric acid, and which tube is in connexion with a Liebig potash-tube. The solution of potash should have a specific gravity of 12·50, and the fermentation should be conducted at a temperature of from 80 to 100° F., and should be allowed to continue for twelve hours. The potash-tube is weighed both before and after fermentation. One grain of carbonic acid corresponds to about two grains of sugar. This operation is very troublesome, requires great nicety, and is then far from accurate. The fermentation test affords results of approximate value only, since the urine contains free carbonic acid, and since some of its constituents, besides sugar, yield during fermentation that acid.

*The Fungus Test.*

This is a particularly valuable test, first pointed out by the author, in a communication published in the 36th volume of the Transactions of the Medico-Chirurgical Society for 1853. He has frequently found it to succeed in cases in which the copper test, most carefully applied, has wholly failed.

It consists in the natural development in urine containing even the minutest amount of glucose or grape-sugar, of the yeast-plant or fungus, which appears first in the form of *sporules*, then *thallus*, and lastly, under favourable circumstances, in that of perfect *aërial fructification*. In order to ascertain by means of this test whether a urine contains sugar or not, it should be set aside in a moderately warm place for a few days, and the scum which always becomes developed upon the surface of urine thus exposed, as well as the sediment at the bottom, should be examined with the microscope for the fungus in question, which possesses well-marked distinctive characters.

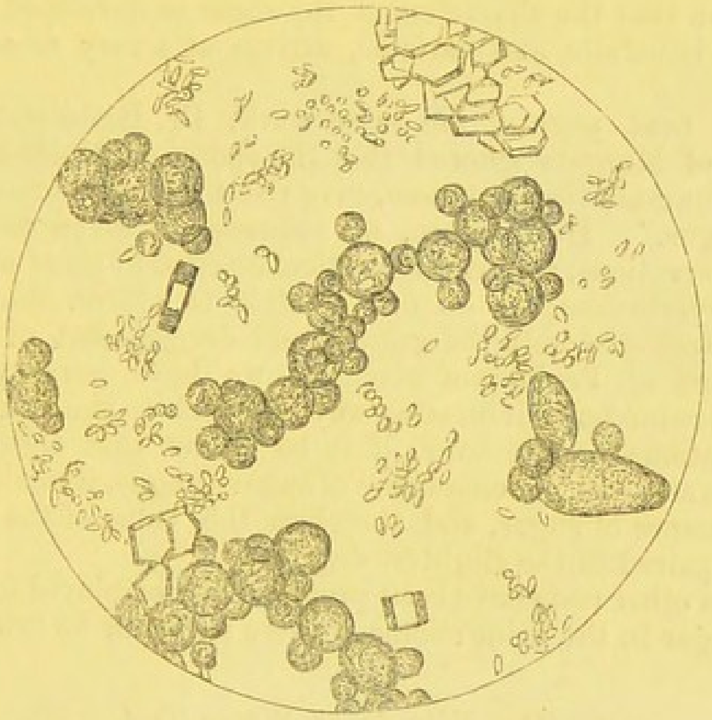
Care must be observed not to confound the sporules or thallus with those of the common fungus, Penicilium glaucum, which becomes developed more or less abundantly on the surface of every acid urine containing mucus or albumen, and exposed to the air for a time, the quantity of mucus present in the urine in health being even sufficient to give rise to a moderate development of the Penicilium. There are at least three species of fungus formed in human urine, and until the error was pointed out by the author, the mistake was uniformly made, of regarding the development of a flour-like scum of fungus upon the surface of the urine as in all cases a sure indication of the presence of sugar.

The sporules and thallus, or root-like portions of the sugar or yeast fungus—for the two are identical—are much larger than those of Penicilium glaucum, while the perfect fructification in the two species is wholly distinct. See Figs. 43, 44, and 45.

The discovery of the perfect aërial fructification of the yeast-plant was a triumph, for it had long baffled the efforts of numerous scientific observers.

For the development of this fungus, as also of Penicilium glaucum, an acid state of the urine is requisite: if, therefore, the urine when voided be alkaline, no formation of this fungus will take place unless it be rendered acid, which it may easily be by the addition of a few drops of acetic acid.

FIG. 43.



*Sporules* of SUGAR FUNGUS, intermixed with those of PENICILIUM GLAUCUM and with hexagonal Crystals of *Uric Acid.* It will be observed that the distinctive characters of the sporules of each species of fungus are clearly defined and closely preserved. Magnified 220 diameters. 1852.

Accompanying the development of the sugar-fungus, there is a free liberation of carbonic acid, the bubbles of which are continually rising to the surface, and the appearance of which is a sufficient indication of the presence of sugar. If a diabetic urine be corked for some days in warm weather, and the cork be then suddenly removed, it will effervesce from the rapid elimination of carbonic acid.

In Dr. Beale's work on the urine, page 257, the following remarks on the sugar-fungus occur:—" Dr. Hassall arrives at the conclusion that there is a species of fungus which is developed in specimens containing even very minute traces of sugar, which may be looked upon as characteristic of the presence of this substance, as it occurs in no other condition of the urine. This is the sugar-fungus; but *most persons* are agreed that the characters of the fungus are by no means sufficiently constant to enable us to conclude as to the presence or absence of sugar in the urine."

Who these "most persons" are, not even a single name being given, and what the precise data upon which a conclusion so utterly groundless has been arrived at, is not stated; but this we do know—that the characters of the sugar-fungus, so far from not being constant, are most definite and precise; and as the result of very great experience in this matter, we affirm, that the observer who forms the opinion that the characters of the sugar as developed in diabetic urine are indefinite and variable, arrives at a very erroneous conclusion.

On the next page of the same work, Dr. Beale states: "Mr. Hoffman of Margate showed that the spores of Penicilium would, under favourable circumstances, give rise to the development of the sugar-fungus." Here, again, no reference is given to Mr. Hoffman's observations, nor are any particulars cited in proof of the statement; nevertheless, we do not hesitate to affirm, that although we have studied closely the growth and development of the sugar-fungus, and of Penicilium glaucum, we have never yet noticed a single circumstance indicating any approach to the transformation above mentioned. Moreover, if it be a fact that the Penicilium sometimes assumes the characters of sugar-fungus, it could only do so in the presence of sugar, and therefore the value of the test would not be impaired in the slightest degree.

Various other tests have been proposed and employed for the detection of sugar in the urine; some of these may now be briefly noticed.

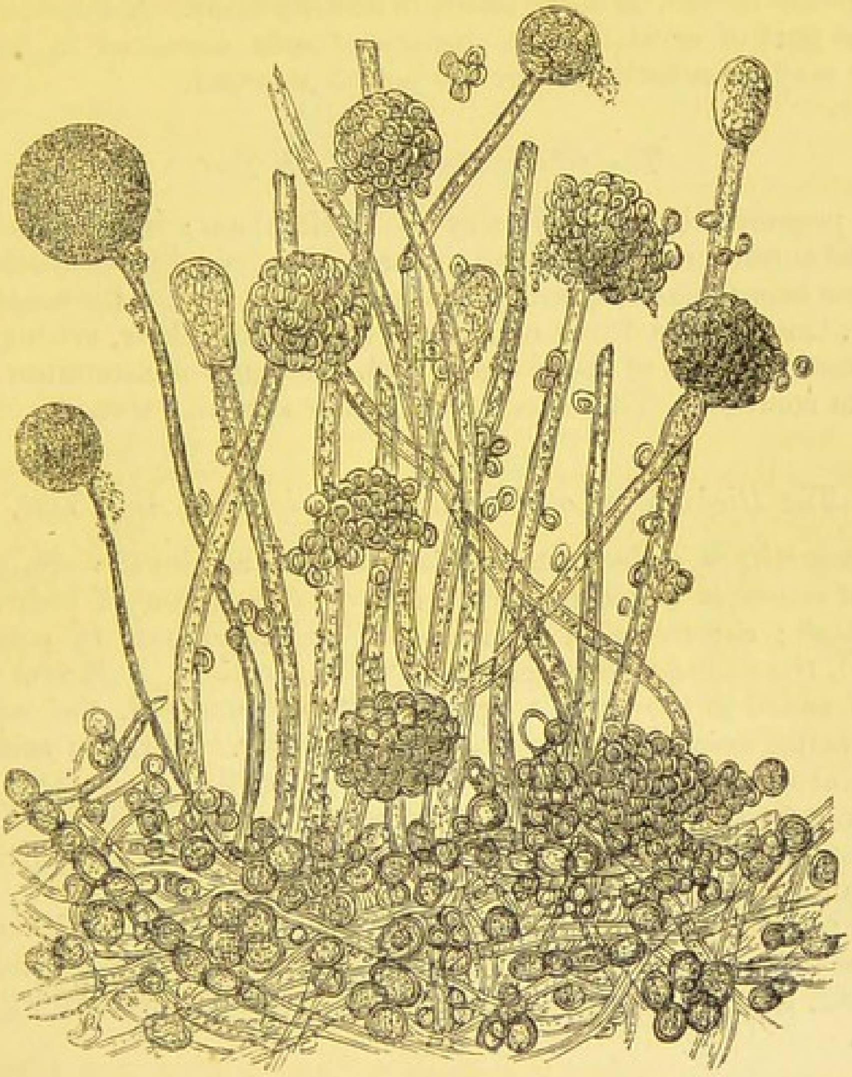
### *The Nitrate of Silver Test.*

This test was suggested by Dr. Bence Jones. If a solution of nitrate of silver be added to diabetic urine, the silver is reduced, by the sugar, to the metallic state, even in the cold, and is deposited, forming a mirror-like coating to the test-tube. This test is very fallacious, for the silver is reduced with the greatest readiness by numerous substances, in the absence of sugar, and even when water only is used. As pointed out by the author some years since, the reduction of the silver is insured in non-saccharine urine, by holding the flame of the spirit-lamp so that it impinges on the surface of the mixture in the test-tube.—*Lancet*, January, 1853.

### *The Bichloride of Tin Test,*

Also called *Maumene's* test, like the copper test, is founded upon the reducing power of sugar. It is thus applied: a piece of white merino, or other woollen fabric, is soaked in a solution of bichloride of tin and dried; the cloth is then wetted in one part with the urine, and made hot by being held over a spirit-lamp, or before a fire. If sugar be present, the moistened part will become of a glistening brown or black colour. It is affirmed that the sugar contained in ten drops of diabetic urine diffused through half a pint of water may be detected with this test.

FIG. 44.



The SUGAR FUNGUS in perfect Aërial Fructification. It will be observed that the characters of each part of the fungus—sporules, thallus, and especially the reproductive tufts—are entirely different from the corresponding part of *Penicilium glaucum*. Magnified 220 diameters. 1852.

Although this test is very delicate, yet it should be remembered that the same black colour is produced by most of the hydrocarbons—as hemp, linen, cotton, paper, starch, &c.

*The Bismuth Test.*

This test, proposed by Bottger, and said to be more delicate than even the copper test, and freer from sources of fallacy, is thus applied: Solution of potash is first added to the urine, then a small quantity of subnitrate of bismuth, and the mixture is boiled. A grey or blackish precipitate is thrown down, if sugar be present, consisting of the suboxide of, or of metallic bismuth. Beneke has shown that the precipitate occurs, in some cases, in healthy urine. A solution made of one part of crystallized carbonate of soda dissolved in three of water may be substituted for the potash solution.

*The Chromate of Potash Test*

Was proposed by Mr. Horsley of Cheltenham: it consists of the neutral chromate of potash and liquor potassa, equal parts of solutions of these being mixed together. On being boiled with urine containing sugar, the mixture turns of a deep sap-green colour, arising from the decomposition of the chromic acid, the oxide of chromium being held in solution. This is certainly a very sensitive test.

*The Bichromate of Potash and Sulphuric Acid Test,*

Also sometimes called *Luton's* test, is thus employed:—Sulphuric acid in excess is added to a cold saturated solution of bichromate of potash; chromic acid is liberated, and bisulphate of potash is formed, the solution being of a beautiful red colour. Sufficient of the test is added to the urine to cause it to become red, the mixture when boiled assuming an emerald-green colour. Chromic acid is a powerful oxidizer, especially mixed with another acid: part of its oxygen goes to the sugar, which is converted into carbonic acid and water, while the free sulphuric acid unites with the sesquioxide of chromium liberated.

The principle of this and the preceding test is similar: it is said to have frequently succeeded after the failure of other tests, and that uric acid, the urates, urea, and albumen do not interfere with its action.

*Polarized Light.*

The application of polarized light to the detection of sugar in the urine requiring a special apparatus, and being adapted only to its discovery when present in considerable amount, it is of but little practical utility; a detailed description of it may therefore be fairly omitted.

This test depends upon the property which a solution of either grape or diabetic sugar possesses of decomposing and deflecting a ray of polarized light to the right, the angle of deflection being greater in proportion to the amount of either of these descriptions of sugar present. The sugar of fruits deflects the ray to the left.

## QUANTITATIVE DETERMINATION OF GLUCOSE.

Hitherto the tests by which the presence of sugar in the urine may be ascertained have been chiefly discussed: a few remarks must now be bestowed upon its quantitative determination.

Fig. 45.

Penicilium glaucum, in perfect Fructification. Magnified 220 diameters. 1852.

There are several methods, more or less exact, by which the amount of sugar contained in any urine may be estimated.

Dr. Garrod arrives at an approximate determination of the quantity of sugar by the tint, more or less deep, developed on boiling, in certain proportions, a mixture of the urine and of a solution of carbonate of potash.

The standard solution exhibits the colour produced by $\frac{1}{2}$ gr. of sugar to the ounce of urine, and it is placed for comparison in a glass tube of one-half inch in diameter.

The solution of potash is made with three ounces of the carbonate to six of water.

Equal parts, say thirty minims, of the urine and solution are to be boiled for five minutes over a spirit-lamp, in a test-tube, or flask.

The mixture is then transferred to a tube similar to that containing the standard solution, and, if necessary, diluted to the exact tint of the standard, when, allowance being made for the quantity of water added, the amount of sugar contained in the thirty minims of urine is approximately determined.

If the amount of sugar be large, the urine will require to be diluted by the addition of a known measure of water, prior to its being boiled with the alkaline solution.

A second means of determining the amount of sugar is by measuring the carbonic acid evolved, on subjecting a measured quantity of the urine to fermentation with yeast, as already described.

A third and more exact method, already noticed, is to collect, dry and weigh the suboxide of copper precipitated on boiling a measured quantity of the urine with an excess of the Barreswil solution, the formula for making which has been already given, or the amount may be calculated from the quantity of the copper test required to precipitate all the sugar.

### *Microscopical Characters of Glucose.*

Grape-sugar used formerly to be described as uncrystallizable; in many fruits, in honey, and under favourable circumstances, in the urine, it readily crystallizes in a very distinct manner: ordinarily the crystals are aggregated, forming roundish granules; but when the glucose is tolerably pure they occur singly as well as in groups; they consist usually of six-sided rhombic plates.

With chloride of sodium it forms a compound the crystals of which are well defined, and have the form of four or six-sided double pyramids. The compound contains 13·3% of chloride of sodium, or of one equivalent of salt with two of sugar.

## THE PATHOLOGICAL OCCURRENCE OF SUGAR IN THE URINE.

It is asserted by several observers, that sugar is constantly present in human urine—that it is, in fact, a normal constituent: of this statement, however, no conclusive evidence has yet been afforded. It is nevertheless proved that it is much more frequently present than was formerly supposed, and it is even probable that it does sometimes occur in the healthy urine. It seems certain that after a highly saccharine diet, small quantities of sugar frequently escape into the urine.

In analysing urine, the tests applied are usually those which are applicable to the detection of grape-sugar only. Now it is possible that cane-sugar derived from the food may be present in some cases, and therefore it would be right to search, also, for this form of sugar: generally, no doubt, cane-sugar is converted in the system, and most probably in the liver, into grape-sugar; but this may not be always the case.

Prout has found sugar in the urine of *gouty and dyspeptic* persons.

Budge has met with it in *abdominal affections* and *hypochondriasis.*

Lehmann found it "in the urine of a *puerperal woman,* in whom, on the fifth day after delivery, the secretion of milk was suddenly suspended."

It is said to occur in the urine in some cases of *phthisis.*

Alvaro Reynoso believes that he has found sugar in cases of *epilepsy* and *hysteria,* and in *pulmonary affections,* including *emphysema* and *asthma.* He likewise believes that it is present in the urine after *narcotization* by ether or chloroform, after narcotic drugs, and after the exhibition of the *metallic salts,* as of mercury, iron, antimony, and arsenic, of sulphate of quinine, &c. The accuracy of these observations is generally doubted, and by some observers most of these statements are positively denied; as by Uhle, Kletzinsky, Beale, and Morse. Michea, who used the potash test, also failed to confirm Reynoso's conclusions.

It is right to remember that Reynoso employed the Barreswil solution: 1500 grains of urine were treated with acetate of lead, the solution filtered, and the excess of lead removed with chloride of sodium. The clear filtered liquid after concentration was subjected to the copper test. Part of the solution was likewise submitted, by Reynoso, to the fermentation test.

In *diabetes,* to the consideration of which disease we shall devote a special section, sugar is found in nearly all the fluids of the body, including especially the saliva. In examining the body of a person who died of diabetes, Bernard only failed to detect it in the brain, spinal cord, pancreas, and spleen.

Beale found sugar in the sputa, in a case of acute *pneumonia,* just before the patient's death.

Gibbs states that it occurs in the urine after *whooping-cough.*

It is found in the urine after *injuries of the head,* probably from irritation or injury to the medulla oblongata or the fourth ventricle.

In the author's report on the urine of *cholera,* elsewhere quoted, it was shown that sugar is of common occurrence in the urine in that disease. It was there remarked: "It will be observed that the sugar-fungus was met with in samples of the urine in nearly every case. Of the value of this fungoid test for sugar, I have elsewhere adduced evidence; but additional proof is now furnished of its great utility. The yeast-plant was met with in different stages of growth in at least fourteen samples, while evidences of its existence were observed in several other specimens; the specific gravity of the urines in which it was actually detected ranged from 1007 to 1018."

Indigo is also frequently present in cholera urine derived from the decomposition of *indican*, the *uroxanthin* of Heller. Now sugar is one of the results of that decomposition: the question therefore arises, does the sugar exist in the urine of cholera when first voided, or does it proceed from the indican? If this latter explanation be correct, then no doubt it will be found to apply equally to other cases in which small quantities of sugar have been detected in the urine.

Heintz has also detected sugar in the urine of cholera.

Dechambre, using the same process as Reynoso, found it in the urine in several *old people*.

Bence Jones also detected slight but distinct evidence of sugar in the urine of a patient who had been twenty-four hours under *chloroform*.

M. Blot confirms several of Reynoso's results; and he found sugar in the urine of *pregnant* and *suckling* women.

## DIABETES.

Having now considered many of the more important facts connected with the occurrence of diabetic sugar, or glucose, in the urine, the disease Diabetes itself may next be treated more specifically.

## VARIETIES OF DIABETES.

It is not to every case in which sugar occurs in the urine that the term diabetes can be properly applied: it should be restricted to those only in which the amount of urinary sugar is considerable and its presence continuous. The propriety of this limitation will be apparent when it is stated that the occurrence of sugar in minute quantities in perfectly normal urine has been rendered, by recent observations, highly probable.

Diabetes may be divided into the *artificial* and the *natural*, or idiopathic,—a variety of the latter form has received the name of *intermittent* diabetes.

The affection denominated *diabetes insipidus*, formerly supposed to be characterized by the presence in the urine, either separately or mixed with the sweet sugar, of a tasteless or insipid sugar, has no existence. What, years ago, was mistaken for tasteless sugar by Dupuytren, Thénard, and Bouchardat, was either ordinary glucose or else inosite.

The term diabetes insipidus is now restricted to cases which resemble diabetes only in the existence of thirst, and in an excessive elimination of urine, which is, however, destitute of sugar: it is therefore obvious that this term, as being calculated to mislead, ought to be entirely discarded.

### *Idiopathic or Ordinary Diabetes.*

Of idiopathic diabetes, as previously mentioned, two varieties have been noticed, the ordinary form and the intermittent variety. The first is characterized by the persistent presence of the sugar in the urine.

### *Intermittent Diabetes.*

The second modification of diabetes has received from Dr. Jones the name of "*intermittent.*" In this variety the sugar sometimes disappears from the urine, returning again from time to time.

It occurs particularly in old people, and is obviously associated with deranged digestion.

### *Artificial Diabetes.*

It has been ascertained by various experiments, performed by Bernard, and subsequently by others including Pavy, that the urine, at will, may, under certain circumstances, be rendered saccharine. These experiments consist in peculiar or special injuries inflicted on the *medulla oblongata*, or the filaments and ganglia of the *sympathetic system*, and in the injection of *woorari*, and of *strychnine*, into the subcutaneous cellular tissue of the back of animals over the *medulla oblongata;* these poisons operating and producing their effects through the cerebro-spinal system. In all these experiments it is necessary that the respiration be maintained, and that the urine be not tested for from one to two hours afterwards.

The first experiment of this kind was performed by Bernard, who ascertained that whenever the floor of the fourth ventricle was punctured, sugar appeared in the urine.

Pavy, more recently, has instituted a variety of experiments resulting in the appearance of sugar in the urine.

Of three of these followed by this effect, one consisted in the division of the lower part of the *medulla oblongata*, artificial respiration being maintained in this as well as in all the other experiments subsequently to be cited; the second in the destruction of the *medulla* through its *centre;* and the third consisted in *decapitation.*

The other set of experiments made by Dr. Pavy were upon the *sympathetic system* of nerves, which he was led to operate upon under the idea that it was the channel through which the previously ascertained influence of the cerebro-spinal system on the liver was conveyed to that organ.

The subjoined experiments were all followed by the appearance of sugar in the urine; division of the filaments of the sympathetic accompanying the vertebral artery; division of the ascending branches of the superior thoracic ganglion; removal of the carotid ganglion of the sympathetic, first on one side and afterwards on the other; division of the sympathetic in the thorax (this experiment was not always followed by the appearance of sugar in the urine); removal of the superior cervical ganglia of the rabbit.

To the above experiments may be added with advantage, an enumeration of those which were not followed by the presence of sugar in the urine:—1. Injury of brain, probably; 2. Separation of the brain from the medulla oblongata by division of the crura cerebri; 3 and 4. Division of the spinal cord in the cervical region, and of both pneumogastrics; 5. Division of the pneumogastric.

In like manner diabetes or glucosuria is not unfrequently produced as the result of accidental injuries to certain portions of the cerebro-spinal system.

Further, it should be held in remembrance that the diabetes experimentally produced is but *temporary*.

Lastly, it has been shown by Harley, that artificial diabetes may be produced independently of injury, as by eating largely of *asparagus*, and by the injection of *alcohol* or *ether* into the vena porta.

The following considerations appear to furnish in a measure the key to the above results:—First, the experiments upon the medulla oblongata seem to show that the liver receives some force or influence which prevents the chemical act of the transformation of glucogen into sugar during life and in health. Second, the experiments show that this force is not transmitted by the spinal cord or pneumogastric nerves. Third, the result of the experiments on the sympathetic go some way to prove that the influence of the medulla is conducted by it to the liver; at the same time it is possible that the sympathetic exerts an independent action on that organ.

## CHARACTERS AND COMPOSITION OF DIABETIC URINE.

### *Quantity.*

The quantity of urine passed in diabetes varies much, but is usually very great—from five to twenty pints, and even upwards, in twenty-four hours.

So large is the quantity passed, in many cases, that it has been suspected that more water is voided than is actually consumed. This, however, is certainly not correct as a rule; since it has been proved by numerous careful observations that the amount, in most cases, is really less. There would appear, however, to be some exceptions to this. A case is recorded by Ormerod, in which 900 grains more urine were passed in twenty-eight days than could be accounted for by the fluid contained in the food and drink consumed; the patient at the same time gained in weight.

Supposing it to be established that in some cases, apart from all inaccuracy or fallacy of observation, there is really an excess of urinary water over the liquid taken, this excess may be explained in one of three ways: either by the body becoming poorer in water, and so losing weight; by absorption of water by the skin; and, lastly, by a formation of water by the union of oxygen and hydrogen in the system.

The quantity of water passed in diabetes is of course greatly augmented by inaction of the skin, and the consequent diminution of insensible perspiration. The normal quantity of water which should escape by the skin and lungs is from 1000 to 1200 grammes, while in several cases of diabetes the amounts recorded are as follow:—198, 204, 529, and 637 grammes of 15·44 grains each.

Observations made for the purpose of determining whether water is passed in excess, in any case of diabetes, should be continued for several successive days, since the water is apt to be retained in the system; it should also be remembered that it is very slowly absorbed from the stomach, and the fact should likewise be noted whether the body gains or loses in weight.

## *Specific Gravity.*

The specific gravity or density of urine containing sugar is subject to a wide range of variation.

In confirmed diabetes it generally ranges from 10·38 to 10·48 and even higher. Bernard gives the maximum height at 10·74, which, however, it very rarely attains. The average may be put down at 10·44. If the disorder progresses favourably, of course a reduction in the weight of the urine takes place until it reaches the healthy standard and becomes free from sugar. It should not be concluded, however, from mere specific gravity, that sugar is absent, since the author has found sugar in urine having a specific gravity of only 1·007; recourse, therefore, should always be had to tests.

There is one very important fact in regard to the specific gravity of diabetic urine which should never be lost sight of—namely, that in arriving at an opinion as to the progress of the case, we must not be guided so much by the weight of the urine passed as by the *quantity;* it is this which is first gradually lessened, the specific gravity remaining, in many cases, nearly unaffected, and this even under a carefully restricted regimen, and becoming lessened only as the cure advances towards completion. The author has had cases under his care, at the Royal Free Hospital, in which this particular has been clearly shown.

The specific gravity of diabetic urine should be determined shortly after it is passed, especially in summer; because, if the temperature be elevated, fermentation speedily sets in, part of the sugar is dissipated, and the density thereby reduced. If a bottle of diabetic urine be kept for some two or three days corked, and the weather be warm, on the removal of the cork it will often froth up like ginger-beer, from the escape of the carbonic acid derived from the sugar, and probably also in part from the urea, both of which entirely disappear during the fermentation.

*Colour.*

Diabetic urine is usually of a very pale straw or sherry colour, as might have been expected would be the case from the large quantity passed, and the consequent dilution of the colouring matter.

Although generally of a pale colour, it is not always so, as cases are sometimes met with in which the urine is of a deep brown colour; the amount of urine passed, however, in such cases has not been very large, which, in a measure, explains the fact.

According to Heller, the normal pigment *urophæin* is always lessened, and the *uroxanthin*, which gives a violet blue colour with hydrochloric acid, is increased. Schunck procured more *indigo* from diabetic urine than from any other. Stockvis has observed that nitric acid gives rise to "peculiar tints." Parkes, in reference to this point, states, "I have sometimes seen this well marked, but in other cases it has been absent."

*Acidity.*

The urine in diabetes is usually acid from the first, becoming more so very soon after it has been passed; and, as fermentation sets in, the *carbonic* and *acetic* acids are formed, with sometimes *formic* or *propionic*, and *butyric* acids. When a very small quantity of sugar is present in any urine, the reaction may be either neutral or slightly alkaline when first passed.

*Sediments.*

Diabetic urine is usually remarkably clear and transparent, depositing only a little mucus after it has stood at rest for some time. During fermentation, uric acid, if present, is set free, and becomes deposited; deposits of crystallized phosphate and oxalate of lime are occasionally met with, the latter not nearly so frequently as might have been anticipated from the chemical relation which exists between oxalic acid and sugar.

*Composition.*

The great and peculiar characteristic of the urine in diabetes consists in the presence of grape-sugar, or glucose, in large amount. This description of sugar occurs in many other diseases; and there now seems reason to believe that it may even be found in the urine, if not as a normal constituent, at all events independent of any appreciable disease. About fourteen years since, the author stated in the *Lancet*, that sugar was contained in the urine in small quantities much more frequently than was generally supposed; and it now appears that it occurs much more generally than even he supposed. In other instances of its occurrence, the amount contained in the renal excretion, as compared with diabetes, is very small; and in many instances, though not in all, its presence is but temporary.

Before proceeding to discuss further the facts connected with the presence of sugar in the urine in diabetes, it will be desirable to ascertain in what condition the urea and other urinary constituents are in that disease.

The *urea*. In general the urea is much increased, and this to an extent which cannot be explained by reference to diet only, or to diminished excretion of nitrogenous products by the skin, lungs, and bowels, or to any complicating febrile disease, or to excessive water drinking. This increase is clearly shown by the following figures.

In the case of a child 9 years of age, recorded by Parkes, the urea amounted to 421 grains, corresponding to 7 grains per lb. avoirdupois. In 11 other cases recorded by different observers, the urea ranged between 454 grains the lowest, and 1411 grains the highest amount. In one case, in which the urea was 700 grains, the amount per lb. avoirdupois was 5·83 grains; in another, in which the urea was 1374 grains, it was per lb. 10·5 grains; and in a third case, in which the total amount of urea is not stated, it amounted, according to body-weight, to 11·2 grains. Thus, the increase was twice and even three times as much as the normal standard, 3·53 grains per lb. In a case of Sydney Ringer's, that of a woman whose weight was only 104 lbs., the average amount of urea, calculated from the observations of 42 days, was 764 grains in the twenty-four hours, corresponding to 7 grains per lb. weight. The majority of the cases in which these observations were made were upon mixed diet; and this was so with Mosler's patient, who excreted the largest amount of urea, namely, 1411 grains.

It appears, therefore, highly probable that the increased formation of urea is, *in part*, due to augmented metamorphosis of the nitrogenous tissues, explained possibly by the circumstance that the oxygen, which by Bernard is believed to go to the oxidation of the sugar, is free in diabetes to act upon the tissues.

In some cases, however, urea is present in normal or diminished amount, or is even absent, and this sometimes on a mixed diet; but these cases form the exceptions rather than the rule. In such cases we must ascertain whether there is any increased discharge of urea by the skin or bowels.

In diabetes the diet exerts its ordinary effect on the urea. Ringer has determined the important fact, from seven series of trials on the same patient, that when sugar of any kind is given in fasting hours, it has the effect of increasing the urea.

The *uric acid*. This would appear not to be present in unusual amount, and in some cases to be even lessened.

The *hippuric acid* has been found to be present in some cases, by Lehmann and others, in large amount; in other cases the quantity was diminished, or it was even absent. It appears that, in some of the cases in which it was absent, the patients were upou a meat diet; but Lehmann states, in the last edition of his handbook, " In the urine of diabetes, on a strict animal diet, the hippuric acid is not absent."

There is no want of *glycine* in the system in diabetes, as shown by the fact that benzoic acid when administered undergoes its usual transformation.

The *sulphuric acid* is often increased in consequence of the meat diet. Böcker in one case found 64·69 grains in 24 hours, and Mosler 83 grains.

The *phosphoric acid* seems to be but little affected.

The *chloride of sodium* varies greatly, but is frequently in large excess. In six recorded cases it ranged between 337 and 568 grains in the twenty-four hours. This increase is explained by increased ingress and diminished egress by the skin.

*Albumen* is sometimes present in diabetic urine. Von Durst found albumen in 8 out of 28 cases, and Heller in 3 out of 8 cases. The quantity is, however, usually very small: according to Heller, seldom exceeding 0·2 per cent. Its persistent occurrence in any amount beyond mere traces may certainly be regarded as an unfavourable symptom.

There appears good reason to believe that *sulpho-cyanogen* is not unfrequently present in diabetic urine. F. Schültze found that in cne case perchloride of iron imparted a deep red colour to the urine; after the administration of chloroform this reaction ceased. Hünefeld and Parkes have observed the same reaction.

Petters found, both in the urine and blood of a patient dying in a narcotized state, *aceton;* and he attributed the narcosis to its presence.

## ON THE QUANTITY OF SUGAR IN DIABETIC URINE.

The amount of sugar in diabetic urine is, of course, very variable, although usually considerable.

A very curious fact, and it is one of much practical value, is, that the presence of ever so small a quantity of sugar in the urine is indicative of considerable excess in the blood; since it does not make its appearance in the urine at all unless the blood is to a certain extent saturated with it.

In a case made the subject of observation by Ringer, that of a woman, the mean daily excretion of sugar was 154 grains, and of urea no less than 1090 grains.

In a second case, also that of a woman, whose weight was only 104 lbs., the mean daily amount of sugar in the urine was 772, and of urea 764 grains.

In some instances diabetic urine has been found to contain as much as 15 per cent. of sugar.

In a case of Dr. Garrod's 1085 grains of urea and 3500 grains of sugar, were discharged in the twenty-four hours, the sugar being determined by his glucometer.

In a woman aged 43, the particulars of whose case have been narrated by Bence Jones, the amount of sugar ascertained by Soleil's saccharometer, ranged, under differences of diet, between 3100 and 5180 grains in 24 hours. Beale found, in the urine of a woman aged 18, no less than 8750 grains of sugar.

*Influence of Food.*

As a rule, *food of all kinds*, whether non-nitrogenous or nitrogenous, increases the amount of sugar in the urine; there are, however, exceptions, as in some cases the whole of the sugar is due to the saccharine and starchy constituents of the food.

It appears further, from the observations of Andral, that any *change of food* for a time lessens the sugar. A woman passing 27 grammes of sugar was placed on meat diet, when the sugar fell to 10 grammes, but gradually, the diet remaining the same, it rose to the original 27 grammes; vegetables being now added to the food, the sugar sank to 15 grammes, and then mounted up as high as 54 grammes.

*Vegetable food* containing sugar or starch, or these substances separately, invariably increases the amount of sugar in the urine in diabetes, and this to a very considerable extent.

There is, indeed, good reason for believing that the whole of the starch absorbed from the food is converted into sugar, since, in many cases, the amount of starch taken, and that of the sugar afterwards found in the urine, almost exactly correspond. The same probably holds good as respects the sugar, only that, when this is given in very large quantities at a time, usually part only is absorbed.

The effect of starch on the presence of sugar in the urine is further shown by the fact that, in some cases of diabetes, abstinence from it occasions the entire disappearance of the sugar.

This is a very important fact, since the cases in which this occurs are of a milder and more promising character than those in which sugar is found in the urine during an exclusively meat diet. It is probable that, in all cases of diabetes, the sugar is, in the earlier stages, formed only from saccharine and starchy food.

In the majority of cases of diabetes the sugar is likewise increased by *nitrogenous* food. When meat only is eaten, the sugar begins to increase soon after the meal, and continues to do so for some time, and then it gradually falls. In a case recorded by Schültze, the amount of sugar in the urine, when the patient was on a mixed diet, was one-third more than could have been derived from the starch of the food. In one of Criesinger's cases, the sugar passed corresponded to two-fifths of the meat consumed, and to three-fifths of the albuminate contained in the meat.

From all the observations and analyses hitherto made, it appears that there is no fixed ratio between the amount of sugar formed and the quantity of albuminous food taken. In some cases a larger amount is passed than in others; and there is reason to believe that the case is the more serious and confirmed in proportion to the extent of the conversion of albuminous food into sugar.

### *Influence of Special Articles of Food.*

The *gelatinous* tissues yield more sugar than washed fibrin. (Bouchardat).

*Milk* does not increase the amount of sugar greatly. (Jones.)

*Rennet* lessens sugar to some extent. (Gray.)

*Gum* does not furnish any sugar according to Graham ; but then it is absorbed only in small amount.

*Asparagus,* when eaten largely, will produce an artificial diabetes. (Harley).

*Pepsin* increases the sugar. (Leubuscher and Parkes.)

### *On the Effect of Abstinence from Food.*

The effect of fasting is, of course, in all cases to occasion a very marked reduction in the amount of sugar in the urine; sometimes it will altogether disappear—abstinence from vegetable food only being even sufficient to cause the disappearance of the sugar.

Unfortunately, however, this is not generally the case; but not unfrequently a large amount of sugar continues to be eliminated during periods of rigorous fasting. In these cases it is obvious that the sugar can only proceed indirectly from the tissues, and most probably immediately from the glucogenic substance formed in the liver, and there is reason to regard such cases as representing the malady in its worst or most advanced form.

Indeed, it would appear that diabetes is divisible into *three stages* —the *first,* or milder form, being indicated by the disappearance of the sugar on abstinence from vegetable food; the *second,* or intermediate form, when the same result ensues on abstinence from all food; and the *third,* worst, and last stage, when the sugar continues to be eliminated even during complete fasting. These facts are of much practical importance, and they will be again more particularly considered.

In a case recorded by Traube, it was found that after the discontinuance of the food, the sugar gradually lessened, but that at length a point was arrived at when it ceased to become diminished, and remained, in fact, almost stationary. He ascertained that the sugar thus excreted, not derived from food, amounted to no less than 1072 grains in twenty-four hours.

In one of Mr. Ringer's cases the excretion of sugar during complete fasting varied per hour from 2·4 to 5·3 grammes, equal to from 37 to 81 grains respectively, the mean being 4·1 grammes, or 63 grains; and in a second case it ranged from 1 to 3·7 grammes, equal to 15, 44, and 57 grains, the mean being 1·93 gramme, or 29 grains. The mean of two series of observations in the first case gave 4·4 grammes, equal to 68 grains, of sugar per hour, and 1632 grains per twenty-four hours.

Ringer ascertained that in these two cases there was a large elimination of urea as well as sugar, and that a rather close and constant relation existed between their respective amounts, not only during fasting, but after nitrogenous food: by starchy food this relation was of course destroyed.

In the first case, during fasting, 48 grammes or 741 grains of urea were eliminated in twenty-four hours, and the relation in the first series of observations made during consecutive hours of the same day between the urea and the sugar was as 1 to 1·2; and in a second series of observations made in consecutive hours on different days the same relation was found to exist.

In the second case, that of a woman who was exceedingly thin, the urea during fasting amounted to 22 grammes in the twenty-four hours, equal to 336 grains, and the relation between it and the sugar was exactly the same as in the first case.

On a *meat* diet, it was found that the urea and the sugar in both cases were increased—the former more than the latter; but still, that, taking the two cases together, a connexion could be traced between the relative amounts of urea and sugar.

Thus, in the first case, the mean of the urea of seven food hours was 2·48 grammes, equal to 38·3 grains, of sugar 4·80, equal to 74·1 grains, and the relation as 1 to 1·9. In a second series of observations in the same case, the relation was 1 to 2·2, that is, the same as in the fasting hours.

In the second case the mean of four hours' excretion of urea was 0·923 gramme, equal to 14·2 grains, of sugar 1·938 gramme, equal to 29·9 grains, and the relation was as 1 to 2·1.

Although food, especially saccharine and starchy food, augments the amount of diabetic sugar in the urine, it must not be understood that this sugar is formed directly from the food by any transmutation of its elements, for this is not the case. It has been clearly proved that the sugar found in the blood and urine not due to direct absorption from the food, is derived from the transformation of a substance discovered by Bernard, which has received the name of "*glucogen*," or "*the glucogenic substance*," which is formed chiefly, and it would appear exclusively, in the liver. Those constituents of the food, therefore, which increase the sugar of the urine, do so by first augmenting the formation of glucogen, upon which important substance some remarks will next be made.

THE GLUCOGENIC SUBSTANCE OF BERNARD.

*Views of Bernard.*

The researches of Bernard have established the fact of the formation of a substance in the liver which, from the circumstance of its ready conversion into that variety of sugar known as glucose, he has termed *glucogen*.

Bernard affirms, as the result of his experiments, that this substance is normally, and as a physiological action of the liver regularly, transformed into glucose; that this, in health, after having been taken up by the hepatic veins, is destroyed by oxidation; but that in certain abnormal conditions, this natural transformation is arrested.

As to the cause which impedes this oxidation, nothing is known: it certainly does not depend upon want of oxygen in the system, since in cases of diabetes, fat, salicine (Ranke), the tartrates (Kletzinsky), and acetates are all oxidized.

Bernard founds the statement of the formation of sugar in the liver and of its subsequent destruction, partly upon the fact,—that while the blood of the portal vein is either entirely free from sugar or contains traces of it only, in that of the hepatic veins it is particularly abundant.

Of the formation of the glucogenic substance, of its transformation, if not as a physiological action of the liver, at least under certain circumstances; of the general absence of sugar in the portal veins, no doubts whatever exist: these particulars may all be looked upon as thoroughly established.

*Views of Pavy.*

In one important particular, however, the views of Bernard have been called in question. Dr. Pavy asserts, founding his statement upon the results of numerous well-devised and carefully conducted experiments, that the glucogenic substance, which he terms *hepatine*, is not normally and physiologically converted into glucose—that is, that the change does not take place during the normal and proper performance of the functions of the organ, but only under certain abnormal or exceptional conditions during life, or else is a *post-mortem* change occurring very speedily after death.

This view is founded by Dr. Pavy mainly on the fact that, according to his experiments, sugar is not found in the liver when examined instantly after life is destroyed, although it speedily makes its appearance there after death; neither is it present in any quantity in the blood of the right side of the heart, as it would be were sugar constantly formed in the liver, and were it conveyed away from that organ by the hepatic veins.

The following particulars will serve to show the nature of the evidence upon which Pavy's views, in opposition to Bernard, are founded.

Dr. Pavy states he noticed, with many others, that when blood is removed during life from the arterial system and examined, the indication of sugar is exceedingly slight; whereas, if the life of the animal were immediately afterwards destroyed, the blood collected from the right side of the heart gave a strong impregnation of sugar. The inference naturally drawn from this observation was, that sugar became destroyed on passing through the lungs, an inference which subsequent observations led him to doubt.

From an experience of upwards of sixty observations, he states he is enabled to affirm that, contrary to what has recently been believed, sugar is only found to the extent of the *merest trace* in the blood of the right side of the heart, under a natural or ordinary condition, *during life*.

Very speedily after death, however, the quantity of sugar, as shown by the following determinations, rapidly increases.

After death, 100 grains of defibrinated right ventricular blood, in five different cases, furnished the following quantities of glucose:—

| | Defibrinated Blood. Per cent. | Liver. Per cent. |
|---|---|---|
| No. 1 | 0·70 | |
| " 2 | 0·65 | 4·10 |
| " 3 | 0·50 | 3·39 |
| " 4 | 0·94 | 2·45 |
| " 5 | 0·70 | 2·44 |

The increase will become very apparent by contrasting the above quantities with the following determinations made from blood from the right side of the heart, taken during life:—

| | |
|---|---|
| No. 1 | ·047 |
| " 2 | ·073 |
| " 3 | ·058 |

The contrast between these results is very striking: it is to be regretted that no particulars are given of the way in which the dogs were fed on which the first experiments were made; of those on which the second set were instituted, two were fed on tripe, and one had been kept fasting for a day.

In procuring the blood of the right side of the heart during life, for the purpose of testing it for sugar, it is requisite that it be removed while the animal is in a state of tranquillity, as any struggling instantly increases the amount of sugar, probably by mechanically forcing the glucogen out of the liver, and which, as soon as it enters the blood, is almost instantly transformed into glucose. The sugar was estimated with the Barreswil solution, according to the process of Bernard. The blood was defibrinated, and about an ounce or an ounce and a half weighed out and treated with three or four times its volume of spirit. The liquid was separated by pressure through flannel, and the solid residue was several times washed with spirit, so as thoroughly to remove all that was soluble. By evaporation, an extract of small bulk was obtained, from which the sugar was estimated.

Dr. Pavy found, moreover, if a ligature was passed round the base of the heart instantly after death by pithing, that the blood of the right ventricle was as *free* from sugar as during life; but that, if even a minute or two were allowed to elapse before the chest was opened, the blood flowing from an incision into the right side of the heart was strongly saccharine.

Having thus determined the important fact of the difference in the amount of sugar contained in the blood of the right side of the heart before and after death, the next point was to determine the amount of sugar in the liver itself under different circumstances.

Thinking that blood might act as a more energetic ferment of the sugar-forming substance than the tissue of the liver alone, a solution of sulphate of soda was injected into the liver as instantaneously as possible, in order to drive out the blood from the vessels. The liver was then tested, and, although it was not entirely free from sugar, it yielded a much smaller reaction than usual. On a second analysis, two hours afterwards, an abundant orange-coloured precipitate was obtained with the Barreswil solution.

Dr. Pavy having found that although saliva instantly converts a neutral solution of the liver-substance into sugar, at a moderately elevated temperature, yet if either a little acid or alkali be added, the change is retarded according to the quantity used, now determined to inject the liver of a dog as instantaneously as practicable after death with a strong solution of potash, 300 grains to 3 oz. of water. It was in vain, he states, that he sought after this experiment for the presence of sugar either in the liver or the contents of the circulatory system.

Subsequently, experiments were instituted to prove that the potash solution used had in no way modified or destroyed the sugar. After injection with potash the liver was thus prepared for analysis: a piece being placed in a mortar was triturated to a pulp; a sufficient quantity of strong sulphuric acid was cautiously added to neutralize the alkali and leave a slight acid reaction, by which a solid mass was procured that yielded a clearish fluid on squeezing in a piece of flannel. This fluid was collected and rendered alkaline with potash, so as to allow of the application of the copper test.

In other experiments citric acid was substituted for the potash, and with the same result, no sugar being found in the liver; and, in preparing a liquid for testing, all that is required is to treat with a little sulphate of soda, filter, and neutralize.

A third series of experiments was now instituted, founded on a knowledge of the fact that an elevated temperature promotes the transformation of the sugar-forming substance into glucose, while cold either retards or stops it altogether, according to its degree.

Thus, if an animal, as a dog, be suddenly killed by the destruction of the *medulla oblongata*, and the abdomen instantly opened, and a piece of liver cut off and plunged into a mixture of ice and salt, the *post-mortem* transformation of the liver-material will be prevented, and an absence of sugar, Dr. Pavy affirms, will be observed. There are certain precautions which should be adhered to in this experiment; thus, the ice and salt should be liquefied before the immersion of the liver; and, since the reduction of the temperature acts gradually from without inwards, the outer parts and thin edges of the liver only should be tested for sugar. The centre of a portion of frozen liver remains soft and dark coloured for some minutes after immersion; while the exterior has become pale, and so hard as to be difficult to cut with a knife.

In preparing the liver for analysis after the operation of freezing, one or other of the following processes should be adopted, because treating with sulphate of soda is obviously objectionable.

The liver should be either cut into thin slices, pounded in a mortar, and thoroughly incorporated with spirit, by which means the glucogen is left behind, and the sugar, if present, is extracted.

Or the liver may be pounded in a mortar with a little solid potash, which, as before stated, prevents the transformation of the glucogen into sugar. The extraction of a liquid for analysis is then effected by the addition of sulphuric acid, as has been already pointed out.

Again, Dr. Pavy refers, in support of his views, to the following experiment of Bernard. If the spinal cord of an animal be divided just below the origin of the phrenics, and life be destroyed a few hours afterwards, the liver will be found free from sugar when examined immediately, but becomes strongly saccharine a little later. Dr. Pavy explains the absence of sugar in this case immediately after death, by the reduction of temperature which takes place, and which renders the transformation of the glucogen gradual in place of rapid. This experiment has been repeated with certain modifications, the results confirming the statement of Bernard as to the absence of sugar, and also the explanation of Dr. Pavy, that the non-formation of the sugar resulted from a reduction of temperature. A rabbit, operated upon as described, was placed on an engine-boiler where the thermometer stood at 88° F. After three hours it was suddenly killed by a blow on the head; and the liver, after trituration with potash, was tested with the Barreswil solution, the indication of the presence of sugar being as strong as if the specimen had been derived from a rabbit in which section of the spinal cord had not been performed.

To demonstrate still more completely the fact that it is to the reduction of temperature solely that the absence of the sugar is to be attributed, Dr. Pavy instituted another experiment.

When the coats of animals, as the rabbit, cat, &c., are oiled, their temperature, when exposed to cold, falls rapidly, and, if the cold be great, they die outright. Dr. Pavy found that, if the animals were killed when the temperature had descended to about 70° or 80° F., the liver immediately after death was likewise found free from sugar.

Lastly, the effect of temperature on the formation of sugar in the livers of cold-blooded animals, as the frog, first observed by Bernard, may be cited in corroboration of the view put forth by Dr. Pavy. Three frogs were exposed for three hours to a temperature of 90° F.; while another three were allowed to remain exposed to the air, which was cold but not frosty at the time; the livers of the first three gave a decided indication of the presence of sugar, but the others exhibited no reaction with the Barreswil solution.

One or two other particulars have still to be considered in connexion with the question of the formation of sugar in the liver during the life of the healthy animal. The presence of sugar in the blood, of course, by no means determines the point, since sugar may be derived directly from the food; or there is reason to believe that it may result from the escape of the glucogenic substance from the liver-tissue into the blood, when it becomes speedily transformed into sugar by the action of that fluid. If, states Dr. Pavy, the glucogenic substance be injected into the jugular vein of a rabbit or a dog, it rapidly gives rise to a strongly marked diabetic condition of the urine.

The escape of the glucogenic substance of the liver into the blood would serve to explain several particulars which have been noticed. It would account for the trace of sugar encountered in the circulation under ordinary circumstances; it would explain the increase in the amount of sugar which occurs, in disturbed states of the circulatory system, from violent struggling, producing compression of the organ, from disturbance of the respiration and from depletion. It has been shown by Bernard that, when an animal is bled to death, the last portion of blood abstracted contains more sugar than the first.

The experiments, as detailed by Dr. Pavy, upon the results of which his view, in opposition to Bernard, is based, seem conclusive: nevertheless, other experiments have been instituted by Dr. Harley with the co-operation of Dr. Sharpey, the conclusions being directly contrary, and confirming the accuracy of Bernard's statements as to the transformation during life and in health of the glucogenic substance into glucose.

### *Experiments of Dr. Harley.*

The experiments undertaken by Dr. Harley were designed expressly with a view to test the accuracy of the statement of Dr. Pavy, that the sugar found in the liver after death is due to a *post-mortem* change of the glucogen.

The mode of proceeding adopted was as follows:—

"In testing the blood, a quantity of distilled water, equal to about four times that of the blood used, was boiled in a capsule. To the water, when boiling, a few drops of acetic acid were added, and afterwards the blood was very gradually introduced. In order that the albumen might be thoroughly coagulated, a drop or two more of acetic acid was added, care being taken to avoid an excess. When the albumen was completely coagulated, which was known by its separating and floating in the clear liquid, the whole was thrown on a filter. The clear filtered liquid was then tested. The same process was followed when operating upon the liver."

The first experiments were so directed as to ascertain whether sugar was present in the blood under circumstances both favourable and unfavourable to its occurrence.

Blood drawn from the *carotid artery* of a dog fed upon bread, milk, and boiled liver, gave "distinct evidence of the presence of sugar."

In the next experiment, a dog which had been running at large was selected: a canula was inserted into the *left carotid artery*, and the blood allowed to flow directly into the boiling acidulated solution. The clear filtered liquid gave "a red precipitate" with the copper test.

The blood from the *right* femoral artery of a dog fed solely on flesh for four days was then tested in the same manner as in the previous experiment, and was found to contain sugar.

The amount of sugar in these experiments was not determined, "because," states Dr. Harley, "I knew that in healthy arterial blood it varied according to the state of digestion, and the kind of food—from an inappreciable quantity to 0·24 per cent."

Dr. Harley next operated upon the frozen liver of a dog fed for fourteen days upon animal food: pieces of the frozen liver were allowed to drop directly into the boiling acidulated liquid. On testing the clear filtrate, "distinct evidence of the presence of sugar was obtained."

The next experiment was undertaken for the purpose of showing that the sugar found in the frozen liver was really formed there, and was not carried to the liver in the portal blood.

The dog, the subject of this experiment, was fed for ten days on boiled tripe, and was killed after a fast of twenty-two hours. In the *portal* blood, "not a trace of sugar could be detected." On the other hand, the *hepatic* blood gave "distinct evidence" of its presence, as also the frozen liver.

Nearly the same results were arrived at in the case of a dog kept fasting for three days; no sugar was found in the blood of the portal vein, nor in that from the aorta, or inferior vena cava; but sugar was present in the frozen liver, in the blood which flowed from it, and perhaps a trace in that of the right side of the heart.

The last experiment instituted had for its object the determination of the relative amounts of sugar contained in a part of the frozen liver, and in another part of the same liver kept in the warm body of the animal. For this experiment a dog was taken, previously fed on animal diet, but which, five hours before it was pithed received a full meal of bread-and-milk. In the frozen portion of liver the sugar amounted to 0·333 per cent., and in that of the other portion to 1·55 per cent. Now, 0·333 per cent. of sugar in a human liver of the average weight of 50 ounces would amount to 70 grains.

From these experiments, Dr. Harley concludes that sugar is a normal constituent of the blood of the general circulation, and that since sugar is found in the liver at the moment of death, it cannot properly be ascribed to a *post-mortem* change. It is nevertheless apparent, especially from the last experiment instituted by Dr. Harley, that a very rapid and considerable formation of sugar takes place after death.

There is one important practical fact which it seems to the author may be deduced from the experiments of Bernard and Pavy, taken in conjunction with the ascertained circumstance that in diabetes there is no deficiency of oxygenating power whereby the accumulation of the sugar formed in the liver until diabetes results would be explained; and it is this—namely, that the presence of sugar in the blood in excess is due, not to lessened destruction of sugar, but to increased transformation of the glucogenic substance. This point once fairly established, a definite clue and direction is given to our treatment. Nevertheless, the discoveries of Bernard, even with a doubt hanging over the point just noticed, are of the very highest importance, from the light which they shed upon the nature of diabetes.

The extraction and properties of the glucogenic substance, and the circumstances which contribute to its formation, may next be considered.

### *Extraction of Glucogen.*

The glucogenic substance is possessed of very distinct chemical characteristics, the exact nature of which has been the more fully ascertained since methods have been devised for its separation and isolation from the tissues and other constituents of the liver, the liver-cells especially, in which it is affirmed to be located.

The method recommended for its extraction by Dr. Pavy is nearly as follows:—As soon after death as possible, the liver must be thoroughly washed to free it from sugar, cut into small pieces and thrown into a sufficient quantity of boiling water to cover it. After half-an-hour's boiling, the liquid is strained off through flannel, and the solid residue, after being pounded in a mortar, is boiled again for about an hour, with a fresh and larger quantity of water; the liquid is again strained; both portions are then mixed and evaporated; the glucogen rises as a scum, which is formed the more quickly as the evaporation proceeds, and is removed from time to time by means of a spatula, or glass rod; this removal of the scum is continued until the liquid is exhausted, or until only a small bulk remains, which may be thrown away. The glucogen thus obtained is, of course, impure; after being drained, it is left as a soft, pulpy, glutinous substance of a somewhat pale yellowish colour. It is now spread out and allowed to dry spontaneously; when dried, it forms a hard, brittle, semi-transparent, and gumlike body.

It may be obtained in a state of greater purity by means of the following process:—

The fresh liver is boiled with a solution of potash, by which it is completely dissolved; the glucogen is precipitated by alcohol, is washed repeatedly, is redissolved, and boiled a second time with potash; is again precipitated, and the alkali neutralized with acetic acid. The process adopted by Dr. Pavy in his determinations of the glucogen was founded on the above.

Two hundred grains of liver were taken and reduced to a pulp in water; two-thirds of its weight of caustic potash were added and incorporated with it; the mass was transferred to a porcelain dish, and sufficient water used to rinse out the mortar. The whole was kept boiling for about half-an-hour, until the liver was entirely dissolved; when cool, five or six times the bulk of redistilled methylated spirit were added, by which the glucogen was precipitated: this addition of spirit should be made at once. The supernatant liquor being drawn off, with its impurities, by means of a pipette, a fresh quantity of spirit was used, and the precipitate well stirred; the liquid was again removed and the washing repeated three or four times; the whole was then poured on to a filter and again washed, until the spirit that ran through became quite colourless; the glucogen was then dried and weighed, the weight of the filter itself having been previously determined. The whole process should be performed in as short a time as possible.

The chief impurity of the glucogen thus prepared consists of potash, which is found to adhere tenaciously to it, and which in one case was ascertained by Pavy to amount to one-fifth of the whole weight obtained.

### *Variation in the Amount of Glucogen.*

The researches of Pavy have clearly demonstrated the following facts in regard to the amount of glucogen in the livers of dogs.

First, that while glucogen is contained in the livers of dogs fed upon a purely animal diet, as tripe, the quantity is by about one-half less than in the livers of those which have been nourished either upon a purely vegetable or upon a mixed diet, as barley-meal and boiled potatoes, grape, and common moist cane-sugar. Thus, while the average weight of the liver of dogs fed on tripe nearly equals *half* *an ounce* to every pound of the animal's weight, that of five dogs under a strictly vegetable diet, exceeded *one ounce* to the pound; whilst upon an animal diet, mixed with sugar—that is, tripe or gut and sugar—the average of four cases amounted to within a fraction of an ounce to the pound.

The first and last results are particularly interesting and important in connexion with diabetes, as showing that glucogen may be formed, first, from substances destitute of sugar, and second, from cane-sugar itself. There is also another particular, of much practical value, resulting from the experiments with the mixed food—namely, that glucose was found in the urine.

The quantity of glucogen was determined in many of the cases experimented upon, and will be found set forth in the following table :—

Tables showing the relative amounts of glucogen in the liver after an *animal*, a *vegetable*, and a *mixed diet*.

| *Animal diet.* Per cent. | *Vegetable diet.* Per cent. | *Mixed diet.* Per cent. |
|---|---|---|
| 5·24 | | |
| 8·29 | | |
| 5·61 | 9·87 | 12·80 |
| 8·45 | 25·30 | 17·55 |
| 4·88 | 16·50 | 12·33 |
| 10·95 | | 15·37 |
| 6·94 | | |
| 5·44 | | |
| Average amount, 6·97. | Average, 17·23. | Average, 14·5. |

To these tables, as confirming in a very marked manner the comparative results therein set forth, may be appended the particulars of two other experiments made upon two half-grown rabbits, as nearly as possible resembling each other. One was kept without food for three days; the other was fed daily for the same period with one ounce of cane-sugar and the same quantity of starch, these being injected into the stomach. On the fourth day the examination was made.

The liver of the rabbit which had not been fed weighed one ounce, and furnished 1·4 per cent. of glucogen; that of the other, fed as above described, weighed 2¾ ounces, and contained 16·9 per cent. of glucogen.

Similar experiments were practised upon two adult rabbits, and with closely approximating results.

Dr. Pavy concludes his remarks on the influence of diet on the liver, by a reference to the views of M. Sanson, who maintains that there is but one source for the sugar found in the body, namely, the food; and further, that the glucogenic substance of Bernard is nothing but *dextrine*, and which he states does not belong exclusively to the liver, but is found in the blood and various organs and tissues of the body. The liver, he says, is not an organ for producing the glucogen, but simply for abstracting it from the blood, and transforming it into sugar with greater activity than is elsewhere effected. Dr. Pavy states, in opposition to these views, that he was unable to detect glucogen in either the spleen, kidney, or blood of dogs; neither did he find that the blood became saccharine after its removal from the body.

### *Properties, Physical and Chemical, of Glucogen.*

Glucogen, when pure, is a colourless, tasteless, inodorous, non-nitrogenous substance, soluble in water but insoluble in alcohol, and unaffected by even boiling solutions of potash: its reaction with iodine is particularly characteristic, that reagent causing it to turn of a wine-red colour.

Its physical appearance differs according to the mode of its preparation. When collected from the surface of its boiling aqueous solution, and when dry, it forms a brittle semi-transparent gumlike substance; when thrown down by alcohol, it occurs as a white flaky precipitate, which, when quickly dried, becomes white, opaque, and friable; but if slowly dried, it forms a hard semi-transparent substance.

It is thus evident that glucogen bears a very close resemblance in all its physical and chemical properties to dextrine, and the view of M. Sanson, that the glucogen of M. Bernard is nothing more than the dextrine of the food, has yet to be satisfactorily refuted.

One of the greatest chemical peculiarities of glucogen is, the extreme facility with which it becomes transformed into glucose, as by contact with animal matters, saliva and blood, which act as ferments, and even by boiling it for a few minutes with dilute sulphuric acid. Again, temperature exerts a great influence over its transformation; an elevated temperature hastens the change, but cold, according to its degree, either retards or altogether prevents the conversion.

Glucogen readily disappears from the liver; extreme and rapid reductions of temperature, and prolonged fasting, are sufficient to occasion its disappearance; any causes which seriously disturb the functions of life have the same effect; it is on this account that glucogen is so seldom found in the liver of the human subject after death.

Saliva, at a temperature of about 100°, as has been pointed out by Dr. Pavy, effects an almost immediate transformation of glucogen into glucose, provided the solution be neutral or nearly so; but if it be rendered either decidedly acid or alkaline, the change is greatly impeded. Thus the glucogen obtained by precipitation with spirit from the plain decoction of the liver is readily acted upon by saliva, while that thrown down from the potash solution is but tardily converted into sugar.

These facts may possibly turn out to be of much practical importance in the treatment of diabetes, and they appear to point to the propriety of the administration of certain acid and alkaline remedies.

### *Office of Glucogen in the Animal Economy.*

It is very certain that glucogen does not ordinarily pass from the liver as such, but that it undergoes a transformation therein. Bernard affirms that it is normally transformed during life into glucose; and Pavy, on the other hand, declares that this change takes place either after death, or, if during life, only as the result of certain abnormal and modifying circumstances.

If Bernard is right, what great purpose, it may be inquired, does this transformation of glucogen into sugar, and of this again into other products, carbonic acid and water, serve? Is it designed to form a channel by which the escape from the system of superfluous carbon is provided for, or is it a means for the maintenance of the temperature of the body?

But if Bernard's view is incorrect, we must then seek for another transformation, and another use of the glucogen. Dr. Pavy hints that it is concerned in the production of fatty matter.

To the author, it appears that one of the strongest facts which has been adduced against the normal conversion of glucogen into glucose, is the augmentation of the liver-substance, which has been shown to occur from the consumption of cane-sugar.

## ON THE ORIGIN OF GLUCOSE.

The glucose found, under certain circumstances, in the blood or urine, may proceed from one or more of several sources.

### *From Articles of Food in which it is present.*

First, it may be derived from articles of food in which it is present, introduced into the stomach: in this case it enters the blood, principally through the portal vein, by simple absorption.

It is obvious that the sugar from this source is incapable of giving rise to diabetes; otherwise, everybody at times would be diabetic. This sugar, therefore, in place of appearing in the urine, is either destroyed in the system in the same manner as Bernard believes the liver-sugar to be in health; or it is appropriated possibly in the formation of fat; or, as seems still more probable, it goes to form the glucogenic substance.

*From the Transformation of certain Constituents of the Food.*

Second, it may proceed from the direct transformation in the stomach of starch and cane-sugar, or of any articles containing them.

In healthy or normal digestion, however, the amount of glucose derived from this source is but very small, the starch being chiefly converted into dextrine, a change which is said to be effected simply by a catalytic action under the influence of warmth and nitrogenous matter, which acts as a ferment.

Now, it was from the transformation of the starchy constituent of the food that, formerly, the sugar found in the urine in diabetes was supposed to proceed; but independently of more recent researches, especially those of Bernard, this notion is controverted by the single fact—that if diabetes consisted only in an abnormal transmutation of starch into sugar, nothing further would be necessary for the cure of the complaint than rigid abstinence from the consumption of all articles containing sugar, dextrine, and starch; whereas it is known that while benefit is derived from such abstinence, it is by no means, in the generality of cases, sufficient to insure the removal of the malady.

Starch and cane-sugar introduced into the stomach, it is true, are converted into glucose; not in the stomach, but in the *liver;* and this not by direct transformation of the one kind of sugar into the other, but the cane-sugar is first changed into glucogen; which is transformed into glucose. This fact appears to be established by the experiments of Pavy, who found that the administration of cane-sugar augmented greatly the amount of glucogen in the liver.

*From Nitrogenous Food.*

A third source is from nitrogenous food, as has been clearly established by the observations and experiments already noticed under the heading *Influence of Nitrogenous Food on the Glucose;* but in this case also, it would appear that the sugar is not formed directly from the food, but from the glucogen of the liver.

*From the Tissues.*

A fourth and last source of glucose, as already pointed out, is in the tissues themselves; but here a difficulty and apparent inconsistency occurs. If in all other cases the glucose in diabetes is formed from the glucogen of the liver, it is not easy to see how, in the present case, the inference is to be avoided, that the glucose proceeds directly from the tissues; unless, indeed, these—instead of breaking down into urea, &c., as under ordinary circumstances—in diabetes give rise to the formation of some albuminous compound capable of being transmuted into glucogen. This inference, although not negatived, is weakened by the fact that in most cases of diabetes the urea is itself greatly augmented.

The following Table exhibits the elementary composition of *dextrine, starch, cane-sugar, muscle-sugar, glucose, glucogen,* and *lactic acid.* From a comparison of the figures given, the close connexion which exists between these bodies is rendered very apparent.

| | Dextrine. | Starch. | Cane-sugar. | Muscle-sugar. | Glucose. | Glucogen. | Lactic acid. |
|---|---|---|---|---|---|---|---|
| Carbon . | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| Hydrogen | 10 | 10 | 11 | 16 | 14 | 12 | 12 |
| Oxygen . | 10 | 10 | 11 | 16 | 14 | 12 | 12 |

If the glucose be anhydrous, its composition is $C_{12}, H_{12}, O_{12}$.

### MODES OF DISAPPEARANCE OF SUGAR IN THE SYSTEM.

That sugar does disappear in the system is undoubted.

There are two ways in which this disappearance may be, and probably is, accomplished.

First (and about the correctness of this there is no doubt), it disappears by appropriation or assimilation, contributing, most probably, to the formation of fat.

Second, it is affirmed that it is destroyed in the blood.

Bernard, as we are aware, states that sugar is always produced in the liver from the glucogenic substance; and also that, normally, it is destroyed on its way to and in the capillaries of the lungs by conversion into *carbonic acid* and *water.*

By some, the opinion is held, that it is converted into lactic acid; but no sufficient evidence would appear to have hitherto been adduced in support of this view.

### SYMPTOMS OF DIABETES.

The symptoms of diabetes, in its early stage, are by no means marked; and hence the disease is very apt at the onset to be overlooked, and too frequently when it falls under the notice of the physician it has become confirmed and advanced.

When advanced, they are so characteristic that they can scarcely fail to excite attention.

The first symptoms which usually attract notice are the frequency with which the urine is voided, and particularly the large quantity passed.

As the disorder progresses, other symptoms arise: the odour of the *breath* is peculiar, resembling, according to Dr. Watson, that of ripe apples; there is great and almost insatiable *thirst*, and obstinate *constipation;* these latter symptoms depend mainly upon the drain of fluid from the system. Gradually, as the amount of urine voided is lessened, the thirst and constipation become relieved.

Another symptom, arising from the same cause, is dryness and harshness of the *skin*.

Lastly, there is *wasting*, which is very great in severe cases, and as a consequence of this *debility*.

As the disease advances towards a close, the *lungs* are apt to become affected, chronic inflammation is set up, ending in the breaking down of the lung-tissue; this is a very frequent complication of the disorder in its worst form, and also a most unfavourable one. Not unfrequently the sight is impaired by the formation of *cataract*.

We must be on our guard against coming to the conclusion, from the large quantity of urine voided, that the case is one of diabetes. Cases are of by no means uncommon occurrence, in which much urine, of pale colour and of low specific gravity, is passed: these cases being likewise attended with thirst and emaciation are very apt to be mistaken for diabetes; they differ, however, in the absence of sugar.

On the other hand, caution is required not to overlook the diabetic element which sometimes exists in such cases; for, notwithstanding the low density of the urine, it does yet not unfrequently contain sugar. The author has met with several such cases in which the health has been considerably impaired.

## TREATMENT OF DIABETES.

We have at length arrived at the important subject of the treatment of diabetes.

With the knowledge which we now possess of this complaint, certain principles upon which that treatment should be based are clearly indicated.

First. The knowledge of the fact that the sugar found in the urine proceeds from a transformation of the glucogenic substance of the liver, and that the amount of this substance is increased by the consumption of saccharine and feculent food, is demonstrative of the paramount importance of strict regulation of the diet in this complaint.

Second. Nutrition being perverted, the food which should nourish and sustain the body escaping so largely by the urine in the form of sugar, the disease, in fact, being so completely of an exhaustive character, it is obvious that the powers of the system must be maintained, not merely by the judicious regulation of the diet, but by every other means by which those powers can be preserved: as by avoiding over-exertion of every kind, fatigue of mind and body, anxiety, and by the administration of restorative and tonic remedies.

Third. The causes which have led to the malady should always be inquired into, as these will sometimes influence the treatment: whether the disease be inherited or not; whether due to any trying circumstances in the life of the patient, over-exertion of mind or body, anxiety, venery, mercury, &c.

In general, in going into the history of these cases, we shall light upon one or more predisposing causes; many of these have clearly been followed by exhaustion of the nervous system, and that this condition is intimately connected with diabetes is unquestionable, since lesion of certain portions of that system, and particularly of the sympathetic, is itself alone sufficient to produce temporary diabetes.

*On the Diet.*—From what has already been stated, it is obvious that, in regard to diet, the main indications to fulfil are, first, to prescribe animal food very freely; and second, to cut off as far as possible all those articles by which either sugar or starch may find an entrance into the system.

If digestion is sufficiently active, the patient should eat meat three or four times a day, especially lamb and mutton.

Other articles of animal diet which may be freely used, are, venison, game, poultry, fish, eggs, plain soups, cured meats, cheese; and milk occasionally only, on account of the sugar which it contains.

Isinglass, gelatine, and all articles, as jellies and blancmange, containing them, are amongst the least desirable of all the nitrogenous articles of food; since they increase considerably the amount of sugar.

Amongst articles of *vegetable diet*, the use of which may be permitted, are gluten bread and biscuits, prepared bran biscuits and cake, and occasionally the green and some other vegetables, as the different kinds of green cabbage, spinach, French beans and scarlet runners, the green tops of asparagus, watercresses, celery, kale, endive, and green lettuce. These vegetables should, however, be partaken of only occasionally and cautiously, and if the case does not progress favourably, they had better be discontinued, especially those of a white colour, as celery, kale, and endive.

The following articles should in general be altogether omitted from the diet of the diabetic:—wheaten bread, fermented or unfermented, white or brown, the white fermented bread being the most objectionable; biscuits, semolina, flour, and all puddings, pies, and other articles made therefrom. Vermicelli and macaroni, Italian paste and semola, on account of the larger proportion of gluten contained in them, are less prejudicial. Arrowroots of all kinds, since they consist wholly of starch, should be avoided; rice, sago, potatoes, parsnips, beetroot, carrots, turnips, Jerusalem artichokes, are all very objectionable; peas, lentils, broad and haricot beans, less so, although still objectionable, as also cauliflower and broccoli, which contain sugar, as do most of the white vegetables.

Of *fruits*, nearly all kinds should be avoided, since they all contain glucose or grape-sugar, the dried fruits especially, such as currants, raisins, figs, dates, &c.; and amongst fresh fruits, peaches, grapes, plums, pears, strawberries, gooseberries, cherries, &c.

It will be apparent, from a consideration of the above lists, that while a person labouring under diabetes is debarred from many articles of diet, yet that a tolerably large number of the more important kinds remain for his use. No patient afflicted with this malady need ever hope to get well, who is incapable of exercising great self-control in respect to diet.

The gluten bread, gluten and bran biscuits and cake, may be used alternately. The bran from which the biscuits and cake are made should be specially prepared, as in its ordinary condition it is coarse, and contains sometimes as much as fifty per cent. of starch. It should therefore be ground very fine, whereby it is rendered more easy of digestion, and less irritating to the bowels; and the starch should be separated from it as much as possible, by friction and sifting, and by washing it first in hot and subsequently in cold water, by pressing and finally drying it; the washed and dried bran is rendered more brittle by this process, and admits of being ground more readily. The bran thus prepared should contain scarcely a trace of starch.

Dr. Camplin recommends that a quart of ordinary bran should be boiled in two successive quarts of water, for a quarter of an hour each time, strained through a sieve, and then washed on the sieve with cold water, until the water runs through clear; lastly, that it should be squeezed in a cloth to free it from water, and then dried slowly in an oven. It is to be feared that after this treatment the bran would be but little nutritive.

Of this prepared bran, three ounces should be taken; three new-laid eggs, $1\frac{1}{2}$ or 2 ounces of butter, and rather more than half a pint of milk; beat up the eggs, mix with a portion of the milk, melt the butter in the other portion, previously made warm, and stir the whole well together; add nutmeg or a little ginger; make into biscuits and bake; they should be kept in a dry place, and in a tin case. They may be obtained of Mr. Blatchley, of Oxford Street, and of Mr. Donges, the successor of Mr. Smith, of Gower-street North. Mr. Blatchley also makes a bran cake which has the advantage of being softer than the biscuit; and he likewise supplies prepared bran-powder of a very superior description.

The bran biscuits, and particularly the cake, are more agreeable to the taste than ordinary gluten bread; and when carefully prepared contain scarcely any starch, and have, moreover, the advantage of assisting in the regulation of the bowels.

Nevertheless, the gluten bread is a valuable article of diet, in the treatment of diabetes. It is very much more nutritious than the prepared bran, containing some 75 per cent. of gluten, but also some 25 per cent. of starch.

Biscuits may be made from gluten, containing scarcely any starch, somewhat after the receipt given above for the bran biscuits; indeed, Mr. Blatchley prepares a gluten biscuit which is nearly free from starch, and which also is of pleasant flavour, and is readily masticated.

A very valuable article would be a biscuit made of equal parts of the prepared bran and pure gluten, and to the preparation of this Mr. Blatchley is now about to turn his attention.

The gluten bread may be procured of Mr. Van Abbott, of Fenchurch-street. The impropriety of using in diabetes ordinary bread, may be judged of when it is stated that wheat flour contains some 80 per cent. of starch.

In order to obviate the objection which exists to the less pure forms of bran and gluten, arising from the presence of more or less starch, Dr. Pavy has had prepared by Mr. Hill of Bishopsgate-street an almond biscuit, the almond-powder being washed in boiling water, and mixed up with eggs. This must be too rich for most stomachs, and should be mixed with some substance which would render it less so, as torrefied cotton-pulp, potato-fibre from a starch manufactory, or the prepared bran-powder.

Under the head of Diet, a few remarks may be made upon the plan of giving in diabetes large quantities of *sugar*.

It does not appear that any great success has attended this mode of treatment; neither on rational grounds was success to have been anticipated. Experiment proves that the sugar given, whether cane or grape-sugar, is converted in the liver into glucogen, and that from this the liver or diabetic sugar is formed. There is therefore good reason to believe that the administration of sugar, like starch, must be positively hurtful.

Amongst the *liquids* which may be partaken of in diabetes may be enumerated water, tea, coffee, pure cocoa; milk sparingly and occasionally only; bitter beer; the light wines, as claret or light dry sherry; the stronger and sweet wines, as Malaga and Madeira, all home-made wines, cyder, and perry, should be avoided. It must be remembered that even beer and the light wines increase sugar somewhat; as does also milk.

Excessive consumption of *water* appears to act on the sugar in the same way as it was shown to do upon the urea, that is, it increases the amount somewhat. This result is no doubt partly due to the washing out some of the sugar from the tissues. Abstinence from water, of course, lessens the sugar, owing, it is believed, simply to retention. A perseverance in abstinence causes patients to feel exceedingly ill and depressed. It thus appears that water should be indulged in to a moderate extent only.

*Coffee* lessens the sugar. *Cocoa* contains a little starch, about

11 per cent., and may tend, therefore, *slightly* to increase the sugar; but it is, in many respects, a most useful article of diet, and it may safely be taken occasionally. The mixtures sold as cocoa nearly all contain large per-centages of starch, and therefore on no account should be used, but the cocoa-nibs, which are nearly always genuine. *Beer*, as already stated, increases the sugar somewhat, the chloride of sodium much, but lessens the urea slightly. Of all the beers brewed, those of Bass and Allsopp are the best, since they contain comparatively but little sugar. The light wines, as *Bordeaux*, exert nearly the same effects. *Alcohol* increases the *sugar*, according to Gunzler, Ott, and Leubuscher, and lessens the *urea;* injected into the *vena portæ*, it produces temporary diabetes (Harley).

It must be constantly held in remembrance, that it is necessary the system should be supplied with heat-producing food of some kind. Starch and sugar are interdicted; but in the various kinds of fatty matters, and in alcohol, we have a class of calorifiants which are not susceptible of the saccharine transformation, and the administration of which, therefore, is specially indicated.

*On Medicine in Diabetes.*—The medicines to be administered in cases of diabetes belong, for the most part, to the class of tonics. There are but few remedies which can be said to exert anything like a specific influence in reducing the amount of sugar; the benefit derived, in most cases, being due to the effect of the medicines prescribed, in improving the tone of the system.

It is, indeed, true, that some few remedies occasion a diminution of the urinary sugar, and therefore the exhibition of them should form part of the treatment.

The following may be enumerated as amongst the more important and useful tonics:—The various preparations of *iron* and *quinine*, as the *citrate of iron, citrate of ammonia and iron, citrate of iron and quinine, mistura ferri composita, liquor cinchonæ, decoctum cinchonæ*, and *sulphate of quinine.*

In the choice of the exact remedy, we must, of course, be guided by the symptoms and general condition of the patient, as in some cases many of the above preparations might not be desirable.

Where there is great depression, *ammonia* will often be found useful; and it may be combined with either infusion of *quassia* or decoction of *bark.*

Where the quantity of urine eliminated is very large, small doses of *morphia* or *opium*, of which remedies there is great tolerance in diabetes, may be occasionally administered.

The *phosphates of soda* and *ammonia* have been administered with a view to improve the nervous energy, but without any very marked results; the amorphous or red phosphorus, given in pills in doses of half a grain, would be likely to have a greater effect.

Taking into consideration the fact that certain *acids* and *alkalies* prevent or retard the conversion of glucogen in the dead body into glucose, benefit will be found to result from the administration of some of these.

*Bicarbonate of soda* lessens the amount of sugar in the urine, according to Gunzler, to the extent of one-fifth.

The *Vichy* waters, which contain a large quantity of that alkali, are said to exert a similar effect.

It is remarkable that these and other alkaline remedies, even when administered in very large doses, do not in diabetes exert their ordinary effect, but fail to render the urine alkaline.

The *Carlsbad* waters, tried in one case only, did not lessen the sugar, and this although the urine was rendered alkaline.

Other remedies which have been tested experimentally, but which did not appear to exert any marked effect, are *permanganate of potash*, an oxydizing substance (Parkes); *lactate of iron, benzoic acid*, and *benzoate of ammonia* (Leubuscher).

*Tartaric acid* increases the sugar (Rosenstein), as does also *pepsin* (Leubuscher).

No precise experiments have as yet been made with a view to determine the action of *the mineral acids.*

*Cod-liver oil*, especially the fresh English oil, will be found highly serviceable in some cases.

M. Bouchardat, in a communication recently addressed to the Academy of Medicine, and which will be further referred to, assigns great therapeutical value to both fatty matters and alcohol. "If," he states, "for those aliments, such as sugar and starch, which are so readily and completely (so to speak) converted into glucose in the system, we substitute either partially or wholly the calorifiant aliments, such as fatty matters and alcohol, which do not undergo the saccharine transformation, then two results present themselves: the glucose either disappears, or is sensibly diminished in quantity."

The *thirst* and *constipation* are very troublesome, especially in the severer cases. Very weak tea, coffee, and toast-and-water are the safest beverages; but these should be indulged in only in moderation. Equal parts of milk and lime-water form another good drink.

For the relief of the constipation, an enema of warm water or gruel is the best, as it does not add to the debility. One of the mildest aperients which can be used is *olive oil.*

Attention to the *skin* is also of great importance in the treatment of diabetes: this is dry and harsh, owing to the draining away of the fluids of the system by the kidneys; and, consequently, its eliminative function is much impeded. Benefit will therefore be derived from occasional tepid bathing and friction, while the clothing should be of the warmest description. Generally, when the sweat is at all abundant, sugar, sometimes in large amount, is present in that excretion. In a case of diabetes attended with profuse sweating, Griesinger found the amount of sugar in the urine to sink in twenty-four hours from 187 grammes to 100 and 85·7 grammes;

while Fletcher procured $6\frac{1}{2}$ grains of sugar from a piece of flannel which was allowed to remain in the axilla for forty-eight hours.

In the intermittent form of diabetes, attention should be specially directed to the improvement of the functions of the digestive organs.

M. Demeaux, in a Memoir read before the Academy of Sciences, has recommended two new remedies for the treatment of diabetes, "I have been," he states, "for several years past in the habit of using, in cases of diabetes mellitus, a mixture of equal parts of *rhatany* and *calcined alum;* and have been so far successful as to think it incumbent upon me to call the notice of the profession to the effects I have witnessed. In all cases I have obtained a decided modification and amelioration of the symptoms; and in two instances in which the disease was well marked, a continuance of the above treatment brought about an entire cure."

## PROGNOSIS.

The prognosis in this disease is now much more favourable than it was some years since, when diabetes was looked upon as incurable, and as necessarily running on, sooner or later, to a fatal termination. At the present time, on the contrary, few cases are met with which may not be materially benefited by appropriate treatment, while many may either be cured absolutely, or the symptoms may be so far ameliorated that patients may live on, with perhaps occasional mild attacks of the disease, for many years. It is in all cases, however, essential to successful treatment, that the patient exercise self-control, and abide rigidly by the instructions of his medical adviser.

There are circumstances which greatly influence the prognosis.

One of the most material of these is the presence or absence of organic disease. In the earlier stages of this affection, in the majority of cases, no organic mischief is discoverable; but as the disorder advances, and as debility and emaciation increase, phthisis too frequently sets in, and when this complication has been superadded to the original complaint the prognosis is anything but favourable.

Respecting the cause of the development of tubercles in the lungs M. Bouchardat addressed to the Academy of Medicine, in 1851, some important practical observations.

He is of opinion that tubercles only appear when the resources of calorification are well nigh exhausted by the advance of the glucosuria, and when, in consequence of this exhaustion, the functions of the lungs and of the entire colorifiant apparatus are indirectly impaired.

He states, further, that having watched, during several years, patients affected with diabetes mellitus, he has invariably remarked that when the nutritive powers were tolerably active, and the quantity of sugar passed in the urine during twenty-four hours did not exceed three ounces and a quarter, the lungs were no longer subject to tubercular deposits; and he holds it, therefore, to be a law that tubercles always appear in the lungs when the elimination of sugar takes place in considerable quantities, and during a sufficiently long space of time. "In some diabetic patients I have seen," states M. Bouchardat, "an elimination of sugar amounting to two pounds daily, this elimination being effected by the non-utilization, by the economy of the ingested aliments, and by the consumption of the tissues it holds in reserve. The office of the eliminated principle is evidently, in the normal state, that of supplying the wants of calorification, consequently the diabetic patient is so situated that he throws off, as waste matter, the aliment by which the calorifiant function is supported."

By similar reasoning M. Bouchardat accounts for the liability of the cow to tubercles of the lungs. Fed upon foods abounding in sugar and starch, and yielding enormous quantities of milk, it, especially if confined in stables and deprived of air and exercise, speedily becomes phthisical.

The condition of the urine will often throw light upon the important question as to whether organic disease exists or not. Thus in some of the severer cases of diabetes the urine is albuminous, indicating constitutional mischief. The presence of albumen is therefore an unfavourable symptom.

The prognosis is also unfavourable when, combined with great emaciation, the *quantity* of saccharine urine passed *is very large*,—from 10 to 12, or more, pints a day.

It is likewise unfavourable where any *hereditary predisposition* to the complaint exists.

The favourable circumstances are the absence of organic disease and of albumen in the urine, a moderate discharge of urine, four or five pints daily only, and a certain stoutness of person.

A careful observation of the effect of diet on the quantity of sugar excreted will materially assist our prognosis.

If, when all saccharine and amylaceous substances are excluded from the diet, the sugar disappears from the urine, the case is probably either in its early stage, or is of a mild character. If, in place of disappearing altogether, it is very much reduced, this again is so far favourable.

If, however, on a meat diet, the quantity of sugar is large, the prognosis is far less favourable.

And if, during complete abstinence, as in the twelfth or fourteenth hour of fasting, it is still considerable, the case is unquestionably of a very serious character, since the sugar can only be formed at the expense of the tissues.

As any case progresses favourably the quantity of urine is gradually diminished, the thirst becomes less, the constipation is not so obstinate, the skin is less harsh, and the strength and weight of the body increase.

It should be remembered that no great change, at first, is in general observed in the specific gravity of the urine passed; but merely in the quantity, the gravity remaining nearly the same. It is only as an approach is made towards recovery that the specific gravity gradually falls, so that, if we would judge correctly of the progress of any case, we must observe, not merely the weight of the urine voided, but the quantity. This is an important practical fact, and, unless attended to, we shall often be led, from observing the specific gravity to remain so stationary, to come to the erroneous conclusion that the case is not being benefited by the treatment. It should also be remembered that on a meat diet the urea, and consequently the specific gravity of the urine, is greatly increased.

There are two other particulars in connexion with a diminution in the amount of sugar, which must not be forgotten.

One is, that *inosite* sometimes replaces the sugar, and for which, therefore, search should always be made in diabetic urine, since this, if overlooked, might mislead. The sugar being lessened, the conclusion might be formed that the case was progressing favourably, whereas inosite, which differs so slightly in composition from glucose, might be substituted for it. In a case which occurred to Vohl, the patient continued to lose ground, although the sugar kept diminishing; but he discovered that inosite was present, and increased in proportion to the diminution of the sugar, and he procured no less than from 278 to 309 grains of that substance per day.

The second fact is, it sometimes happens that, for some days before *death*, the sugar entirely disappears from the urine.

## INOSITE.

This body, allied closely to glucose, was discovered by Scherer in the decoction of muscle, and has hence been termed "muscle-sugar." It has since been found in the lungs, kidneys, spleen, liver, and urine.

*Chemical Characters.*—It has a sweet taste, is readily soluble in water, slightly so in spirits of wine, and not at all in alcohol and ether; it crystallizes from a boiling spirituous solution as it becomes cold. In its crystallized state it contains four atoms of water; it effloresces on exposure to the atmosphere, and at 200° F. it loses its water of crystallization; at 410° F. it fuses, and at a higher temperature it becomes decomposed. Evaporated with hydrochloric acid it is unchanged, as, also, when boiled with caustic potash; neither does it throw down the suboxide of copper, with the copper test for glucose: it is not susceptible of the vinous fermentation; but with yeast and in the presence of animal matter, it undergoes the lactic and butyric fermentations.

*Composition.*—Carbon, 12; Hydrogen, 12; Oxygen, 12+HO 4.

*Preparation.*—The juice of the heart of the ox is to be treated in the same manner as in the preparation of creatine from muscle. The baryta is to be separated from the mother-liquor, decanted from the creatine by means of sulphuric acid; the sulphate of baryta is removed by filtration; the liquid is then to be evaporated, to free it from the volatile acids. Strong alcohol is to be gradually added, when the *inosite*, together with sulphate of potash, will separate in a crystalline state; the mother-liquor may then be removed, when the crystals of inosite may be picked out, or they may be separated by means of boiling water, in which they are more soluble than sulphate of potash.

Scherer has pointed out the following characteristic *test* for inosite. The solution of inosite, or mixture containing it, is to be evaporated, with a little nitric acid, almost to dryness on platinum foil; the residue is to be treated with ammonia and a little chloride of calcium and evaporated to dryness, when a *vivid rose-red tint* is developed. No similar reaction takes place with any other sugar or carbohydron.

*Microscopical Characters.*—Inosite crystallizes in four-sided prisms. The crystals usually occur in groups, but sometimes singly.

### *Pathology of Inosite.*

Inosite has been found in the urine in diabetes, in two cases, by different observers; in one it was observed, by Vohl, to replace the glucose: as this lessened, the inosite increased, and Vohl obtained from 18 to 20 grammes of inosite from the day's urine, equal to 278 and 309 grains. It has likewise been discovered by Cloetta and Neukomm in the urine in Bright's disease. The tasteless sugar of Bouchardat and others was probably inosite.

Its pathology is very closely connected with that of glucose.

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# CHAPTER VIII.

## VARIOUS ORGANIC ACIDS.



### CARBONIC ACID.

Carbonic Acid ($CO_2$), both free and combined, is frequently present in the urine; it may be traced to several sources.

Thus sometimes it is introduced into the system from without, through the various carbonated beverages and carbonates of the alkalies consumed.

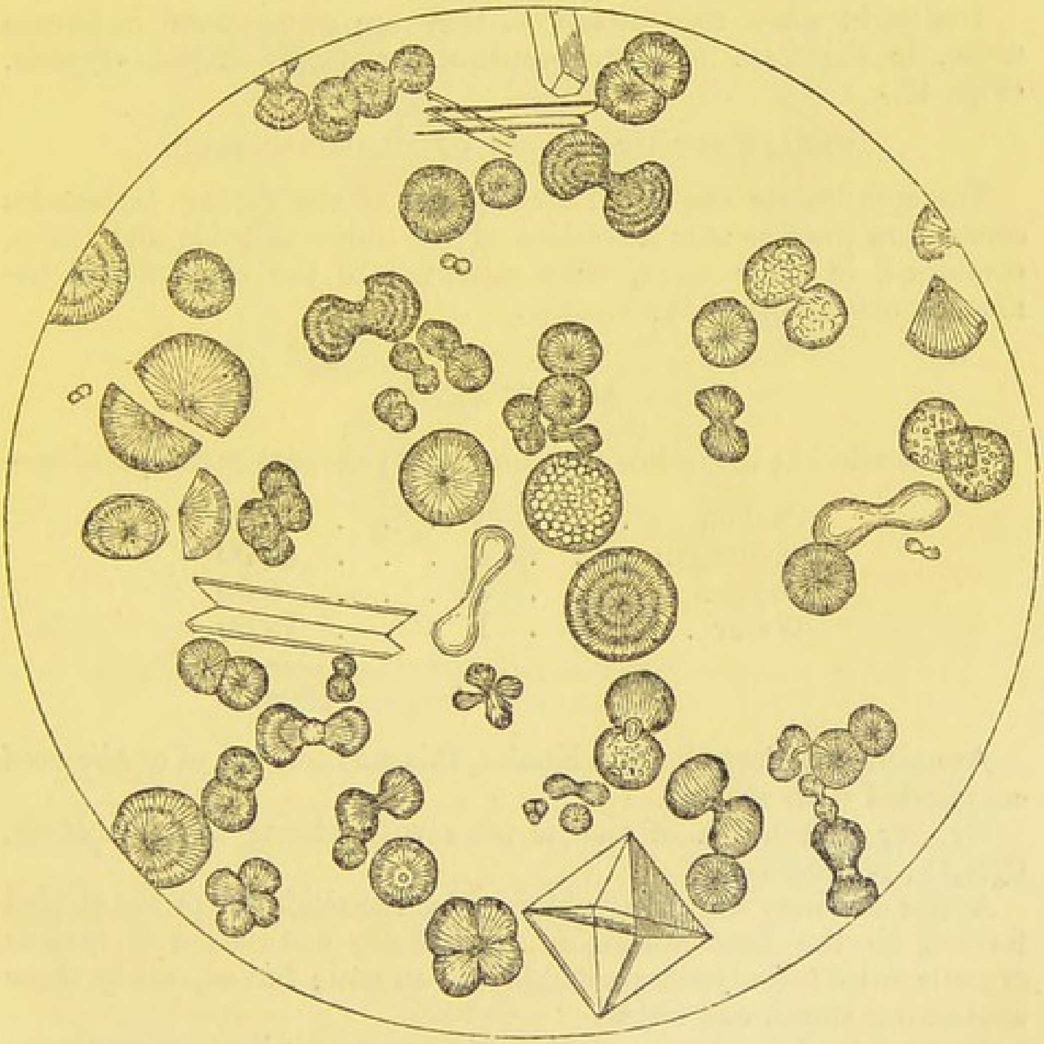
At others it is formed within the organism, as from the transformation of various vegetable acids, as citric, malic, tartaric, and acetic acids.

Or, lastly, it may be derived from the decomposition of urea.

The most frequent combinations of carbonic acid in the urine are with lime and magnesia: when either of these salts occurs, the carbonic acid is usually derived from urea, while the base is obtained by the decomposition of the earthy phosphates.

Usually the earthy carbonates occur in an amorphous state, but

FIG. 46.



*Spherical* and *Dumb-bell* Crystals of CARBONATE of LIME; from the *Urine of the Horse.* Magnified 220 diameters.

the late Dr. Golding Bird met with carbonate of lime in the globular and stellar forms. "The few instances of this kind I have met with occurred in neutral or faintly acid urine, a condition probably necessary to ensure the regular structure of the little crystalline masses." Examined with polarized light, a black cross becomes visible in the centre of each spherule.

Crystalline deposits of carbonate of lime are of constant occurrence in the urine of the herbivora, especially in that of the horse and ox: they form very beautiful microscopic objects, consisting of regular globules of various sizes, resembling pearls, and exhibiting very clearly, when immersed in Canada balsam, a radiated texture, owing to their being composed of numerous acicular crystals. (Fig. 46.)

Not unfrequently, the crystals of carbonate of lime assume the dumb-bell form. (Fig. 46.)

Lastly, in some rare instances, they are encountered in human urine, in the form of very beautiful cornucopia-shaped crystals. (Fig. 47.)

### TREATMENT OF EXCESS OF CARBONIC ACID.

The appropriate treatment for deposits of the earthy carbonates consists in the free administration of the mineral acids and tonics, combined, in some cases, with attention to the condition of the mucous membrane of the bladder.

## ACETIC ACID.

Acetic acid has the following atomic and per-centage composition—

| | | |
|---|---|---|
| Carbon | 4 | 40·00 |
| Hydrogen | 3 | 40·00 |
| Oxygen | 3 | 5·00 |
| Water | 1 | 15·00 |
| | | 100·000 |

According to Berzelius and Kohler, this acid consists of *oxalic acid* conjugated with *methyl.*

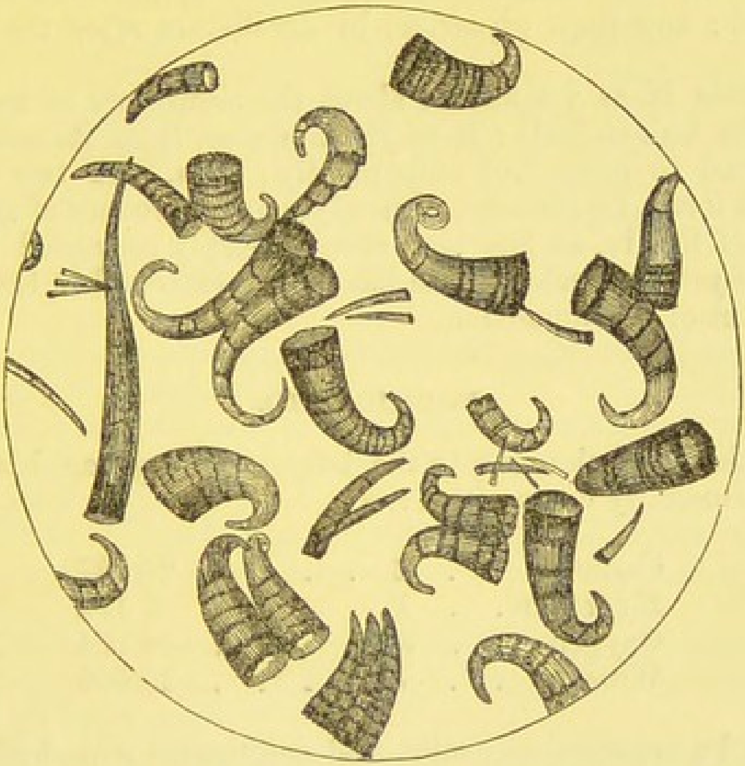
By dry distillation of the acetates with strong bases, *acetone,* $C_6H_6O_2$, is produced.

Acetic acid may be readily obtained by the oxidation of the alcohol formed by the fermentation or by the dry distillation of various organic substances, both vegetable and animal; but especially those containing starch and sugar.

In a moderately strong solution of an acetate, nitrate of protoxide of mercury produces, after a time, a precipitation of glistening fatty-looking crystalline scales, while on the addition of a persalt of iron a somewhat intense red colour is produced.

This acid is met with sometimes in the *stomach,* and it is probable that alcohol may in some cases be in part converted into it in that organ. Scherer has found it in the *juice of flesh*. Bouchardat and Sandras think they have discovered it in the *blood* of animals whose food has been steeped in brandy. It has been detected in *saccharine urine*, resulting, probably, from the oxidation of the alcohol formed during the fermentation of the sugar.

FIG. 47.



Remarkable *Cornucopia-shaped* Crystals of CARBONATE of LIME; from *Human Urine*. 220 diameters. 1851.

*Acetone* has been obtained by Petters, by the distillation of the urine in a case of diabetes, and in one of measles.

Acetic acid would doubtless be more frequently present in the urine, but for the fact that the acetates, in their passage through the system, are converted into carbonates.

## METACETONIC ACID.

This acid, also known by the names *butyro-acetic* and *proprionic acids*, has the following composition: $C_6H_5O_3+HO$.

Kolbe regards it as *ethyloxalic acid*, $=C_4H_5,C_2O_3,HO$.

It forms, with various bases,salts having a fatty appearance, and imparting an oily sensation to the touch.

It is a volatile acid, like the others of the same group: it may be separated from formic acid, by means of oxide of mercury; and should acetic acid be also present, soda should be added, when, on evaporation, the acetate will crystallize before the metacetonate; or oxide of lead may be employed, it forming with the one acid a crystallizable, and with the other a non-crystallizable salt.

It is generated during the decomposition of many vegetable substances, as peas and lentils; by the action of potash on sugar, starch, and gum; in the oxidation of fats and of albuminous bodies, by nitric acid; and from glycerine, by distillation after the action of yeast.

But little is as yet known about the occurrence of metacetonic acid in the human body: it might, however, from its composition, be expected to occur not unfrequently; thus, with two atoms of oxygen it forms *lactic acid*, while glycerine, a product of the decomposition of fat, is, as has been stated, readily converted into this acid. As yet, metacetonic acid has only been found in the urine as the product of decomposition.

## FORMIC ACID.

This acid, also belonging to the butyric acid group, has the following elementary composition:—

| | | |
|---|---|---|
| Carbon . . . | 2 . . . . . | 26·087 |
| Hydrogen . . | 1 . . . . . | 2·174 |
| Oxygen . . | 3 . . . . . | 52·174 |
| Water . . . | 1 . . . . . | 19·565 |

It may be regarded as oxalic acid conjugated with hydrogen, or as containing the radical *formyle* ($C_2H$), which with chlorine forms *chloroform*.

It is a volatile acid, and is distinguished from the other acids of this group by its power of reducing, when solutions containing it are warmed, the oxides of silver and mercury; and since its boiling-point is lower, it may be separated from them by fractional distillation.

Formic acid exists ready formed in ants, especially *formica rufa*, and in caterpillars (Will): it has been found by Scherer in the juice of muscle, in the fluid of the spleen, in the blood in leucæmia; and by Lehmann and Campbell in normal human sweat. Bouchardat and Sandras believe that they have detected it in the blood of dogs fed for a long time upon sugar. Lastly it has been found by Campbell in the urine in phthisis.

Formic acid may be artificially prepared by the oxidation of various animal and vegetable substances—as by distilling sugar with water, sulphuric acid, and bichromate of potash. Bouchardat and

Sandras are of opinion that starch and sugar in the blood, before they are reduced to oxygen and water, are first decomposed into formic acid.

## BUTYRIC ACID.

This acid at ordinary temperatures forms an oily rancid-smelling volatile fluid, and may be regarded as oxalic acid, conjugated with the hydrocarbon, $C_6H_7$.

It has the following composition :—

| | | |
|---|---|---|
| Carbon | 8 | 54·545 |
| Hydrogen | 7 | 7·955 |
| Oxygen | 3 | 27·273 |
| Water | 1 | 10·227 |
| | | 100·000 |

It forms various salts with the alkalies, earths, and metallic oxides.

Butyric acid exists in rancid butter, and is also found amongst the products of its saponification.

It is likewise produced from nitrogenous matters—as albumen, fibrin, and gelatine—during their putrefaction or decomposition by strong oxidizing agents.

Lastly, it is formed during the fermentation of starch and sugar, the nitrogenous matters with which these are intermixed acting only as ferments.

Lactate of lime, in the presence of a ferment becomes converted into a butyrate of lime, and it is from that salt that butyric acid is prepared on the large scale.

When present with other acids of this group, it may be obtained according to the process given by Lehmann,—first, it is separated by distillation from the non-volatile acids, as lactic acid; we may have, however, in the distillate, formic, acetic, and metacetonic acids. The first is removed by means of its property of reducing the oxides of gold and silver; the remaining acids must then be combined with soda. The greater part of the acetate of soda may be separated by crystallization; the other soda-salts are to be decomposed with moderately concentrated sulphuric acid, yielding in the receiver metacetonic and butyric acids, with a little acetic acid, and from these the butyric acid may be separated by fractional distillation, the metacetonic acid passing over at 284° F., and the butyric acid not till the temperature is raised to 320° F. or 329° F.

Butyric acid has been detected in the food rejected from the stomach, in the *urine* (especially diabetic urine, being formed after emission), in the *sweat*, and in *milk*.

Nothing of a definite character is at present known respecting the precise origin in the animal body of butyric acid: it is a product of the decomposition of certain of the nitrogenous tissues, and of some of the non-nitrogenous substances, as the fats.

## VALERIANIC ACID.

This acid is distinguished by its odour and hot burning taste; it is so powerful, that when applied to the tongue it almost blisters it, producing a white spot wherever it touches it.

It consists of

| | | |
|---|---|---|
| Carbon | 10 | 58·824 |
| Hydrogen | 9 | 8·823 |
| Oxygen | 3 | 23·530 |
| Water | 1 | 8·823 |
| | | 100·000 |

It forms various salts, from which it is separated by acetic acid.

It is not unfrequently produced during the decomposition or oxidation of various vegetable and animal substances, both nitrogenous and non-nitrogenous: it may be formed from fats, by oxidizing them with fuming nitric acid; it is readily obtained from the potato fusel oil, by the action of spongy platinum and atmospheric air; also from oil of valerian, by oxidation by means of an alkali; lastly, leucine allowed to putrefy, or treated with caustic potash, is converted into valerianic acid, ammonia and hydrogen being given off.

It may be separated from several of the acids of this group by fractional distillation, it boiling only at 349° F.; from butyric acid it may be removed by crystallization of the baryta salts, the valerianate and butyrate of baryta assuming different forms.

This acid has been frequently found in the urine, being derived in some cases from the decomposition of leucine.

## LACTIC ACID.

*Occurrence.*—Lactic acid occurs in great abundance in the *juices* of both striped and unstriped *muscles*, whether of the carnivora or herbivora; it is found in the *spleen* and most of the *glands*, and in the *brain;* it is also frequently, but not invariably, present in the *gastric juice* in conjunction with hydrochloric acid, in *chyle*, in the *blood* sometimes, especially when this is acid; in many specimens of perfectly *fresh urine*, but more frequently in stale urine: it is a result of the acid fermentation of Scherer, being derived, it is presumed, from the decomposition of the urine pigment, and which fermentation sometimes takes place while the urine is still retained in the bladder: it may also be formed in the urine after emission, from the decomposition of *diabetic sugar*, or from the transformation of *indican*. According to Lehmann, it is constantly present in the urine of stall-fed animals subsisting on amylaceous food.

It has been frequently affirmed to be contained in sweat, especially the acid *sweat* of rheumatism; but the investigations of Schottin are said to have disproved this statement as regards both normal and morbid sweat.

It is contained in *sour milk*, and also, according to Schlossberger, in the normally *acid milk of the carnivora.*

Lastly, it is present in many *sour vegetable substances*, as in sour cabbage (the *sauer-kraut* of the Germans), in the acid waters of starch-works, &c., being derived from the starch or sugar therein contained.

Lactic acid has the following atomic and percentage composition:—

| | Atomic. | Percentage. |
|---|---|---|
| Carbon | 12 | 40·00 |
| Hydrogen | 10 | 6·67 |
| Oxygen | 10+2 HO. | 53·33 |

## *Chemical Characters of Lactic Acid.*

It forms a syrupy liquid, the aqueous solution of which, when heated, is in part volatilized; at 266° F. it loses its two atoms of water, and becomes anhydrous, forming a firm yellowish substance; at 500° F., *lactide* is formed, which sublimes, and is reconverted into lactic acid by the prolonged action of water. According to Strecker, lactic acid may be regarded as *formic acid*, conjoined with *aldehyde*, which is alcohol deprived of part of its hydrogen.

When in contact with putrefying substances at a moderate temperature, it yields *butyric acid*, carbonic acid and hydrogen being evolved.

The alkaline lactates, as also lactate of baryta, are non-crystallizable, but those of lime, copper, and zinc are so, and they are all insoluble in ether.

## *Determination of Lactic Acid.*

The perfectly fresh urine must be inspissated, at a low temperature, on the water-bath, to the consistence of syrup, the residue treated with alcohol holding oxalic acid in solution: the alcohol extract is next treated with an excess of hydrated oxide of lead; the solution filtered, excess of lead removed by means of sulphuretted hydrogen, and the filtrate finally boiled with oxide of zinc, when, after filtration and concentration by evaporation, crystals of lactate of zinc will be formed.

Or we may proceed as follows:—A baryta salt of lactic acid, which is very soluble, should be first formed, then a lactate of lime by the addition of sulphate of lime.

Lactate of lime crystallizes in double brushes, easily recognisable under the microscope. From the lactate of lime, a salt of copper may be formed by the addition of sulphate of copper, the crystals of which are also characteristic.

Lastly, the lactate of copper may be decomposed, and well-formed crystals of lactate of zinc, the angles of which may be measured by the goniometer, will gradually appear on immersion in the solution of a small piece or bar of zinc. For further particulars, the reader is referred to Lehmann's "Chemistry."

### *Origin of Lactic Acid.*

The lactic acid found more particularly in the juice of muscles, in the chyle, and in the urine, may be traced to several distinct sources.

That in the fluids of the stomach and intestines may be traced to the transformation of the amylaceous and saccharine constituents of the food.

That of the muscular juice, to the disintegration of the muscular tissue, and more immediately to *inosite*, or muscle-sugar.

Thirdly, that formed independently in the urine may proceed from the fermentation and decomposition of glucose, or from the sugar derived from the decomposition of Scherer's *uroxanthin*, which is identical with *indican*.

Thus, lactic acid may occur whenever sugar, or any substance which readily yields sugar, is present, and no matter whether this proceeds from without—as in the case of saccharine or amylaceous food—or is formed within the body.

According to Scherer, it is a result of the decomposition of normal urine-pigment; and if this really be so, there can be no doubt about its being sometimes generated from the variety of sugar which is formed on the disintegration of indican.

### *Uses of Lactic Acid.*

A few remarks will not be out of place, respecting the uses of lactic acid in the animal economy, in order to enable us the better to understand its pathology.

First, it aids digestion powerfully, by promoting the solution of the food.

Second, by its rapid combustion in the blood—that is, by its conversion into carbonic acid—and the consequent evolution of caloric, it greatly assists in maintaining the warmth of the body.

That it is very quickly changed, when introduced into the system, has been repeatedly proved by direct experiment. Thus, in the course of a few minutes after any large dose of a lactate, the urine is rendered alkaline from the presence of an alkaline carbonate.

Were it not for this circumstance—since there are at least two constant sources of its production, namely, food, and the disintegration of the muscular tissue—it would be invariably present in the urine, and this frequently in very large amount.

Thirdly, Liebig believes that the muscles are kept in a state of tension by the electric action maintained through the agency of the acid muscular juice and the alkaline blood of the capillaries.

From the preceding remarks, it therefore becomes apparent that lactic acid can only make its appearance in the perfectly fresh urine, when, from impeded oxygenation, arising from any cause, the conversion of the lactates into carbonates is prevented.

## PATHOLOGY OF LACTIC ACID.

The acid fermentation of Scherer, as already stated, results in part in the formation of lactic acid, and which fermentation, according to Lehmann, sometimes takes place while the urine is still retained in the bladder.

According to the same observer, lactic acid is frequently present in the urine under a variety of circumstances.

It occurs in most *febrile diseases.*

It is affirmed to be constantly present in the urine of persons who, in consequence of repeated *catarrhs*, suffer from partial relaxation of the pulmonary tissue, and yet often think themselves perfectly well.

It is likewise said to occur generally in the urine wherever *oxalate of lime* (Lehmann) and *uric acid* (Parkes) are present in large quantities.

It is very commonly contained in the urine in *diabetes*, resulting generally from the decomposition of the sugar; but Lehmann states that it is also usually found, in cases of that malady, in the perfectly recent saliva.

Scherer and Lehmann have found much lactic acid in the urine in some cases of *rickets*, and also in the *osteomalacea* of adults. C. Schmidt has likewise detected it in the long bones, in a case of the latter disease.

It has been stated to occur abundantly in the urine in *rheumatism*, of which disease it has been even assumed to form the *materies morbi*. No sufficient proof has, however, as yet been afforded of its occurrence.

In cases of *puerperal fever*, *pyæmia*, and *leucæmia*, according to Scherer, the *blood* and the *purulent secretions* have an acid reaction from the presence of lactic acid, which of course is liable, under such circumstances, to find its way into the urine.

The presence of lactic acid in the urine in many of the preceding cases would appear to be indicative of deficient oxidation.

Lehmann sums up his views as to the occurrence of lactic acid in the renal excretion, in the following words:—

"In all cases where the supply of lactates to the blood is very great—whether this depends upon an excess of acid being formed in [illegible] imperfect process of oxidation in the blood—lactic acid may be detected in the urine."

### TREATMENT OF EXCESS OF LACTIC ACID.

From what has been already advanced, the principles upon which the treatment of excess of lactic acid in the urine should be conducted, are rendered obvious.

If it be traceable to diet, this must be carefully modified and regulated.

If it be independent of food, its source may be traced to undue waste of the muscular tissue.

Or, lastly, when its presence is attributable to deficient oxidation, this condition must be obviated by pure air, exercise, and the administration of invigorating remedies.

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# CHAPTER IX.

## DIABETES INSIPIDUS.

It was formerly generally believed that the disease denominated diabetes insipidus was characterized by the presence, in the urine, of a tasteless or insipid sugar; that it differed, in fact, only from ordinary sweet diabetes in the character of the sugar eliminated.

Thénard and Bouchardat separated, indeed, from the urine a substance which they described as this tasteless sugar. Nevertheless, the opinion entertained by these chemists, and which at one time so generally prevailed, is now acknowledged to be incorrect; the urine eliminated, in cases of diabetes insipidus, does not usually or necessarily contain a particle of sugar of any kind. Thus the disease in question has no title to be called diabetes at all.

But although sugar is absent, yet this so-called diabetes insipidus possesses, in common with true diabetes, two very striking symptoms—namely, thirst, often insatiable, and which causes large quantities of fluid to be drunk; and a greatly increased elimination of urinary water: so that often, the malady in question bears much resemblance to saccharine diabetes.

Moreover, this resemblance is still further increased by the fact that, as in diabetes, there is marked implication of the nervous system, and upon which the excessive thirst in all probability depends.

The increase in the quantity of water passed is usually very great. Henry records the case of a woman aged 34, who passed in 24 hours nearly 501 ounces; in that of a man aged 25, Poggiale found that the water excreted amounted to 612 ounces; while in one of hysteric polydipsia, according to Alfred Vogel, it was 190 ounces.

At the same time that the water is much increased, the specific gravity of the urine is, in nearly all cases, greatly reduced, ranging from 1001 to about 1010.

It appears further, that, as a rule, the urinary solids are diminished.

In Henry's case, the urea excreted in 24 hours amounted to only 101·13 grains, and the salts to 221·29 grains; there was no uric or hippuric acid.

In Poggiale's case, the urea was 173 grains, the uric acid 9·63 grains, and the other ingredients—except the phosphate of soda, which was in very small amount, 3·61 grains—were in nearly their normal proportions.

These and other corresponding analyses prove that in diabetes insipidus, in its typical and usual form, there is no excessive waste of tissue.

Baron has made the singular observation, that in two cases of this disorder the urine was greatly augmented by starchy food. Martin records a case in which the disease ensued from a blow on the head; while Lacombe states that "great muscular exertion, mental anxiety, and even the drinking of large quantities of cold water, have induced, more or less, long-continued diuresis." (Parkes.)

In ordinary cases of this disease, although the rule is that the solids of the urine are deficient, yet, according to Becquerel, cases occur in which the amount is the same as in health, or nearly so; while, in a third class of cases, there is an increase of the solids.

Thus, in a case of Parkes, a man passed, as the average of 14 days, 104 ounces of urine, 545 grains of urea, and 279 grains of chloride of sodium: the urea was therefore slightly in excess, but the chloride of sodium was very much increased.

In Dr. Golding Bird's case the urine voided was 138 ounces, the urea 376 grains, the uric acid 21 grains, and the fixed salts 462 grains: that is, the urea was deficient, the uric acid greatly increased, as also the fixed salts, especially chloride of sodium.

Professor Vogel records the case of a woman aged 36, suffering from hysteria, in which the urine ranged from 96 to 129 ounces, the urea from 417 to 756 grains, the chlorine from 308 to 463 grains, the sulphuric acid from 47 to 77 grains, and the phosphoric acid from 77 to 139 grains. Here there is an increase of both the sulphuric and phosphoric acids, as well as of the urea and chloride of sodium; the free acid and the pigment were lessened.

Parkes remarks on these cases:—"Thus, in complete contrast to the former series of cases, we see that all the chief ingredients may be increased, except perhaps the pigment, the alterations in which have not yet been made out. Only it is to be remarked, that in none of these cases was the amount of urine so excessive as in the first series."

The increased discharge of chloride of sodium in some of these cases was obviously due to retention; while in others, the augmentation in the amount of the urea and other organic constituents was due to abnormal disintegration of tissue, as shown by the rapid wasting which sometimes occurred.

Cases of increased elimination of urine, owing to diminished escape of water by the skin, lungs, or bowels, cannot be classified with the disorder we have been considering: neither can cases of diuresis resulting from the absorption of effused water, as sometimes occurs in anasarca, from the removal of obstruction in the kidneys, as after acute disease of those organs, be considered to be the same nature as those of diabetes insipidus in its ordinary form.

### TREATMENT OF DIABETES INSIPIDUS.

The treatment must of course vary according to whether the solids of the urine are deficient, in normal amount, or in excess.

In the first class of cases, tonics, especially preparations of iron, astringents, and sedatives, including small doses of opium, are the classes of remedies the administration of which is especially indicated.

In those cases attended by increased metamorphosis, and consequent wasting, the treatment requisite is of a totally different character. Here, fever, if present, must be moderated, and the nervous system must be quieted; ends which may be attained by means of liquor ammoniæ acetatis, small doses of ipecacuanha wine, hydrocyanic acid, hyoscyamus, and even small doses of opium.

In particular, restriction must be placed upon the quantity of water drunk; since this, as has been elsewhere shown, exercises such marked effect in increasing the disintegration of tissue.

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## CHAPTER X.

## SULPHURIC ACID.



Until recently, but little that was definite was known in regard to the sulphuric acid of the urine: now, however, it has been determined that it is as important as any other urinary constituent.

QUANTITY.

According to the table given in Parkes's work on the urine, compiled from the calculations of nineteen different observers, the range of sulphuric acid in twenty-four hours in men between the ages of twenty and forty, is from 17·34 to 41·14 grains, and the mean 31·11 grains.

The variation, therefore, is very great, owing partly to the unequal quantity of sulphuric acid introduced into the system in the food and drink consumed.

The range in the same individual is often quite as great as that of a number of people.

Parkes calculates the amount of sulphuric acid excreted in twenty-four hours to each pound avoirdupois of body-weight, at 0·214 of a grain.

It appears also, and the observation is a very important one, that the amount of sulphuric acid formed in the body stands in a definite relation to that of the urea, the proportions being about as 1 to 15 or 20.

It must be remembered that the whole of the sulphuric acid contained in the body is not excreted by the urine; but that part escapes by the intestines and skin.

*Influence of Food.*

Food containing sulphates or unoxidized sulphur, of course increases the sulphuric acid of the urine.

The increase usually begins in the second hour after such food, and continues from six to eight hours.

According to Parkes's observations, the amount increases from 1·1 grain per hour to 2·1 grains. The mean of analyses by Gruner gave 1·03 grains in each fasting hour, and 1·50 in each food hour.

The total increase in the twenty-four hours resulting from food, according to Buckheim's experiments, amounted to about one-third of the whole amount.

It occasionally happens, however, that the sulphates are not increased: this may result from two causes, either from retention or from absence or deficiency of sulphates in the food.

The increase is greatest after *nitrogenous food*, owing partly to the large amount of sulphates which this description of food contains, and partly to oxidation of its sulphur, as well as probably that of the tissues themselves.

After *non-nitrogenous food*, it appears to be diminished. Again, the sulphuric acid is much increased when, the diet being the same, a large quantity of *water* is drunk. The increase, according to Böcker, amounted to over five grains daily, while in Genth's experiments it reached nearly eight grains daily.

This increase no doubt results in part, as shown by the simultaneous increase in the urea, from increased metamorphosis of tissue and oxidation of sulphur; and in part from augmented elimination.

Like the urea, it is decreased by *alcohol*, added to a regulated diet, to the extent, in a case recorded by Hammond, of no less than 13 grains daily.

When *beer* is taken in moderate quantities, as a daily constituent of the food, it also lessens the sulphuric acid and the urea much. (Böcker.)

It is likewise slightly lessened by *coffee* and *tea*.

### *Influence of Exercise, Bodily and Mental.*

On the other hand, it is increased by *exercise* and by *mental exertion*.

### *Effects of the Administration of Sulphates and of Sulphur.*

The sulphuric acid of the urine is of course increased when that acid is taken as a medicine: it does not appear, however, in the free but in the combined state, it having, in its passage through the system, become united to potash or soda. It is also increased when the *sulphates*, as of soda or magnesia, are taken; but not in proportion to the amounts administered, since much of these salts, especially when they act as purgatives, escapes by the intestines.

When *sulphur* is given, the greater part of it is oxidized; but a portion also makes its way into the urine unchanged. In the case of a man who passed in the twenty-four hours 36 grains of sulphuric acid, and 4 of sulphur, Griffiths found, after taking a dose of sulphur, 76 grains of the acid and 7 or 8 of unoxidized sulphur; so that the quantities of each excreted were doubled.

The sulphurets are also oxidized, and appear in the urine as sulphates.

It does not appear that the *urea* is augmented when sulphur is taken, even in large quantities. (Böcker.)

### *Determination of Sulphuric Acid.*

The amount of sulphuric acid present in any urine may be ascertained in one of two ways—either by the weight of sulphate of baryta precipitated on the addition of chloride of barium or nitrate of baryta; or volumetrically, by noting the amount of a solution of known strength of either of those salts required to precipitate the whole of the sulphuric acid.

Whichever process is adopted (and of course the volumetric method is the most speedy), the urine must be first acidulated with either nitric or hydrochloric acid, in order to prevent the precipitation of the phosphate of baryta formed, and which is readily soluble in either of the above acids. The addition of the baryta salt to the boiling urine ensures a quicker separation of the sulphate of baryta.

If in the volumetric method it is suspected that too much of the baryta solution has been added, a drop or two of a dilute solution of sulphate of soda must be added to a similar quantity of the clear urine, when, if no precipitate occurs, more of the baryta solution must be added.

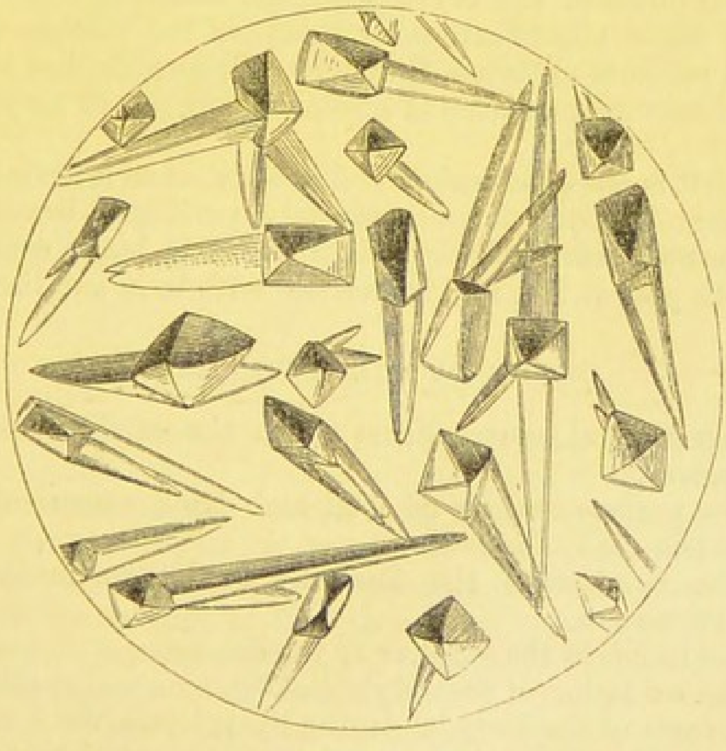
The sulphuric acid may also be determined from the carefully incinerated solids of the urine.

The amount of *unoxidized sulphur* in the urine may be thus determined: the sulphuric acid is ascertained in the ordinary way in one portion of the urine; a second quantity is evaporated to dryness, nitric acid is added, and after some time the extract is carefully incinerated; by this process the uncombined sulphur is oxidized, and the difference between the two amounts of sulphuric acid obtained represents the quantity of unoxidized sulphur present.

## MICROSCOPICAL CHARACTERS OF THE SULPHATES.

The sulphates crystallize readily from the urine, and the crystals, more or less approximating to their typical forms, may be seen frequently on examination with the microscope, of the residues of a few drops of urine spontaneously evaporated on slips of glass.

FIG. 48.



Peculiar *Nail-like* Crystals of a Sulphate, probably SULPHATE OF POTASH; from *Human Urine*. 100 diameters. 1852.

The sulphuric acid of the urine occurs chiefly in combination with potash, forming *a sulphate of potash*. The crystals of this salt are anhydrous, and occur in the form of short six-sided prisms terminated by six-sided pyramids; but often, and particularly in the urine, the body of the crystal is absent, and then the triangular-faced dodecahedron results. The primary form, according to Phillips, is a right rhombic prism; and according to Mitscherlich, a rhombic octahedron.

It frequently crystallizes in the urine in the form of beautiful rosettes and perfect and elegant dumb-bells. Whether these crystals are pure, and are composed only of the sulphate, has not yet been determined. Attention was called to the frequent occurrence, in the residues of small quantities of evaporated urine, of these soluble dumb-bells, by the author, many years since, and the annexed figure was drawn in 1850, and appeared in the *Lancet* in March, 1858.

The ordinary crystals of *sulphate of soda*, when deposited from aqueous solutions, as from the urine, occur in the form of decahydrated crystals: they are transparent striated prisms, belonging to the oblique prismatic system, and are efflorescent.

These sulphates are insoluble in alcohol; by means of that reagent, therefore, urea, and many other urinary constituents, may be removed from the evaporated extract of the urine, so as to allow of the more complete crystallization of the sulphates.

When the forms of the crystals are not sufficiently characteristic to allow of their identification by means of the microscope in the evaporated residues of urine, they may still be identified by the application of minute quantities of a solution of a salt of baryta. (Figs. 48, 49, 50.)

Although it is more convenient and definite, when referring to quantities, to treat of sulphuric acid separately, yet it must be remembered that it does not occur in the urine in a free state, but in combination; usually with potash, but also sometimes with soda and lime.

## ORIGIN OF SULPHURIC ACID.

There are several sources from which the sulphuric acid of the urine is derived.

From the various articles of food and drink consumed, and in which it exists ready formed.

From the sulphur of the food, by oxidation, in its passage through the system.

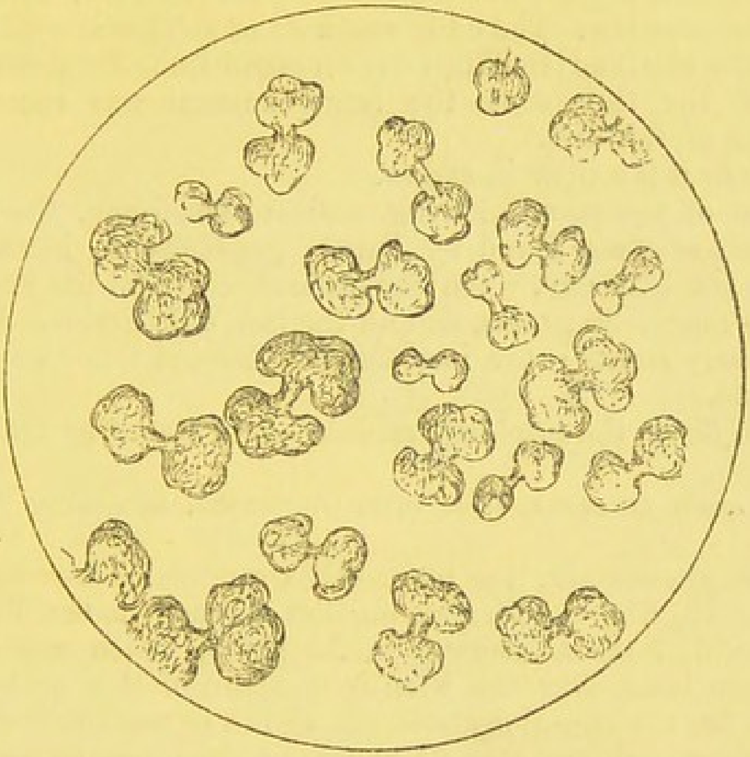
From oxidation of the sulphur of the tissues.

From the oxidation of the sulphur of *taurine* and *cystine* present in several parts of the body, as in the liver, lungs, &c.

From experiments made *during fasting*, it appears that about *one-third* of the sulphuric acid of the urine is derived from the food, and the remaining *two-thirds* from the tissues and sulphur compounds.

It is probable that the greater the activity of digestion and the rapidity with which the tissues are built up and oxidized, the larger is the amount of sulphuric acid eliminated. It appears to be greater during fasting hours, *according to weight,* and in this respect it agrees with urea.

FIG. 49.



Beautifully formed *Dumb-bell* Crystals of a SULPHATE; from *Human Urine.* 100 diameters. 1850.

## PATHOLOGY OF SULPHURIC ACID.

In simple uncomplicated fever (*febricula*), in which the urine is high-coloured, and has all the usual characters of febrile urine, the sulphuric acid is increased. Parkes found that a boy 14 years of age, on meagre diet, passed, as the average of three days, 29½ grains of sulphuric acid; and the urine of a man aged 21, on "starving" diet, furnished, as the average of four days, the same amount. It will be remembered that the mean daily amount in healthy men, on full diet, between the ages of 20 and 40, is 31·11 grains.

In *typhus abdominalis* there is also an increase, considering the spare diet, amounting sometimes almost to abstinence.

A young man on very meagre diet passed during the height of the disease 26·45 grains, while during health, and on good diet, he passed only 26·67 grains. Another young man on low diet, on the fifteenth and sixteenth days of the fever, passed 20 grains, and when well and on generous food, 20 grains. (Parkes.) From the results of several other cases, it also appeared that the sulphuric acid was in excess, in proportion nearly to the degree of wasting and the amount of destruction of tissue. Where sweating, or purging, or retention exists, the amount will of course be diminished.

In one case of *typhus exanthematus*, Parkes found the sulphuric acid to be rather high. The patient weighed 129 lbs. avoirdupois, and the diet was low. The daily amounts of sulphuric acid excreted between the 8th and the 26th days ranged from 34 to nearly 50 grains: at the time when the larger amount was excreted, the patient was on full diet.

In *variola* it is a little in excess.

In a case of *pyæmia* following confluent small-pox, the quantity of sulphuric acid was found by Parkes gradually to increase from the 7th to the 17th day, when the patient died: on the first-named day it was nearly 24 grains, and on the last 44½ grains. The diet was extremely scanty; the increase, therefore, in this case was very considerable.

In *milk fever*, the sulphuric acid has been stated by Heller to be in excess.

In *delirium tremens*, it is often increased, according to Bence Jones.

In *acute pneumonia*, it is frequently considerably increased. "In a girl aged 19, who was on starving diet, I found, on the fifth day of the disease, 37·7 grains excreted in 24 hours, which was certainly one-third, at least, over the healthy standard of this person. In a man aged 22, the excretion about the eighth or tenth day of disease averaged 58·8 grains in each 24 hours, no food having been taken for several days." (Parkes.)

Parkes also mentions a case in which 59 grains were excreted; and Professor J. Vogel met with an instance in which no less than 70 grains were eliminated the day before death.

As in most other diseases, cases occur depending upon various complications, but particularly upon retention, in which the sulphuric acid and other urinary solids are excreted in less than the normal amounts.

During convalescence, the sulphuric acid, urea, uric acid, pigment, &c., fall for a short time below the average.

The sulphuric acid is but little affected in *acute pleurisy*.

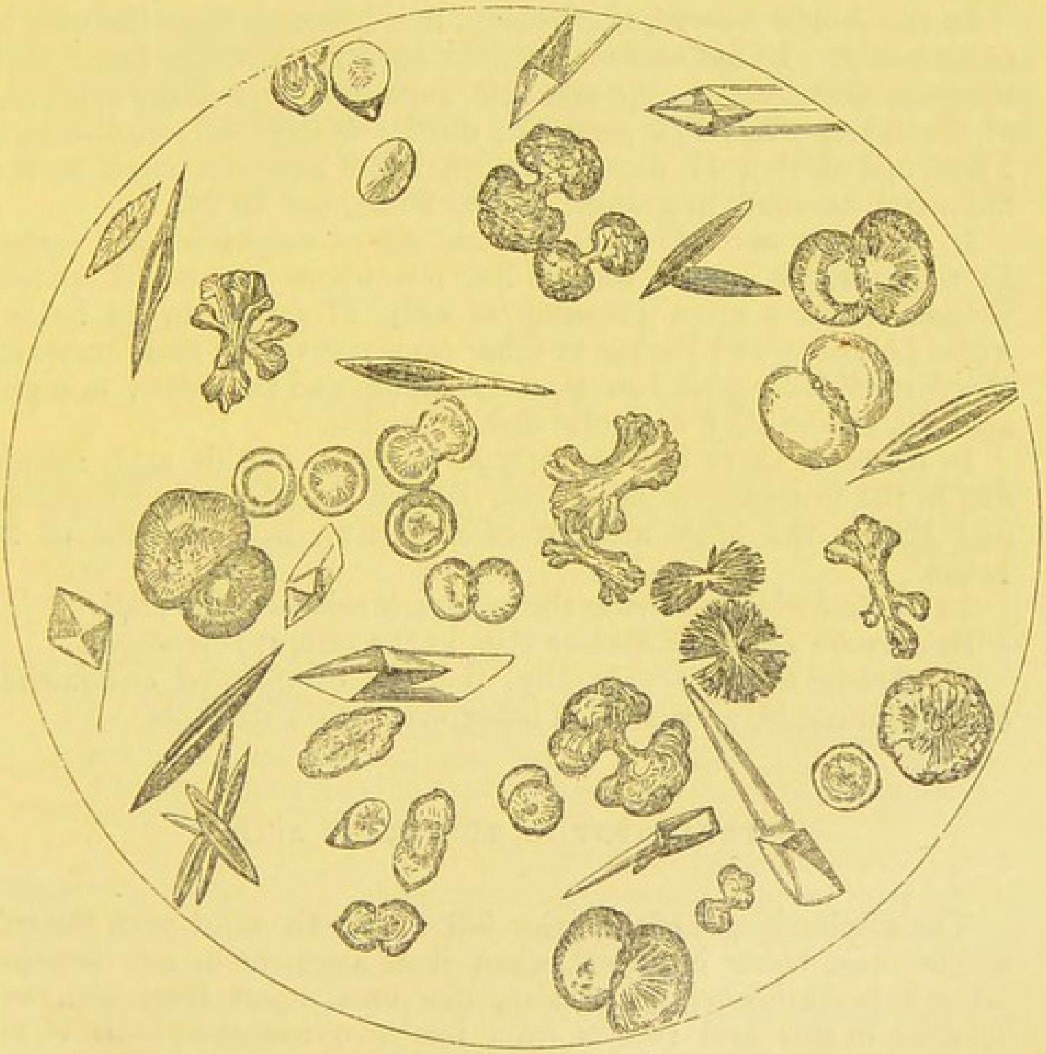
In *acute capillary bronchitis* and in *acute phthisis*, there is good reason to believe that it is augmented.

In *rheumatic fever* it is usually much increased. Parkes found it so in five cases, in all of which "the fever was intense, and the joint-affection severe." In one case it reached nearly 53 grains in 24 hours; the normal amount on recovery being only 24 grains.

In some exceptional cases it was decreased; this may be owing to retention, local inflammation, or excessive action of the skin or bowels; of course we must not look for a great increase when the attack is mild or chronic, nor when exudation has taken place, as into the pericardium.

It is probable that the *non-oxidized sulphur* is also somewhat increased in rheumatic fever: this was the case in one of Parkes's analyses, in which it amounted to about 5½ grains; the mean amount in five healthy cases, as determined by Ronald, being 4·125 grains.

FIG. 50.



Represents several modifications of Crystals of the Sulphates, chiefly SULPHATE OF POTASH; from *Human Urine*. 100 diameters.

So far as present observations extend, there does not appear to be any diminution of sulphuric acid, or urea, during the paroxysm of *acute gout*.

It thus appears that the urine, in almost all diseases accompanied by *fever*, contains *an excess* of sulphuric acid, as well as of its other constituents,

In *cholera* the sulphuric acid has been found to be sometimes increased, and at others decreased.

In a case of *chorea*, Bence Jones found an increase.

No definite conclusions have yet been arrived at, as to whether the sulphuric acid is lessened or increased in *non-acute phthisis*: from the observations hitherto made, it does not appear to be much affected.

Nothing is known respecting the amount of sulphuric acid excreted in *cirrhosis*.

In non-febrile *icterus*, if anything, it is lessened, since the urea is so certainly. In the case of a woman aged 25, Kölliker found that the mean excretion of sulphuric acid, during 16 days of the existence of the fever, was 1·714 gramme; during 9 days of convalescence 1·508, and during 17 days of health 1·898 gramme, equal to the following amounts in grains: 26·46, 23·28, and 29·30.

In *anæmia* and *chlorosis*, the amount of sulphuric acid varies. In a girl whose weight was 85 lbs. but whose age is not stated, Gruner found a mean excretion of only 17 grains in 24 hours; while Lehmann and Parkes in other cases met with a great increase, the former finding no less than 54 grains, and the latter, in a girl aged 19, and on very moderate diet, 30 grains.

In *diabetes* there is frequently an increase of this acid, mainly due to the nitrogenous diet: thus Böcker found nearly 65 grains, and Mosler the large amount of 83 grains, in the urine of 24 hours.

In *acute Bright's disease* the sulphuric acid is diminished.

In *chronic Bright's disease* also, as the rule, it is lessened.

In *chronic diseases* generally, there is *diminished elimination* of sulphuric acid, as well as of other urinary constituents.

## TREATMENT OF SULPHURIC ACID.

The sulphuric acid of the urine follows, for the most part, the rule of the urea, being increased when it is augmented, and lessened when it is diminished; and also, like urea, apart from diet, any increase in this acid results from increased metamorphosis of the sulphur-holding tissues.

The great object, then, to be fulfilled in the treatment of cases of great *excess of sulphuric acid* due to increased destruction of tissue, is to diminish the metamorphosis. This increased metamorphosis may be accompanied by fever of an active and sthenic, or of a low and asthenic type.

When the former, the treatment must be antiphlogistic; and when the latter, tonics and stimulants will frequently be required.

Thus, in active fever, in pneumonia, and in acute rheumatism, the treatment pursued must be antiphlogistic and eliminative; whereas, in *typhus*, it must be tonic and conservative.

In *pyæmia*, again, the treatment must be tonic, antiseptic, and eliminative.

In *delirium tremens* it must be sedative.

In cases of *deficiency of sulphuric acid* in the urine, arising from retention, as in Bright's disease, elimination by the skin, bowels, and urine must be promoted.

Of course it must not be understood that the whole of the indications for the treatment of any disease can be determined from the excess or deficiency of any one urinary constituent: regard must be had to the general composition of the urine, and not only so, but to the age and constitution of the patient, and the precise character of the symptoms.

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# CHAPTER XI.

## PHOSPHORIC ACID.



PHOSPHORUS and the phosphates are found in every part of the body. There are, however, certain fluids and solids in which they occur in greater abundance than others.

Amongst liquids, in the *blood*, *seminal fluid*, and particularly the *urine*.

Amongst solids, in the nitrogenous, but especially in the *nervous* and *osseous* tissues.

The phosphorus occurs partly in the unoxidized state, and partly in the form of phosphoric acid.

The phosphoric acid is combined in part with the *alkalies*, usually with soda, but sometimes partially or even wholly with potash; and in part with the earths, as lime and magnesia, forming with magnesia and ammonia a triple compound.

Now, the phosphoric is one of those acids which has the property of combining with one, two, or even three atoms of base; but the phosphates of the urine are all *tribasic*.

The following salts of phosphoric acid have been ascertained to be present in the *renal excretion*, either constantly or occasionally:—

*Alkaline Phosphates.*

| | |
|---|---|
| Common or rhombic phosphate of soda, with alkaline reaction . . | $2\,NaO,HO,PO_5+24$ Aq. |
| Acid phosphate of soda . . . . | $NaO,2\,HO,PO_5+2$ Aq. |

*Earthy Phosphates.*

| | |
|---|---|
| Phosphate of lime, or bone-earth phosphate . . . . . . . . . | $3\,CaO+PO_5$. |
| Acid phosphate of lime . . . . | $2\,CaO,HO,PO_5+3$ Aq. |
| Phosphate of magnesia . . . . | $3\,MgO,PO_5+5$ Aq. |
| Phosphate of magnesia and ammonia . . . . . . . . . . | $2\,MgO,NH_4O,PO_5$, and 12 Aq. |

*Phosphate of ammonia and soda* ($NaO,NH_4O,HO,PO_5+8$ Aq.) the microcosmic salt, is stated to be a constituent of human urine; but it is probable that it is formed only as the urea becomes decomposed. Its crystals are very characteristic.

The *alkaline phosphate of soda* ($3\,NaO,PO_5+24$ Aq.) has also been stated to be present in urine; but Liebig denies that it is ever found in healthy urine. It is a very unstable salt, and is readily decomposed even by the presence of carbonic acid in the urine, carbonate of soda and common phosphate of soda being formed.

*Phosphate of potash* ($KO\,3PO_5$) may be sometimes contained in urine, but probably only when chloride of sodium is either absent, or present only in small amount.

## CHEMICAL CHARACTERS OF THE PHOSPHATES.

The phosphates are divisible into alkaline and earthy phosphates. The *alkaline*, unlike the earthy phosphates, are not precipitated by ammonia or other alkalies; the phosphoric acid of both the alkaline and earthy phosphates is thrown down by nitrate of silver; and that of the alkalies by sulphate of magnesia or chloride of magnesium with chloride of ammonium and ammonia. The precipitate by nitrate of silver is soluble in nitric acid and ammonia; that by acetate of lead is soluble in nitric acid, but insoluble in acetic acid and ammonia; chlorides of barium and calcium occasion precipitates with the soluble phosphates, soluble in hydrochloric, nitric, and acetic acids.

The *earthy phosphates* are insoluble in water, soluble in most organic acids, if not too dilute, as acetic and carbonic acids, in chloride of ammonium, and readily so in the mineral acids. They are precipitated on the addition of ammonia; and also sometimes by simply boiling the urine. The cause of this precipitation is attributed by Dr. Owen Rees to the expulsion of chloride of ammonium, by which he is of opinion they are partly held dissolved; and by Dr. Brett to the carbonic acid being driven off. In some cases it is occasioned by the alkali formed, during the act of boiling, from the decomposition of urea. Dr. Bence Jones has shown that if a little common phosphate of soda be added to urine, a precipitation of earthy phosphates will take place on the subsequent application of heat; he therefore infers that if more than an average amount of this phosphate be present, the precipitation of the earthy phosphates by heat is insured. Lastly, Scherer long since pointed out that the precipitation occurs when the neutral earthy phosphates of lime and magnesia are present, and results from their conversion, in the act of boiling, into basic salts. Thus, 2 $MgO,HO,PO_5$ and 2 $CaO,HOPO_5$ pass into 3 $MgO,PO_5$ and 3 $CaO,PO_5$. This Parkes regards as no doubt the true explanation.

Albuminous compounds dissolve earthy phosphates, as does casein also to a considerable extent.

From the solution of phosphate of lime in acetic acid, the lime is precipitated by oxalate of ammonia; and from the nitric or hydrochloric acid solutions, by means of sulphuric acid and alcohol, as a sulphate of lime.

### *Determination of the Phosphates.*

The phosphates, both alkaline and earthy, are at once distinguished by forming the golden yellow phosphate of silver when treated with a solution of nitrate of silver. This reagent, applied to crystals of the phosphates contained in the evaporated residues of drops of urine, serves, with the aid of the microscope, at once to distinguish them from all the other urinary constituents.

In some cases, it is sufficient for the object in view to determine the whole of the phosphoric acid of the urine, without distinguishing that which is in union with the alkaline from that united to the earthy phosphates. It is better, however, in most cases, to ascertain the quantities of each separately.

The analysis may be made either from the urine itself, or from its ash; and the quantities may be determined either by the weight of the precipitates, or by the amount of the solution of the precipitant required to throw down all the phosphoric acid.

The precipitant employed is usually a solution of perchloride of iron. Acetate of soda must first be added, then acetic acid, and finally a solution of perchloride of iron.

When the phosphoric acid is determined by the volumetric method, of course the test-solution of perchloride of iron must be of a definite strength: a solution of ferrocyanide of potassium is employed in order to ascertain the point at which sufficient of the perchloride has been added to precipitate all the phosphoric acid, and which is indicated by the appearance of a blue colour, arising from the formation of Prussian blue.

The earthy phosphates are readily and completely separated from the alkaline phosphates by means of ammonia free from carbonate, by which the former are precipitated; and they may then be collected by filtration, washed with ammoniacal water, heated to redness, adding, lastly, a drop or two of nitric acid, and weighed; or if we desire to estimate the phosphoric acid alone, the earthy phosphates must be dissolved in acetic acid, and the phosphoric acid precipitated in the manner above described.

Should it be necessary to determine the lime and magnesia, we must proceed as follows:—

The urine must be acidulated with acetic acid, and the *lime* precipitated by means of a solution of oxalate of ammonia.

The *magnesia* may be estimated from the same portion of urine after the removal of the lime: this must be concentrated by evaporation, rendered alkaline with ammonia, and a small quantity of a solution of phosphate of soda and some chloride of ammonium added, as the magnesian phosphate is slightly soluble in water, but not in chloride of ammonium. The precipitate must be ignited and weighed, and the magnesia calculated therefrom.

The *alkaline phosphates* may be estimated in the following way:—

After the removal of the earthy phosphates the remaining phosphoric acid may be precipitated by the addition to the liquor of a soluble salt of lime or magnesia, when a phosphate of lime or magnesia will be formed, from which, after ignition, the phosphoric acid may be calculated. The quantity of the calcareous phosphate thus obtained, corresponds within a fraction to that of the alkaline phosphates, so that, except when extreme accuracy is required, no special calculation is necessary. The phosphoric acid is generally in combination with soda.

Phosphoric acid is precipitated as a tribasic phosphate of silver, by means of a solution of nitrate of silver; but since the chlorides are thrown down by the same reagent, it cannot in the case of urine be estimated in this way. While chloride of silver is insoluble in nitric acid, phosphate of silver is readily so; these salts may therefore be easily separated; both precipitates are soluble in ammonia.

## MICROSCOPICAL CHARACTERS OF THE PHOSPHATES.

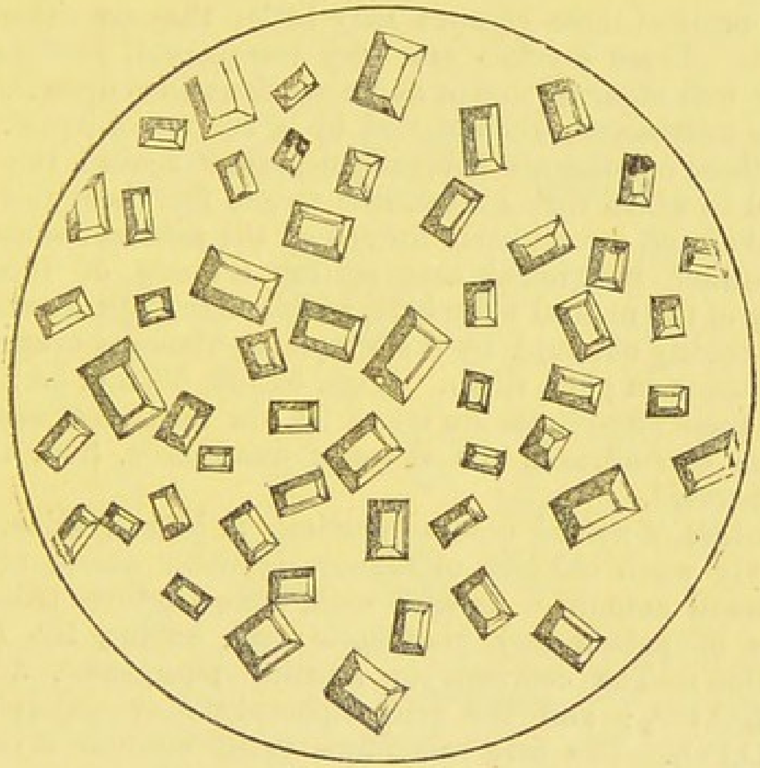
*Forms of Crystals of the Alkaline Phosphates.*—The alkaline phosphates which have been separated from human urine are the neutral and the acid phosphates of soda.

These phosphates have been particularly described by MM. Robin and Verdeil, who have published processes for their extraction from the urine, and have figured the crystals.

These authors give the following directions for obtaining the *neutral phosphate of soda* from urine:—

"When we decant the fluid from highly concentrated urine, to separate the saline deposit, and add to it absolute alcohol, there are deposited slowly upon the sides of the vessel crystals of neutral phos-

FIG. 51.



*Prismatic* Crystals of NEUTRAL PHOSPHATE of SODA; from *Human Urine* evaporated on a glass slide. 220 diameters.

phate of soda. These are plates derived from the rectangular or right rhombic prism, with truncation of the edges.

"Sometimes these plates are irregular, and striated upon their surfaces in different ways. They polarize light; the last forms particularly give colours most remarkable for their tint and intensity.

"It is easy, with a little practice, to distinguish these crystals from all other kinds in the urine, and above all from the acid phosphate."

On the extraction of *the acid phosphate of soda*, MM. Robin and Verdeil have the following remarks:—

"The acid phosphate of soda may be obtained crystallized in the urine, by following the same course which we have indicated in treating of the neutral phosphate of soda. When this is crystallized, there is deposited, three or four days after, crystals much more soluble in water than the neutral salt: we may hasten the deposit by adding ether to the liquid already treated with absolute alcohol. These crystals, from the mode of truncation of their angles on the sides of the base, appear to be derived from the rectangular or right rhomboidal prism. The truncation usually marks the whole of the base.

"The forms of these crystals vary little; they are either prisms or plates. These crystals are very transparent, and their faces cannot be well observed except as we see them turn upon themselves under the microscope, when carried by a current of liquid. Moreover, as these crystals are generally deposited against the sides of the vessel to which they adhere, it is rare to find them well shaped; they are flat and incompletely formed on the adherent sides."

The author has found that perfect crystals of these salts, especially of the neutral phosphate, visible with the microscope, may often be readily obtained by the simple spontaneous evaporation of drops of urine on glass slides. (Figs. 51, 52, 53, and 54.)

When these phosphates are taken for the purpose of experiment, they often crystallize in the shape of dumb-bells, from the urine thus evaporated.

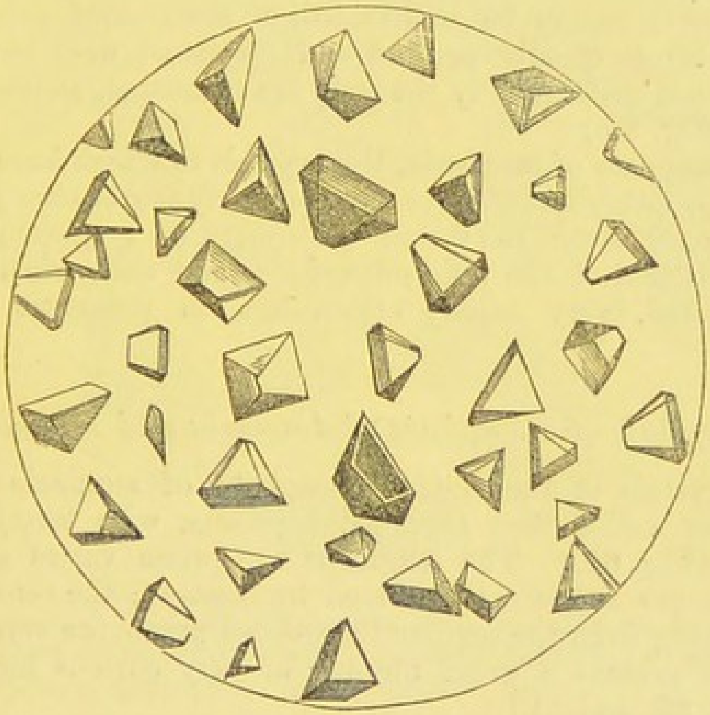
*Phosphate of potash* occurs sometimes in human urine, but it is stated only when chloride of sodium is either absent or present only in small amount. As with soda, there are three tribasic combinations of potash and phosphoric acid, having the following composition:—The common or alkaline phosphates, $3\ KO,PO_5$, and $2\ KO,PO_5$; and the acid biphosphate or superphosphate, $KO,2\ HO,PO_5$. The first salt forms small acicular crystals, the second does not crystallize, and the third crystallizes on evaporation; but the crystals, which are very soluble, contain only basic water.

### *Forms of the Crystals of Phosphate of Lime.*

The size, form, and arrangement of the crystals of phosphate of lime as they occur in human urine vary greatly, but the peculiarities are in all cases sufficiently characteristic to allow of the ready identification of this phosphate by means of the microscope. The crystals are either single or aggregated, most frequently the latter, forming glomeruli or rosettes more or less perfect. (Figs. 56, 57, and 58.) Sometimes they are small and needle-like, and then they generally form, by their crossing and union at right angles, glomeruli or spherules. (Fig. 57.) Sometimes the crystals are thin and flat, having oblique or pointed terminations. (Fig. 56.) Very frequently, however, they are thick, wedge-shaped, and united by their thin narrow extremities, so as to form more or less complete portions of a circle. (Fig. 58.) The free larger ends of the crystals are usually somewhat oblique, and when perfect present a six-sided facette. (Fig. 59.) The author has never yet met with these crystals having both ends complete, owing, he believes, to the tendency which they have to crystallize from a centre in rosettes.

The *penniform* crystals, described by the late Dr. Golding Bird as a variety of the crystals of the magnesian phosphate, un-

FIG. 52.



Crystals of NEUTRAL PHOSPHATE of SODA; from *Human Urine*. 100 diameters.

doubtedly represent a modification of those of phosphate of lime. (Fig. 55.)

Dr. Beale states that he has met with minute dumb-bell crystals of phosphate of lime in human urine.

MM. Robin and Verdeil describe an *acid phosphate of lime* as occurring in the urine of man and the dog, differing in the form of its crystals from that just described.

It crystallizes, on evaporation, on the surface of the urine.

"The crystals have all the form of half octohedra elongated, being derived from the right prism with a rectangular base. Some are large, others very small. They may be isolated, but the majority are united, one to the other, in different ways, either two-and-two or in large groups. They are soluble in acetic acid. The edges of the crystals are well marked; their dihedral angles are very sharp; they refract light but little."

### *Crystals of Phosphate of Magnesia.*

The crystals of phosphate of magnesia sometimes consist of a great number of long and slender crystals, stretching right across the field of vision, pointed at either extremity, frequently split or divided into smaller secondary crystals, and more or less aggregated into bundles. At others the crystals are broader and larger, having the form, as near as can be ascertained, of a six-sided prism, the extremities being usually pointed and furnished with two unequal facettes; not unfrequently the ends are truncated, and occasionally oblique. (Fig. 60.)

The phosphate of magnesia, the crystals of which have just been described, is either a *neutral* or more probably an *alkaline phosphate.* The ordinary form in which phosphate of magnesia exists in the urine is that of the *acid phosphate;* and this, when the urine is evaporated, very readily crystallizes in prismatic triangular crystals.

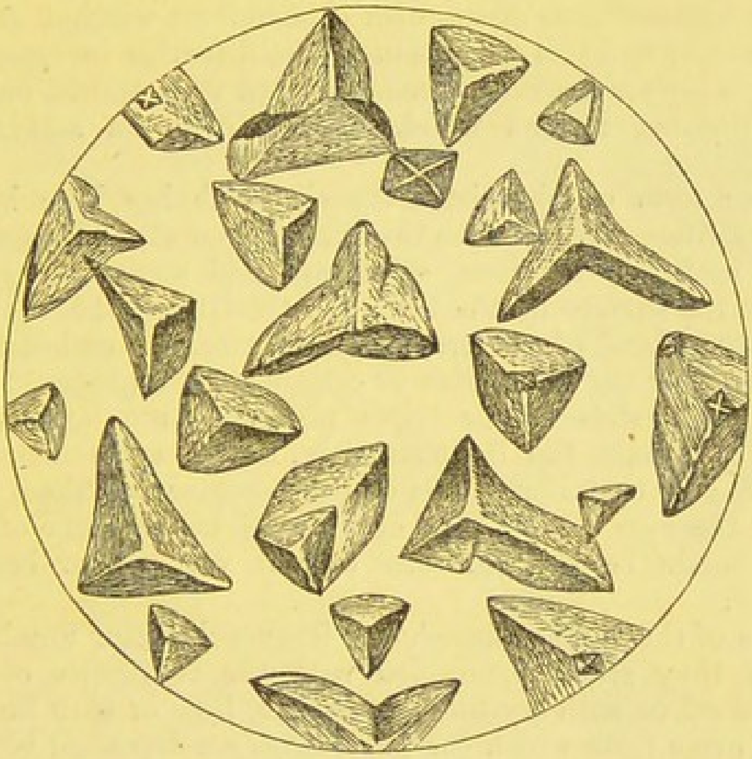
### *Crystals of Phosphate of Ammonia and Magnesia.*

The crystals of the neutral phosphate of ammonia and magnesia form well-defined three-sided prisms, with terminal sloping facettes. (Fig. 61.) The length of the prism varies greatly, and its angles are sometimes replaced by facettes; the consequence is, that, starting from the regular three-sided prism, the crystals of this phosphate present a great number of very curious modifications. (Figs. 62, 63, and 64.)

In old stale urines the crystals are sometimes observed to be aggregated into masses, and they even assume occasionally a branched arrangement. (Fig. 66.) In other instances the prismatic crystals become split at the ends, and gradually spread out and assume the crucial shape of the crystals of the *bibasic phosphate.* (Fig. 67.) Crystals of triple phosphate are said to be sometimes deposited from urine which still exhibits an acid reaction: this, however, may be due, not to the presence of free acid, but of some salt, or salts having an acid reaction.

If the triple phosphate is ever really deposited from an acid urine (and there certainly appears no reason to doubt that it is so sometimes), the ammonia entering into its composition must be derived from the blood, *possibly* from chloride of ammonium in some cases, and in others from carbonate of ammonia derived from the decomposition of urea. Several observers have noticed the deposition of crystals of triple phosphate from acid urines. Dr. Bird has remarked of one of his cases—"The urine was always acid, and remained so for a day after emission, even in hot weather; . . . . and soon after passing, even before it was perfectly cold, a copious deposit of prismatic crystals of triple phosphate appeared. I have seen an

FIG. 53.



Crystals of a Soluble Phosphate, most probably of NEUTRAL PHOSPHATE of SODA, with nucleus of CHLORIDE of SODIUM; from *Human Urine*. 100 diameters. 1850.

ounce bottle of this urine let fall a deposit reaching to one-tenth the height of the fluid."

It must not be forgotten, however, that the crystals of the acid phosphates of lime and magnesia have the same prismatic form as those of the triple phosphate.

When ammonia is added to recent urine, from four to six-rayed star-like feathery crystals immediately appear, these being formed by the union of the ammonia with the phosphate of magnesia of the urine; these crystals used to be described as consisting of the *bibasic phosphate of ammonia and magnesia.*

This phosphate occurs only in stale urine, and then usually the crystals are cruciform and flattened.

Crystals of triple phosphate form beautiful objects under the polariscope.

## CHARACTERS OF DEPOSITS OF EARTHY PHOSPHATES.

The deposits of earthy phosphates, whether crystalline or granular, are white, presenting a chalky or earthy appearance.

The triple phosphate, when deposited in the form of small prisms, and in considerable quantity, sometimes has a greenish tinge, and then so closely resembles pus in its texture and tint, that it is quite impossible to distinguish it therefrom without the aid of the microscope; and this resemblance is still further increased by its exhibiting a certain degree of tenacity when it is poured out of the vessel containing it, and which depends upon an admixture of mucus.

There is a form of phosphatic deposit which has been but little noticed by writers, but to which the author drew attention some years since. It occurs as a brittle, colourless, and structureless pellicle floating on the surface of the urine; it constitutes the well-known "iridescent pellicle" of writers, and often contains embedded in it crystals of either the magnesian or calcareous phosphates.

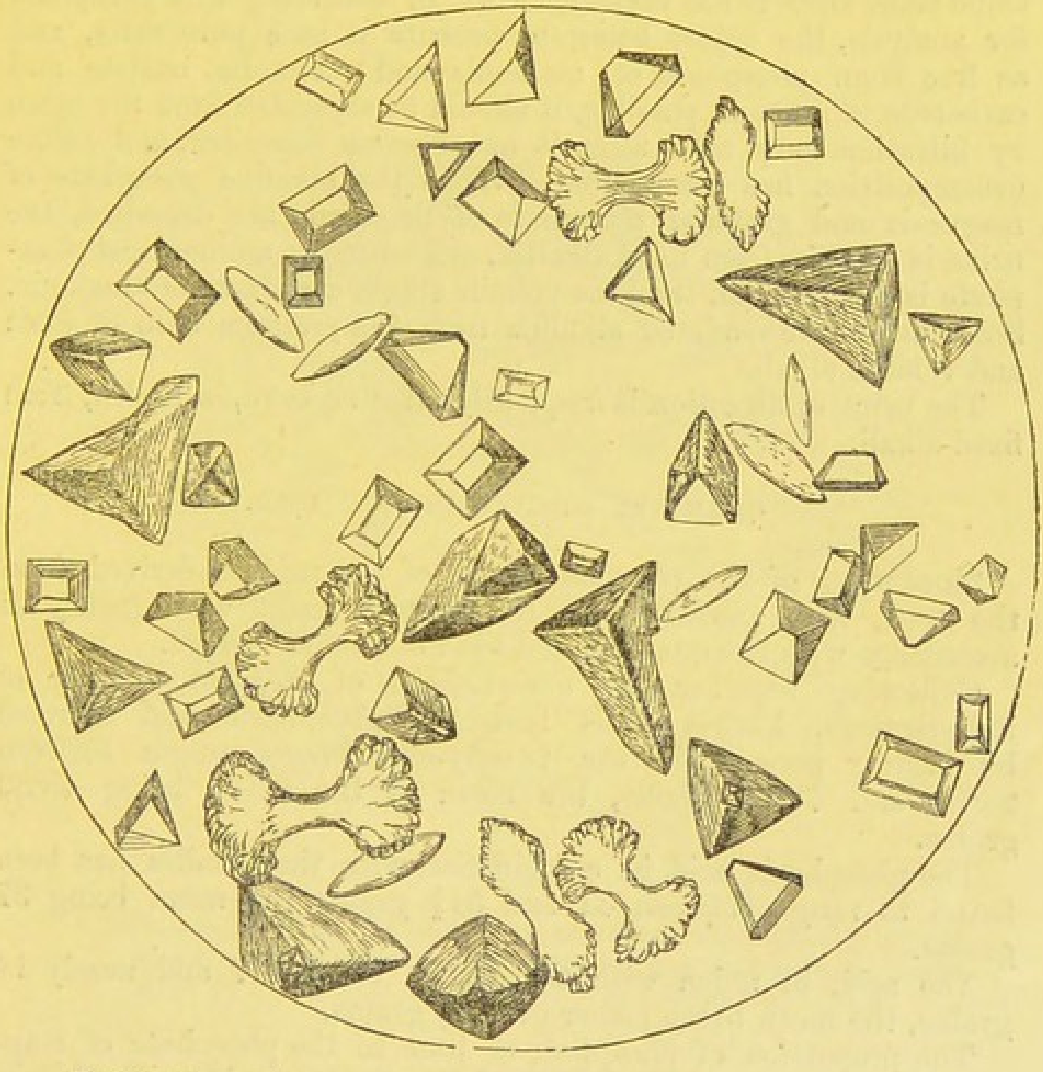
When the crystals of the triple phosphate are large and well formed, they refract the light strongly, in the same manner as a glass prism; so that if a bottle of urine containing them be held up before the eyes in the light of the sun or the flame of a lamp, and the bottle be shaken, each crystal will appear beautifully illuminated.

Deposits of the earthy phosphates frequently occur unmixed, but sometimes they are intermingled with the corpuscles of mucus, pus, and blood, or with crystals of oxalate of lime or with the urates. When the urine from which the phosphates are deposited is pale, the urates are also of a pale, usually fawn colour, or even nearly white: when thrown down from highly coloured urine, as sometimes happens, they are more deeply tinted.

### *Characters of Urine depositing Earthy Phosphates.*

The urines from which the earthy phosphates are deposited are usually pale, but occasionally high coloured. The quantity passed is ordinarily in excess, and the calls to void it frequent, more or less uneasiness and smarting being occasioned by its passage at the neck of the bladder and along the course of the urethra. The specific gravity varies greatly: if the quantity of urine voided be large and the phosphates persistent, and especially if it be alkaline from fixed alkali, it is usually pale and of low specific gravity; if, however, much food is taken, and digestion not seriously impaired, it may be of deeper colour and of high gravity; and if, again, the deposits of phosphates are occasioned by local disease, the fault not being in the urine itself, the colour and weight of the urine will necessarily vary greatly at different times and in different cases. Phosphatic urine generally contains more than the normal quantity of mucus : indeed, when triple

FIG. 54.



Represents various modifications of the Crystals of the Soluble Phosphates, chiefly NEUTRAL PHOSPHATE of SODA ; from *Human Urine.* The *dumb-bell* crystals were found in drops of evaporated urine after a dose of Phosphate of Soda. 100 diameters.

phosphate is present, the quantity of mucus is generally large, and the urine may contain pus as well. Its reaction likewise varies. When crystalline phosphate of lime is deposited, it is generally feebly acid, often decidedly so when first voided, the greater part of the phosphate of lime becoming deposited, while the urine still retains some degree of acidity; it, however, speedily becomes alkaline, owing partly to the additional mucus which it contains. Sometimes the crystals of phosphate of lime are thrown down from the urine before its escape from the bladder; ordinarily, however, the urine is bright and clear when passed, and they are not formed until some time after it has been voided. In collecting this phosphate for analysis, the object being to procure it in a pure state, and as free from phosphate of ammonia and magnesia, oxalate and carbonate of lime, as possible, it should be separated from the urine by filtration very soon after it has become deposited, and before decomposition has commenced. When the alkaline phosphate of magnesia and granular phosphate of lime only are deposited, the urine is alkaline from fixed alkalies, and when the ammoniacal phosphate is precipitated, from the volatile alkali, carbonate of ammonia. Some urines are rendered alkaline from the presence both of fixed and volatile alkali.

The urine of digestion is frequently alkaline even, in health, from fixed alkali.

## QUANTITY OF PHOSPHORIC ACID.

Since much of the phosphoric acid of the urine is derived from the food, it is obvious that the amount must vary greatly in accordance with the quantity and kind of food consumed.

Collecting together the observations of a great number of investigators, Parkes finds that the phosphoric acid excreted by healthy persons, in the twenty-four hours, ranges between 24·70 and 79·07 grains, the mean of the whole being 48·80 grains.

The phosphoric acid in combination with the alkalies has been found to range between 41 and 51½ grains, the mean being 37 grains.

The acid, in union with the earths, between 7 and nearly 18 grains, the mean being rather over 8½ grains.

The proportion of phosphate of lime to the phosphate of magnesia is, according to Lehmann and Kletzinsky, as 15 to 7; that is, there is usually rather more than twice as much of the calcareous phosphate: Böcker makes the proportion as 3 to 1.

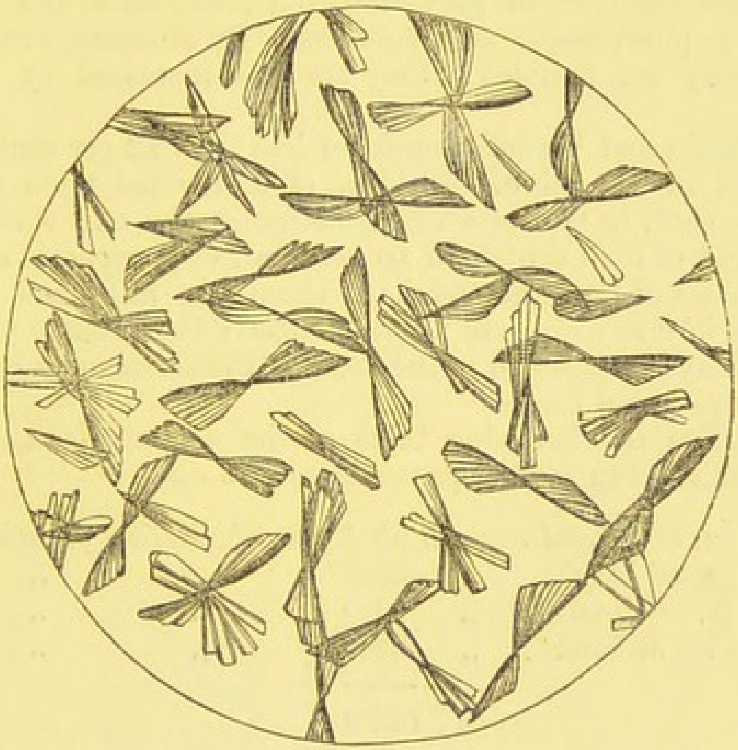
On the other hand, Neubauer and Kerner both found the phosphate of magnesia to be in excess; and the first-named observer gives the proportion of phosphate of magnesia to the phosphate of lime as 2 to 1, while the latter found the disproportion to be even greater, as 14·97 to 5·71 grains.

These differences in health depend mainly, of course, upon peculiarities in the food consumed, and on digestion.

Parkes computes, from various reliable data, that the mean excretion of phosphoric acid in the 24 hours, per pound avoirdupois, is 0·336 of a grain; and this quantity approximates closely to the mean of the experiments of Hegar, Jenner, Winter, and Beneke.

But little has hitherto been done in determining the amount of *unoxidized phosphorus* in the urine. In one case Ronalds found 5·9, or nearly 6 grains, in the urine of 24 hours.

FIG. 55.



*Penniform* Crystals of PHOSPHATE of LIME: from *Human Urine*. Drawing made from preparation lent the author many years since by the late Dr. Golding Bird. 220 diameters. 1852.

### ORIGIN OF PHOSPHORIC ACID.

The whole of the phosphorus, oxidized and unoxidized, found in the animal body and in the urine, is of course derived from without.

Part escapes from the system without having entered into the composition of the tissues, while another portion combines therewith, especially with the muscular, nervous, and osseous tissues, and only becomes liberated by their metamorphosis.

It is therefore evident that, as is the case with sulphur and the sulphates, part of the phosphorus and phosphates is derived from the disintegration of the tissues, and therefore represents a certain amount of tissue-change or waste.

Further, a large portion of the earthy phosphates of the food is unabsorbed, and escapes with the fæces.

### *Effects of Food.*

After food, the phosphates are of course increased; according to Jones and Beneke, the earthy more than the alkaline phosphates. Mosler makes the increase amount to about *one-fifth.*

After *animal food* in particular, the phosphates, and especially the earthy phosphates, are increased. By albumen, according to Mosler, they are doubled: they are less increased by *vegetable food.*

MM. Robin and Verdeil found no less than 12 per cent. of phosphoric acid in the ash of the blood of a dog fed upon meat, and only 3 per cent. in that of a vegetable-feeder, the ox; while the ash of the blood of man contained 10 per cent. of phosphoric acid.

Phosphates of lime and magnesia abound in milk, and the latter phosphate in many kinds of vegetable food; the alkaline phosphates are abundant in flesh, and in the seeds of the cereals and leguminous plants, as peas and beans.

Beale gives the following table of the amount of alkaline phosphates contained in several prime articles of diet:—

| | | | | |
|---|---|---|---|---|
| 14 oz. of *Bread* | contain | 53·2 | grs. | of alkaline phosphates. |
| 12 oz. of *Beef* | " | 40·7 | " | " |
| ½ lb. of Potatoes | " | 11·0 | " | " |
| ½ pint of Milk | " | 32·0 | " | " |
| | | 136·9 | | |

Bread, beef, and milk, it is evident from the above figures, are all rich in alkaline phosphates; but potatoes much less so. Now the daily ingestion of these phosphates by most healthy adults is scarcely less than the sum total of the above numbers, namely, 136·9 grains.

It must be remembered that part only of the earthy phosphates of the food enters the system, and that they are principally discharged in the fæces, the ashes of which often contain over 80 per cent. of these phosphates. The proportion of alkaline phosphates in the fæces, owing to their greater solubility, is but small.

Whether the unoxidized phosphorus is augmented by food has not yet been determined.

By *non-nitrogenous food* the phosphates are lessened. When *fat* is added in excess to an ordinary diet, the phosphates as well as the other constituents of the urine are unaffected.

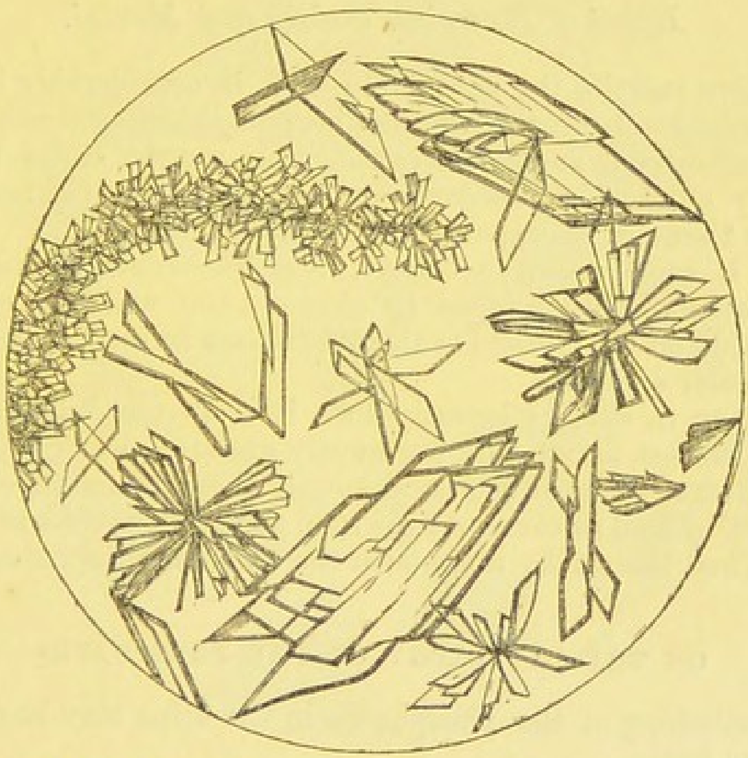
When *sugar*, another non-nitrogenous substance, is superadded to the usual diet, the effect is different; the phosphoric acid, and especially the phosphate of lime, is lessened. (Böcker and Hegar.) In a period of 9 days, according to Böcker, the diminution in the excretion of phosphate of lime amounted to 147 grains. This is a highly important practical fact, as will be shown presently.

When *starch* is added to ordinary food the phosphates are lessened, not, apparently, as in the case of sugar, from retention of phosphate of lime, but simply from diminished ingress.

When a large quantity of *water* is taken *fasting*, they are slightly lessened. (Böcker.)

When much *water* is added to the *ordinary diet* they are increased; but not to the same extent as the sulphates.

FIG. 56.



*Aggregated* and *Compound* Crystals of PHOSPHATE of LIME; from *Human Urine*. 220 diameters. 1852.

When *alcohol* is added to a regulated diet the phosphates are lessened; the earthy to the extent of four grains per day.

According to Hammond's experiments, alcohol has the same effect when given to persons *fasting*, or who are *overfed*.

Böcker found that a white and a red Rhine *wine* increased slightly all the constituents of the urine, the phosphates amongst the rest.

By *beer* the phosphate of lime is lessened. (Böcker.)

By *tea* the phosphates are considerably lessened; to the extent of upwards of eighteen grains in Hammond's experiments.

By *coffee* the diminution is affirmed, by Böcker and Lehmann, to be still more considerable. Hammond, however, found the excretion to be normal.

By abstaining from solid food, the usual amount of liquid being taken, the phosphates are reduced one-third, or even one-half.

By abstinence from liquids, the same amount of solid food being consumed, the excretion of the solids of the urine generally, including phosphoric acid, is much diminished. The lessening of this acid in Mosler's experiments amounted to 44 grains daily; and there is reason to believe that this results not merely from retention, but in part also from lessened metamorphosis.

### *Effect of Exercise, Bodily and Mental.*

By active exercise the phosphoric acid is considerably increased, and, according to Lehmann, the alkaline phosphates especially. Speck, whose authority is entitled to considerable weight, states that it is materially affected by this cause—a fact which the richness of the muscular tissue in phosphates sufficiently explains.

There is some reason to believe, from Böcker's experiments, that it is considerably diminished by *sleep*—a fact which, if confirmed, is explicable on the ground of the diminished activity of the nervous and muscular systems.

According to several investigators, it is increased by *mental exertion*. Mosler found that the hourly excretion was greatest when the intellect was most active, although these hours were the least influenced by food or exercise; the total phosphoric acid was increased one-half, and the earthy more than the alkaline phosphates.

## ON THE PATHOLOGY OF THE PHOSPHATES.

The pathology of the phosphates in the urine may be considered under two heads.

1st. When the phosphates are in *excess*, or are *deficient*.

2nd. When they occur as *deposits*.

We will now specify whether the phosphates are in excess or are deficient in some of the principal diseases, according to the observations of various physicians and experimentalists: and, first, in acute diseases, including fevers and inflammations.

Further observations are required to determine whether the phosphates are increased or lessened in *ague;* but it appears probable that they are diminished.

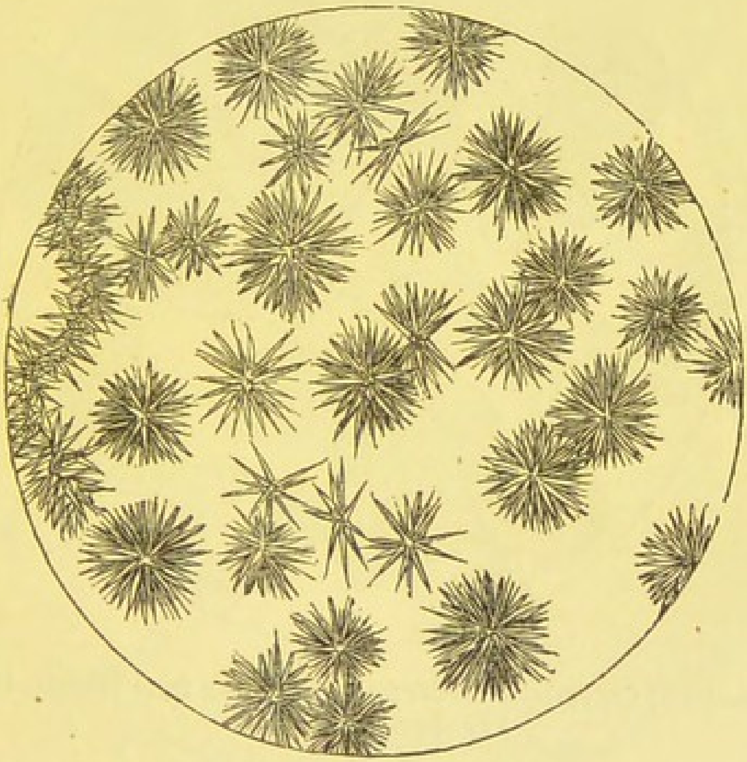
In *typhus abdominalis* the phosphoric acid varies much; but, as a rule, is somewhat lessened, especially during the period of inanition. Whether it is increased during delirium has not yet been determined.

In *meningitis* the phosphoric acid is probably much increased. (Bence Jones and Tomowitz.)

In *delirium tremens* it is remarkably decreased, according to Bence Jones.

In *acute mania* and *acute dementia*, according to Alexander Sutherland, it is increased during the paroxysm, and lessened during the periods of subsequent exhaustion: it is diminished in the third stage of the *paralysis of the insane.*

FIG. 57.



*Glomeruli* of *acicular* Crystals of PHOSPHATE of LIME; from *Human Urine*. 220 diameters. 1852.

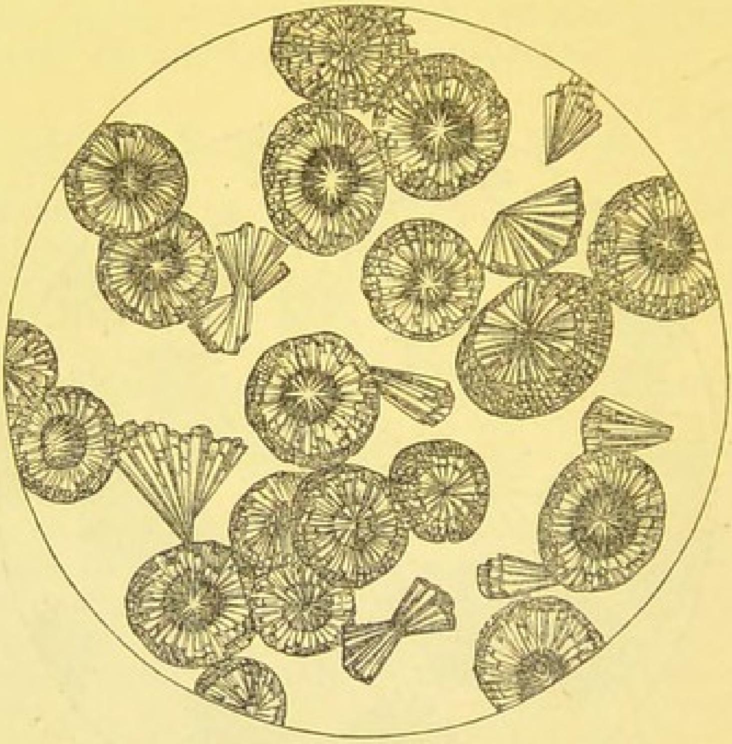
In *pneumonia* it is lessened, and probably beyond what can be explained by the altered diet. Professor Vogel in one case found the mean excretion of 8 days to be rather over 22½ grains during the height of the disease; and in another case the mean of 5 days was 28 grains, Vogel's standard in health being 54 grains.

In *acute pleurisy* the phosphoric acid is probably lessened.

In *acute rheumatism* the alteration in the amount of that acid is not considerable; in some cases it is somewhat increased, in others diminished.

In a case of *acute gout*, ten days before an attack Böcker found the phosphate of lime to be very deficient, while it was also greatly lessened during the fit. (Böcker and Parkes.) This is in accordance with what might be expected when the retention of the uric acid is remembered, and also the fact that gouty deposits, or chalk-stones, contain a proportion of phosphate of lime.

FIG. 58.



*Rosettes* of Crystals of PHOSPHATE of LIME; from *Human Urine*. 220 diameters. 1852.

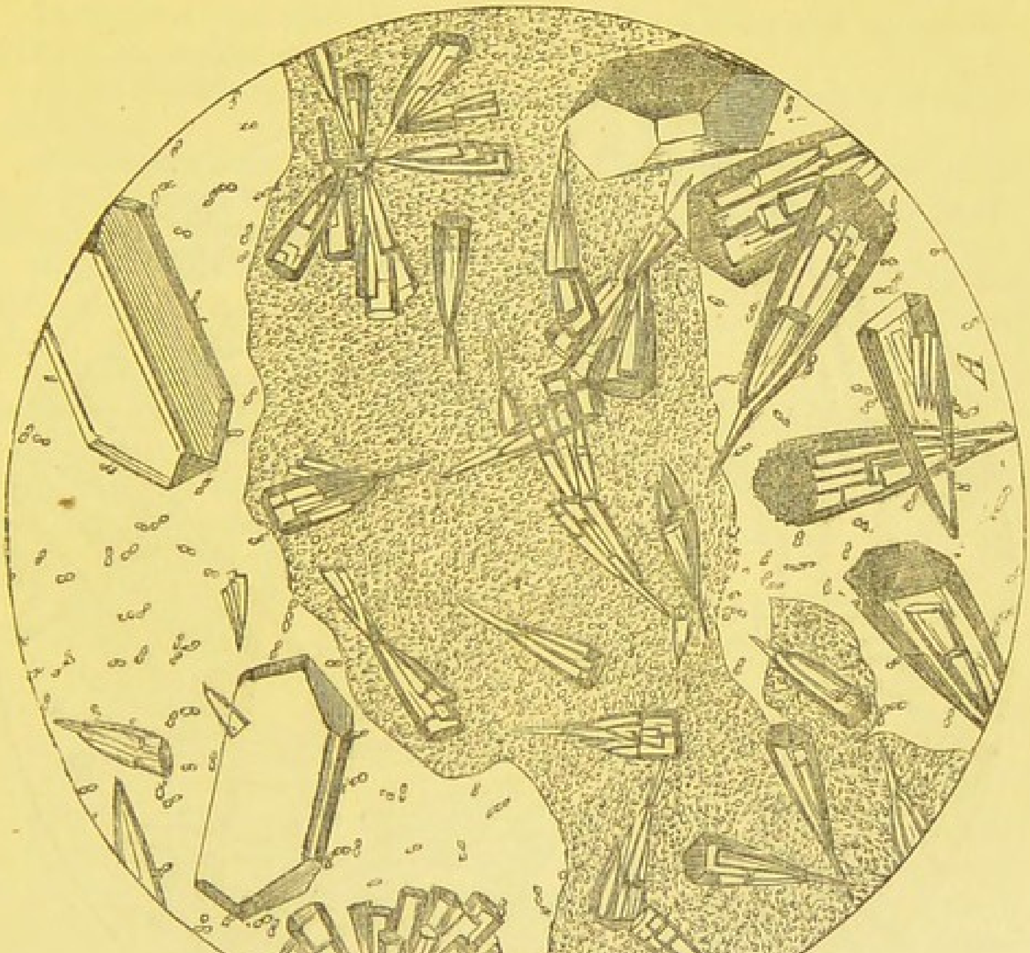
It is thus evident that the information hitherto obtained in regard to the phosphates of the urine in acute febrile diseases is very meagre: altogether it appears, however, that the phosphates, like the chlorides, are either not increased or are decreased; and this decrease appears to be greater than can be explained by the altered diet alone.

To the above rule, acute inflammation of the *muscular*, and especially the *nervous* tissues, form, so far as has yet been determined, exceptions.

In *cholera* the phosphoric acid is at first much lessened, probably simply from retention; but gradually increases until it exceeds the normal amount; it ranges on the first day between 2·92 and 34·96 grains, and from the third to the sixth days from 92·64 to 138·96 grains. (Parkes.)

In *Chronic Phthisis*, with emaciation, the earthy phosphates, according to Beneke, are increased; but further observations are required on this point.

FIG. 59.



More perfect Crystals of PHOSPHATE of LIME: from *Human Urine*; showing their oblique six-sided prismatic form. 220 and 420 diameters. 1852.

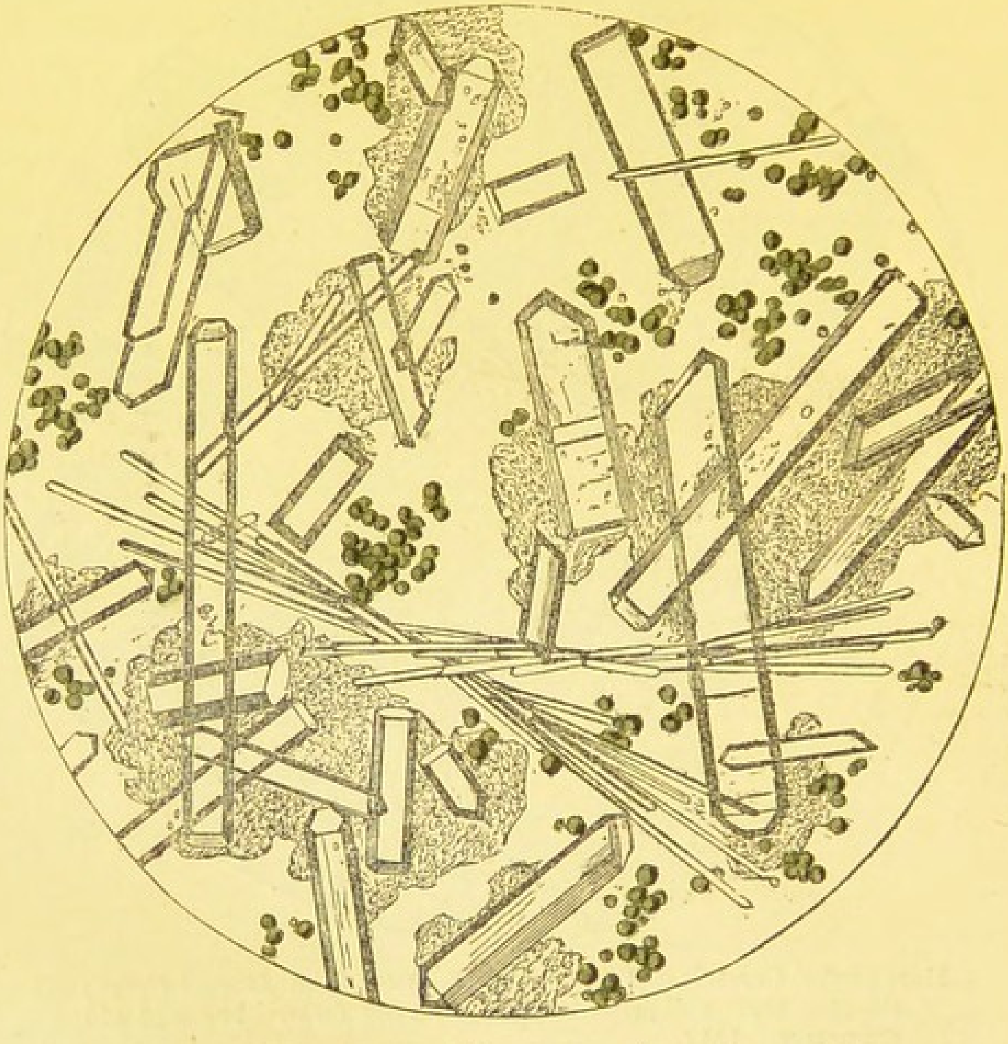
In *Rickets*, as might naturally be expected, there is a great increase in the earthy phosphates. In a child four years old Lehmann found 7·68 grains in the urine of 24 hours, or more than half as much as the mean amount for adult men, given by Neubauer, namely 14·57 grains.

Beale has also found the earthy phosphates much increased in three cases of *mollities ossium:* in two the amounts were equal to those of the alkaline phosphates.

In *diabetes* the phosphates appear to be but little affected, and sometimes they are lessened.

In *acute* and *chronic Bright's disease*, the phosphoric acid is diminished. It has elsewhere been observed, that, as a rule, in *chronic diseases* urinary excretion is diminished, the urea, pigment,

FIG. 60.



Crystals of PHOSPHATE of MAGNESIA; from *Human Urine*. 220 diameters. 1852.

sulphuric and hydrochloric acids in particular, being lessened; on the other hand, the earthy phosphates are subject to much variation, and may be present in lessened, normal, or increased amounts.

ON DEPOSITS OF THE EARTHY PHOSPHATES.

The alkaline phosphates, owing to their great solubility, never spontaneously form deposits in the urine; the earthy phosphates do so, however, very commonly, and especially in alkaline urine.

Now these deposits of the earthy phosphates denote sometimes excess, but they occur also more frequently independently of any excess.

In the first case their precipitation is due to the acid urine containing more than it can hold dissolved.

In the second, to the urine having a feebly acid, neutral, or alkaline reaction.

This reaction the urine may possess when first voided; but it is mostly acquired with varying degrees of rapidity subsequent to its elimination by the kidneys.

Further, the alkalinity is of two kinds, and may result either from fixed or volatile alkali, or both may be present at the same time.

When from the latter, the ammonia, which acts as the precipitant, is derived nearly always, not from the blood, although this may possibly occur sometimes, but from the decomposition of the urea of the urine.

This decomposition occurs sometimes in the bladder; but more frequently in the urine subsequent to its emission.

The transformation of the urea is brought about in two or three different ways.

If the urine be alkaline from fixed alkali, the urea becomes speedily decomposed.

If, again, it contain much mucus, this, by acting as a ferment, speedily effects the decomposition of the urea.

Thirdly, according to Owen Rees, the mucous membrane of the bladder, under irritation or inflammation, secretes an alkaline mucus or fluid, by which the urine is rendered alkaline, occasioning, either with or without ureal decomposition, the precipitation of the phosphates.

Now the phosphates which form precipitates are of three kinds, and they may occur separately or together. Namely—

Phosphate of lime.
Phosphate of magnesia.
Phosphate of ammonia and magnesia.

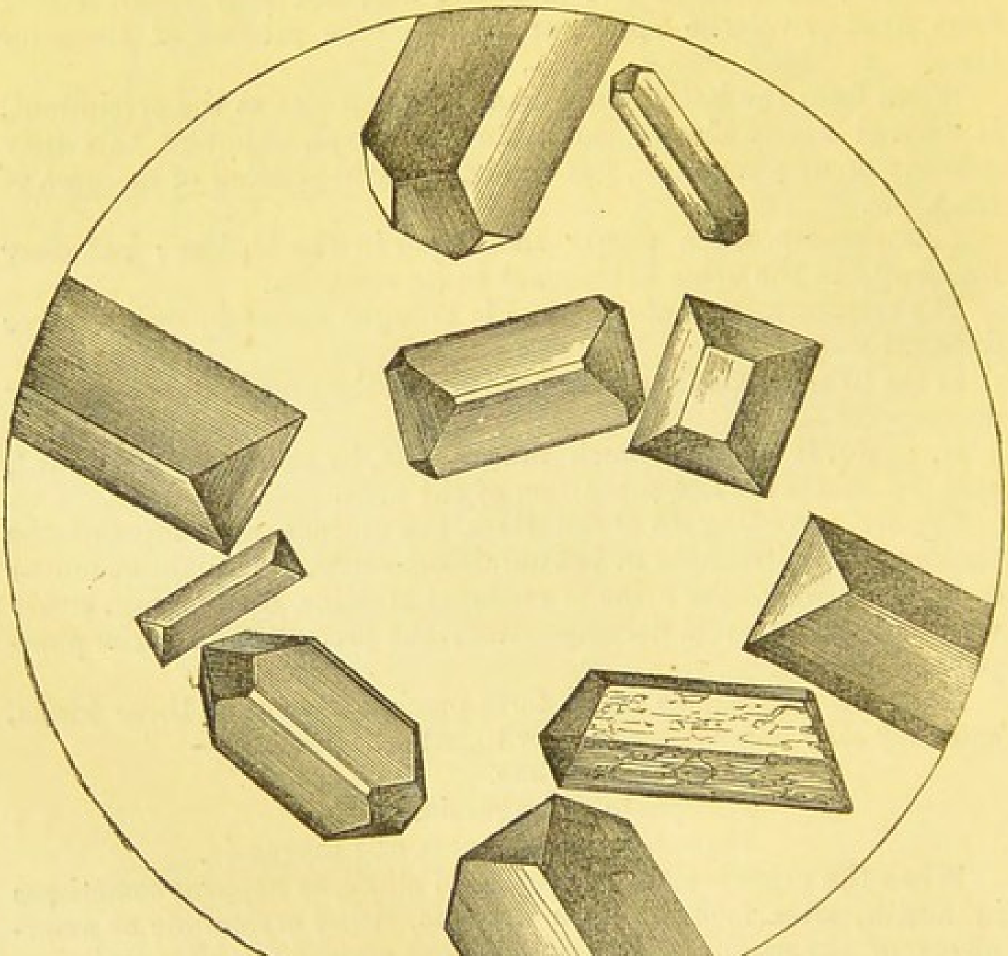
When the urine is alkaline from fixed alkali, as happens sometimes in health, after food, we have deposits, either crystalline or amorphous, of the earthy phosphates without ammonia: after emission, the urine being alkaline, urea is speedily decomposed, and then in addition a deposit of triple phosphate occurs; but the latter very frequently is the only deposit. Or it may be formed first, and the phosphates of lime and magnesia be subsequently deposited.

*Phosphate of Lime.*

This phosphate occurs as a deposit in the urine in two states, either as an amorphous granular powder, or in the crystalline form.

Until special attention was directed to the point by the author, first in the *Lancet*, in 1850, again in his memoir on the Development of Torulæ in Human Urine, published in the thirty-sixth volume of the "Medico-Chirurgical Transactions," in 1852, and subsequently, more particularly, in a communication brought before the Royal Society in January, 1860, it was uniformly stated in works on the urine, that this earthy phosphate occurs only in the granular state, and never in the crystalline form.

FIG. 61.

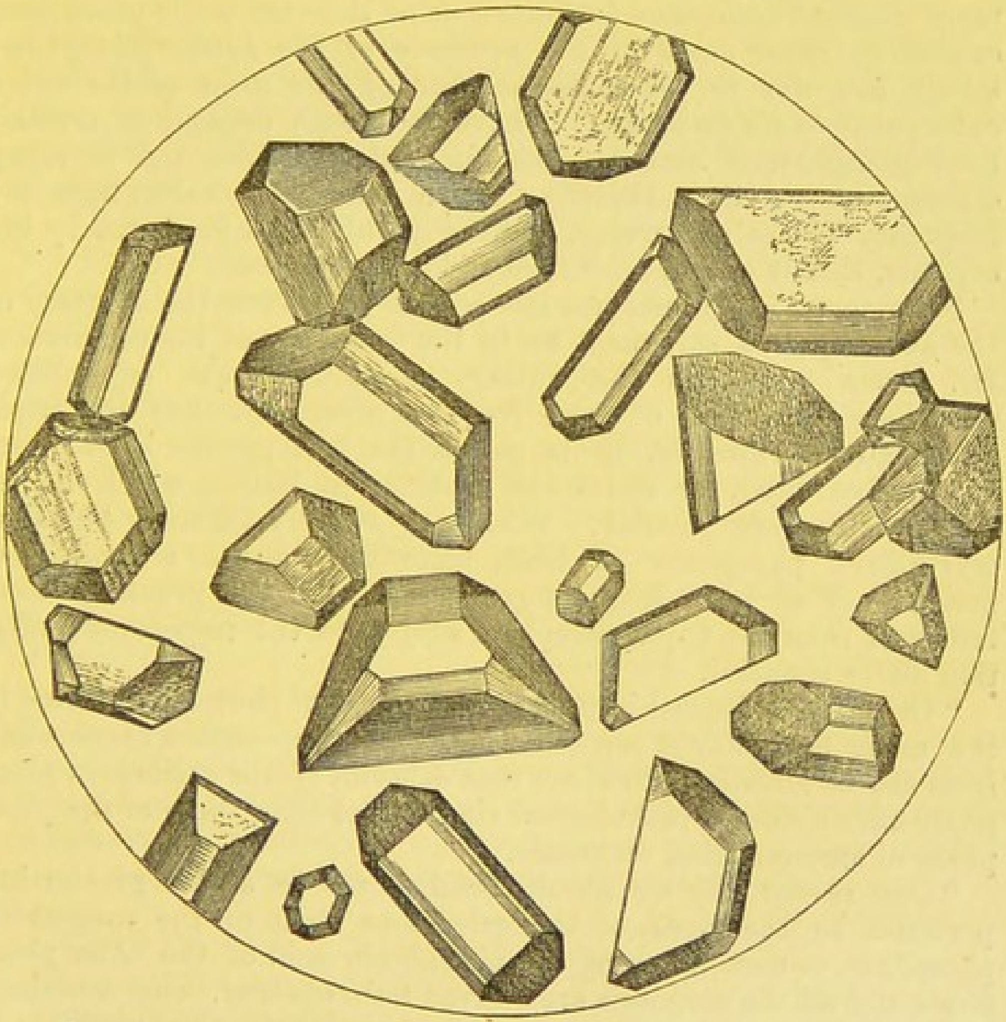


Crystals of NEUTRAL PHOSPHATE of MAGNESIA and AMMONIA, of the typical form; from *Human Urine*. 100 diameters.

The erroneousness of this statement was demonstrated by the author at the periods above alluded to, and in the communication to the Royal Society it was shown—

1st. That there is a crystalline deposit occurring in human urine which really consists of phosphate of lime; 2nd. That it is of frequent occurrence; and 3rd. That it is of greater pathological importance than the triple phosphate.

Fig. 62.



Peculiar *hexagonal* Crystals of Triple Phosphate; from *Human Urine.* 60 diameters.

The results of the quantitative analysis of four samples of the deposit were given, and were as follow:—

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Bibasic phosphate of magnesia . | 0·15 | 0·47 | 4·30 | |
| Bibasic phosphate of lime . . | 1·85 | 6·18 | 5·41 | 1·96 |
| Grains, | 2·00 | 6·65 | 9·70 | 1·96 |

The admixture of the phosphate of magnesia in the first three samples was due solely to the fact that the phosphate of lime, deposited at first in the pure state from more or less acid urine, was allowed to remain therein until decomposition had commenced, and the phosphate of magnesia and ammonia had in consequence become formed.

With regard to the frequency of the occurrence of this phosphate, in amount more or less considerable, it was stated—

"That phosphate of lime in the form of crystals is of much more frequent occurrence in human urine than the triple phosphate, *excluding those cases of the presence of the latter phosphate, which are due to the decomposition of the urea of the urine subsequent to its emission.* I have met with deposits of crystallized phosphate of lime in some hundreds of urines, and in many different cases: it is therefore not a little remarkable, from the frequency of its occurrence, and the peculiarities presented by the crystals, that it should have been so long overlooked."

Subsequent experience has but served to confirm the accuracy of the above-quoted statement as to the frequency of its occurrence. Dr. Beale represents the author as stating that crystallized phosphate of lime is of more frequent occurrence than the triple phosphate. While Dr. Beale quotes the first portion of the passage above cited, he omits the sentence in italics, which makes all the difference possible. What was actually affirmed was, that crystallized phosphate of lime, according to the author's experience, is of more frequent occurrence than the granular calcareous, or than the triple phosphate subject to the important limitation above specified.

"Of the pathological importance of excess of phosphate of lime in the urine not a doubt can be entertained; but certain reasons and facts can be advanced to show that deposits of the calcareous phosphate have a deeper pathological significance than those of the phosphate of ammonia and magnesia.

"One reason why we should be disposed to attach greater importance to the excess of the calcareous than of the magnesian phosphate, is that much of the phosphoric acid of the latter phosphate and all the magnesia are derived from *without*, being contained in the various articles consumed as food; while for the phosphate of lime we have, in the system, in the bones and teeth, and also in the nitrogenous tissues, independent sources of supply amounting to some pounds' weight.

"The particular or special reasons for regarding deposits of phosphate of lime as of more moment than those of the triple phosphate are derived from direct pathological observation. I have observed that when this deposit occurs, it is very apt to be persistent; and when it has disappeared, to return whenever the health is reduced from any cause. I have also noticed that when it is persistent it is usually associated with marked impairment of the health, and this often where organic disease does not exist.

"The prominent symptoms, in one case of calcareous phosphatic deposit I have had under observation for some years, were, great disorder of the digestive organs, frequent and distressing headaches, occasional vomiting, debility, emaciation, great irritability of the nervous system, sexual powers weak, pulse slow and feeble, skin cold, urine in excess, of rather low specific gravity, acid when passed but soon becoming alkaline; micturition frequent, with irritation of neck of bladder; teeth much decayed. It should be stated that there was in this case a very slight tendency to paralysis of the right leg, as shown by an occasional sensation of coldness in the limb, and slight deficiency of power at times only. The last symptom is, however, by no means a constant or necessary one in such cases.

"If these views of the pathology of phosphate of lime be correct, we should expect to find an excess of that phosphate in the urine when there is much waste of tissue, during the rapid decay of the teeth, and in cases of *rickets* and *mollities ossium.* That there is an excess of the calcareous phosphate in the urine in the two last of these cases, is shown alike by observation and analysis."

It will be apparent, from the following quotation, that the late Dr. Golding Bird, referring, however, exclusively to the granular phosphate, regarded deposits of phosphate of lime as of more consequence than those of the triple phosphate :—

"The pathological state of the system accompanying the appearance of deposits of phosphate of lime is analogous to that occurring with the triple phosphate; indeed, as has been already observed, they often, and in alkaline urine always, occur simultaneously. So far as my own experience has extended, when the deposit has consisted chiefly of the calcareous salt, the patients have appeared to present more marked evidence of exhaustion, and of the previous existence of some drain on the nervous system, than when the triple salt alone existed, unless its source is strictly local."

### *Phosphate of Magnesia.*

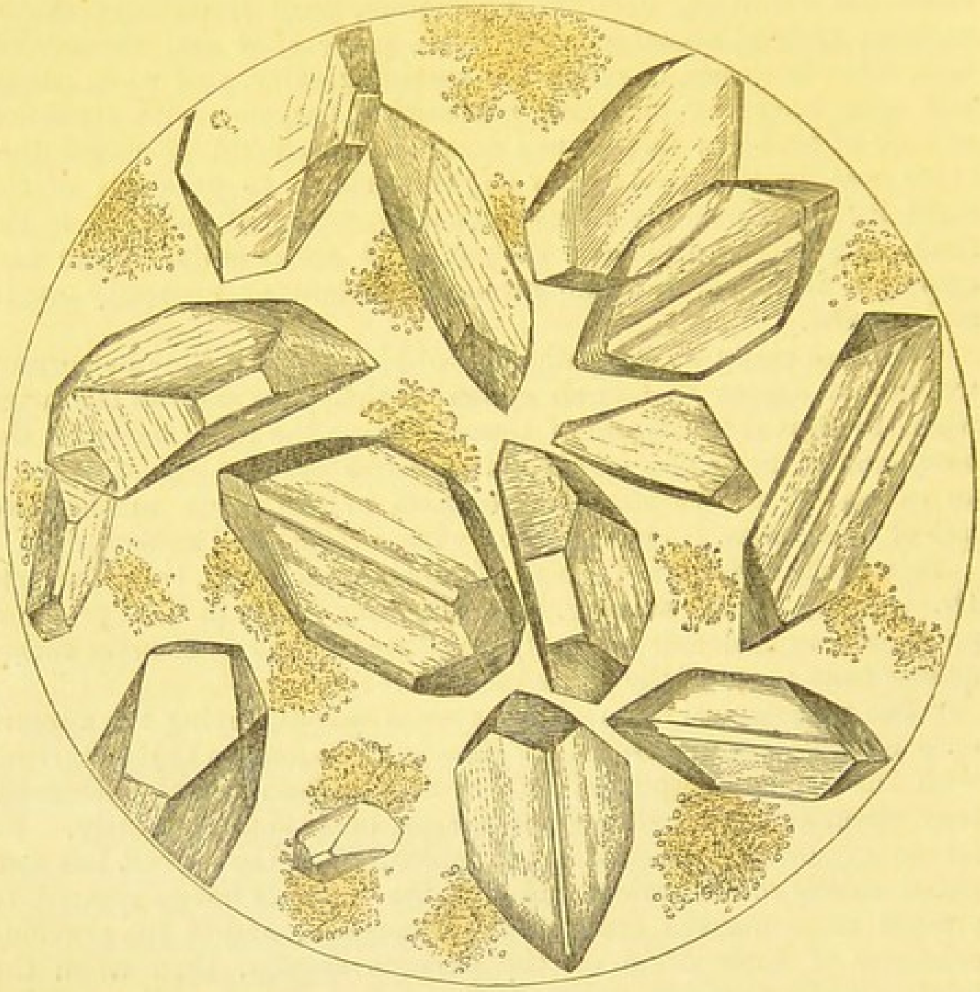
Phosphate of magnesia sometimes occurs in human urine in the crystalline state, as first shown by the author in a paper read before the Medical Society of London in 1853, and again in the *Lancet* in April, 1853.

It has likewise more recently been observed by Dr. Birkett, the judicious editor of Bird's "Urinary Deposits."

It is singular that both my own and Dr. Birkett's patient should have been under treatment with hyposulphite of soda for *Sarcina ventriculi.*

Phosphate of magnesia is stated by MM. Robin and Verdeil to be commonly present in a crystalline condition in the urine of domestic rabbits. The characters of the crystals will be found elsewhere described and figured.

FIG. 63.



Peculiar modification of the Crystals of TRIPLE PHOSPHATE; from *Human Urine*. 100 diameters. 1853.

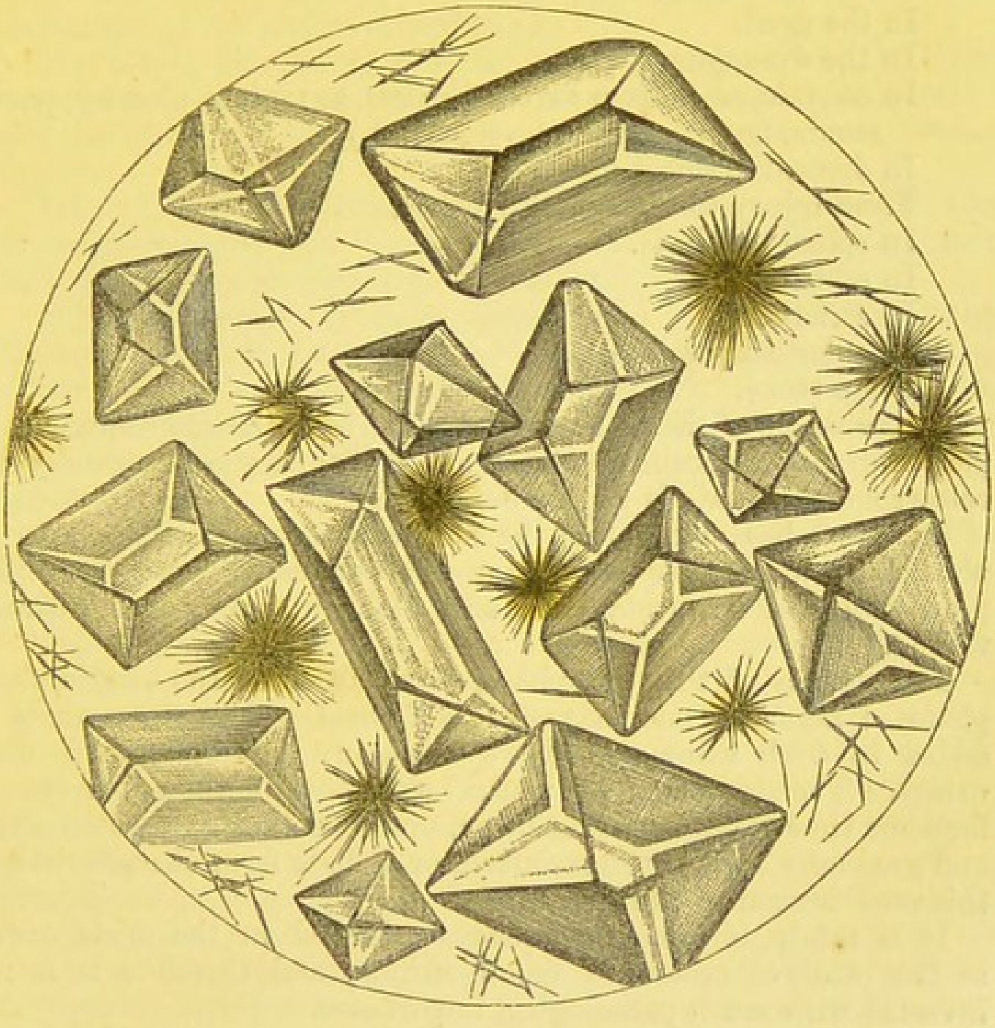
### *Phosphate of Magnesia and Ammonia.*

This phosphate occurs in the urine chiefly as a neutral salt.

According to most writers, the ammonia which enters into the composition of the neutral triple phosphate is derived from two different sources, the blood and the urine; but in both cases as a result of the decomposition of urea.

There is no doubt that it is usually obtained from the urea of the urine; that is, that the formation of the neutral triple phosphate ordinarily takes place in the bladder, or, at all events, in the urine subsequent to its having been voided. This explanation gives it, in fact, a local origin.

FIG. 64.



Remarkable *oblique double* Crystals of TRIPLE PHOSPHATE; from *Human Urine.* 220 diameters. 1853.

Of the formation of triple phosphate from ammonia in the blood, derived from the decomposition of urea, or some other ammoniacal compound, we have, as yet, no clear proof, although it is usually considered that it has in some cases such an origin.

If the observation recorded by Bird, of the occurrence of crystals of triple phosphate as a deposit on the papillæ of the kidney be comfirmed, it tends to prove the probability of its occasional formation in the blood.

Triple phosphate is met with in the urine :—

First. Whenever that secretion is alkaline from fixed alkali, the alkalinity occasioning, after *the lapse of some time,* the decomposition of the urea.

Second. Whenever it is alkaline from the presence of the volatile alkali, carbonate of ammonia, as

In the debilitated.
In the aged.
In the dyspeptic.
In convalescents from severe diseases, as typhus, pleurisy, pneumonia, and rheumatic fever. (Bird.)
In dementia, sometimes.
From injury to the spine by blows.
In spinal paralysis.
In cystitis.
In stricture.
In enlarged prostate.
From stone.

In the whole of these cases the deposit is frequently composed in part of granular phosphate of lime; in spinal paralysis especially the calcareous phosphate is largely deposited.

Dr. Bird has stated that he met with more than one case of phosphatic urine from the secretion of unhealthy mucus "by the propagation of irritation from an irritable uterus or even inflamed vagina."

The variety of this phosphate, formerly called the bibasic phosphate of ammonia and magnesia, is formed whenever ammonia is added to fresh urine, and also without any such addition in stale urines. The crystals of the neutral phosphate, if allowed to remain for some time in decomposing urine, even lose their prismatic shape, and gradually acquire the cruciform or stellate form characteristic of this modification of the salt.

It is rarely, if ever, spontaneously formed in the urine, except as the result of prolonged decomposition, and therefore it is not invested with much pathological importance.

The frequency of the occurrence of deposits of the earthy phosphates, either with or without ammonia, in aged persons, is explained partly by the reduced acidity of the urine, even apart from any local complication. Nutrition and metamorphosis both go on slower in old age, and hence a deficiency of free acid in the urine.

This appears to be the place to notice the very peculiar fact, that the urine has, in some very rare instances, been seen to emit a *phosphorescent light.* In some cases it was luminous as it escaped; in others the light did not appear until it fell upon some hard body, as a stone. The exact cause of this phenomenon has not yet been explained, although it is probably due to the presence of phosphorus in some form or combination.

### *General Symptoms of Excess of Phosphoric Acid.*

There are no general symptoms, so far as is yet known, characteristic of excess of the alkaline phosphates; but on the other hand, there are usually well-marked indications attending the prolonged deposition of the earthy phosphates.

The extent and precise character of the symptoms will, of course, vary with the cause, nature, and amount of the deposit, its duration, and also according to whether it proceeds from constitutional or local causes.

When the deposit consists of triple phosphate only, and this not in large amount, and its presence is only occasional and unconnected with any obvious local disease, the case is a mild one.

When the deposit of triple phosphate is great, is persistent, and there is well-marked constitutional or local disease, the case is more serious and the symptoms naturally more severe. Cases of this kind have been noticed to occur in the persons of clergymen, and others who are called upon to exert themselves greatly at stated intervals.

Lastly, when the deposits consist of phosphate of magnesia, and particularly of phosphate of lime, and they occur without admixture with the ammoniacal phosphate, the case is still more serious.

It would appear, however, that in certain exceptional and unexplained cases, large quantities of phosphate of lime may be excreted by the urine, and the discharge be unattended with severe constitutional symptoms. Dr. Golding Bird has related one very singular case of this description. The patient was an old man, an habitual dyspeptic, and had suffered from pyrosis from boyhood. For many years he had been in the habit of passing urine, milky from the presence of an extraordinary quantity of phosphate of lime, and at one time he brought Dr. Bird more than an ounce of the salt. He had been under treatment for this affection, at different times, for fifty years; but his urine "had never at any time exhibited any signs of improvement. Indeed, all the remedies appeared quite useless; at the same time the man's general health was so good, that there was scarcely an excuse for submitting him to any course of treatment." In this case, phosphate of lime no doubt proceeded mainly from the food consumed, and hence the absence of constitutional symptoms.

Usually, however, there are well-marked constitutional symptoms.

There is often extreme irritability of temper; great despondency, arising from depression of the nervous system; impaired digestion, more or less wasting, pain across the loins, great weakness, both of body and mind, incapacitating from any active exertion. In some cases, but by no means generally, the symptoms are in part explained by the elimination of an excess of urea, indicating increased waste of tissue.

## TREATMENT OF EXCESS OF PHOSPHORIC ACID AND OF PHOSPHATIC DEPOSITS.

So far as has yet been determined, there are few diseases in which both the alkaline and earthy phosphates are eliminated in excess: the only class of maladies in which it is probable that they are excreted in abnormal proportion is the acute diseases of the nervous system.

FIG. 65.

*Cruciform* Crystals of BIBASIC TRIPLE PHOSPHATE; from *Human Urine.* 100 diameters.

Of the pathology of the *alkaline phosphates,* little of a sufficiently precise character is known to serve as a guide to treatment.
It is in regard to the earthy phosphates that our knowledge is

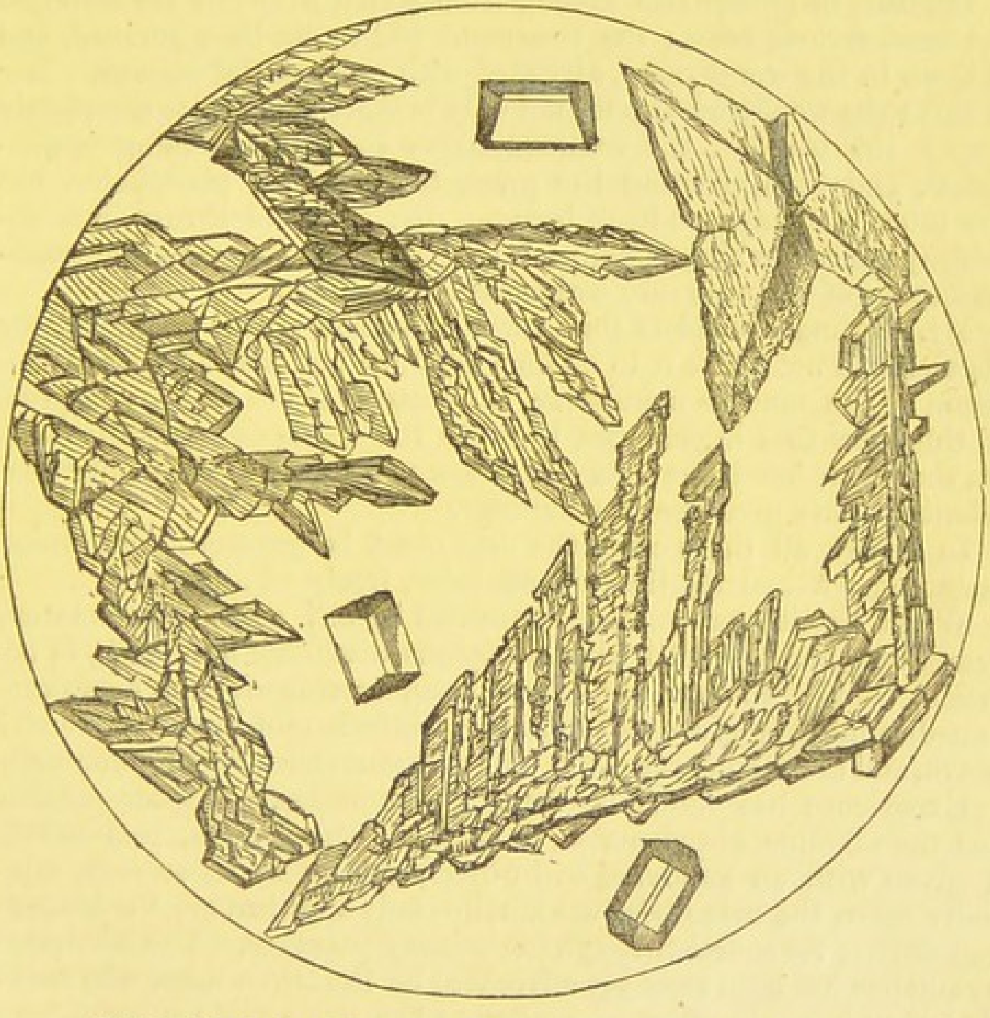
the more extensive, and that the therapeutical indications are clear and decisive.

In all cases of the deposition of earthy phosphates in the urine, we must determine the kind of phosphate, whether it is precipitated in excess or in the normal amount or not, and the cause of such precipitation.

Thus it should be ascertained whether the urine is acid when first voided, and deposits crystallized phosphate of lime.

Whether it is alkaline from fixed alkali, and deposits either phosphate of lime or magnesia.

FIG. 66.



*Ramose* Crystals of BIBASIC TRIPLE PHOSPHATE; from stale *Human Urine.* 40 diameters.

Or, whether its alkalinity proceeds from volatile alkali, causing the formation and precipitation of phosphate of ammonia or magnesia.

Lastly, it should be determined whether the deposit is due to peculiarities of diet, to deranged digestion, to debility, to affection of the brain and nervous system, or to a diseased condition of the mucous membrane of the bladder, the result of spinal paralysis, or of cystitis induced by stricture, stone, enlarged prostate, or other cause.

The iridescent membranous pellicle so often observed on the surface of phosphatic urine, there is reason to believe is usually indicative of a form of dyspepsia termed by Bird irritative, and which is common in gout.

When the phosphates appear after the principal meals and during digestion, while some hours after food the urine is free from them, the deposition in all probability is to be referred to mal-assimilation, or to deranged digestion.

Deposits of phosphates arising from spinal paralysis are amongst the most serious cases: the treatment has to be long pursued, and is then, in the worst cases, attended with only partial success. Nor is this to be wondered at; for not only is there inability to completely empty the bladder, the retained urine speedily becoming ammoniacal, and thus effecting the precipitation of the phosphates, but the mucous membrane itself becomes diseased, and throws out unhealthy mucus, which speedily decomposes and occasions the transformation of the urea into carbonate of ammonia.

Mr. Curling considers that mere retention of the urine in the bladder will not cause it to become alkaline, but that a diseased condition of the mucous membrane is necessary; and he cites in proof of this view that in enlarged prostate the urine is generally acid. On the other hand, the late Dr. Snow proved by experiments that retention does give rise to alkalinity.

In nearly all these cases the diet must be generous, and tonics, including particularly the mineral acids, freely administered.

When cystitis exists, unaccompanied by any active inflammatory symptoms, and attended with a copious discharge of mucus, in addition to the mineral acids, anodynes, astringent and demulcent remedies must be given—as gallic acid, infusions of buchu, of Pereira brava, and of triticum repens, as lately recommended by Mr. Thompson.

Experience has shown that alkaline remedies, as liquor potassæ and the alkaline bicarbonates, in many of these cases, particularly if given with an anodyne, will often prove of much service, especially when the urine becomes alkaline only after leaving the kidneys and during its course through the urinary passages. The treatment by alkalies has been strongly advocated by Dr. Owen Rees, who states that they have the effect of rendering the urine acid; a result very contrary to what might have been anticipated. Dr. Rees believes their beneficial action to be due to their lessening the acidity of the urine as secreted by the kidneys; the urine, he considers, is thus rendered less irritating to the mucous membrane of the bladder, which consequently pours out less of the acrid alkaline mucus.

The alkalies should not, however, be given in too large doses, nor be continued too long.

Mr. Ure has particularly recommended benzoic acid to increase the acidity of the urine.

Tincture of sesquichloride of iron is a very valuable remedy in these cases.

It is very desirable, also, that the bladder should be well washed out from time to time, and great benefit is sometimes experienced from the use of weak acid injections; by the adoption of these means, as well as by the administration of acids, tonics, opium, &c., we shall have done all in our power to diminish the risk of the formation of a calculus.

Dr. Golding Bird has spoken highly of the effects of sulphate of zinc, and also of strychnia, in cases of irritative dyspepsia unaccompanied by inflammation of the mucous membrane of the stomach.

Of course, if stricture exist, this must be treated; and if a stone be present, this must be removed before any considerable improvement in the case can be reasonably anticipated.

Cold bathing, the shower-bath and douche, will in some cases prove highly beneficial.

Urine containing sugar very frequently deposits, after standing a short time, a small quantity of phosphate of lime in the crystalline state. This fact was recorded by the author in his memoir on the "Development of Torulæ in Human Urine," published in the "Medico-Chirurgical Transactions" for 1852. So frequently was it observed, that he was then led to believe that some connexion existed between sugar and phosphate of lime in the urine, and that probably sugar, or its derivative, lactic acid, acted as a solvent of the phosphate of lime. The experiments of Böcker, already noticed, render this view extremely doubtful; for when sugar was added in excess to the ordinary diet, he found that in nine days the phosphate of lime was reduced to the extent of no less than 47 grains. Now if this result is due to a lessened metamorphosis of the osseous and other lime-containing tissues; and if the diminution be a constant result of the remedy, the administration of sugar in cases of rickets and mollities ossium is plainly suggested.

Dr. Prout particularly recommends the employment of *opium*, especially in cases dependent upon spinal derangement; and Dr. Watson has repeated the recommendation. The latter physician thus graphically epitomizes the principles of treatment to be kept in view in these cases,—

"You must cautiously abstain from all drugs or measures that are calculated to lower the vital powers; from saline draughts, and alkalies of every kind; from mercury and colchicum; from bleeding and even from active purgatives; or you will add to the patient's dangerous weakness, and promote the more abundant deposit of the phosphates. But you may do more than abstain from what is hurtful; you may counteract the alkalescent tendency by a generous diet, and by the exhibition of tonic medicine—bark, wine, and acids (the muriatic or the nitric, or both together), may be given in such cases with vast advantage; sometimes opium is also a remedy to be employed in this form of disease. No single drug, probably, has so much power in rendering alkaline urine acid as opium; and it is indicated for other reasons: it composes the nervous anxiety, to which these patients are mostly a prey. Mental relaxation, freedom from care, the relinquishing of all exhausting habits and pursuits—these, too, are points of vast importance whenever they are attainable."

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# CHAPTER XII.

## CHLORINE.



The principal portion of the chlorine of the urine is in combination with sodium, but part also occasionally with potassium and ammonium. That chloride of sodium is of much importance in the animal economy is proved, not only by its almost universal consumption, but also by its effects on the more important constituents of the blood; thus it increases the solubility of albumen, impedes the coagulation of fibrin, and also exerts remarkable effects upon the colour, form, and composition of the red corpuscles of the blood.

### QUANTITY.

Vogel gives the mean amounts of chlorine passed in the twenty-four hours at from 6 to 8 grammes, equal to 92·64 and 123·52 grains. Taking the mean of these two numbers, 7, and uniting the chlorine with sodium, with which it is principally combined, we obtain 177 grains of chloride of sodium as the average daily excretion. In this estimate Vogel is followed by Parkes. Hegar's mean excretion closely corresponds with this, namely, 161 grains.

As might be expected, the range above and below this mean is very great. Parkes, in one of his cases, that of a healthy person on full hospital diet, obtained only 51·87 grains of chlorine, equal to 85·0 grains of salt; while Genth found no less than 173·23 grains of chlorine, corresponding to 283·9 grains of salt.

Taking the mean amount of chlorine daily excreted at 108·08 grains, and adopting 145 lbs. as the mean weight of all the men whose urine has been analysed, it is found that 1 lb. avoirdupois of body-weight furnishes in 24 hours 0·875 of a grain of chlorine.

In women the amount is somewhat less, 0·817 of a grain. (Parkes.)

Bischoff has calculated that about two-thirds, and Kaupp three-fourths, of the chlorine consumed in the food escape by the urine, and the other third or fourth chiefly by the skin, but little being found in the fæces. The difference between ingress and egress is less when the quantity is small than when it is large.

## ORIGIN OF THE CHLORIDES.

The whole of the chlorine contained in the urine is derived from the food.

Part, chiefly united with sodium, passes out of the system without having entered into the composition of the tissues.

Another portion becomes united with the tissues, and is set free only on their disintegration, and this therefore is derived from and represents change of tissue.

### *Influence of Age.*

Taking children of both sexes between the ages of 3 and 7, it appears from Uhle's calculations, that each pound of body-weight excretes 2·15 grains of chlorine per day; that is, the amount eliminated by children in relation to body-weight is nearly three times as great as in adults, in whom, according to Uhle, it is 0·738 of a gramme, equal to about 8-tenths of a grain. This increase is due partly to increased ingestion, and partly to rapid tissue transformation.

### *Influence of Food.*

The chlorine is lessened after animal, and largely increased after vegetable food. This depends upon the relative amounts of chlorine salts in the two descriptions of food.

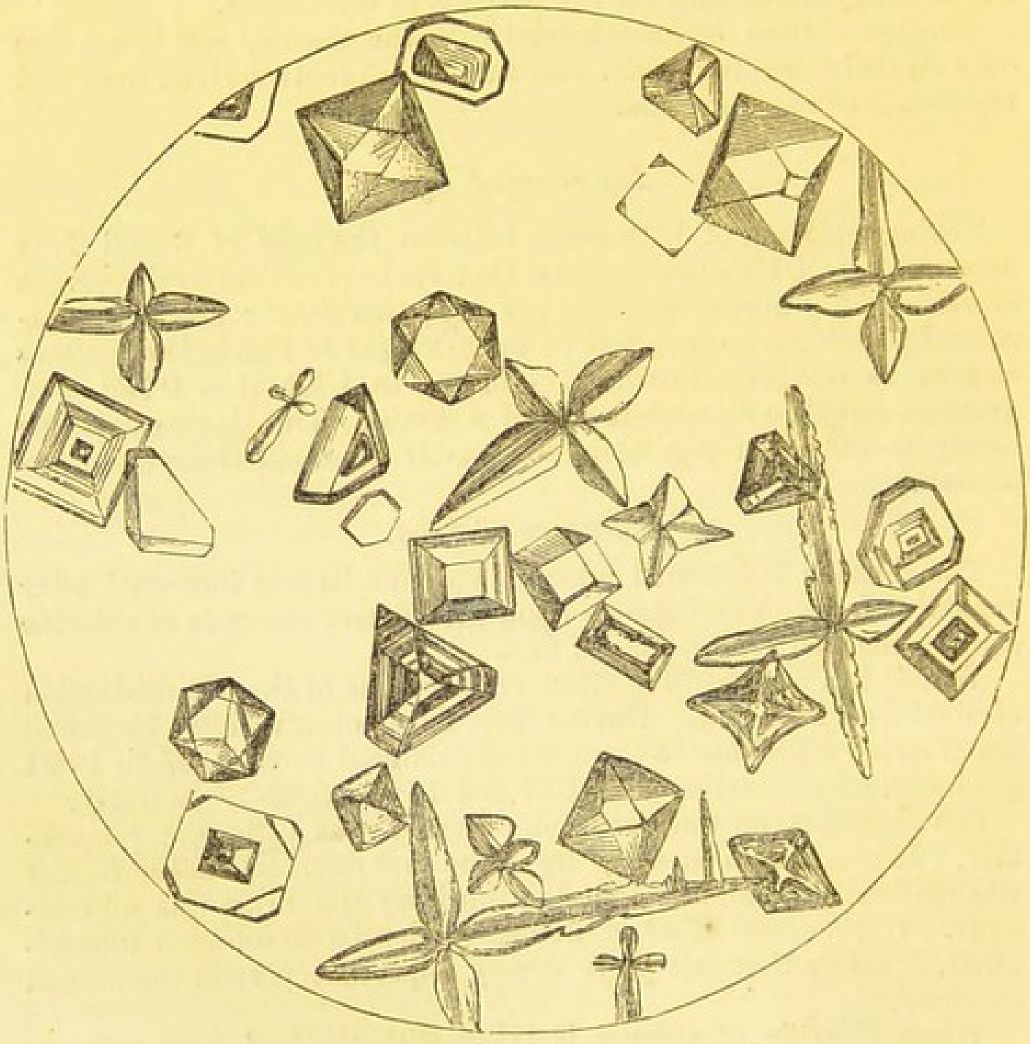
Wundt has observed the effect on the urine of the administration of food free from salt. During five days' observations, he found the chloride of sodium to become daily reduced from 7·207 to 1·091 grammes, corresponding to 111·27 and 16·86 grains respectively.

But the effect on the excretion of water was still more remarkable. It gradually decreased from the first day, till on the fifth it was reduced to one-half. On the third day the urine was albuminous. If the usual effect of its deprivation be to occasion albuminuria, it shows that salt plays a very important part in the animal economy.

When chloride of sodium is taken with the food, part only, as previously stated, escapes by the urine, and there is some reason to believe that a portion is decomposed, the chlorine and the base, it is presumed, reuniting previous to their excretion. The free chlorine has been supposed to aid digestion by the formation of hydrochloric acid in the stomach, and the base to furnish soda to the bile. Given by itself in large doses, it does not appear that either the water or the urea is much affected; the former is perhaps on the whole somewhat lessened, and the latter perhaps slightly increased.

M. Baud believed, from experiments on sheep, that he had determined the fact of an increased excretion of urea and other nitrogenous compounds consequent upon the addition of salt to the food; but this result has not been confirmed by more recent observations, which show that the urea is scarcely at all affected. If correct, the increase would indicate augmented metamorphosis of the nitrogenous tissues.

FIG. 67.



Represents several modifications of the Crystals of CHLORIDE of SODIUM. Magnified 100 diameters.

When large quantities of water are drunk *fasting*, or in addition to the ordinary diet, there is a temporary increase of chlorine salts.

By *alcohol*, the chlorine is greatly lessened, doubtless from retention, and this whether given fasting or with food.

By *beer*, taken in moderate quantities and added to the ordinary diet, according to Böcker's experiments, it is augmented; but the urea, extractives, &c. lessened, the former considerably.

By *tea*, it is somewhat lessened, but by coffee to a greater extent. (Böcker, Lehmann, and Hammond.)

### *Effect of Exercise, &c.*

The chlorides are increased by *exercise*, as also by *sleeplessness* and *mental activity*. (Hegar, Kaupp.)

### *Abstinence from Food.*

Abstinence from food does not occasion a total disappearance of chlorides from the urine.

### *Determination of Chlorine.*

The chlorine may be estimated either from the urine itself, or from its ash; the former method is to be preferred, as some of the chlorine is lost by incineration; in either case, the liquid should be first acidulated with nitric acid, to prevent the precipitation of the phosphoric acid on the addition of a solution of nitrate of silver, whereby the chlorine is thrown down.

The quantity is ascertained either by weighing the precipitated chloride of silver, or else is determined by the volumetric method, which is by far the most expeditious; that is, by carefully noting the quantity of a solution of nitrate of silver, of known and appropriate strength, required to separate the whole of the chlorine.

Or it may be determined volumetrically, as is now usually done, by means of a graduated solution of pernitrate of mercury. Chlorine forms a soluble compound, corrosive sublimate; and urea, an insoluble one with peroxide of mercury; it also has a stronger affinity for the mercury than urea; so that, if the solution of the pernitrate be added to urine, no precipitate will appear until all the chlorine has combined with the urea. When this has occurred, then the compound of urea and mercury will begin to be precipitated. In adopting this plan, however, the phosphates must be previously removed by means of the *baryta solution*, described under the head of the quantitative determination of urea.

### *Microscopical Characters of Chloride of Sodium.*

The chlorine of the urine is principally in combination with sodium, the resulting chloride of sodium being a readily crystallizable salt.

The primary form of its crystals is cubical, and well-formed cubes may frequently be obtained from the syrup-like extract of the urine. The ordinary form, however, in which they are met with in urine evaporated on slips of glass is the octohedron, the octohedra being distinguished from those of oxalate of lime by their being longer in their principal axis, and by not polarizing light.

Sometimes the crystals occur in the form of half octohedra, when they are occasionally striated.

More rarely they present the form of dodecahedra, more or less perfect.

From the solution of the ash of urine, it often crystallizes in the form of crosslets and daggers. (Fig. 67.)

Out of the system, chloride of sodium enters into a definite combination with urea, but whether this ever exists in the urine is uncertain. The crystals of the compound of urea and salt assume usually the octohedral form.

## PATHOLOGY OF THE CHLORIDES.

In *ague* the chlorine is greatly increased during the cold and hot stages. Franke found as much as 293 grains of chloride of sodium excreted in six hours, while Sidney Ringer ascertained it to be increased ten, and even twentyfold. The water and the chlorine were observed by Ringer to be closely related.

In simple continued fever, *febricula*, chloride of sodium is somewhat lessened, but is reduced to a greater extent in *typhus abdominalis* and *typhus exanthematus*. In a case of the latter fever recorded by Parkes, the chlorides were entirely absent.

The diminution depends partly upon diminished ingestion and partly upon the profuse sweating and diarrhœa which frequently accompany these diseases; but there seems reason to believe also that, in some cases, there is retention, and this in the absence of pneumonia or other local inflammatory implication. During convalescence the chloride of sodium and water become abundant.

In *scarlatina* the chlorides, according to Brattler, are often much lessened, but increased during convalescence.

In *erysipelas* of the head and face, in a man aged 20, Parkes found the chlorine reduced to 19 grains on the fifth and sixth days of the disease.

In *puerperal fever*, Chiori found the chlorides lessened, and after some days they disappeared altogether.

In *milk fever* they are also diminished.

In *acute pneumonia* the chlorides are greatly lessened, and often entirely absent, reappearing in the urine only, some time after resolution has set in (occasionally as many as eight or ten days), and the excess of urea has passed away. This deficiency is due to retention, and from the large amount of salt in the sputa, as shown by Beale and others, it evidently accumulates in the inflamed lungs. The chlorides are also in excess in the sputa of *phthisis* and in *purulent* and *fibrinous exudations*.

Some days after resolution has taken place, and when there is but little expectoration and no purging, the quantity excreted may amount to 232 or even 286 grains in the 24 hours.

In *pleurisy*, both with and without pneumonia, but with effusion, the chlorides are diminished: they escape from the blood with the effused liquid, and reappear in the urine as this is absorbed.

In *acute capillary bronchitis*, the reduction in their amount is almost as great as in pneumonia, and in both diseases they are sometimes entirely absent.

In *acute pulmonary phthisis*, they are either deficient or absent. It must, however, be remembered, that in these cases the diet is low, and that there is expectoration, as well as, frequently, sweating and diarrhœa.

In *acute rheumatism*, the chlorides are usually much lessened or even wholly absent; but in this disease there are several causes in action which explain the diminution or absence—namely, exudation, lessened diet, profuse sweating, and sometimes diarrhœa.

It thus appears that in all the diseases previously enumerated, except ague, there is a diminution of the chlorides, due in part in many cases obviously to retention. These diseases, being all of an active character, and accompanied by fever, may therefore be placed amongst the *pyrexiæ*.

The rule, therefore, in this class of cases, as regards the chlorides, and, as we have seen, the phosphates also, is the reverse of that which obtains with most of the other urinary constituents. While the chlorides are diminished, the urea, uric acid, pigment, extractives, and sulphates, with some exceptions, are augmented.

The exceptional increase in the chlorides, in ague, cannot at present be explained.

It further appears that a close connexion exists between the water and the chlorides, and that when the latter is lessened the former is also diminished.

*Chronic febrile diseases* are frequently the results of the acute forms; and hence, as a rule, the urine resembles more or less that excreted in the acute diseases, and consequently the chlorides are more or less deficient.

The condition of the urine as to the chlorides in *non-febrile diseases* may now be considered.

In *cholera* the chlorine is at first nearly absent; but from the fifth to the eighth day it gradually returns, the amount eliminated not being large, and the greatest excretion occurring a day or two after that of the urea.

In *chronic phthisis* during a fit of hectic, as is the case in ague, the chlorides increase during the cold and hot stages, and even still more remarkably for the first two hours of the sweating stage. In a case in which the urine was analysed by Mr. Ringer, it increased from 7·22 and 5·51 grains per hour before the shivering to 10·20 grains per hour in the cold stage; to 12·49 grains in the hot stage; and to 22·86 and 19·27 grains per hour in the first two hours of the sweating stage. In the third and fourth hours it fell to the normal amount 6·50 and 6·94 grains, and after the fit was over it rose to 15·74, and then fell to 10·68 grains. Thus there was in this case no diminution of the chlorides during the sweating stage.

As in ague, the water and the chlorides exhibited a close relationship.

The state of the appetite, the bowels, skin, and also the amount of expectoration, in phthisis, influence greatly the excretion of the chlorides by the urine.

In *dropsy*, whether proceeding from disease of the heart, liver, or kidneys, there is great diminution of the chlorides; but when diuresis supervenes and the dropsical fluid is absorbed, they are proportionately increased.

In cases of *diabetes*, owing to the increased ingestion of food and the inactivity of the skin, they are usually very greatly augmented; the quantity in adults having been observed to range between 337 grains (Böcker) and 568 grains (Thierfelder and Uhle).

In *acute Bright's disease* the chlorine is lessened, or sometimes absent. (Mosler and Heller.)

It is also diminished in *chronic Bright's disease*, and this sometimes to an extent greater than can be explained by the reduced diet, and inversely to the amount of albumen. (Rosenstein.)

It is thus apparent that in *chronic diseases* generally, there is diminished elimination of the chlorides, and, it may be added, lessened excretion of the water and of the other urinary constituents, resulting from diminished food, impaired digestion, defective innervation, and feeble circulation.

## TREATMENT.

Reviewing all the facts which have hitherto been determined respecting the occurrence of the chlorides (chiefly chloride of sodium) in the urine, some degree of surprise may be expressed at the fact that this salt has not been proved to play so important a part in the animal economy as from its very general use might have been anticipated: in particular, it does not appear to exert any marked influence over the nutrition and metamorphosis of the tissues, present investigations merely showing that it stands in close relation to the water of the urine.

The retention, either partial or complete, of the chlorides in acute pyrexial or inflammatory disease is remarkable, and indications for treatment are thereby afforded—thus, one of the objects to be aimed at is increased elimination of the chlorides, an object to be effected through the skin, bowels, and urine.

There is one remedy in particular which has been found by the experiments of Parkes, to generally augment the chlorides in the urine—namely, *liquor potassæ*.

The presence or absence of the chlorides from the renal excretion often affords valuable aid in diagnosis and prognosis; thus if, in a case of pneumonia, they are entirely absent, it may be inferred that the attack is a very severe one; and again, their reappearance in the urine after a period of retention is usually a favourable symptom.

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## CHAPTER XIII.

## ON THE ACIDITY AND ALKALINITY OF THE URINE.



The normal *acidity* of the urine is due to the presence of certain acid or super-salts, principally of phosphoric and uric acids, but also in some cases of hippuric and possibly sulphuric acids.

Occasionally—either as the result of decomposition, fermentation, or disease—other acids are present—as carbonic, lactic, acetic, butyric, and, rarely, valerianic acids.

The *alkalinity* of the urine may be occasioned in several ways, as by the absence of any excess of phosphoric or other acid to which the normal acidity of the urine is due; by the presence of an increased amount of the normal alkaline salts; by certain alkaline salts not ordinarily present in the urine—as, for example, carbonate of ammonia.

There are two kinds of alkalinity of the urine, the one from fixed, and the other from volatile alkali.

The urine may be alkaline, as secreted by the kidneys, from fixed alkali; it is highly probable that it may be so likewise from volatile alkali, but the fact does not appear as yet to be unequivocally established; usually, when alkaline from volatile alkali, it becomes so subsequent to its secretion, and as the result of the decomposition of the urea.

Carbonate of ammonia is doubtless sometimes present in the blood from the decomposition of urea and even chloride of ammonium, and hence its occasional presence in the urine as eliminated by the kidneys may be inferred.

There are several causes which favour this decomposition of the urea in the urine, and which have been in a measure already dwelt upon—such as retention in the bladder from stricture, or enlarged prostate, the irritation of a stone, cystitis, however induced, spinal paralysis, &c.

A urine acid when voided, when kept for any time, passes through a series of changes. At first it usually becomes more acid, and subsequently alkaline, chiefly from the decomposition of the urea.

These changes occur with varying degrees of rapidity, not only according to the composition of the urine itself, but also to temperature, and the amount of mucus, pus, or other putrescible and fermentable nitrogenous matter which it may contain.

Accompanying these changes in the reaction of the urine, other material alterations in its condition take place—such as, on account of increased acidity the precipitation of uric acid, and, as a consequence of alkalinity, the deposition of the earthy phosphates. After a time, different species of fungi and animalcules become developed in the urine according as it is acid or alkaline, and which will be described hereafter.

It must be remembered that the urine may have an acid reaction, and yet not contain any free acid.

### *Degree of Acidity.*

The acidity of the urine is usually determined by an alkali, such as soda; but a closer idea of the actual acidity is conveyed by comparing it with the amount of oxalic acid equivalent to the alkali used.

Winter found in one man the mean acidity of the urine of twenty-four hours to equal 36·67 grains of crystallized oxalic acid, and in another, 29·70 grains; Kerner 30; and Vogel from 30·88 to 61·76 grains.

It does not appear that the relative acidity of the urine in children has been ascertained and compared with that of adults; but in old age there is a lessening of the acidity.

Dr. Roberts found the free acid, on an average of 19 days, to equal only 16·76 grains of oxalic acid. The maximum quantity was 26·55 grains, and occurred under an animal diet, and the minimum 7·01 grains, under a mixed diet—a very wide difference.

As shown by Scherer, the acidity of very many urines, especially those that are high-coloured and concentrated, increases after excretion. This increase, according to Scherer, is due to an acid fermentation, and by some is attributed to oxidation of pigment. Certainly, it does not generally result from oxidation of uroxanthin, as suggested by Virchow, since it occurs most frequently in urines in which that indigo-yielding substance is very deficient.

"The acid thus produced is probably the lactic, but it has been supposed that acetic (Liebig), butyric, metacetonic, and even oxalic acid (Zimmermann) may be thus formed." (Parkes.)

The duration of the acidity varies, but may continue for many days in some cases, while in others, the urine begins at once to lose its acidity and to become alkaline, the change constituting what has been termed the "alkaline fermentation."

*Effects of Food.*

The urine of the herbivora is alkaline, and is rendered so by the alkaline carbonates and salts of the vegetable acids, converted into carbonates, in their passage through the system. That the food is the cause of the alkalinity, is shown by the fact, that when such animals are made to fast, the urine becomes acid. The effect of food upon the reaction of the urine is still further exemplified by the following circumstances: when rabbits are fed upon an animal diet for some time, the urine passed is acid, and when dogs are restricted to vegetable food it is rendered alkaline. (Cl. Bernard.)

That food, therefore, in the human subject should exercise a marked effect upon the reaction of the urine, is only what might have been anticipated; and some years since Bence Jones deduced the following conclusions from the inquiries which he instituted :—

That after 3 days of a *mixed* diet, the acidity after meals was found to decrease, and to attain its lowest limits from three to five hours after breakfast and dinner; sooner, however, after breakfast than after dinner. It then gradually increased, and obtained its highest limit just before food. If no food was taken, " the acid of the urine did not decrease, but remained nearly the same for twelve hours."

When *animal food* only was consumed, the diminution of the acidity was more marked and more lasting than when a mixed diet was taken; and the acidity before food rose rather higher with a mixed than it did with animal diet.

When *vegetable food* only was taken, the decrease in acidity was not so marked: though the urine became neutral, it did not become highly alkaline. " The increase in the acidity of the urine was by no means so marked as the decrease in the alkalescence. The acidity of the urine was rather higher with the vegetable food than it was with animal food."

The accuracy of these results has been questioned, insomuch that it appeared to Dr. Roberts desirable to put them to the test by the institution of a number of careful and elaborate experiments, the chief results of which are embodied in the following conclusions. The observations were carried out on the same individual, and for a lengthened period.

The *primary* effect of a meal—whether of purely vegetable, animal, or mixed food—was, in from one to three hours, to diminish the acidity of the urine, and very frequently to render it alkaline.

After thirty-six breakfasts, the urine became alkaline seventeen times, neutral five, and remained acid fourteen times: after thirty-six dinners it became alkaline twenty-eight times, neutral in two cases, and it continued acid in six.

The remote or *secondary* effect was to increase the acidity of the urine, an effect observed especially over-night after supper, and which appeared greater after animal than vegetable food, "so that a highly-animalized diet tends in the long run to heighten the acidity of the urine."

The depression of the acidity after breakfast occurred at the second hour, and continued from two to four hours; while after dinner it occurred at the third, fourth and fifth hours, and lasted from four to six hours. The effect, therefore, of dinner was less quickly manifest, but was greater and more prolonged than that of breakfast.

The effect of mixed and animal diet appeared almost identical. Vegetable food given on alternate days, with either mixed or animal food, had a more feeble effect; but when taken continuously for several days its effect was equally powerful.

The depression of acidity after a meal coincided in point of time with *absorption* rather than with digestion.

The *solids* of the urine increased in proportion to the declension of the acidity, so that the passage of food into the blood, and the diminished acidity of the urine, seemed to stand in the relation of cause and effect. The increase in the solids was partly due to an augmentation of the phosphates and of uric acid, which were ascertained to be in excess in the more alkaline urines. No ammonia or carbonates were present in any of the urines.

The greater number of the alkaline urines were turbid from precipitated phosphates, but some, notwithstanding their alkalinity, and that they contained an excess of phosphates, retained their transparency, and they all possessed the pleasant and characteristic odour of the urine of the horse. These results confirm, in the main, the prior conclusions of Bence Jones.

There is one point connected with the results of Dr. Roberts's experiments which it appears important should be noticed.

The amount of free acid separated in the course of 24 hours, on an average of 19 days, was only sufficient to neutralize 14·10 grains of dried carbonate of soda, an amount which corresponds to but 16·76 grains of crystallized oxalic acid, and which is not half the quantity given by Winter and others as the normal mean acidity of the urine. The low acidity of the urine of the person upon whom Dr. Roberts's experiments were carried out, appears to explain the occurrence of so large a proportion of alkaline samples. The average daily alkalinity was equal to 3·32 grains of dried carbonate of soda.

It cannot, however, be expected that similar observations, made upon the same plan and with the same care, will invariably yield identical results, since considerable allowance must be made for individual peculiarities, as of diet and digestion, and the varying action of the skin, lungs, and bowels, exercise, &c.; possibly these causes serve to explain some of the decrepancies occurring in the statements of other experimenters.

The results of Winter's experiments differ in one important particular from those just recorded, explained possibly in part by the fact that the urine was not examined at sufficiently short intervals, and partly by some individual peculiarity. Winter found that the urine was least acid after breakfast, more acid after dinner, at one o'clock, and most so during the night.

Thus it was equal to, in every hour

| | Crystallized Oxalic Acid. Grains. |
|---|---|
| After breakfast . . . . . . | 1·20 |
| „ dinner . . . . . . . . | 1·54 |
| During the night . . . . . | 1·93 |

Dr. Herman Weber's experiments on himself, extending over a period of two months, and of which some particulars are given by Parkes, agree to a great extent with those of Winter. He found that during the night, from 11 P.M. to 7 A.M., the urine was most acid; that in the following hour, no food being taken, namely, from 7 to 8 A.M., the acidity was nearly but not quite so great; that from 8 A.M. to 1 P.M., breakfast only having been taken at 8 o'clock, the acidity was reduced on the average one-third; while from 1 P.M. to 8 P.M., a dinner of meat and potatoes having been taken at 1 o'clock, it was rather more reduced; while from 8 P.M. to 11 P.M., tea having been taken at eight o'clock, the acidity gradually rose, notwithstanding the tea, till it nearly reached the mean acidity of the night urine.

Dr. Weber also specially observed that when he went without his breakfast, the acidity still became reduced, though to a less degree; and the same occurred when no dinner was taken. It sometimes even happened that after dinner the urine was more acid than at night, and still more so after tea. Again, the urine after breakfast and tea was sometimes found to be neutral, and after dinner slightly alkaline.

In experimenting upon others, Dr. Weber in some cases met with different and still opposite results, the acidity being increased by food—a result possibly due to indigestion. It is obvious, however, from this and other facts, that the acidity does not follow the same rule in all even apparently healthy individuals.

It is not stated of what the tea consisted; but the increase of acidity after that meal may possibly admit of explanation by reference to its composition. If this meal was a light one only, then the effect of the dinner having passed away, the urine would naturally assume the acidity, the result of the remote effect of the food consumed: again, the diminution of the acidity in the morning, when no breakfast was taken, might merely show that the remote effect of food in increasing the acidity of the urine had reached its limit and was passing away, and the same explanation would apply to the reduction of acidity noticed when no dinner was taken.

These explanations, if correct, have at least the effect of reconciling more closely the results of the experiments of Roberts and Weber: if incorrect, we appear driven to the conclusion that, independent of food, the night urine is more acid than that passed during the day, a conclusion in the present state of the inquiry by no means warranted. Dr. Roberts, however, records this curious observation: a supper of milk and bread with a pint of ale, had not the effect of lowering the acidity of the night urine. How is this result to be explained? Is it due to the fact that the secondary effect overpowered the immediate effect, and so the urine retained its usual acidity?

We have now to consider why it is that food so generally lowers the acidity of the urine, and by what means it again recovers its acidity.

Dr. Bence Jones suggested that the blood, and consequently the urine, were rendered more alkaline by the withdrawal of acids from the blood for the purposes of digestion. It is possible that this diversion of the acid may occur to some extent, and exert some small effect upon the reactions of the blood and urine; but since the decrease of acidity corresponds not with the commencement of digestion when the stomach contains most acid, but occurs at a much later period, and coincides rather with absorption, it can scarcely be the principal cause of this change of reaction.

The depression of the acidity of the urine, as originally pointed out by Liebig in regard to the blood, is therefore really due to the alkalies present in the food.

The subsequent increase of acidity which takes place some hours after food, is due, doubtless, in part, to increased metamorphosis of the tissues, and the consequent formation of uric, hippuric, phosphoric, and sulphuric acids, and partly sometimes to acids generated in the stomach or blood, and independent of metamorphosis.

By *cane-sugar*, and *honey*, the acidity of the urine, as shown by Roberts, is not diminished.

By *alcohol*, added to a regulated diet, as might be expected from its general effect in impeding metamorphosis, the acidity is reduced.

As by *tea* and *coffee* the sulphuric and phosphoric acids are lessened, the acidity is in all probability reduced by these beverages.

By *fasting*, the urine is rendered scanty and relatively to its quantity the acidity is increased.

*Effect of Exercise.*

By *exercise*, according to Professor Lehmann, the acidity is increased, but J. Lehmann's more numerous experiments appear to show that it is not augmented.

## *On the Determination of the Reaction of the Urine.*

Strictly speaking, there are but two varieties of urine—*urina cibi* and *urina sanguinis. Urina potus* has no existence as a distinct form of urine; and when the term is employed, it must be understood that it merely signifies that a urine—it may be urina cibi or urina sanguinis—has been rendered dilute by the quantity of fluid taken.

Now, as we have seen, urina cibi is of low acidity, or is even alkaline; urini sanguinis, just the reverse, being usually very acid: in conducting experiments, therefore, upon the acidity of the urine in connexion with food, care must be taken to keep these two urines distinct; and this may be done by examining the renal excretion at stated times. If long intervals between each examination be allowed to elapse, the urine in the bladder will on some occasions be a mixed urine, and so, unless guarded against, the results may be more or less vitiated.

The urine should therefore be examined at short and indeed almost hourly intervals during the day, the quantity passed must be measured, and its acidity and specific gravity determined, and the day and hour at which each observation was made, together with any remarks in regard to diet, and the time of the meals, &c., which may appear necessary, should be regularly recorded. It is best, in order to avoid mixture of the two kinds of urine, that food should be taken twice only each day.

The acidity is usually determined by means of a solution, of known strength, of dried or anhydrous carbonate of soda. The soda used by a simple calculation may be converted into crystallized oxalic acid, in which form the acidity of the urine is now usually represented by most observers. The atomic weight of carbonate of soda is 53, and of ordinary crystallized oxalic acid 63.

For most ordinary purposes, it is sufficient to determine the acidity of the whole of the urine passed in 24 hours, distinguishing in some cases the day from the night urine, as also the after-breakfast and after-dinner urines.

It is obvious, from all that has now been advanced, that the inquiry as to the varying reactions of the urine is one of considerable nicety, demanding the strict observance of certain precautions.

### ORGANIC PRODUCTIONS FOUND IN THE URINE.

In urine left exposed to the atmosphere, certain organic productions become developed. For the growth of some of these three things are required—the presence of a nitrogenous substance, oxygen derived from the air, and a fluid either acid or alkaline.

When developed in normal urine, the mucus furnishes the material for the development and growth of these productions; but in morbid urine it may consist of albumen or any fluid containing it, as pus or blood.

According as the urine is acid or alkaline, the character of the growths varies.

If acid, the fungus known as *Penicilium glaucum* is developed, and if in addition the urine contain sugar, then *the yeast fungus, Myko-derma Cerevisiæ*, is also formed. Both these productions will be found described and figured in connexion with albumen and sugar.

The developments occurring in feebly acid, neutral, or alkaline urine are of a different kind, and were fully described in a communication* by the author, published in the *Lancet* for November, 1859, and from which most of the following particulars are abridged.

Amongst these are included *Vibriones*, which are minute living bodies the diameter of which is the $\frac{1}{25000}$th, and the average length the $\frac{1}{5000}$th of an inch. When living, they are in a state of ceaseless activity; when examined with a quarter-inch object-glass, the motions present an oscillating character; but with a higher power it is seen that in progression they move in a rolling or spiral manner.

When they first make their appearance in urine they are comparatively not numerous, and diffused throughout the whole liquid; afterwards, very frequently, they are developed in multitudes, and then the greater part of them collect on the surface, forming a thick and greasy-looking pellicle. If a minute portion of this scum be broken up and examined under the microscope, myriads of vibriones are beheld, sometimes aggregated into little roundish masses, which are probably so many centres of germination. In old and stale urines the pellicle usually breaks up and disappears, the vibriones for the most part falling to the bottom of the glass.

Again, very frequently, the scum which collects on the surface of the urine does not consist entirely of vibriones, but is composed in part of different kinds of crystals, chiefly triple phosphate, and also of fungi, especially *Penicilium glaucum*, so often found in the urine, in different proportions and conditions of development.

The causes which determine their development are, first, a fluid either feebly acid or alkaline: if strongly acid when voided, fungi first appear, and then as the urine loses its acidity the vibriones become developed, and it is in this way that the occurrence of both torulæ and vibriones in the same urine is explained; second, the presence of animal matter, as mucus, epithelium, pus, albumen, &c.; and thirdly and lastly, exposure to the air. Whenever these three conditions coexist, vibriones become developed, and their presence, therefore, when taken by itself, is not necessarily indicative of any serious mischief or derangement; but when they occur in a number of

* On the Development and Signification of Vibrio lineola, Bodo urinarius, and certain Fungoid and other Organic Productions generated in Alkaline and Albuminous Urine.

samples consecutively, they show that the urine is deficient of its proper degree of acidity, and this it rarely is except in states of debility. Vibriones are, then, most apt to occur in the urine in diseases accompanied by extreme debility.

The late Dr. Golding Bird looked upon the occurrence of vibriones as of serious import; thus we meet with, in his work on "Urinary Deposits," the following remarks: "I have only met with these animalcules in the urine of persons in an excessively low and depressed state; in cases of syphilitic cachexia, when the prostration of strength is extreme, and in mesenteric diseases, I have repeatedly found them abundantly developed with remarkable rapidity. They appeared in great abundance in the urine of a patient under my care at Guy's Hospital during the past summer. The subject of this case was a most miserable-looking young man, who entered the hospital half starved and labouring under polydipsia, passing a very large quantity of urine of low specific gravity. He died of rapid phthisis in a few weeks: the urine became full of vibriones in active motion a few hours after being passed."

Dr. Basham, many years since, published some observations on the development of vibriones, and amongst them the following remark occurs: "They appear almost simultaneously with hydro-sulphuric acid and its compounds; and all fluids that decompose into hydrosulphuret of ammonia and its allied compounds, promote most rapidly the development of these vibriones."—On the Cholera-Sporules, *Medical Gazette*, 1849.

An animalcule of frequent occurrence in alkaline human urine is one which, many years since, the author named *Bodo urinarius*, and of which a full description was given in the *Lancet*, in the paper already referred to.

The infusoria in question are about the $\frac{1}{1800}$ of an inch in length, and the $\frac{1}{3000}$ in breadth; they appear, when living and in motion, of an oval or rounded form, and they present a granular aspect, not unlike that of a delicate mucus corpuscle: sometimes they are broader at one end, and are furnished with one, but usually two, and occasionally even three, long lashes, or cilia, by means of which they move themselves with the greatest rapidity; these proceed, when there are two or three lashes to each animalcule, from opposite extremities.

When these animalcules as contained in a drop of urine are first placed under the microscope, they usually appear rounded or oval; but gradually, as the water evaporates and their motion slackens and they are about to die, it is seen that they are really flattened and somewhat twisted. It is when they are dying or just dead, that the organs of locomotion are best seen; when they are in full activity, it is impossible to discover any indications of them.

One method by which these animalcules are multiplied is by *fissiparous* reproduction: the different stages of division and separation may in some cases be clearly traced out.

The circumstances which lead to the development of *bodo urinarius* are to a considerable extent similar to those under which

FIG. 68.

BODO URINARIUS. *a a.* Bodo. *b b.* Particles of indigo. From *Human Urine.* 420 diameters.

vibriones make their appearance; since, however, it does not become developed in all urines in which the latter are formed, it is obvious that there must exist some special circumstance or condition necessary to its growth. The author has observed particularly that it is in the more decidedly alkaline urines that it usually occurs, and especially in connexion with *indigo;* indeed, when this substance is present in any quantity, the bodos are developed by myriads. When they first appear, like vibriones, they are diffused throughout the whole bulk of the liquid, but as soon as they have multiplied to any extent, they collect on the surface, forming a soft and greasy-looking pellicle, which when much indigo is present, is often of a slaty or bluish colour.

An animalcule somewhat resembling the preceding is the *Trichomonas vaginæ*, described many years since by Donnè; it occurs in the vaginal mucus of women affected with leucorrhœa, and is sometimes found in the urine.

In addition to the two animalcules just noticed, several other animal organisms have been at rare intervals discovered; these are not, for the most part, developed in the urine, but are generated in the kidney, or bladder, and sometimes in both situations. They belong to different genera, appertaining chiefly to the Anthelmineæ, and a very good account of most of them will be found in Beale's work on the urine.

One of these is the *Echinococcus hominis*, which has been detected in the urine in several cases: it is developed in the kidneys. The cyst containing the echinococci bursting, at length they make their way, mostly in a broken and imperfect state, along the urethra into the bladder: their organisation, and especially the form of the hooklets, is so characteristic, that when found in the urine they may be readily recognised.

*Dactylius aculeatus* has been found in one case only, that of a girl aged 5 years, under the care of Mr. Drake. Several of the worms voided were examined by Mr. Curling, whose paper on the subject will be found in the twenty-second volume of the Transactions of the Medico-Chirurgical Society. The female worm was nearly an inch in length, and the male about half the size: the surface is covered with spines, as indicated by the specific name, and these are disposed in clusters.

*Strongylus gigas* is another species of parasitic worm, sometimes found in the kidneys of the lower animals, and which appears also to have been discovered, on one occasion only, in the kidney of the human subject. The female worm is several inches in length, nearly twice the size of the male worm; the ova make their way into the bladder, and are discharged in great numbers in the urine.

A woman, whose case is recorded by Dr. Arthur Farre, passed, in 1811, in the course of two or three months, from 800 to 1000 worms belonging to two different species, but consisting, except on one occasion, of a worm to which Dr. Farre has given the name of *Diplosoma crenata*, on account of the double body. It varied from four to six inches in length.

The other worms were smaller, from half an inch to an inch in length, and were passed once only. Rudolphi has given this worm the name of *Spiroptera hominis*.

Another parasitic worm, *Distoma hæmatobium*, now called by Cobbold *Bilharzia hæmatobia*, has been found not only in the pelvis of the kidney, the ureters, and bladder, the gall-bladder, and the small intestines, but, still more strange to say, in the veins of the small intestines and in the portal veins. The eggs were found embedded in and adhering to the mucous membrane of the kidneys, ureter, and bladder.

A few other cases in which worms have been voided in the urine have been recorded, but the species have not been identified. The author has himself detected certain *eel-like productions*, which closely resembled the animalcules of sour paste and vinegar, and the so-called *Vibrio tritici*. Besides the parasites noticed, the *ova* and *larvæ of flies* and other *insects* are occasionally found in stale, and particularly saccharine urines, exposed to the air. One larva noticed was distinguished by its jointed body, furnished with numerous hairs or bristles.

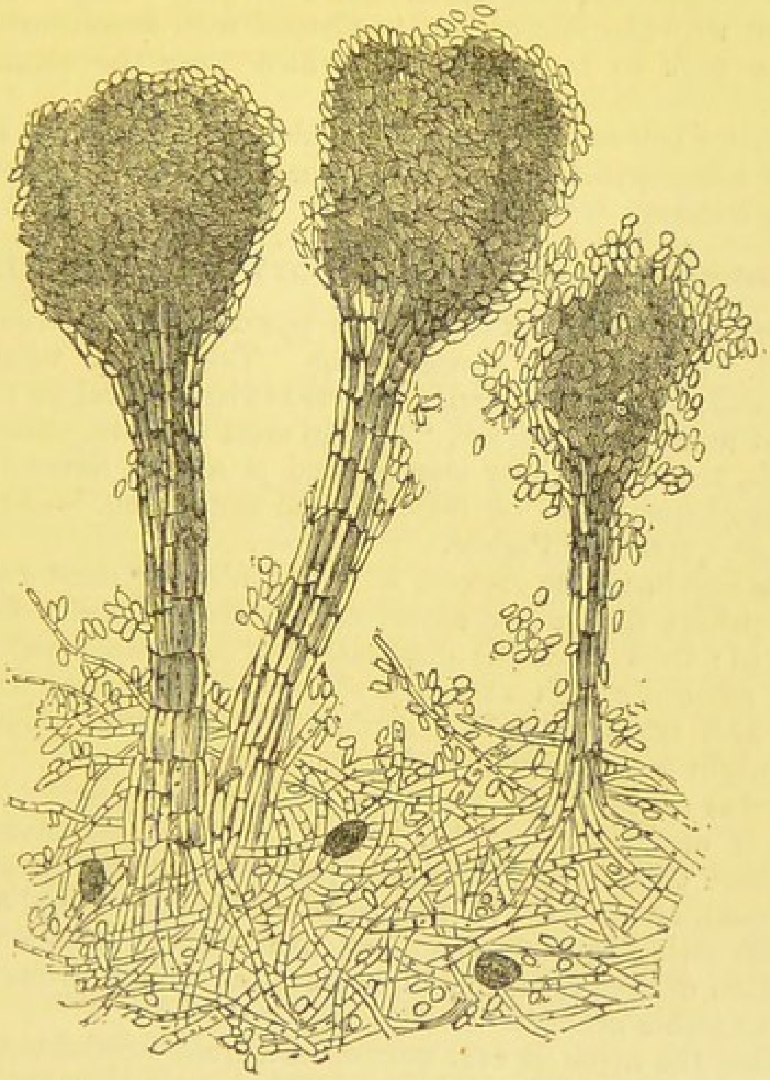
The reaction of the urine has doubtless but little to do with the development of some of the productions just described; it was yet considered that it was more convenient they should be noticed in connexion with the other vegetable and animal organisms which occur in urines which are either acid or alkaline. A brief description may now be given of three vegetable productions sometimes present in human urine.

One of these, described by the author some years since as occurring in alkaline urine, is a species of fungus. It differs materially in several respects from either *Penicilium glaucum* or *Mykoderma cerevisiæ*. The *sporules*, unlike those of the Penicilium, are for the most part oval, and about the $\frac{1}{2420}$th of an inch in length, and the $\frac{1}{3280}$th of an inch in diameter: that is, while they differ in form from those of Penicilium glaucum they are at the same time considerably larger. The *thallus* consists of threads, which are very slender and but little branched, and which have a soft and jelly-like consistence, so that when the tufts are raised from the urine on the point of a needle, they look like little portions of jelly, an appearance which is very characteristic of this fungus. The aërial fructification is also very distinct; the stems bearing the masses or heads of oval sporules do not consist, as in the other fungi found in the urine, of a single-jointed thread, but one made up of several such threads, united and bound together into one stem; these filaments terminate in and break up into the numerous sporules composing the reproductive tufts. The name of *Penicilium mucosum* would not be inappropriate. (Fig. 69.)

A species of Sarcina, probably distinct from *Sarcina ventriculi*, has been found in the urine by several observers, amongst others, by Mackay in 1848, and subsequently by Heller, Welcker, Begbie, Johnston, and Beale; it is smaller than the species developed in the stomach, and has been named by Rossmann *Sarcina Welckeri*. Hepwood found it even in the pelvis of the kidneys.

Lastly, on several occasions the author has encountered a number of "oval or rounded membranous bodies or *vesicles* of about the $\frac{1}{1194}$th of an inch in diameter, and the $\frac{1}{800}$th of an inch in length, and of a *deep brown* colour. Some of these bodies are separate, while others are united together so as to form bunches; more rarely, three or four of them are joined end to end, and thus form a short beaded thread. When quite fresh, the interiors of these vesicles

FIG. 69.



PENICILIUM MUCOSUM. From *Human Urine*. Magnified 220 diameters.

appear to be occupied by a fluid, but sometimes they have the appearance of being empty, as frequently a large rounded aperture may be seen in the wall of each cell. Unlike most of the other productions occurring in the urine, they are not met with on the surface of the fluid, but at the bottom."—*Lancet*, 1859.

Respecting the nature of these bodies, some uncertainty exists whether they should be regarded as the sporules of a species of fungus, or as the ova-cases of some animal production.

In 1850, Dr. Cotton forwarded the author for examination some urine which he had received from Dr. Nicholson of Antigua, and which deposited a copious sediment, composed almost entirely of the bodies in question. The patient was attacked suddenly with acute pain in the right lumbar region, for which he was treated antiphlogistically. On the subsidence of the inflammatory symptoms a very large quantity of urine was passed, of a brown colour and high specific gravity, and which Dr. Nicholson discovered, on examination with the microscope, to abound with moniliform bodies, which he took to be torulæ, but which were the structures in question.

The writer has met with these vesicles, though not in anything like the same quantity, in many other urines, and also in some drinking-waters.

## PATHOLOGY OF ABNORMAL ACIDITY AND ALKALINITY.

In most febrile diseases during the pyrexial periods, the urine is very acid, due mainly to concentration. Taking the whole of the urine passed, Professor Vogel is reported to have found, as the result of a great many observations, " that in most diseases, acute as well as chronic, the free acidity lessens, and is almost never increased unless large quantities of mineral acid are taken."—Neubauer's *Anleitung*, quoted by Parkes.

If this conclusion be correct, it is undoubtedly most important, and one which from other considerations would hardly have been anticipated: thus from the diminution of food consumed in most diseases, especially such as are acute, and from the destruction of tissue which takes place in disorders of that type, an increase of acidity might rather have been expected.

In *typhus abdominalis*, the urine at first is very acid; but if the acidity per day be determined, it will be found one-fifth or one-fourth below the average. At a later period it may either be alkaline when passed, or speedily become so when voided. The alkalinity is sometimes owing to fixed alkali, but more usually it is due to decomposition of urea resulting from retention of the urine, excess of mucus, or feeble acidity.

Whether the urine is ever ammoniacal from ureal decomposition as *secreted* by the kidney, has not yet been satisfactorily determined; but the point is one of the highest practical importance.

In *typhus exanthematus*, in a case of Parkes, the free acidity was very slight.

In *scarlet fever*, on the subsidence of the active symptoms, the urine is either neutral or slightly acid.

In *pneumonia*, according to Vogel, taking the whole quantity passed in the day, the acidity is diminished; the urine is, however, excreted in lessened amount, and is very acid.

In *rheumatic fever*, the urine is highly acid from concentration, but, according to Vogel, the total daily acidity is greatly reduced: this result is very different from the belief generally entertained.

In *acute gout*, during the paroxysm, it is doubtful whether there is increase or diminution of acidity. In a case of Parkes, the free acidity was equal to 28 grains of crystallized oxalic acid; and as the sulphuric acid was not in large amount, and the phosphoric acid was very small, it was supposed that some other acid, probably organic—such as lactic, acetic, or formic acid—was present in the urine.

In *cholera*, the first urine voided is usually acid, but becomes more so in that passed subsequently.

After a fit of *epilepsy*, the urine is copious, pale, and only feebly acid. The urine of *hysteria* is of the same character.

In *spinal paralysis* it is either feebly acid, neutral, or frequently alkaline from ureal decomposition. According to Rayer, Andral, Bullock, and Becquerel, the urine is usually acid in the absence of cystitis, although there is no doubt but that its general acidity is lowered in consequence of the lessened activity of all the vital functions.

In *chronic phthisis*, except during hectic, the acidity is but little affected: when hectic is present, the urine corresponds to that of the other pyrexiæ.

In *chronic diseases of the stomach*, including dyspepsia, the acidity of the urine may be increased, or it may be alkaline.

The normal effect of food, as we have seen, is to reduce the acidity, and even to render, in some cases, the urine alkaline: but in organic affections of the stomach attended with obstinate vomiting, the author has found the urine to be very alkaline; indeed, it has been in such cases that deposits of crystallized phosphate of magnesia have been met with. This result may possibly be due to the discharge of acid by the stomach.

In other cases, arising from some fault of digestion, the urine is abnormally acid: this would be owing chiefly to the formation of some acid not usually contained in the urine.

Parkes states that "when the urine is more acid than usual after food, it is also often scanty, and deposits urates and oxalate of lime. The symptoms connected with this state are chiefly cardialgia, nausea, and frontal headache."

In one case of *rickets*, Gorup-Besanez discovered lactic acid in the urine.

In *anæmia* and *chlorosis*, the acidity is usually lessened.

In *diabetes mellitus*, it is said not to be considerable at first, but it increases rapidly after the urine has been voided and before fermentation has perceptibly set in.

The acids which have been detected in diabetic urine are lactic acid (Lehmann), butyric acid (Fonberg and Scherer), acetic, formic, and proprionic acids (Klinger). During fermentation, carbonic acid is of course generated, also acetic acid, derived chiefly from oxidation of the alcohol.

In *chronic Bright's disease*, with diminished excretion, the acidity is usually lessened. Mosler found it in one case equal to only 10·19 grains of crystallized oxalic acid in the 24 hours; but Parkes, in another exceptional case, found it equal 37·4 grains. In this case, contrary to what is usual, the acidity rose greatly in place of falling in the second hour after food, equal, if it had continued at the same rate throughout the day, to about 76 grains.

In *chronic cystitis, stricture,* and *enlarged prostate,* the urine as secreted by the kidneys presents its normal reaction and characters, but speedily becomes alkaline in the bladder from ureal decomposition.

### TREATMENT OF ABNORMAL ACIDITY AND ALKALINITY.

Very many useful indications for treatment are derived from a knowledge of the varying reactions of the urine.

As has already been mentioned, its reactions have much to do with the occurrence of urinary deposits: if unduly acid, then uric acid is thrown down; and if alkaline, the earthy phosphates.

Before proceeding to administer remedies with a view to correct the reaction of the urine, care must be taken to ensure our obtaining accurate knowledge of the degree of acidity or alkalinity. In very many cases, one or two samples of urine only are examined, and strips of turmeric or litmus-paper alone used; and if the first turn brown, and the latter red, the administration of alkaline or acid remedies is too frequently at once decided upon. Now this proceeding is very fallacious; for first, as has been shown, the night urine in health is very acid, while that passed after meals is sometimes decidedly alkaline; and second, no judgment approaching to accuracy can be formed by such means as to the amount of excess of acid or alkali contained in the whole day's urine.

It is necessary, therefore, that the acidity or alkalinity of the urine of each day should be determined, distinguishing between the night and the day urine.

Having determined the amount, regard must be had to the quality and quantity of the food consumed, in order to ascertain whether the results are in any manner explained thereby.

Next, we must determine as far as possible the cause of the abnormal reaction, and especially whether it is dependent upon the state of digestion, or upon some affection of the bladder.

The special treatment of deposits of uric acid and of the earthy phosphates will be found discussed in connexion with those subjects, and we have in this place only to refer to the question of treatment generally.

It must be borne in mind that it is frequently necessary to reduce the acidity of the urine in cases in which there is no absolute but only a relative excess of acidity, as when deposits of the urates are occasioned by an undue acidity of highly concentrated urine. Lastly, a possible source of error must carefully be guarded against:—if the examination of the urine be delayed even a few hours, especially in warm weather, the abnormal acidity or alkalinity may be due to changes which have occurred in the renal excretion subsequent to its emission, resulting from what have been termed the acid and alkaline fermentations: in diabetic urine, again, various organic acids become rapidly developed.

The determination of the nature of the acids or alkalies abnormally present, and especially of the bases with which the alkalies are united, will often throw much light upon the case. So far as the earthy phosphates are concerned this is not difficult, but is sometimes more so in that of the organic acids.

The line of treatment to be adopted must depend upon the cause and nature of each case.

If the whole day's urine be abnormally acid, some derangement of digestion will generally exist; and this view will be specially confirmed, if it be found that the acidity of the urina cibi is considerable. The diet particularly must be carefully regulated both as to quality and quantity, and the habits pursued must be such as are not calculated to disturb digestion. Mild tonics, alkalies, and sedatives, will mostly prove useful—as infusion of calumba, bicarbonate of potash, tincture of hops, or hyoscyamus.

The fact that with acid vomiting the urine becomes sometimes very alkaline from fixed alkali, would appear to support Bence Jones's view, that the reaction of the urine has much to do, at least in some cases, with the amount of free acid poured into the stomach.

If the urine be but feebly acid, neutral, or alkaline, and this condition be not explained by any vesical complication, constitutional debility will generally exist, which will have to be treated by tonics, the mineral acids, &c.

If it be alkaline from volatile alkali we must look well for vesical complication, which is usually present in such cases; and here again tonics and mineral acids will be required, in addition to the special treatment needed by the existing local affection, and the nature of which, in the chapter on the Phosphates, has already been considered.

Amongst the principal remedies used in the treatment of abnormal acidity and alkalinity of the urine, are, of course, the alkalies and acids, the precise effects of the administration of which may now be considered.

When the uncombined *vegetable* or *organic* acids are administered —as the oxalic, tartaric, malic, citric, and acetic acids—they are for the most part converted in the system into carbonic acid; citric acid is said to be wholly transformed, while of the other acids a minute quantity only makes its way into the urine unchanged. (Piotrowsky and Magawly.)

These acids, therefore, when administered freely, increase the acidity of the urine, partly by the small amount of undecomposed acid which escapes, but principally by the large quantity of carbonic acid discharged. Fruits, therefore, which contain organic acids, likewise increase the acidity of the urine.

By *benzoic acid* the acidity has been asserted to be greatly increased, by Ure and Keller; but Kerner has proved that it exerted in his case no appreciable effect. It is therefore obvious that little or no reliance can be placed upon this remedy for increasing the acidity of the urine.

The *mineral acids*—sulphuric, nitric, and hydrochloric acids—all pass into the urine, and consequently augment its acidity. They appear, however, in part, in the combined state, taking potash or soda from the blood. Nitric acid is probably decomposed to some extent in the system.

It is therefore obvious, that when it is desired to increase the acidity of the urine, the mineral acids should be employed, and of these the hydrochloric is probably the best. To the sulphuric acid it may be objected that it forms, with lime at least, a salt of sparing solubility; and to nitric acid possibly, that it is partly decomposed in the system. They should be administered in considerable doses.

The influence of the mineral acids on the general composition of the urine is undetermined.

From the consideration of the effects of acids upon the urine, we turn to that of the alkalies.

*Carbonates of soda* and *potash*, and also all *the organic salts of those bases* convertible in the system into carbonates, quickly render the urine alkaline: but when these alkalies are discontinued after having been taken for some days, the singular observation has been made by Parkes and Beneke, that the acidity of the urine is increased much beyond what it was before the alkali was administered.

Further, bicarbonate of potash, it would also appear from Parkes's observations, increases remarkably the phosphoric acid of the urine, and on the first day of its administration the urea also.

The late Dr. Golding Bird was of opinion that the alkaline carbonates, acetates, citrates, tartrates, &c., were blood-depurants; and that by increasing metamorphosis they increased the solids of the urine, including urea, uric acid, and the extractives.

This view is slightly supported by the results of Parkes's experiments with *bicarbonate of potash* given in a case of gout.

The careful experiments of Böcker, however, made with *acetate of potash*, on two healthy young men, furnished very different results; the water, urea, extractives, and the *earthy salts* particularly, were diminished.

Parkes's experiments with acetate of potash also confirm fully Böcker's observations, although in some exceptional cases it is certain that the acetate does act as a diuretic and increase the water.

Altogether, the weight of evidence is against the opinion of Bird, that acetate of potash is a blood-depurant, increases metamorphosis, and augments the elimination of the organic solids. It is still possible, however, that the alkaline carbonates may produce some of these effects, although more conclusive evidence than has yet been produced is required to establish this point.

It has, further, been proved by Parkes, that *liquor potassa*, while it increases the alkalinity of the urine likewise augments the organic solids, the sulphuric acid, and probably also, in some cases, the phosphoric and uric acids. This medicine, at least, therefore, is a blood-depurant.

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# CHAPTER XIV.

## THE EXTRACTIVES.



UNDER the name of "The Extractives" a great variety of substances is included; and as it would be impossible, in the clinical examination of the urine, to determine each constituent separately, we must be satisfied to ascertain their gross amount, the knowledge of which often furnishes, as will appear hereafter, information of an important character.

*Composition.*—The principal constituents of which the extractives consist are, *creatine, creatinine; xanthine,* and *hypoxanthine*; *xanthoglobulin*, discovered in normal human urine by Scherer, who considers that it is identical with the *sarcine* of Strecker, present in the juice of flesh; *phosphorus* and *sulphur; the two acids of Marcet; the colouring-matter; the resin of Harley*, which adheres so strongly to the pigment; and the resinous bodies termed by Scharling *omichmyloxide*. Frequently also a little *sugar* is present, derived possibly, in some cases, from Heller's *uroxanthin*.

It is very difficult wholly to isolate the extractives from some of the other urinary constituents, so that many of the determinations hitherto made include other substances besides those above enumerated.

*Quantity.*—The mean of the "extractives and volatile salts" furnished by four series of observations by Böcker, was 247·6 grains in the 24 hours.

In a man aged 22, Scherer found "the extractives and uric acid" to be 375·7 grains; and in a man aged 38, and weighing 45 kilogrammes, 318 grains.

The amount of extractives, mucus, and uric acid, given by Rummel, is 236·7 grains. While Becquerel's average for the "extractives" was only 180·6 grains.

Taking the average of these various numbers, and deducting 35 grains for the volatile salts, 8 grains for the uric acid, and 7 for the mucus, we obtain an average of 236·3 grains. This Parkes regards as much too high, and considers, without stating the precise reasons for his opinion, that " we may provisionally assume the true number to be about 154 grains."

Parkes gives the mean amount of " pigment and extractives" excreted in 24 hours by each pound of body-weight at 1·062 grains.

In children the mean of whose ages was 4 years and 2 months, Parkes, calculating from the data furnished by the observations of Scherer, Rummel, Bischoff, and Lecanu, finds the extractives and volatile salts to amount to 1·96, or nearly 2 grains to the pound avoirdupois, nearly double the average for adults.

According to Uhle's calculation, made partly from his own analyses, and partly from those of other observers, " the extractives and volatile salts" in children between the ages of 3 and 7, amount to 0·279 gramme or 4·3 grains per pound avoirdupois.

### *Influence of Food.*

The effect of ordinary meals upon the extractives is as yet undetermined, but the pigment is increased.

By *nitrogenous food*, the extractives, including the pigment, are much decreased: according to Lehmann to the extent of one-third.

By *non-nitrogenous food*, according to the same authority, they are increased one-third.

By *vegetable diet*, the extractives, including the pigment, are also much increased.

By *alcohol*, according to Böcker, they, as well as the pigment, are considerably reduced.

By *tea*, Böcker found the extractives and volatile salts greatly lessened.

By *fasting*, of course they are diminished.

By *exercise*, according to Lehmann, they are lessened; but this statement requires confirmation.

By *mental exertion*, Mosler found the pigment increased.

## PATHOLOGY OF THE EXTRACTIVES.

It may be remarked that there is no necessary connexion between urea and either the pigment or extractives, although an increase of the former is usually accompanied by an augmentation of normal pigment.

During the fit of *ague*, in some cases there is no increase of pigment, but in others it would appear to be augmented.

In simple fever (*febricula*), the pigment and probably the extractives generally, are increased; and this increase likewise occurs in most diseases accompanied by pyrexia.

In *typhus abdominalis*, the pigment is sometimes very greatly increased; according to Vogel's scale of colours, from 3 to 6, the normal amount, to 80 and even 100. This increase appears to be due mainly to normal pigment. At a later period of the fever, according to Parkes, the pigment and extractives are decreased. In *typhus exanthematus* the creatinine and creatine are increased. (Schottin.) The pigment and extractives were throughout in small amounts in Parkes's case.

In *variola*, the pigment is increased.

The same is the case in *scarlatina* during the febrile period.

In *milk fever*, it is likewise increased, as also in *puerperal fever*.

In *acute pneumonia*, the pigment and extractives are considerably increased.

In *acute pleurisy*, the pigment is in excess, but not to the same extent as in pneumonia.

In *acute bronchitis*, there is a similar increase.

As also in *acute pulmonary phthisis*.

In *acute hepatitis*, it is greatly augmented.

In *rheumatic fever*, the pigment and extractives are always greatly increased.

In *acute gout*, during the paroxysm, the pigment is sometimes in excess, and at others deficient. Before the paroxysm, there is diminution of pigment and extractives.

In *cholera*, the normal pigment for the first few days is deficient; sometimes the urine contains *hæmatin*, and then it presents a brownish smoky look; it nearly always contains more or less *uroxanthin* or *indican*.

The formation of a blue pigmentary substance in the urine, in cases of cholera, was first noticed by Heller, who bestowed upon it the name of *uroglaucin*.

The author has elsewhere shown that *indigo*, derived from *indican*, is of frequent occurrence in human urine; and in his communication to the Royal Society, he advanced certain reasons to prove that the uroglaucin of Heller is really indigo. Of this fact no doubt now whatever remains; he succeeded in obtaining from several samples of blue pigment from cholera and other urines, all the well marked reactions which characterize indigo.*

The indigo-yielding substance, indican, exists in the blood and rice-water dejections of cholera, as well as in the urine.

In *epilepsy* and *hysteria*, the urine is pale, showing a deficiency of pigment.

In *spinal paralysis*, it is also pale and the pigment deficient.

In *chronic phthisis*, especially where hectic is present, it is high coloured, and frequently deposits urates, deeply tinted with *uroerythrin*.

* Report on the Urine of Cholera Patients during the Epidemic of 1854. By Arthur Hill Hassall, M.D., General Board of Health. 1855.

In *chronic diseases of the heart*, the urine is often high coloured, the urates abundant and deeply stained.

In *cirrhosis*, it is also high coloured, depositing deeply-stained urates; and *bilephæin* may sometimes be detected, even when there is no jaundice.

In *chronic enlargement of the spleen*, according to Golding Bird, the pigment is increased.

In *anæmia* and *chlorosis*, there is a diminution of normal pigment.

In a case of diabetes recorded by Böcker, "the volatile salts and extractives" were very greatly increased. In Mosler's case, the pigment was also increased. Heller considered the *normal pigment* to be lessened, and the *uroxanthin* increased; and Schunk procured more *indigo* from diabetic than from any other urine.

In *acute Bright's disease*, the urine is often high coloured from increased pigment.

In *chronic Bright's disease*, on the contrary, the pigment and extractives are reduced in amount.

### TREATMENT OF EXCESS AND DEFICIENCY OF EXTRACTIVES.

We have seen that, as a rule, the extractives are increased in diseases of an active or inflammatory character, this increase indicating augmented metamorphosis; and further, that they are decreased in those of a chronic or asthenic character. In accordance therefore with the nature or type of the disorder, so must the treatment, based upon the ordinary principles, be regulated.

Although usually the pigment is increased simultaneously with the other extractive matters, this is not always so; and the urinary colouring-matter may be either augmented or lessened independent of the remaining extractives.

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## CHAPTER XV.

## THE COLOURING-MATTERS, NORMAL AND ABNORMAL.



*Extraneous Colouring Matters.*—Various pigmentary substances derived from articles of food, drink, or medicine, make their way into the urine and alter its colour. The principal of these were noticed when the colour of the urine of health was treated of in connexion with its other physical characters.

The subject of the colouring-matters proper of the urine is a most difficult one, and at the same time is of the highest pathological importance. Formerly, all was obscurity in regard to it; of late years, however, it has been much elucidated.

### HÆMATIN, OR BLOOD-PIGMENT.

Unaltered blood-pigment frequently makes its way into the urine: it occurs in two very different states; enclosed in the red blood-corpuscles, and free, when it is called "dissolved" hæmatin. Of course, in either form, it is accompanied by the presence of albumen in the urine.

It occurs in the free or dissolved state in the urine in connexion with certain eruptive, malignant, and cachectic diseases, and in which the blood itself is specially affected; the urine being usually rendered by its presence of a brown or blackish-brown colour.

In a state of purity, hæmatin is dark brown, and is slightly lustrous, insoluble in water, alcohol, and ether, but readily dissolved by weak alcohol to which sulphuric or hydrochloric acid has been added, and from this mixture it is precipitated, on the addition of water: by the caustic alkalies or their carbonates it is also readily dissolved. It has the following *composition*—

| | |
|---|---|
| Carbon . . . . . . . . . . | 65·347 |
| Hydrogen . . . . . . . . . | 5·445 |
| Nitrogen . . . . . . . . . | 10·396 |
| Oxygen . . . . . . . . . . | 11·881 |
| Iron . . . . . . . . . . . | 6·931 |
| | 100·000 |

### UROHÆMATIN, OR URINE-PIGMENT.

There is good reason for believing that *urohæmatin*, or urine pigment, the *urophæin* of Simon, is simply altered hæmatin or blood-pigment; and if this view be correct, it follows that the quantity of this pigment is in proportion to, and is a measure of, the destruction or metamorphosis of the blood-corpuscles which takes place in the blood. This fact is the key to the pathology of urine-pigment, and it shows how much importance must necessarily be attached to that pigmentary substance.

Like hæmatin, it contains *iron*, and the following is its *composition*, according to Scherer—

| | Per cent. |
|---|---|
| Carbon . . . . . . . . . . | 58·43 |
| Hydrogen . . . . . . . . . | 5·16 |
| Nitrogen . . . . . . . . . | 8·83 |
| Oxygen . . . . . . . . . . | 27·58 |
| | 100·00 |

Scherer considered that urine-pigment was in a constant state of change, and that it was decomposed by neutral and basic acetate of lead into two substances, differing in their respective amounts of carbon and hydrogen: one of these was certainly the cyanourine of Heller.

It is uncertain whether the urine-pigment is formed directly from the blood-pigment, or in the liver through the bile-pigment.

The ruby-red crystalline substance *hæmatoidin*, and the crystalline *bilifulvin* of Virchow found in bile which has been retained in the system, there is every reason to believe are identical—at all events, the latter is convertible into hæmatoidin—and urine-pigment very closely resembles bilifulvin. Thus Kühne has shown that the blood-cells are destroyed by the colourless biliary acids and their salts, and that biliary colouring-matter is thus formed, the acids themselves being unchanged. These facts, as well as the effect of diseases of the liver on the urine-pigment, all appear to point to an *hepatic* source.

Robin assigns to hæmatoidin the formula $C_{14}H_9NO_3$, and considers that it is formed from hæmatin by the abstraction of water and iron.

The amount of urine-pigment may be approximately determined by comparing a definite stratum of urine with a standard table of colours, as proposed by Vogel. In most analyses urohæmatin is included in the "Extractives."

## UROERYTHRIN.

A red pigment, wholly distinct from indigo-red, and termed by Simon *uroerythrin*, is of frequent occurrence in urine. It is identical with the *rosacic acid* and *purpurate of ammonia* of Prout, and the *purpurine* of Bird in part. The exact tint of deposits stained with this pigment is subject to great variation, it ranging from *deep red* and *carmine* to *pink* and *salmon colour*. It is present in the urine when first voided, but becomes deeper from exposure. The urates, when they form a deposit in the urine, are usually more or less stained or dyed with this pigment.

Marcet believes that the red pigment differs only from normal urine-pigment in the presence of one of the acids discovered by him. The pink pigment, Parkes thinks, may probably be indigo-red; but this appears doubtful.

The red pigment is partly dissolved by alcohol, ether, and hot water.

Uroerythrin is obtained by the action of warm absolute alcohol on the well-washed urates coloured with that pigment. If held in solution in the urine, it must first be precipitated either by the addition of colourless urate, or in the following manner: a little ammonia, or carbonate of ammonia, is added to the urine, which, however, must still be allowed to remain somewhat acid; the urine, after being well shaken, must stand at rest for some hours, a few drops of acetic acid must then be added, and the urine set aside for a time again, when a red or pink deposit will soon become visible.

It is precipitated from urine by acetate of lead, the precipitate being of a pinkish colour, provided the pigment be present in any considerable amount, and from this deposit it may be separated by treatment with boiling alcohol.

Urea, uric acid, and urohæmatin, are usually in excess in urines containing much uroerythin.

A colouring-matter, possibly identical with uroerythrin, has been observed, by Landerer, in connexion with the cutaneous exhalation, a piece of flannel placed under the axillæ became stained with a red pigment.

## INDICAN AND INDIGO.

Three closely allied pigmentary substances occur in the urine—namely, *indican*, *blue* and *red* indigo.

Heller long since affirmed that there existed in urine, normal and abnormal, a pigment which was colourless, or almost so, which under different circumstances furnished several pigments, and to this substance he gave the name of *uroxanthin*. It is distinguished by the action of a large excess of strong nitric or hydrochloric acid, which causes the urine containing it to assume a purple, violet, or blue colour, and which tints Golding Bird thought were characteristic of his *purpurine*, under which name he, however, obviously confounded *uroxanthin* and *uroerythrin*, most of his observations applying to the latter pigment.

Sulphuric acid of specific gravity 1830 added to urine, in the proportion of about one-third of its volume, also gives rise to a pink, lilac, or deep blue colour, according to the amount of uroxanthin present. (Carter.)

Heller obtained uroxanthin from the urine by the following simple process: acetate of lead was added, the urine filtered, the filtrate evaporated to dryness at a low temperature, and the uroxanthin extracted with ether. It is also soluble in water and alcohol.

The urine in which it occurs is usually of a pale yellow colour, and is stated to be very acid.

About four years since Dr. Schunk, of Manchester, discovered in some specimens of urine, a substance which he had also found in plants, which he termed *vegetable indican*, and which he believed to be identical with Heller's uroxanthin.

According to Schunk, vegetable indican has the following composition:—$C_{52}H_{31}N_{34}O$. It does not therefore quite correspond in composition with indigo-white.

When treated with acids and other reagents, it yields indigo-blue and indigo-red, together with other pigments and substances, particularly sugar, leucine, and certain volatile substances.

*Schunk's Process.*—The following is Schunk's process for obtaining indigo from urine:—

The urine is treated with basic acetate of lead, filtered, and the precipitate being washed with water, the liquid is mixed with an excess of ammonia, which occasions more or less of a white, or yellowish-white precipitate. This precipitate is collected on a filter, slightly washed with water, and then treated with dilute sulphuric or hydrochloric acid. After the whole of the oxide of lead has combined with the acid employed, the liquid is filtered.

When there is much indican present, the filter acquires a blue tinge; and the liquid, which is of a brownish-purple colour, gradually becomes covered with a thin pellicle, blue by transmitted, and copper-coloured by reflected light.

When there is less indican the pellicle only appears after some time, or not till the next day; if, however, no indigo appears after 24 hours, the absence of indican may be inferred.

By most observers the urine depositing indigo largely has been described as very acid when passed, or as quickly becoming so; this the author has not found to be the case in many of the instances which have fallen under his observation. The urines have usually been deficient in acid, quickly becoming ammoniacal, and have given rise to the development of multitudes of vibriones, and, in particular, an animalcule which he long since named *Bodo urinarius*.

The acid urines, on the contrary, as those giving rise to the formation of *Penicilium glaucum*, have contained the pigment only in very small amount.

The addition of acids, as the hydrochloric acid, it is true, quickens the formation and precipitation of indigo-blue.

So far as the other constituents are concerned, it does not appear that the indigoferous urines present anything abnormal (Scherer), if we except the fact that "large quantities of indican and of uric acid are often found together." (Parkes.)

*Heller's Process.*—Fresh urine is precipitated with a hot solution of acetate of lead, the urine quickly filtered, and the excess of lead removed with sulphuretted hydrogen; the urine is again filtered, and the free sulphuretted hydrogen expelled by boiling. The hot liquid is now gradually added to an equal quantity of highly concentrated hydrochloric acid, the mixture being well stirred during the addition; if the mixture become decidedly blue, it is a proof that much indigo will be obtained, but if only violet-red, none is present.

After standing at rest for some time, a blue pellicle appears; at the end of 12 hours the mixture is diluted with an equal quantity of water, shaken, and set aside for 24 hours. The deposit which takes place is separated by filtration, first washed with boiling water until the acid has been wholly removed, then treated with dilute spirits of wine; lastly, it is dried.

The blue precipitate on the dried filter is now drenched with ether so long as this is coloured red; the etherial solution is evaporated, and the residue is again treated with ether or alcohol, which takes up the *urrhodin* or *indigo-red* in a nearly pure state.

The substance on the filter now consists almost entirely of blue indigo; but for its isolation we must proceed as follows: the filter is cut into pieces, which are introduced into a flask, and boiled repeatedly with alcohol of specific gravity of 0·83 to 0·90, until it ceases to be coloured blue. The alcoholic extracts are to be filtered while hot, evaporated to about half, and the residue put aside for some hours in a closed bottle. The *indigo-blue* then becomes precipitated.

It is obvious that for merely clinical purposes this process need not be followed to its last results; in fact, in general it will be sufficient to evaporate a considerable bulk of urine and to treat the extract with ether, dilute the solution with water, and expose the mixture to the atmosphere for some time. Indeed, in most cases, all that is necessary is to expose about a pint of urine to the air for several days, when if indican be present in abnormal amount, it will become decomposed, and indigo-blue will appear.

### *Indigo-Blue.*

Heller found that urine containing uroxanthin furnished, on exposure to the air, or by treatment with acids, a blue pigment which he named *uroglaucin*, but which he never suspected was in any way related to indigo.

"Some years before this (before 1840) Prout had observed indigo in the urine of a patient, especially after taking seidlitz-powders. The indigo was sublimed and perfectly recognised. In 1850 Debuyne noticed the urine of a dropsical patient to have a blue colour, and on examination he discovered that the pigment was indigo. In 1853, Hassall* examined this subject, and may be said to have first given it its true standing. He not only proved the blue colouring-matter to be indigo (having obtained isatin and anilin from it), but affirmed the possibility of producing it in a great number of urines by exposure to the air. He thought it was derived from white indigo. Very soon afterwards, Scherer examined the same point, and came to the same conclusion.

"In succeeding years many observations were made on the blue urinary pigment, and its identity with indigo was more or less clearly acknowledged, until the observations of Schunk defined the subject still more by his examination of indican. Schunk obtained a small quantity of indigo arising from indican, from almost every specimen of urine. It then became evident that Heller was perfectly right in his repeated assertions, that the blue pigment was derived from the substance he called uroxanthin (the indican of Schunk) solely: if any more doubt could be said to exist on the subject, it has been set at rest by a comparative elementary analysis by Kletzinsky." (Parkes.)

* Transactions of the Royal Society, 1853 and 1854.

| | C. | H. | N. | O. |
|---|---|---|---|---|
| Uroglaucin . . | 73·469 | 3·864 | 10·407 | 12·260 |
| Indigo-blue . . | 73·282 | 3·817 | 10·680 | 12·221 |

The *cyanourin* of Braconnot is also identical with blue indigo.

The *urines* which furnished the blue indigo obtained by the author possessed, for the most part, the following characters :—

They were of low or medium specific gravity, ranging for the most part from 1007 to 1019; they were either faintly acid, neutral, or alkaline, and they were at first of a pale colour, indicating a deficiency of ordinary urine-pigment.

Set aside in an open vessel, the urine was in most samples observed to undergo the following changes :—

After a few days' exposure it gradually changed colour, the pellicle or scum which had formed on the surface became at first slate-coloured, and at length deep blue, presenting here and there, where the scum had been disturbed or broken, a rusty-red tint, due to the formation of *indigo-red* : the urine itself also underwent, during the same period, further remarkable changes, becoming thick and turbid, deep brown, greenish, bluish-green, and finally, as the blue pigment became deposited, of a faded yellowish-green colour; a considerable sediment collected at the bottom of the glass; this was of a deep brown colour, soft, deliquescent, intermixed with a little blue colouring-matter, and possessing a medicinal smell resembling somewhat *valerian*.

Examined with the microscope, the scum or pellicle was found to consist of vibriones, of innumerable animalcules, elsewhere described, and crystals of triple phosphate, with a great many fragments and granules, which, under the microscope, were seen to be of a deep and bright blue colour.

In some urines the quantity of indigo formed was so small as not to affect their colour, and to be discoverable only by the aid of the microscope.

In other samples the amount was so great that the bulk of the urine was, at a certain stage of the transformation of the colouring-matter, of a grass-*green* colour, and in others, after the indigo-blue had subsided, it was brownish black, almost *black*. Thus, doubtless, some of the green and black urines, the occurrence of which has been recorded at times by different observers, were due to the presence of indigo-blue, or allied substances associated therewith.

The formation of the indigo-blue in any urine may be hastened by the addition of hydrochloric or some other acid.

*Sugar* is also generally present. The urine of cholera usually contains much indican. Now "the yeast-fungus was also met with in different samples of the urine in nearly every case."—(Author's Report on the Urine of Cholera, 1854, Board of Health.) It has been stated that one of the principal products of the decomposition of indican is a variety of sugar allied to glucose: hence urines containing indigo throw down usually the red oxide of copper when treated with the copper test. (Virchow.)

In all urines containing much indigo, there are three things which require to be specially noticed—the *blue scum*, the *light-green*, *brown*, or *blackish-green urine*, and the *brown sedimentary extractive*.

If the *urine* containing blue indigo be introduced into a bottle and corked, after a few days the blue colour will have disappeared, but if now the contents of the bottle be exposed to the air, it will after a time reappear. The first of these changes is due to the deoxidation of the indigo-blue, and the second to its reoxygenation.

If the indigo-blue be removed by filtration fromy an urine in which all the indican has not yet been converted, and the filtered urine be exposed to the air, a fresh quantity of the blue pigment will be formed.

If the *brown extractive*, containing *indifuscin* resulting from the decomposition of indican, be treated with alcohol, the solution will acquire a deep brownish colour, and on evaporation will furnish a brown extractive, soluble in water, but not in dilute acids; nitric acid does not indicate in this the presence of bile-pigment, nor does the precipitate formed with basic acetate of lead furnish a purple liquid with alcohol and free acid; a strong solution of potash dissolves the extractive, and yields a deep blood-red fluid, which is rendered green and opalescent by boiling. These reactions show that the brown pigment resembles hæmatin in its chemical manifestations.

During evaporation, the *aqueous* solution of the brown extractive of some of the samples examined gave a further supply of indigo. The residue was made black by concentrated sulphuric acid, and deep brown by potash.

A portion of the *alcoholic* extract of the brown extractive was treated with potash for the purpose of ascertaining whether it contained *leucine*, and the product, on the addition of hydrochloric acid, gave off a powerful odour of *valerianic acid*. The moist extractive of the urines containing the indigo was likewise observed to emit the peculiar smell of valerian.

Before proceeding to the analysis of *the blue colouring-matter* formed spontaneously in certain urines exposed for some days to the air, it is almost always necessary to purify it, or the characteristic reactions will be obscured, owing to the presence of animal matter, partly in the form of vibriones and animalcules, as well as of crystals of triple phosphate. Thus, if much animal matter be present, concentrated sulphuric acid will give a dirty brown in place of a blue solution, and on subjecting the dry precipitate to heat, the violet vapours will be obscured by white empyreumatic fumes generated by the destruction of the animal matter.

The urea, chlorides, and some other impurities, may be removed by water, and the phosphates by digestion in weak hydrochloric acid.

Now the purified blue colouring-matter was found to possess the following characters, chemical and general.

It exhibits a coppery lustre on being rubbed with the nail. It is not soluble in water, dilute acids, alcohol, or turpentine, nor is it affected by spirits of wine in which there is a little free acid.

It is not attacked by liquor potassæ at ordinary temperatures, but when heated therewith, it is converted into a dirty yellowish-brown solution.

It is freely dissolved by strong sulphuric acid, producing a deep blue liquid miscible with water, and which chlorine has the power of bleaching.

Heated with fuming nitric acid, it yields a greenish-yellow solution, which becomes of a brilliant yellow with liquor potassæ.

On diffusing it through water and boiling with lime and grape-sugar, it furnishes a wine-red fluid, which on being filtered and then neutralized with hydrochloric acid, gives a greenish-blue precipitate. Another portion of the liquor, if exposed to the air for a few hours, reacquires its blue colour.

When heated in a test-tube, it evolves vapours of a rich violet-red colour, and produces the characteristic odour of sublimed indigo.

When boiled with dilute nitric acid, and evaporated to dryness, it yields a dirty orange-yellow material, *isatin*, which, when subjected to heat and the action of potash, gives an alkaline volatile liquor, and this when tested with a solution of chloride of lime and with a piece of deal moistened with hydrochloric acid, furnishes the characteristic reactions of *aniline*.

Aniline was likewise procured by the simple distillation of the pigment with a concentrated solution of caustic potash, as shown by the development of the well-known violet-blue colour on the addition of a solution of chloride of lime.

### *Indigo-Red.*

Heller succeeded in obtaining from his uroxanthin, a red pigment which he termed *urrhodin*, and which is identical with indigo-red; it is of the same composition as indigo-blue, consisting of, according to Schunk, $C_{16}H_5NO_2$. When the crust of indigo-blue on the surface of any urine is broken, in the course of a short time indigo-red always makes its appearance at the place where the disturbance has occurred. The red modification of indigo is met with much more sparingly than the blue, and it often assumes the crystalline form, the crystals being needle-shaped, and sometimes crossing each other so as to form little rosettes. From indigo-blue, *indigo-white* may be readily obtained.

### *On the Source of Indigo in Urine.*

The important question of the source or origin of indigo in urine may now be considered.

That indigo-blue and indigo-red are derived from indican, a substance approximating closely to white or colourless indigo, is certain.

It is also equally certain that a very close relation exists between the several varieties of indigo and both hæmatin and urine-pigment, which is but modified hæmatin.

Bile-pigment and melanin likewise are not very dissimilar from any of the above-named pigments in their elementary composition, as shown by the following table, copied from the author's paper in the "Philosophical Transactions."

| Composition. | White Indigo. (Cream.) | Blue Indigo. (Cream.) | Blue Pigment of Scherer. (Indigo.) | Hæmatin. (Mulder.) | Bile-Pigment. (Scherer.) | Urine Pigment (in disease.) (Scherer.) | Urine-Pigment (in Health). (Scherer.) | Melanin. Scherer. |
|---|---|---|---|---|---|---|---|---|
| Carbon ...... | 72·72 | 73·22 | 66·99 | 70·49 | 68·19 | 61·65 | 58·43 | 58·08 |
| Hydrogen ... | 4·54 | 2·92 | 5·95 | 5·76 | 7·47 | 5·60 | 5·16 | 5·91 |
| Nitrogen ...... | 10·60 | 11·26 | 7·12 | 11·16 | 7·07 | 7·29 | 8·83 | 13·76 |
| Oxygen ...... | 12·12 | 12·60 | 19·94 | 12·59 | 17·26 | 25·46 | 27·58 | 22·23 |

These numbers not only indicate the relation which exists between these substances, but they also show that there is for the most part a progressive removal of carbon and an increase of oxygen.

The relationship may be exhibited in another way: it will be seen that there is a difference of only four atoms of carbon and four of hydrogen between the composition of three atoms of indigo and one of hæmatin—

1 atom of hæmatin $=C_{44}H_{22}N_3O_6$.
3 atoms of indigo $=C_{48}H_{18}N_{,3}O_6$.

Again, *leucine* is a common product of the decomposition of albuminous matters, and it was thought that this body was present in the alcoholic extractive: now 1 equivalent of hæmatin and 2 of water contain the elements of 2 atoms of indigo and 1 of leucine:—

| | C | H | N | O | | | C | H | N | O |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. Hæmatin | =44 | 22 | 3 | 6 | =2. | Indigo | 32 | 12 | 2 | 4 |
| 2. Water | = | 2 | | 2 | =1. | Leucine | 12 | 12 | 1 | 4 |
| | 44 | 24 | 3 | 8 | | | 44 | 24 | 3 | 8 |

Lastly, Herring has pointed out that *hæmatin*, with water and oxygen, will furnish indigo and benzoic acid, converted in the urine into hippuric acid and ammonia.

These suggestions at present are merely theoretical; but the time is not very distant when the nature of the chemical changes resulting in the formation and transformation of hæmatin will be more clearly determined.

It must not be understood from the above formularies that hæmatin was present in the urine in which blue indigo became developed, for this was not the case; so that the transformation of the hæmatin into indican, if it really occurred, must have taken place in the blood. Further, it does not appear that hæmatin, when present in the urine, manifests any peculiar tendency to become converted into indigo.

The same statement applies equally to the ordinary urine-pigment, for by no treatment of the urine with reagents can indigo be developed in the urine at will. The urines, moreover, which have been found to deposit the indigo most freely have nearly always been of a pale colour when first voided, showing a deficiency of normal urine-pigment.

There is no reason whatever for believing that the indigo met with in the urine is derived from the colouring-matter of bile, as in the urines in which indigo was found no traces of the presence of that secretion could be discovered; while in one only of three samples of urine examined, highly charged with bile, was any indigo formed, and then but in small quantity.

### *Schlossberger's Blue Pigment.*

There is some reason to believe, from the observations of Schlossberger, that another blue pigment is occasionally, though rarely, met with in the urine: it was not Prussian blue nor Vivianite, nor could it be reduced to indigo-white, or any compounds of the phenyl series be produced therefrom, and only once met with: it was soluble in ether.

### *Green Pigment.*

In several instances the urine has been observed, on exposure to the air, to become green; and in one case it was green when voided.

There is no question but that the green colour, in all or nearly all these cases, was due to the presence of indigo. The blue pigment, when finely divided and dispersed through the urine, this being yellow or brown, gives rise to various shades of green. The author has met with several cases of grass-green urine in which the colour has been due to indigo.

In cases in which bile is present in considerable amount, the urine also sometimes presents a brown or blackish-green colour, very different to the grass-green tint just noticed.

### *Brown and Black Pigment.—Melanourin.*

Urines are occasionally met with which are more or less brown or black; these colours may arise from several different causes.

They may be connected with the occurrence of *indigo* in urine, as the author can testify from personal observation. Schunk considers the black substance formed by the action of the strong acids on the urine to be due to the oxidation of indigo-blue.

They may be connected with the presence of *bile.*

With that of *hæmatin,* when the urine will be *albuminous.*

They may arise, it is affirmed, from the presence of *melanin;* but this appears doubtful.

The urine has also been observed to be of a very dark colour after certain medicines, as tar (Weber), and creosote (Pereira and Hughes). In one case, the dense black precipitate which was thrown down by boiling nitric acid was converted on exposure into blue indigo. (Odling.)

Between indigo and the creosote series of compounds, there is an intimate chemical relationship.

## ON THE PATHOLOGY OF THE URINARY PIGMENTS.

Even in the present state of our knowledge of the subject, it is obvious that the pathology of the pigments found in the urine is of very great importance.

### *Hæmatin, or Blood-Pigment.*

Of hæmatin as contained in the blood-corpuscles, it is not necessary to treat in this place, but only of free or dissolved hæmatin.

It occurs in the latter state in the urine in connexion with certain eruptive, malignant, and cachectic diseases in which the blood itself is specially affected, as in *scarlet fever, measles, putrid typhus, severe remittents,* in *scurvy* and *purpura,* and sometimes in *Bright's disease.*

### *Urohæmatin, or Urine-Pigment.*

Since there is no doubt but that urine-pigment is derived from hæmatin, the consideration of the pathology of urohæmatin follows naturally in this place.

The quantity of urine-pigment, it has already been remarked, is to be taken as a measure of the destruction of the red corpuscles of the blood; whenever therefore the amount of that pigment is considerable, there must be increased disintegration of the blood-corpuscles indicated by the depth of colour of the urine.

Now this increased colour is observed specially in *all active and inflammatory diseases,* and probably also in *certain chronic structural affections.*

### *Red and Pink Pigments—Uroerythrin.*

Uroerythrin, like urohæmatin, appears to indicate increased metamorphosis.

The *red* or *carmine* pigment occurs frequently in the urine of *fever,* of *acute rheumatism* and *gout,* of *acute pneumonia, pleurisy, peritonitis,* and *meningitis.*

It occurs also specially in *organic affections* of the *liver, spleen,* and *heart.*

Uroerythrin, it is obvious, is present therefore in excess in the same cases in which urohæmatin is also in abnormal amount.

The *pink* pigment is met with in *hectic*, and in *organic diseases accompanied by fever*; but "the pink and the red pigment are very generally mixed up." (Parkes.)

*The Indigo Pigments.*

That coloured indigo should be frequently found in the urine is not so remarkable when the fact is known that indican, so readily convertible into coloured indigo, has been discovered in several parts of the body, in the *blood* by several observers, rarely in the *bile* (Chevreul), in the *skin* frequently, in the *bones* of an infant (Herring), in the *brain* (Guntz), in the voluntary *muscles* (Coccius), in a pleuritic *fibrinous exudation* (Carter), in the *excrements* (Coccius), and in the *stools of some cholera patients* (Parkes).

So frequently indeed has indigo been discovered in human urine, that the question has at length arisen, whether it is not to be regarded as a normal constituent. The author met with it nearly ten years since, in very variable quantities, in a great variety of urines, and hence announced its frequent presence in the renal excretion. Schunk obtained indigo in small quantity in almost every sample he examined, while Carter, from an investigation of 300 cases, has come to the conclusion that indican is normal to the urine.

If really normal, the quantity usually present is very minute; but when it is found in the renal excretion in large amount, its occurrence is undoubtedly pathological.

Again, it seems to some extent to take the place of normal urine-pigment, and since it is one of the most carbonaceous and the least oxygenated of all the animal pigments, its occurrence appears to be indicative of defective oxygenation.

The diseases may now be enumerated in which it has been found more particularly to occur. It may be premised that these are for the most part chronic and atonic, rather than acute and pyrexial.

It has been stated to occur particularly in diseases of the *nervous tissue* (Heller); in *ague* (Dressler); in *scarlatina* occasionally (Author and Carter); in *phthisis* (Author), in *pleurisy* (Carter); in *Diabetes* (Heller and Schunk); in *gout* sometimes (Parkes); in *dysentery* (Virchow and Parkes); in *cholera*, often in immense amount (Simon, Heller, Author, Begbie and Parkes); in *lead colic*, and after the use of *mineral acids* (Virchow); in *Bright's disease* (Heller, Author, and others); in *perforation of intestines* (Carter); in a case of *tumour below hepatic region* (Hughes); in *strumous peritonitis* (Wilks); and in a great number of other cases. On the other hand, it is less common in acute febrile diseases (Heller).

It should be noted particularly, that the urines in which indigo appears in large quantity are at first usually pale and deficient in normal colouring-matter.

Virchow is of opinion that indigo is found in large amount whenever the formation of bile is impeded.

*Green Pigments.*

A grass-green urine has been observed to be passed by a child with enlarged *spleen* after *intermittent fever* (Landerer); green urines have likewise been met with in *Bright's disease, peritonitis, spinal disease,* and *cystitis* (Heller).

ON THE TREATMENT OF URINARY PIGMENTS.

The treatment must of course vary, not only with the kind of pigment, its source and origin, and the general cause or condition which has given rise to it, but it must also be shaped and varied according to the malady with which it is associated. This is as much as to say, that the existence of any normal pigment in the urine in abnormal amount, or the presence of any abnormal pigment, does not in itself afford sufficient indications for treatment apart from other considerations, as of the special derangement or disease with which it is connected. The mere observance of the presence of certain pigments affords, however, in many cases, most valuable information, and frequently throws light upon the case not otherwise obtainable.

The presence of *hæmatin* in the urine in the *free* or *dissolved* state implies great alteration and degradation of the blood.

The treatment must vary with the disease; but generous diet, the mineral acids, tonics, especially bark, quinine, &c., are in most cases required.

It must be remembered that excess of *urohæmatin*, or urine-pigment, denotes increased metamorphosis of the red blood-corpuscles, and also usually augmented transformation of the tissues generally.

The indication in this case is to lessen this metamorphosis, an object best effected by the administration of such remedies as reduce the accompanying fever or pyrexia, as by antiphlogistics, nauseants, purgatives, diuretics, &c.

Of course, the precise means employed, and the extent to which they are carried, must be determined by the nature of the attendant disease.

The presence of *uroerythrin*, in combination with the urates, indicates for the most part increased metamorphosis, and therefore is to be treated upon the same principles as excess of *urohæmatin* or normal pigment.

When it occurs in connexion with organic diseases of the liver, spleen, and heart, the treatment required is different. In such cases, it appears to denote increased elimination of carbon, rather than heightened metamorphosis. The object here would appear to be, rather to favour elimination and promote oxygenation than to reduce the activity of the functions by antiphlogistic remedies.

The occurrence of *indican* or deposits of *indigo* is indicative of increased elimination as compared with normal urine-pigment, which it replaces, of carbon in union with more nitrogen, but less oxygen. The objects to be fulfilled are therefore to increase oxygenation and to promote the elimination of the carbon in a more oxidized state; in fact, in the form of normal urine-pigment.

These aims we must endeavour to accomplish by a nitrogenous diet, by pure air, gentle exercise, friction to the skin, by tonics, and by the exhibition of oxygenating remedies, as nitric acid and chlorate of potash; but it should be remembered that the best oxygenating remedy is to be found in abundance of pure air.

The *green* and *black* pigments, it has already been stated, nearly always, and perhaps always, consist of indigo, hæmatin, or bile.

We shall now proceed to treat of the biliary colouring-matters and the allied constituents of the bile, sometimes encountered in the renal secretion.

## BILE AND BILIARY COLOURING-MATTER.

Bile is a very complex fluid; its chief constituents consist of fatty matters, *oleic, margaric,* and *stearic acids; taurine, cholesterine;* two colouring-matters, the one green, *biliverdin,* and the other brown, *bilifulvin;* two nitrogenous acids peculiar to bile, *cholic* and *cholinic acids;* and, lastly, *various salts,* especially of *soda.*

It will not be necessary to describe in detail the whole of these constituents, but chiefly the colouring-matters, the bile acids, cholesterine, and taurine.

The colouring-matters are sometimes present in the urine without the bile-acids, and sometimes the latter are present and the former absent.

### *Bilifulvin and Biliverdin.*

The brown pigment, *bilifulvin,* is insoluble in water, very slightly so in ether, more so in alcohol; more soluble in caustic potash than caustic ammonia. It is from this modification of the bile-pigment that the characteristic changes result on the addition of nitric acid—it turning green, blue, violet, red, and finally, after a time, yellow. When hydrochloric acid is added to a potash solution, it is precipitated of a green tint, the precipitate forming a red solution with nitric acid, and a green one with alkalies, and being apparently identical with biliverdin. The brown pigment has a strong affinity for bases, and forms with the alkaline earths insoluble compounds.

The green pigment, *biliverdin,* is slightly soluble in alcohol only, but dissolves in ether, forming a red solution; in hydrochloric and sulphuric acids, it dissolves with a green colour, and in the alkalies with a yellowish-red tint. It does not change colour on the addition of nitric acid, although green bile-pigment is sometimes met with possessing this property.

The reddish-yellow crystals found in bile by Berzelius, and to which he has given the name of bilifulvin, as well as the bilifulvin of Virchow, consisting of zigzag crystals, both of which are probably, and the latter certainly, identical with the *hæmatoidin* also discovered by Virchow,—must not be confounded with the brown pigment above described.

Biliverdin and bilifulvin may be entirely removed from the other constituents of the bile by means of animal charcoal.

They may thus be obtained:—

The solution of bile is treated with baryta-water or a solution of chloride of barium, so long as a green precipitate is thrown down; this precipitate is then treated first with hydrochloric acid and then with ether, to separate the baryta and fatty matter, *biliverdin*, a substance which closely resembles chlorophyll, remaining.

When bile is evaporated, and treated with alcohol, there remains a residue, consisting of mucus and a brown colouring-matter, *bilifulvin*, the *cholepyrrhin* of Berzelius, and the *bilephæin* of Simon: this is dissolved by warm dilute spirits of wine, and is thrown down from the solution again by alcohol, when it may be collected and dried. Biliverdin is derived from bilifulvin, and is often alone present in the urine.

Now these colouring-matters resemble very closely, in their chemical composition and reactions, blood and urine-pigments, and there appears much reason to believe that they consist of altered hæmatin. Both Zenker and Funke have established the fact of the conversion of Virchow's bilifulvin into hæmatoidin, and Mettenheimer has shown that crystals of hæmatoidin may be procured from bile-pigment. Frerichs and Städeler maintain, however, that they may be formed from the metamorphosis of the biliary acids. (See p. 287.)

Again, it has been shown that when the alcoholic solution of bile is exposed to the air, the green colouring-matter turns red, and then closely resembles hæmatin.

## *Cholic and Cholinic Acids.*

The bile-acids occur in the urine both with and without the pigment.

*Cholic* or *Glycocholic* acid has the following composition: $HO\,C_{52}H_{32}O_{11}$.

It forms needle-shaped glistening crystals; it is but little soluble in cold water, more so in boiling water, is readily dissolved by alcohol, and but little so by ether. When heated, it melts, evolving a peculiar odour; its salts with alkalies or alkaline earths are soluble in water.

It may be obtained pure from the solution of bile decolorized by animal charcoal. The cholic acid is precipitated with acetate of lead, the lead is removed by means of sulphuretted hydrogen, and the acid obtained by evaporation.

*When warmed with sulphuric acid and sugar, an intense violet colour is developed.* This is Pettenkofer's test.

When cholic acid is boiled with sulphuric or hydrochloric acid, a nitrogenous body, glycocol, $C_4H_5NO_4$, and a non-nitrogenous resinous substance, choloidinic acid, $C_{48}H_{39}O_9$, are formed.

Heated for a considerable time with hydrochloric acid, it is converted into *dyslysin*, $C_{48}H_{36}O_6$, and which therefore differs only in composition from choloidinic acid in containing 3 atoms less water. Unlike choloidinic acid, dyslysin is insoluble in alcohol, but is soluble in ether.

Further, cholic acid is decomposed by the caustic alkalies and alkaline earths into glycocol and cholalic acid, which has 1 atom more water than choloidinic acid. It crystallizes from its hot alcoholic solution in octa and tetrahedra.

Cholic acid agrees in its composition with hippuric acid.

Between cholic and oleic acids a very close relation obviously exists. Thus Lehmann states that acids of the butyric and succinic acid groups may be produced alike from cholic and oleic acids, by the action of nitric acid. Further, Kühne has shown that all fats containing olein give with sulphuric acid and sugar an intense purple-violet colour, a reaction which, according to Lehmann, differs only from that of cholic acid in occurring more slowly, and requiring the access of atmospheric air.

*Cholinic*, also called *taurochloric acid*, $C_{52}H_{45}NO_{14}S_2$, differs from cholic acid in containing 2 atoms more water and 2 atoms of sulphur. On the presence of sulphur, therefore, the distinctive characters of this acid mainly depend.

It may be thus obtained:—The cholic acid and colouring-matter must be precipitated with neutral acetate of lead; the cholinic acid is then thrown down by means of a solution of basic acetate of lead and ammonia, the precipitate is freed from lead with sulphuretted hydrogen, and free cholinic acid remains.

By the evaporation of the solution the free acid is decomposed; but in combination with the alkalies, it may be evaporated even at the temperature of boiling water.

Treated with the caustic alkalies it is converted into *cholacic acid*, $C_{48}H_{40}O_{10}$, and *taurine*, $C_4H_7NO_6S_2$. In bile, cholinic acid is usually in combination with soda.

## *Taurine.*

Taurine was first discovered in *bile* by Gmelin, and is found in the urine whenever that fluid is contained in the renal excretion: it does not usually occur separately, but conjugated with cholic acid, forming cholinic or tauro-cholic acid.

It is soluble in water and in spirits of wine, but not in anhydrous ether or alcohol: it is dissolved by even the boiling mineral acids without change, and without forming combinations with them: it is not precipitated from its solution by the metallic salts: it may be heated to 464° F. without decomposition or fusion.

It has the following *composition* :—

| | | |
|---|---|---|
| Carbon | 4 | 19·20 |
| Hydrogen | 7 | 5·60 |
| Nitrogen | 1 | 11·20 |
| Oxygen | 6 | 38·40 |
| Sulphur | 2 | 25·60 |
| | | 100·00 |

It therefore resembles, in the presence of sulphur, cystine: from the fact that the sulphur of taurine cannot be recognised by means of ordinary fluid oxidizing agents, it is supposed that it is present in that body in an *oxidized condition.*

*Formation.*—It has been prepared artificially by Strecker from isæthionate of ammonia, which differs in its elementary composition from taurine only in containing two elements more water.

*Preparation.*—Lehmann's process for obtaining taurine is as follows:—The bile is freed from its mucus by an acid, or the alcoholic extract is mixed with hydrochloric acid, and boiled for some hours, till the choloidic acid is completely formed from the nitrogenous acids of the bile. The fluid is then filtered, whereby the choloidic acid is removed, and rapidly evaporated until the chloride of sodium has crystallized out of the mother-liquor; five or six times its bulk of boiling alcohol is added, the taurine being deposited as the solution becomes cold. The following directions are given in Thudichum's work for the separation of taurine from bile. The bile is boiled for some length of time with hydrochloric acid, the fluid is filtered from the precipitate of dyslysin, evaporated, and mixed with spirits of wine; the taurine is precipitated, and chloride of sodium and hydrochlorate of glycocoll remain in solution.

*Tests.*—Taurine is distinguished by the form of its crystals, by the generation of sulphurous acid when heated with access of air, and when boiled with caustic potash by developing ammonia and sulphurous and acetic acids, which combine with the potash.

The *crystals* of taurine are very characteristic, so that they are readily distinguished under the microscope. They occur as regular hexagonal prisms, with four or six-sided sharp summits or extremities, the elementary form being a right rhombic prism.

## *Detection of Bile.*

For ordinary practical purposes, the urine is usually tested only for the colouring-matter and bile acids.

Urine containing bile in large quantity is of a dark olive-green or blackish colour, and its appearance sufficiently indicates the presence of that fluid; but when the amount is small, we may have to resort to chemical processes for its detection.

One very characteristic test of the presence of the colouring-matter of bile in urine is furnished by the action of *nitric acid*: if a drop or two of this be added to a few drops of the suspected urine, and placed upon a white porcelain plate, and bile be present, a blue tint will be developed, rapidly passing successively into violet and red, the tints being very fugitive.

If bile be present in small amount only, the urine may be either evaporated to dryness and the pigment extracted with alcohol, or the urine may be precipitated with diacetate of lead, and the colouring-matter extracted with spirit slightly acidulated with sulphuric acid, when, if bile be present, the alcohol assumes a greenish tint.

Again, if it be present, in even minute amount, many of the substances precipitated from the urine become stained by it in a very characteristic manner, as albumen, the cells of the vesical epithelium, and, as long since pointed out by the author, the crystals of triple phosphate. This latter is both a delicate and pretty test of the presence of bile.

Heller's test consists in adding a little albumen to urine, when, on precipitation with nitric acid, the albumen will be found to be more or less tinted.

The existence of the bile acids in urine is determined by *Pettenkofer's* well-known test of sugar and sulphuric acid, and which is thus applied:—

The dry extract of the urine is treated with alcohol, the alcoholic solution is evaporated, the residue dissolved in a few drops of water, and placed in a little porcelain capsule; a small quantity of a solution of sugar is added, and lastly, three or four drops in succession of strong sulphuric acid, when shades of red, pink, crimson, and lastly violet, appear more or less intense, according to the quantity of the acids present. In applying this test, in order to prevent any undue action of the sulphuric acid upon the sugar, it is necessary to keep the contents of the capsule as cold as possible, which is effected by adding the acid gradually, and by floating the capsule upon cold water.

The method devised by Hoppe is still more delicate, but is exceedingly tedious:—

The urine is treated with excess of milk-of-lime, boiled for half an hour, filtered, evaporated nearly to dryness, and excess of strong hydrochloric acid added: the mixture must be boiled for another half-hour, and the acid is to be removed from time to time, to prevent spurting; when cold, five or six times the volume of water is to be added, the liquid filtered, and the resinous mass washed with water, and dissolved in spirit containing 90 per cent. of absolute alcohol, decolorized with animal charcoal, again filtered, and evaporated to dryness over a water-bath. The residue is pure choloidic acid, and when warmed, it emits an odour resembling musk: it is now dissolved in a small quantity of caustic soda and warm water, and the sugar and sulphuric acid added in the usual manner, when a beautiful dark-violet colour will be developed. (See *Archives of Med.*, vol. i.)

PATHOLOGY OF BILE IN THE URINE.

The appearance of bile in the urine depends in general upon some impediment to its escape from the liver into the intestines: accumulating in the liver, it is absorbed into the blood, whence, being a foreign body, it is excreted by the kidneys.

*Bile-pigment* is sometimes found in small quantity in the urine in *hot weather*. (Scherer.)

In *variola*, it is often present.

In *scarlatina*, according to Heller, during the first six days.

In *puerperal fever*, according to Chiari.

In *pyæmia*. (Parkes.)

In *pneumonia*, even without jaundice, although this in a slight form not unfrequently occurs in pneumonia of the right lung. (Parkes.) The bile acids are also often present. (Pettenkofer.)

In *acute hepatitis*, an affection not often occurring in this country, *the bile acids* have been found in the urine in one case by Gorup-Besanez. According to Parkes, pigment is not usually present unless the hepatitis be accompanied by jaundice, which is not very common.

In *acute yellow atrophy* of the liver, the urine frequently contains both bile-pigment and *bile acids*. (Frerichs and Scherer.)

Sanders on one occasion found bile-pigment, but no bile acids, although he tested the urine for them by Hoppe's method.

In *cirrhosis*, the pigment is frequently present.

In *icterus* from obstruction, pigment is of course abundant. The bile acids appear to be sometimes present, but frequently to be absent; and when present, to be so only in small amount. Since the adoption of the method of Hoppe, they have been more frequently discovered than previously, though still in small amount only.

Frerichs and Staedeler have recently endeavoured to prove that the bile-pigment is formed from the bile acids, and in this way they explain why it is that the acids are usually more abundant in the less deeply-tinted urines than in those which are highly-coloured with the pigment.

They refer, in proof, to the fact that with sulphuric acid, glycocholic acid, and chycochlolate of soda, a constituent of bile, give rise to the formation of a coloured compound; and they state further, that taurochloric acid gives with nitric acid the characteristic reactions of bile-pigment.

Lastly, they found that when the bile acids were given to a dog, bile-pigment appeared in the urine but not the acids. Kühne confirms this observation so far as the appearance of the pigment is concerned, but states that the acids may be detected after injection into the veins.

Kühne, therefore, does not attribute the appearance of the pigment to the transformation of the acids, but to the destructive effect exerted on the blood-corpuscles by the alkaline salts of the acids in question, and which is sometimes so great as to occasion hæmaturia.

From his experiments with glycocholate of soda and hæmatin, Kühne concludes that blood-pigment was changed into bile-pigment, and that an, as "yet inexplicable, influence in this direction must be attributed to the bile acids."

Kühne also affirms, that not only is hippuric acid absent from the urine in icterus, but that benzoic acid when administered does not appear as hippuric acid in the urine; and hence he infers that glycocholic acid is then not formed in the liver, but only taurochloric acid and perhaps cholacic acid; indeed, in his experiments on the urine of dogs, he found only the latter acid.

*Taurine.*

Taurine has been found in a free state in the *liver* by Gorup-Besanez, in a person who died of *arachnitis.*

It has also been detected in the *urine* in some cases of *icterus.*

*Cholesterine*

is a product of the metamorphosis of *the fatty tissues*, and is eliminated from the system, especially in the bile. Cholesterine has been found in *urine* by Gmelin, Möller, and Beale.

*Gall-stones* are composed almost entirely of cholesterine.

Gmelin is stated to have discovered it in the urine in a case in which there was *obstruction* to the escape of bile from the liver.

Möller detected it twice in the pellicle formed on the urine of *pregnant women.*

Lastly, Beale has obtained it from the urine in four cases of *fatty degeneration of the kidney;* the fatty deposit was separated from a very large quantity of urine, treated with alcohol, crystals of cholesterine becoming deposited as the solution evaporated.

TREATMENT REQUIRED BY THE PRESENCE OF BILE.

The presence of bile in the urine is dependent either upon functional derangement or organic disease of the liver, impeding its escape into the intestines. The treatment therefore rendered necessary by the occurrence of any of the elements of bile in the urine, involves the determination of the nature of the hepatic affection, and the use of the appropriate means and remedies. One indication in all cases is to endeavour to remove the obstruction which impedes the free discharge of the bile.

In cases of icterus, much valuable information is afforded by the extent of the discoloration of the urine, since it indicates the intensity and progress of the disease.

# CHAPTER XVI.

## XANTHINE AND HYPOXANTHINE.



A CLOSE connexion, chemical, physiological, and pathological, exists between these two substances.

### XANTHINE.

Xanthine, formerly known by the names of *xanthic oxide, urous acid,* and *uric oxide,* was discovered by Marcet in 1819.

It has been frequently found in the *urine,* of which it appears to be a normal constituent, although present in very small quantities, and in the *blood;* it is also met with in the *muscles, spleen, liver, pancreas, thymus gland,* and *brain.*

#### CHEMICAL CHARACTERS.

Xanthine is an uncrystallizable substance: subjected to dry distillation it breaks up into prussic acid and carbonate of ammonia, but does not yield urea. It is slightly soluble in boiling water, from which it is precipitated on cooling; it is soluble in ammonia, leaving on evaporation a yellow foliaceous mass, and is readily so in caustic potash, from which solution it is precipitated by acids, or even by the transmission of carbonic acid through the liquid; also by chloride of ammonium, as the volatile alkali evaporates. It is dissolved by oil of vitriol, and is not thrown down from this solution on the addition of water; also by nitric acid, a lemon-yellow residue being left on evaporation, partly soluble in water; the aqueous solution treated with caustic potash, and evaporated, changes to a characteristic blood-red or carmine colour.

It is slightly soluble in a dilute solution of carbonate of potash, but insoluble in the alkaline bicarbonates; it is very little soluble in the dilute mineral acids, scarcely at all so in strong hydrochloric acid; it is also insoluble in alcohol, spirits of wine, and ether.

*Composition.*—Xanthine has the following elementary composition—

| | | |
|---|---|---|
| Carbon . . . | 10 . . . . | 39·48 |
| Hydrogen . . | 4 . . . . | 36·84 |
| Nitrogen . . . | 4 . . . . | 2·63 |
| Oxygen . . . | 4 . . . . | 21·05 |
| | | 100·00 |

It is thus evident that xanthine resembles very closely in its chief chemical characteristics uric acid, and to hypoxanthine the relation is still stronger.

It is distinguished from hypoxanthine mainly by its greater insolubility in water.

Considering the similarity of composition, it is singular that uric acid has never yet been converted into xanthine.

### DISCRIMINATION OF XANTHINE.

Concretions of xanthine are often mistaken for those of uric acid, which they nearly resemble; their sections present, according to Bird, a well-marked salmon, or rather cinnamon tint: when it occurs as a deposit in the urine, Berzelius states that it appears as a grey powder. When fragments of a xanthine calculus are subjected to friction they present a wax-like surface.

Dr. Bird has pointed out the following distinctions between xanthine and uric acid:—

| *Xanthine.* | *Uric Acid.* |
|---|---|
| 1. Dissolves slowly in nitric acid, almost without the evolution of bubbles of gas. | 1. Dissolves readily in nitric acid, with copious effervescence. |
| 2. The nitric acid solution leaves by evaporation a yellow residue. | 2. The nitric solution leaves by evaporation a pink residue. |
| 3. Soluble in strong sulphuric acid, not precipitated on the addition of water. | 3. Is precipitated by water from its solution in concentrated sulphuric acid. |
| 4. Its solution in liquor potassæ not disturbed by hydrochlorate of ammonia. | 4. Hydrochlorate of ammonia precipitates it, combined with ammonia, from its solution in liquor potassæ. |
| 5. Precipitated uncombined when a current of carbonic acid traverses its solution in potash. | 5. A current of carbonic acid throws down from the alkaline solution an acid urate of potash. |
| 6. Insoluble in solution of carbonate of potash. | 6. Readily soluble in dilute solution of carbonate of potash. |
| 7. Ignited in a tube does not yield urea. | 7. When ignited yields urea as one of its products. |

## ON THE SOURCE OR ORIGIN OF XANTHINE.

Xanthine is undoubtedly an excrementitious substance, and a product of the disintegration of some of the nitrogenous tissues. From its chemical relationship with uric acid, and from the fact of it, as well as hypoxanthine, being found in the same situations and under the same circumstances as that acid, it is highly probable that these three bodies all have a common origin. By the simple addition of two atoms of oxygen, xanthine is converted into uric acid, and by the subtraction of an equal amount of oxygen it becomes hypoxanthine.

## ON THE PATHOLOGY OF XANTHINE.

From the similarity of composition of xanthine, hypoxanthine, and uric acid, the observations already made respecting the pathology of uric acid apply in the main to that of the other two bodies. They may all, in fact, be regarded as the same body in different degrees of oxidation, hypoxanthine being the lowest oxide and uric acid the highest.

It has already been mentioned, that xanthine has been found in the liver, and this fact serves to explain its occurrence in pathological amount in the urine, in cases of *acute yellow atrophy* of that organ.

Several of the cases of deposits and calculi of xanthine recorded have occurred in children.

## ON THE TREATMENT OF XANTHINE DEPOSITS.

But little can as yet be advanced, based upon practical knowledge and experience, relative to the treatment which ought to be pursued in cases of xanthine deposits. The opinion has before been noticed, that the appearance of excess of uric acid in the urine denotes deficient oxidation; and if this be true, then the occurrence of xanthine and hypoxanthine indicates still more defective oxidation. This view once established (and the chemical composition of these substances rather confirms it), we are furnished with the theoretical basis for the treatment of deposits of xanthine and hypoxanthine, which are, however, of extremely rare occurrence.

## HYPOXANTHINE.

This substance was discovered by Scherer, and may be identical with sarcine or sarkine, the elementary composition of which is the same.

It has been found in the *blood* and *urine*; in the *muscles*, especially those of the heart; in the *spleen*, *kidneys*, *pancreas*, *thyroid* and *thymus glands*, and in the *brain*; indeed, wherever and whenever xanthine is found, hypoxanthine is almost invariably present.

## CHEMICAL CHARACTERS.

These are, for the most part, similar to those of xanthine. It is soluble in 1090 parts of cold, and in 180 of boiling water; slightly soluble in boiling alcohol, from which it is thrown down as the solution becomes cold; it dissolves with effervescence in nitric acid, the solution when evaporated leaving an intensely yellow residue, which, treated with caustic potash, turns to orange.

Hypoxanthine forms an indistinctly crystalline powder, which does not assume a waxy texture when triturated.

It has the following elementary *composition*:—

| | | |
|---|---|---|
| Carbon . . . | 10 . . . | 44·257 |
| Hydrogen . . | 4 . . . | 3·219 |
| Nitrogen . . | 4 . . . | 40·820 |
| Oxygen . . . | 2 . . . | 11·704 |
| | | 100·000 |

Strecker has shown that xanthine may be obtained from hypoxanthine by oxidation with nitric acid.

## EXTRACTION OF HYPOXANTHINE.

The spleen, liver, or other tissue, must be finely divided and boiled in water: the strained solution treated with baryta-water, by which the phosphoric acid is precipitated, and again filtered and evaporated to a small bulk; sulphuric acid is now added, which throws down not only the excess of baryta added, but uric acid and hypoxanthine: these are dissolved in boiling solution of potash, and to this solution chloride of ammonium is added; this precipitates the uric acid, which may be separated when the hypoxanthine in its turn is thrown down by a stream of carbonic acid gas.

## ORIGIN OF HYPOXANTHINE.

The same as xanthine: in the normal condition of the organism it is no doubt converted into that substance, and this again probably into uric acid.

## PATHOLOGY OF HYPOXANTHINE.

Similar to that of xanthine, but apparently indicating a lower condition of oxygenation.

It has been found in the urine, particularly in cases of *leucocythemia*.

In this place *sarkine* and *guanine* may be noticed: they are obviously closely related, and sarkine is probably identical with xanthine.

### SARKINE

is obtained from the juice of flesh; it is said to differ from *hypoxanthine* in its greater solubility in water and hydrochloric acid; in forming salts with acids, in which respect it agrees with *guanine;* in dissolving in nitric acid without evolution of gas; and in leaving on evaporation a colourless residue.

### GUANINE.

This body is also nearly related to *hypoxanthine,* for which it has been mistaken; it differs from it only in containing one atom more of nitrogen and of hydrogen—thus, $C_{10}H_5N_5O_2$. It is obtained from Peruvian guano, and has been stated to occur in the urine, but the evidence on this point is not conclusive.

It differs from xanthine and hypoxanthine not only in its elementary composition, but in some other respects: thus it is a weak base, dissolves readily in hydrochloric acid, and forms unstable salts with acids; on diluting its sulphate with a large quantity of water, the guanine is thrown down as a hydrate.

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# CHAPTER XVII.

## ALLANTOINE.



### ALLANTOINE.

This compound occurs in the *liquor allantoidis,* in the *urine* of sucking calves, but disappears as soon as they take vegetable food, when it is replaced by hippuric acid; in that of dogs whose respiration is impeded, and probably also in the urine of young children.

### CHEMICAL CHARACTERS.

It is soluble in 160 parts of cold water, but more so in hot wâter, and crystallizes from its hot solution in alcohol; it is insoluble in ether; it dissolves in warm solutions of the caustic alkalies and their carbonates, but is deposited unchanged as these become cold. It combines with the oxides of lead and silver; it is also precipitated the same as urea with nitrate of protoxide of mercury, and, like sugar, reduces the oxide of copper.

*Composition.*—Allantoine has the following elementary composition:—

| | | |
|---|---|---|
| Carbon . . . | 8 . . . | 30·38 |
| Hydrogen . . | 6 . . . | 3·80 |
| Nitrogen . . | 4 . . . | 35·44 |
| Oxygen . . . | 6 . . . | 30·38 |
| | | 100·00 |

*Decomposition.*—It is decomposed by the concentrated alkalies, absorbing water and forming *oxalic acid* and ammonia; boiled with concentrated sulphuric acid it is also decomposed, taking up water and carbonic acid, carbonic oxide and sulphate of ammonia being formed; warmed with nitric acid it is resolved into *urea* and allantoic acid. It is one of the products of the decomposition of uric acid by means of peroxide of lead. By fermentation with yeast, *urea* and carbonate and oxalate of urea are formed.

*Preparation.*—The urine of the calf must be evaporated below the boiling-point to the consistence of a syrup, and set aside for a few days, when the allantoine, together with the urates and earthy phosphates, will have crystallized out. By adding cold water, and decanting, most of the extractive matter and the urates are removed; lastly, the allantoine is separated from the earthy phosphates by means of hot water.

It may be also obtained, as already pointed out, by the decomposition of uric acid.

There is no special *test* for allantoine, but it is best recognised, apart from an elementary analysis, by the form of its crystals.

### MICROSCOPICAL CHARACTERS.

The crystals are hard and vitreous, and occur as four-sided prisms, which belong to the rhombohedric type.

### ORIGIN OF ALLANTOINE.

It is clearly, from the circumstances under which it occurs, an excrementitious substance, derived from the decomposition of some of the nitrogenous tissues, and closely related to *urea*, *uric* and *oxalic acids*.

### PATHOLOGY OF ALLANTOINE.

It has been found by more than one observer in the *urine* of dogs and rabbits into whose lungs oil had been injected; it was also detected in the urine of a dog which had been made to inhale chlorine. It could not be discovered in the urine of man during violent dyspnœa.

From the fact that the urine of sucking calves contains allantoine, but no hippuric acid, Lehmann has suggested that possibly it may replace the latter body. Chemically, it seems to occupy an intermediate position between uric acid and urea: it, as well as urea, may be formed from uric acid, and urea again may be procured from allantoine.

# CHAPTER XVIII.

## LEUCINE AND TYROSINE.



BETWEEN leucine and tyrosine a very close connexion exists: they are furnished by the disintegration of the same animal substances, and they occur together both in the body and in the urine in health or disease.

### LEUCINE

was discovered by Prout in 1818, in rotten cheese, and hence he named it *oxide of cheese;* it has since been procured from a variety of animal substances. It is identical with the *lienine* of Scherer and the *thymine* of Gorup-Besanez.

Leucine has been found in nearly the whole of the glands, the *thymus* and *thyroid*, the *liver, spleen*, and *kidneys;* in the *pancreas, salivary* and *lymphatic glands;* in the *lungs*, and in a diseased *brain;* in *pus*, and in the *blood, bile*, and *urine*. Its presence in the spleen, liver, pancreas, and thymus glands is normal, but its occurrence in the urine is strictly pathological. It does not occur in the muscular tissue. It has been found to be abundant in the pancreas, spleen, and liver. In the urine it may occur as a deposit, but more generally it is in solution.

#### PROPERTIES AND CHEMICAL CHARACTERS.

It forms glistening, colourless, foliaceous masses, which convey the impression of being of a fatty nature; it is devoid of taste and smell, is lighter than water, fuses at 212°, sublimes unchanged at 338°; it is very soluble in cold water, less so in hot; it is much less soluble in alcohol than water, and is insoluble in ether; it is dissolved by caustic ammonia; it is unchanged by the concentrated mineral acids when cold, but when boiled with nitric acid it is entirely converted into volatile products. On heating its aqueous solution with nitric oxide, or any other oxidizing agent, it is converted into leucic acid, nitrogen escaping. It forms with acids crystallizable salts containing one atom of the acid; with nitric acid it forms a salt which crepitates when heated. The only reagent which precipitates leucine from its aqueous solution is basic acetate of lead.

*Composition.*—Leucine has the subjoined composition:—

| | | |
|---|---|---|
| Carbon . . . | 12 . . . | 54·96 |
| Hydrogen . . | 13 . . . | 9·92 |
| Nitrogen. . . | 1 . . . | 10·68 |
| Oxygen . . . | 4 . . . | 24·44 |
| | | 100·00 |

*Decompositions.*—Fused with hydrated potash, it is resolved into valerianate of potash, cyanide of potassium, water, and hydrogen, which escapes. A similar decomposition ensues when the aqueous infusion of leucine contains a putrefying animal substance, as albumen.

*Formation.*—Leucine is formed by the action of alkalies and acids on albuminous substances, and by the fermentation and putrefaction of the same. Thus it is present in decomposing cheese and gluten.

If caseine, or any other albuminous body, be fused with equal parts of hydrated potash, and the tyrosine be extracted in the manner hereafter to be described, the leucine crystallizes from the mother-liquor, and may be purified by recrystallization from alcohol.

If, on fusing equal parts of a protein-compound and hydrated potash, we interrupt the operation before the mass has become yellow, we obtain only leucine according to the method given for tyrosine, the latter appearing to be formed from the former by continued action.

If *gelatine* be treated in the same manner, or be boiled for a long time in caustic potash, *glycine* as well as leucine is formed; the potash is then saturated with sulphuric acid, and the sulphate of potash removed by alcohol; glycine being far less soluble in alcohol, the two substances may thus be easily separated.

Leucine may also be formed by the action of strong sulphuric or hydrochloric acid; equal parts of an albuminous substance, as flesh and sulphuric acid, are to be gently warmed, then boiled for nine hours with the addition of double the weight of water, the acid neutralized with lime, and the residue of the filtered solution extracted with alcohol, which will contain the leucine.

The sublimation of leucine, its decomposition, by fermentation or hydrated potash, into valerianic acid, and its total dissipation when boiled with nitric acid, afford tests by which it may be clearly distinguished.

### ON THE SEPARATION OF LEUCINE FROM URINE.

The concentrated urine should be digested with cold absolute alcohol, and the residue treated with boiling spirits of wine; this removes the leucine, which becomes deposited on evaporation.

### *Microscopical Characters.*

The *sublimate* of pure dry leucine is said to crystallize in rhombic plates and needles, usually arranged so as to form stars or glomeruli; Virchow, however, has never been able to discover these rhombic plates or crystals, but has found only the acicular crystals.

When crystallized from its *alcoholic* solution, it appears in the form of scales having the lustre of mother-of-pearl, and resembling closely cholesterine. Under the microscope the crystals are seen to be aggregated, rounded, and flattened.

From its watery solution it crystallizes usually in globules, which often combine and form compound nodular masses.

In the *liver* leucine crystallizes in little balls or spheres, in some of which a radiated or stellar arrangement may be detected.

## ORIGIN OF LEUCINE.

Leucine would appear to be a normal product of the disintegration of certain of the nitrogenous tissues of the principal glands.

Neukomm regards it as the product of the too rapid destruction of tissue, a process which occurs particularly in acute yellow atrophy of the liver. From the ease with which leucine is obtained from all the protein-compounds, it is obviously not the product of the disintegration of any one particular tissue.

## PATHOLOGY OF LEUCINE.

Leucine has been detected in the *urine* in cases of *variola,* in a case of *typhus, typhoid* (?) fever, and particularly in *acute yellow atrophy of the liver.*

It has been found in the *liver* itself in large quantities in acute yellow atrophy, and this sometimes in the crystalline state, in *typhus, variola, rheumatic fever,* and *tuberculosis.*

Crystals of leucine have also been detected in sections of liver in cases of *jaundice.*

So far as is known at present, its occurrence is chiefly associated with disordered or diseased liver, although, since it is found in a variety of other organs, its occurrence in the urine might be looked for in connexion with disease of any one of those organs or glands.

## TYROSINE.

This compound was described by Liebig as a product of the decomposition of cheese by means of caustic potash.

It is found wherever leucine is met with, either in the *glands* or in the *blood, bile,* or *urine.*

### PROPERTIES AND CHEMICAL CHARACTERS.

Tyrosine is of very difficult solubility in cold, but is more soluble in hot water: it is insoluble in alcohol and ether; it dissolves readily in alkaline solutions, and it forms salts with the acids, excepting *acetic acid.*

*Composition.*—Its elementary composition is as follows:—

| | | |
|---|---|---|
| Carbon | 18 | 59·67 |
| Hydrogen | 11 | 6·08 |
| Nitrogen | 1 | 7·73 |
| Oxygen | 6 | 26·52 |
| | | 100·00 |

It thus appears that tyrosine has a very different elementary composition to leucine.

*Decomposition.*—Treated with boiling nitric acid, it yields, according to Strecker, a large quantity of *oxalic acid* as one of the principal products of its decomposition.

*Formation and Preparation.*—The protein substance must be fused with an equal weight of hydrated potash, till both ammonia and hydrogen are developed; this is indicated by the original dark brown colour merging into yellow; the mass is then dissolved in hot water, and the solution slightly supersaturated with acetic acid; the tyrosine is deposited in needlelike crystals, which may be purified by solution in potash-water and reprecipitation with acetic acid.

Tyrosine, like leucine, is also formed by the action of concentrated sulphuric or hydrochloric acid, and by putrefactive fermentation.

The best *test* for tyrosine is that named after its discoverer Piria. A small quantity of tyrosine is placed in a watchglass; this is moistened with two or three drops of sulphuric acid; after half-an-hour a little water is added, the solution is neutralized with carbonate of lime, and the liquid filtered; lastly, perchloride of iron, free from acid, is added, when a dark rich *violet* colour is developed.

Another very beautiful *test* has been suggested by Hoffman. Nitrate of protoxide of mercury added to a boiling aqueous solution of tyrosine causes a precipitation of red flakes, the clear liquid being of a *deep pink* or *dark rose*-red colour.

### *Microscopical Characters.*

Tyrosine crystallizes in long needles, which occur singly, or may be arranged in tufts; when dried, they form a silky, glistening, white powder.

### PATHOLOGY OF TYROSINE.

The same as leucine, as far as is yet known.

# CHAPTER XIX.

## CYSTINE.



CYSTINE, originally called by its discoverer, Wollaston, *cystic oxide*, has been found in the *liver* by several observers, and in the *kidneys*, *bladder*, and *urine*, forming in the kidneys granules and calculi, and in the urine occurring chiefly as white or fawn-coloured sand-like and crystalline deposits.

### CHEMICAL CHARACTERS OF CYSTINE.

Cystine occurs nearly always in the crystalline form; it is devoid of colour or taste, is insoluble in water and alcohol; it dissolves in the mineral and oxalic acids, forming combinations which are for the most part crystallizable, but it does not combine with citric, tartaric, or acetic acids; it is also dissolved freely by the fixed alkalies and their carbonates. It is soluble in ammonia, from which it is again deposited unchanged, on the evaporation of the volatile alkali, but it is insoluble in carbonate of ammonia, hence it is best precipitated from its acid solutions by that reagent, and from its alkaline solutions by acetic acid. It burns with a bluish-green flame, giving rise to a very peculiar odour: submitted to dry distillation, it yields ammonia, and developes a very offensive smell; it leaves a bulky and porous ash; boiled with alkalies, ammonia is first formed, and subsequently a gas which, when ignited, burns with a blue flame.

The following is the elementary *composition* of cystine:—

| | | |
|---|---|---|
| Carbon | 6 | 30·000 |
| Hydrogen | 6 | 5·000 |
| Nitrogen | 1 | 11·666 |
| Sulphur | 2 | 26·667 |
| Oxygen | 4 | 26·667 |
| | | 100·000 |

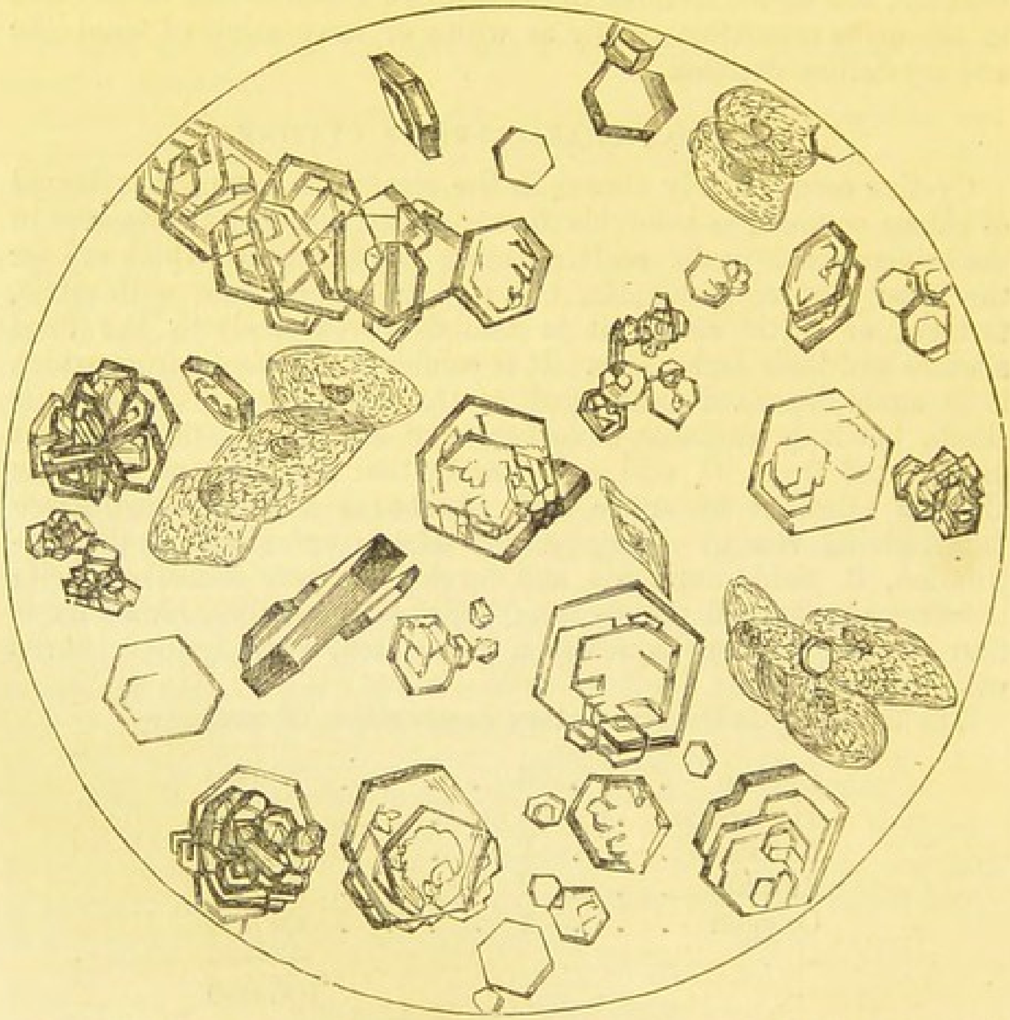
Cystine is distinguished with great ease by its microscopical characters, by its solubility both in alkalies and mineral acids, and by the odour which it developes when submitted to dry distillation, or when burned.

Liebig has given the following directions for the detection of cystine:—The potash extract of the substance suspected to contain the cystine is to be decomposed with a solution of oxide of lead in caustic potash; heat is to be applied, when, if cystine be present, a precipitation of sulphite of lead will occur. It should be recollected that the same result will ensue with any other body containing sulphur, as albumen, mucus, &c., although these substances contain at most but 2% of sulphur, and cystine, 25%.

### MICROSCOPICAL CHARACTERS OF CYSTINE.

The microscopical characters of cystine are peculiarly distinctive; a mere glance at this deposit under the microscope is sufficient for

Fig. 70.



Crystals of Cystine, magnified 230 diameters. Drawing made April, 1853, from urine furnished by Dr. Mott.

its identification. The ordinary form in which the crystals occur is in thin regularly-shaped hexagonal plates, these being often composed of one larger crystal, splitting up into several smaller hexagonal crystals. Sometimes a number of hexagonal plates partially coalesce, forming glomeruli; occasionally long four-sided prisms are met with, the extremities of which are truncate. These long prismatic crystals are well figured by MM. Robin and Verdeil; they occur chiefly amongst the crystals deposited from the ammoniacal solution of cystine.

Another characteristic of the crystals of cystine is derived from the manner in which they reflect the light transmitted from the mirror of the microscope; when this traverses the face of the crystals directly opposed to it, it causes them to appear particularly clear and brilliant, but the light is altogether excluded from those faces or surfaces on which it falls obliquely, and hence they appear as black or nearly black. This appearance is observed particularly in the thicker hexagonal plates.

### CHARACTERS OF URINE DEPOSITING CYSTINE.

Urine depositing cystine is usually of a pale colour, frequently possessing, according to Bird, an oily appearance, like diabetic urine. Its specific gravity is generally below the average, although one case has been met with, that of a child, in which it was 1·030. The quantity passed is often considerable, and it is ordinarily either neutral or feebly acid, speedily becoming alkaline by keeping. Bird describes its odour as peculiar, bearing in general a close resemblance to that of sweetbriar. Less frequently the odour is fœtid, like putrid cabbage, owing to the partial decomposition of the cystine, and the escape of sulphuretted hydrogen. In these cases, the colour of the urine changes from pale yellow to apple-green. Kept a short time, cystine urine becomes covered with a greasy-looking pellicle, consisting of a mixture of crystals of cystine and triple phosphate; and in warm weather, according to Bird, it frequently undergoes a kind of viscous fermentation, bubbles of gas being evolved, and the whole becoming ropy and rather viscid.

The crystals of cystine are generally present in the urine, rendering it somewhat turbid at the moment it is passed; but a small quantity remains in solution, and is precipitated by the addition of acetic acid.

The deposit is usually white or pale fawn-coloured, and often copious. It is sometimes pure and unmixed, but not unfrequently mixed with triple phosphate, phosphate and oxalate of lime; but the urates are not of common occurrence. It will sometimes be found to vanish from the urine for days together, but crystals of cystine are even then precipitated by acetic acid. The urea and uric acid are usually much diminished.

Calculi of cystine are either pale yellow or fawn-coloured, changing by long keeping to greenish-grey, and even a fine greenish-blue tint; they are transparent and crystalline.

The following analyses of cystine urine are by Golding Bird :—

*Boy.*

| | |
|---|---|
| Water | 974·444 |
| Solids | 25·556 |
| Urea, impure | 5·7 |
| Uric acid | ·016 |
| Cystine | ·340 |
| Extract containing fixed salts | 19·5 |

*Strumous Child with Pneumonia.*

Fluid ounce of urine.

| | |
|---|---|
| Uric acid | 0·2 |
| Urea | 3·7 |
| Cystine, Creatinine, Extractives | 8·1 |
| Earthy phosphates | 0·2 |
| Alkaline phosphates, sulphates, and chloride of sodium | 2·8 |
| | 15· |

In Fuch's analysis of the urine of two sisters, thirty and twenty-eight years of age, who were chlorotic, and who had some hereditary disposition to calculi, the uric acid was somewhat diminished, and the urea greatly lessened. In an analysis by Dr. Beale the sulphuric acid was relatively large, 3·74 and 5·35 per cent. of the dried solids, but in neither of the samples was the quantity of cystine great; in one it was 1·8 per cent. of the solids, and in the other too little to estimate.

A deficiency of uric acid and urea has been observed in other cases. Cystine calculi are usually remarkably free from uric acid or the urates. Fat and albumen are sometimes present in cystine urine.

"PATHOLOGICAL ORIGIN AND INDICATIONS OF CYSTINE."

Under the above heading we meet with, in Bird's "Urinary Deposits," the following remarks in regard to the pathology of cystine:—

"This curious substance is, in all probability, a derivative of albumen, or of structures into which it enters, and appears to be the result of the derangement of the secondary assimilative processes, essentially connected with the excessive elimination of sulphur, every ounce of cystine containing more than two drachms of this element. A question may be entertained whether cystine may not be a metamorphic form of the normal sulphur extractive of the urine, or the condition assumed by this extractive when an excess of sulphur is eliminated. From an examination of its chemical composition, there appears no difficulty in explaining the origin of cystine by supposing that it is formed by those elements of our tissues which would normally have been converted into urea or uric acid, in consequence of the presence of an excess of sulphur, probably connected essentially with a scrofulous diathesis."

A very remarkable circumstance connected with the history of cystine in the urine is its *hereditary* character; it has been found in the urine of several members of the same family, and nearly at the same time. In one instance, according to Dr. Bird, it has been traced through three generations.

Again, there is reason for believing that its presence, in some instances, is associated with *derangement* or *disease* of the *liver*, including, according to Prout, *fatty liver*. According to Day, unquestionable evidence of the presence of cystine in the aqueous decoction of the liver of a typhus patient has been recently obtained by Virchow. Scherer has also found it to be present in the liver of typhus patients. The relation which exists between cystine and taurine, into which bile is partly converted by digestion with hydrochloric acid, gives much probability to this view, as does also the observation of Dr. Prout, who has seen fatty matter mixed with the cystine urine, and who himself was hence led to suspect that the deposit was associated with fatty degeneration of the liver. If this view were correct, the excretion of cystine would serve to compensate for deficient elimination of sulphur by the liver, through its ordinary channel, the bile.

Mr. Luke, in a case of cystine calculus, met with extensive disorganization of the kidneys.

Another affection in which cystine is very apt to occur is *chlorosis*. In several cases the patients have been sisters.

The occurrence of cystine in connexion with hepatic derangement or degeneration, and in chlorosis, appears to show that there is a general deficiency of oxidation in these cases. The symptoms usually associated with deposits of cystine are debility, pain in the back, and a pallid and unhealthy-looking complexion.

The relative elementary *composition* of cystine and taurine are exhibited in the following formula:—

| | Cystine. | Taurine. |
|---|---|---|
| Carbon | 30·000 | 19·20 |
| Hydrogen | 5·000 | 5·60 |
| Nitrogen | 11·666 | 11·20 |
| Oxygen | 26·667 | 38·40 |
| Sulphur | 26·667 | 25·60 |
| | 100·00 | 100·0 |

It is in infants and adults chiefly that deposits of cystine occur, and scarcely ever in the aged.

It does not appear that there is any deficiency of sulphuric acid in urine containing cystine, and this again points to the liver as its source.

## TREATMENT OF DEPOSITS OF CYSTINE.

Before proceeding to treat cases of cystine deposit correctly, we must determine the nature of the constitutional cause or condition upon which it depends. If it be associated with the *scrofulous diathesis*, the treatment must be directed mainly to this and to the improvement of the constitution. Iron, especially the milder preparations, as the citrate, tartrate, and iodide of iron, will be found invaluable, attention being at the same time paid to the general health, and especially to the condition of the functions of digestion and assimilation, as by tonics, by bathing or sponging the body, exercise, and light and nutritious diet.

If the *liver* be at fault, we must particularly attend to and watch that organ.

If the deposit be associated with *chlorosis*, here again iron will be most serviceable.

With the view of improving the constitutional powers, and at the same time of dissolving the deposit, Dr. Prout has recommended the persistent use of nitro-hydrochloric acid, of the results of the exhibition of which, however, Dr. Golding Bird has not spoken very favourably.

Great attention should be paid to the diet, since Dr. Pletzer found that in two cases the amount of cystine was much increased by the use of fish and leguminous vegetables.

The administration of sulphur has no effect in producing a deposit of cystine.

Whatever treatment be adopted must be perseveringly followed out, for, since in these cases we have to treat an hereditary disease, recovery cannot be otherwise than a work of time.

Lastly, it should be stated that cystine deposits have been observed in some cases to continue for years without seriously affecting the health. The great danger to be apprehended in such cases is the occurrence of stone.

It is most desirable that in any future analyses of the urine in these cases, the amount of oxidized sulphur, in the form of sulphuric acid, should be determined. The point being settled whether that acid is present in normal amount, or is deficient, light would be thrown upon the question whether the sulphur of the cystine is derived from the disintegration of the nitrogenous tissues, the ordinary oxidation being prevented, or whether it proceeds from the liver.

# CHAPTER XX.

## ON ALBUMEN, ALBUMINURIA, AND BRIGHT'S DISEASE.



It has been affirmed by some observers that albumen is a normal constituent of the urine: if it were so, the quantity must be exceedingly minute; it appears certain, however, that what has been mistaken for that substance has been mucus, derived, not like albumen, from the blood, but from the genito-urinary passages.

Nevertheless, albumen is occasionally found, under certain circumstances, in the urine of persons apparently in good health. Several instances of this kind have been recorded, especially connected with peculiarities of *diet* and with *indigestion*.

Independent of diet, however, very slight causes are in some persons sufficient to occasion temporary albuminuria. Beneke some eleven years since found albumen in his urine on four occasions in as many weeks, and to this time no symptoms of renal disease have appeared; and the same fact has been noticed by other observers, as Clemens and Solon; nevertheless, it is probable that in all these cases some pathological condition, either of the kidneys themselves or of the blood, existed, although not recognised.

Some years since, the occurrence of albumen in the urine was looked upon as always a very serious symptom, and indicative in most cases of disease of the kidney: it is now known, however, that its presence is very frequently unconnected with any organic affection of the renal organs, and that the pathological importance to be attached to it varies greatly, it being in some cases of slight, and in others of the gravest import.

Its importance or otherwise of course depends mainly upon whether it is connected or not with disease of the kidneys.

In those cases in which it is independent of disease of those organs, its presence is generally but temporary, the quantity usually small, and the importance not ordinarily very great.

When, however, disease of the kidneys exists, its presence is more permanent, the quantity greater—often very large—and its significance more serious.

It is therefore apparent that albuminuria admits of division, which, however convenient for purposes of description, and although natural to a certain extent, is yet arbitrary, into "temporary" and "permanent."

In some instances the albumen found in the urine is due simply to admixture with other animal fluids, as the *lochia*, and may be wholly unconnected with disease.

In others again it depends upon the presence of *blood*, proceeding from some part of the genito-urinary passages; in these instances it may simply indicate local lesion, and be wholly independent of any constitutional or general malady.

Lastly, its occurrence may be connected with excessive discharge of *mucus* or *pus* from the genito-urinary surfaces.

The presence of blood-corpuscles in the urine is invariably indicative of lesion of bloodvessels somewhere. When the rupture occurs in the vessels of the kidneys, and is independent of renal calculus or cancer, the amount of blood in the urine is usually but very small.

The rupture of the renal capillaries may depend upon several very different causes:—1st. As active congestion, when the hæmorrhage is analogous to that which occurs in acute pneumonia. 2nd. Passive congestion, a state allied to that of the vessels in purpura. And 3rd. Degeneration, as occurs frequently in chronic Bright's disease. It is always of the utmost moment, since it affords such material aid in diagnosis, to determine whether blood or blood-corpuscles, even in the most minute quantity, occur with the albumen in the urine. If blood be present, albumen of course will always be found, but the reverse is very far from being the case.

In some cases blood escapes into the urine without rupture of vessels, the blood-corpuscles having become *dissolved*.

The microscope affords the best means of detecting minute quantities of blood in the urine.

*Composition.*—The following is the per-centage composition of albumen from blood:—

| | |
|---|---|
| Carbon | 53·0 |
| Hydrogen | 7·1 |
| Nitrogen | 15·6 |
| Oxygen | 23·1 |
| Sulphur | 1·2 |
| | 100·0 |

Albumen not specially purified contains usually much phosphate of lime and some sulphur.

*On the Detection of Albumen.*

Two of the principal characteristics of albumen are its coagulability by the mineral acids, especially nitric acid, and by heat; and hence these reagents are generally employed for its discovery in the urine.

Either the nitric acid or heat is usually sufficient to ensure the coagulation of the albumen, but when both are used—the acid first, and heat afterwards—in the manner generally practised, these tests rarely fail.

Failure, however, does occasionally occur, this being attributable sometimes to the composition and reaction of the urine, especially its alkalinity, and at others to the condition of the albumen itself.

Thus not unfrequently nitric acid alone applied to the cold urine produces no precipitate of albumen, although both the acid and heat used together occasion it; and more rarely, as in acid, *chylous* urine more particularly, nitric acid coagulates the albumen when heat will not.

Albumen is also precipitated from its solutions by *alcohol, alum,* and many *metallic salts,* especially those of mercury.

The polariscope may likewise be employed not alone for the detection of albumen, but for the determination of its amount, the plane of polarization being deflected to the left, and the degree of deflection being proportionate to the amount of albumen contained in the urine examined. This method is affirmed by Becquerel to be very trustworthy.

*Modifications of Albumen.*

The albumen not precipitated by heat, but by nitric acid, Prout regarded to be in an *imperfect* or *hydrated* condition.

In a case of *mollities ossium,* Bence Jones detected a peculiar albuminous substance: nitric acid, when added to the cold urine in which it was present, produced no immediate change, nor did heat occasion a precipitate; even after boiling, the acid produced no effect; but as the urine became cold it solidified; it liquefied again, however, when heat was applied. Hydrochloric acid acted similarly to the nitric acid. On one occasion it did coagulate by heat. From analysis, Dr. Jones regarded it as a hydrated deutoxide of protein.

The urine from which this substance was obtained was of high specific gravity, and slightly acid.

Mialhe recognises three varieties of albumen, all of which, he states, occur in the urine. 1. Ordinary *albumen.* 2. *Albuminose* (the *peptone* of Lehmann), or *digested albumen,* characterized by being very diffusible, passing readily through membranes, and not precipitated by heat and acids. 3. *Modified albumen,* a transitional form between the others, it being precipitated by heat and acids, but *soluble in excess of nitric acid.*

### *Sources of Fallacy of Tests.*

There are several fallacies to which the tests of heat and nitric acid are liable.

Thus heat produces a deposit in urine which contains an excess of earthy phosphates: this precipitate is distinguished from albumen by its solubility in nitric acid.

It does not coagulate albumen when the urine is *alkaline*, and which therefore should in such cases be rendered acid previous to boiling.

Neither will the urine, when very acid, coagulate by heat alone.

Nitric acid, when added in minute quantity to urine, prevents the coagulation of the albumen, and even when coagulated, added in too large amount, dissolves it in some cases; the acid should therefore be freely, but still not too largely added.

Jones considers that the precipitation is prevented by the formation of a nitrate of albumen, which is soluble in a weak solution of nitric acid; but Beale's observations seem to prove that it results from the liberation by the nitric acid of a portion of the phosphoric acid of the urine, by which albumen is freely dissolved.

Nitric acid in urines rich in urates occasions a precipitate of *uric acid*, which, however, does not occur when the urine, without the addition of the acid, is simply boiled. A precipitate of *nitrate of urea* also sometimes occurs on the addition of nitric acid, and which may possibly be mistaken for albumen.

The above acid likewise produces a turbidity, but no precipitate, in the urine of persons taking *copaiba* and *cubebs*.

The best plan, in order to avoid fallacy, is to boil a drachm of the urine in a test-tube, to which several drops of nitric acid have been previously added.

### *Estimation.*

A rough approximation to the amount of albumen present in any urine is arrived at by simply noting the bulk of the precipitate which subsides when a sample of boiled albuminous urine is allowed to stand at rest for a time; but for its precise determination, either of the following processes must be adopted:—

Five hundred grains of the urine of twenty-four hours should be boiled in a flask, nitric acid being subsequently added, in order to ensure the coagulation of the albumen as well as the resolution of the phosphates which may have become precipitated in consequence of the boiling. The boiled urine may be allowed to stand at rest until the albumen has subsided; the clear part then be poured off, and the residue thrown upon a weighed filter. The albumen thus collected must be thoroughly washed on the filter with hot distilled water, to free it from salts; lastly, it must be placed on the water-bath, dried, and weighed.

Or acetic acid may be added, not in too great excess, and the urine boiled; this suffices to ensure the precipitation of the albumen. When urine is boiled, part of the alkali ordinarily contained in it is set free, and this forms a soluble albuminate, not precipitated by heat; the addition of the acetic or other acid prevents this formation, but the acid itself must not be added in too large amount, or part of the albumen will be equally lost, in consequence of the formation of a soluble compound with the acid.

### *Quantity.*

The quantity of albumen contained in the urine varies from a mere trace to some 545 grains in the twenty-four hours, an amount met with by Parkes in one of his cases.

The range in the cases of renal disease recorded by Frerichs was between 59 and 286 grains; in Rosenstein's cases the range was nearly the same; the mean of Schmidt's cases was 204 grains, and of those of Gorup-Besanez 237 grains.

Sometimes when the urine is boiled, it is rendered only slightly opalescent, and at others it becomes solid and white, like the coagulated albumen of an egg. Between these extremes every degree of variation occurs. If the test-tube containing the boiled urine be set aside, the albumen, even if only a small quantity be present, becomes deposited, and a rough estimate, as already pointed out, may thus be formed of its quantity.

The quantity of albumen, according to the observations of Becquerel, Rodier, and Scherer, ranges in normal *blood* between 6·3 and 7·1 per cent., and in normal blood *serum* between 7·9 and 9·8 per cent.

The specific gravity of the serum of the blood in health ranges between 1029 and 1031, while in Bright's disease it is reduced as low as 1018, and even 1015.

### *Origin of Albumen.*

The albumen of the blood is formed chiefly from the protein constituents of the food: it has not yet been shown whether it ever results in part from the disintegration of the nitrogenous tissues. There is reason to believe that prior to its entering into the formation of the tissues, it must be converted into fibrin.

### *Effects of Food.*

The amount of albumen in the urine is greatly influenced in the majority, but not in all cases, by food, especially in the second and third hours of digestion: it is reduced by fasting.

These effects are observed particularly in cases of chronic Bright's disease, but, as appears from some of Latour's observations, in other cases as well.

In two cases of Dr. Parkes, the particulars of which were published in 1854, the amounts passed before and after food were:—

| | Case I. | | Case II. | |
|---|---|---|---|---|
| | *First Experiment.* | | | |
| | Fifteen hours after food. | Second hour after food. | Fasting. | Second hour after food. |
| Water | $3\frac{1}{3}$ oz. | $3\frac{2}{3}$ oz. | $4\frac{2}{3}$ oz. | $4\frac{1}{2}$ oz. |
| Albumen | 14·3 grs. | 34·0 grs. | 9·28 grs. | 17·2 grs. |
| | *Second Experiment.* | | | |
| Water | $1\frac{2}{3}$ oz. | $2\frac{2}{3}$ oz. | 4·0 oz. | $2\frac{1}{2}$ oz. |
| Albumen | 11·2 grs. | 30·4 grs. | 4·68 grs. | 6·75 grs. |

In the majority of Latour's cases published in 1857, the *urina sanguinis* was free from albumen, while the *urina cibi* contained a large quantity.

This effect of food is no doubt partly due to increased pressure on the walls of the bloodvessels, partly to the larger amount of albumen in the blood, and in some cases, no doubt, to differences in the condition of the albumen itself.

It has been noticed by several observers, that certain articles of food, especially *eggs*, give rise, in some persons, to the presence of albumen in the urine. *Cheese* and *pastry* taken in excess likewise appear occasionally to produce temporary albuminuria.

Dr. Mariano Seminola, in a communication on albuminuria recently addressed to the Academy of Medicine of Paris, states that in symptomatic albuminuria, the albumen is but little influenced by diet, but that in the idiopathic form, an exclusively nitrogenous diet will double the amount of albumen.

### *On the Causes which determine the Appearance of Albumen in the Urine.*

One of the causes which occasionally determines the presence of albumen in the urine is an altered or abnormal condition of the blood, and particularly of the serum, such as exists in anæmia. This, however, is by no means the only cause. Another is an altered condition of the albumen itself; but the more usual cause consists in impeded circulation through the capillaries of the kidneys, producing pressure by the blood upon the walls of the vessels, especially those of the Malpighian corpuscles, and consequent escape of the serum with its albumen.

This impediment or obstruction may be produced in one or more of several ways—as by simple congestion of the capillaries wholly independent of disease; by thickening or other disease of the capillaries themselves, either in their walls or by the blocking up of their cavities; by impaction of the tubules with fibrinous casts; by amyloid or fatty deposits resulting from degeneration, either without or within the tubules.

Dr. Mariano Seminola thus explains the elimination of albumen by the kidneys. In idiopathic albuminuria unassimilable albumen accumulates in the blood, which the kidneys throw off as a foreign body, and it is by this deficient assimilation of the albumen that he would account for the diminution in the amount of urea excreted. The disease of the kidneys he regards as the *result* of continued albuminuria, and not the cause.

Robin's theory is that albumen is an excrementitious substance, and that normally it is converted into urea and uric acid, carbonic acid and water, so that whatever prevents this transformation of the albumen causes its appearance in the urine.

## TEMPORARY ALBUMINURIA.

Temporary albuminuria is occasioned in some persons by very slight causes, independent of certain indigestible articles of food, and, so far as can be ascertained, without the existence of renal disease, or any apparent derangement of health. Such cases are, however, rare. As before remarked, the division of albuminuria into temporary and permanent is extremely arbitrary, and it is not easy to define the line of demarcation.

Under the first division all those cases of albuminuria will be included unconnected with structural disease of the kidneys.

By some writers albuminuria has been divided into *idiopathic* and *symptomatic*, a division which closely corresponds to that into temporary and permanent albuminuria.

Dr. Seminola affirms that these two forms of albuminuria may be distinguished by the character of the albumen, which, in the idiopathic form, is like white of egg, and in the symptomatic variety has a caseiform appearance.

Albuminuria may and does occur in connexion with almost every known disease; not unfrequently the association is purely accidental, but usually there is some relation of cause and effect. This is especially the case in certain diseases.

Excluding cases of cholera and pregnancy, and also for the most part those of small-pox and scarlatina, Dr. Parkes found that of 203 cases under observation in University College Hospital, 12·35 per cent. of the men had temporary albuminuria, and 12·03 per cent. of the women, thus showing but little difference between the sexes in this particular. The entire per-centage of albuminous cases, both temporary and permanent, was in men a fraction over 26 per cent., and in women 22½, or together nearly one-fourth of the whole. Of 300 cases investigated by Dr. Barlow, 9 per cent. only, or one-tenth, had albuminuria.

Under temporary albuminuria, Dr. Parkes includes all cases in which the albumen disappeared from the urine previous to the patient quitting the hospital; and under permanent albuminuria, those in which it did not disappear while the patient was under observation. Practically, this division accords very nearly with that adopted by the author, though Parkes includes cases of acute morbus Brightii under temporary albuminuria, and some cases of heart disease under the permanent form.

The maladies with which temporary albuminuria is more frequently associated, are

Certain diseases of the respiratory organs, as *phthisis* and *pneumonia.*

Of 186 cases of *phthisis* albumen was found in the urine, according to Finger in 46; of these 35 died, and in two only was kidney disease found. Of 27 cases tabulated by Parkes, one only had albuminous urine.

Basham believes that the presence of albumen in phthisis always indicates a form of morbus Brightii.

Of 16 cases of *bronchitis*, the urine was albuminous in three. (Finger.)

Of 33 cases of *pneumonia*, albumen was found in the urine in 15 (Finger), and of 10 other cases in 7 by Parkes. Basham states that as the chlorides reappear the albumen disappears.

Of 14 cases of *pleurisy*, it was found but in two by Finger, and of 17 other cases in one only by Parkes. It thus appears, as might have been expected, that inflammation of serous membranes does not predispose to albuminuria.

Of 6 cases of *peritonitis*, albumen was present in but two. (Finger.)

Of 65 cases of *intestinal catarrh* or *diarrhœa*, the urine was albuminous in 8. (Finger).

Passing now to *fevers*, it appears—

That of 18 cases of *intermittent fever*, temporary albuminuria existed in 3 only. (Solon and Finger.)

Of 42 cases of *typhoid fever*, albumen was present in 9 cases. (Solon and Parkes.)

Of 88 cases of typhus (typhoid fever?), the urine in 29 contained albumen, a very large proportion. (Finger.)

Of 7 cases of *rubeola*, or measles, it occurred in 1. (Solon.)

Of 13 of *variola*, or small-pox, it was present in 3. (Solon and Parkes.)

Of 5 cases of *scarlatina*, in 3 the urine was albuminous. (Solon and Parkes.)

Of 46 cases of *puerperal fever*, it occurred in the very large proportion of 32 cases, or nearly three-fourths. (Finger.)

It is almost always present in *puerperal convulsions*.

Of 35 cases of *acute rheumatism*, albumen was found in 6 cases. (Finger and Parkes.)

In 8 cases of *subacute rheumatism*, it was found by Parkes in 1 case.

Of 6 cases of *chlorosis*, it was detected in 2 cases. (Finger.)

Of 39 cases of *disease of the heart*, the urine was albuminous in 13 cases (Finger and Parkes). Of the 4 cases of heart disease in which the albuminuria was permanent, Dr. Parkes states that the kidneys were found on post-mortem examination to be healthy in 3 cases.

Albumen is generally present in the first urine passed in *cholera*. It would appear, however, to be occasionally absent, from the observations of Busk, Begbie, Farre, and Dundas Thomson.

In the Author's Report on the Urine of Cholera Patients, published in the Appendix to Report of the Committee for Scientific Inquiries in relation to the Cholera Epidemic of 1854, various details are given respecting the occurrence in the urine of albumen, sugar, indigo, and oxalate of lime; and in regard to albumen, the following remark occurs:—

"That the urine in cholera is frequently albuminous has long been known, but it now appears that it is almost constantly so, and that this condition of the urine persists for a considerable period after the attack has passed away, facts particularly worthy of notice. I have not met with a single undoubted instance of the absence of albumen from the early samples of urine passed in cholera; while in one or two of the cases here recorded, the patients were actually dismissed from the hospital as well, and apparently they were so, although the urine still continued to be albuminous.

"In the case of Thomas Richardson, it was present in the urine from October 15th to the 28th inclusive."

These observations correspond with those of Buhl and Pfeuffer, who believe that albumen is very seldom, if ever, absent, if the first urine be examined.

Other diseases, in addition to those above named, in which albumen occurs in the urine temporarily, but in which the frequency or otherwise of its occurrence has not yet been determined statistically, are *erysipelas*, *purpura*, *paraplegia*, and *hemiplegia*.

The urine is not unfrequently albuminous in *pregnancy*.

The *amount* of albumen in the urine in *pneumonia* is usually large, and often somewhat so in *typhoid* and *puerperal* fevers; in *small-pox* and severe cases of *scarlet fever*. In most of the other cases, excepting, perhaps, some of *purpura* and *erysipelas*, the quantity is very small.

The diseases in which blood, sometimes in very minute amount, is apt to occur, are *scarlatina* and *purpura*. To these, according to Heywood Thomson, may be added *rheumatism*, *arthritis*, *typhus* (second week), *pneumonia*, *erysipelas*, *torpor hepatis*, *peritonitis*, and *chlorosis.* It is obvious that the diseases here enumerated belong to two very different types—the active and the passive.

"The urine found in the bladder after death is, I believe, universally albuminous." (Basham.)

## ON PERMANENT ALBUMINURIA.

The urine is usually persistently albuminous in acute and chronic Bright's disease, as well as in most other structural affections of the kidneys.

From Parkes's tables, it appears that the per-centage of hospital cases in which the urine was permanently albuminous was in *men* 14·71, and in *women* 10·53, showing a difference of over 4 per cent. in favour of women.

The cases from which these per-centages were calculated included a few in which no renal disease was detected or even present; but of the 39 cases of permanent albuminuria recorded, in 32 the existence of kidney disease was ascertained, and in 3 other cases not disproved: excluding these cases and the 4 cases of heart disease, the conclusion arrived at is, that permanent albuminuria is always indicative of structural disease of the kidney.

## ACUTE BRIGHT'S DISEASE.

This disease consists in congestion and inflammation of the kidneys supervening especially upon scarlatina, less commonly on the other exanthema, and occurring sometimes from other causes—as cold, and checked cutaneous exhalation.

### *Symptoms.*

It is accompanied with symptoms more or less febrile, including particularly headache: there is pallor, nausea, sometimes vomiting, lassitude, loss of appetite, pain (not often severe), or sense of aching and weight in the lumbar region, extending sometimes down the inside of the thighs. Inflammation of one or more of the serous membranes is apt to supervene, and effusion into the air-cells and smaller bronchial tubes, producing bronchitis.

As the disease progresses, general anasarca and symptoms of uræmia ensue, resulting from the retention of urea and other excrementitious substances, the consequence of mechanically impeded elimination. The first symptoms of dropsy are, a slight puffiness of the under eyelids and œdema about the ankles.

The symptoms of uræmia or uræmic poisoning are, a dry, brown tongue, great thirst, stupor, and coma, with or without convulsions, and usually terminating in death.

In advanced stages of the disease, the density of the serum of the blood is reduced from 1031 to 1020, or even less.

In those cases in which recovery is about to take place, increased elimination of water and the other urinary constituents, especially urea, and salt occurs; sometimes diuresis sets in, and the amount of water discharged is very great; in a case related by Brattler, it amounted to 12½ imperial pints.

In some cases the albumen quickly disappears wholly, in others it continues for some time, and no doubt acute nephritis in some instances lays the foundation of the chronic form of the disease which becomes developed in after years.

*Characters and Composition of the Urine.*

During the acute stage, the urine has a dull and semi-opaque aspect, is very scanty and high coloured, often perceptibly tinged with blood; and when not thus obviously coloured, yet containing blood-corpuscles, as shown by the microscope.

The *albumen* is always present in large amount, the urine sometimes becoming nearly solidified by heat.

Frerichs found it to range between 77 and 386 grains in the twenty-four hours, or between 1 and 5.

The *urea* is sometimes increased, as in other febrile diseases, but generally diminished, the diminution depending upon impeded elimination through the congested, inflamed, and obstructed kidney.

Frerichs found, as the mean of two experiments, 154·24 grains; Becquerel obtained a nearly similar amount; and Gorup-Besanez, 335·66 grains, or rather more than twice the amount.

The *uric acid* is increased, except when retained.

The *chlorine* is lessened, also from retention merely, and often disappears altogether.

The *sulphuric* and *phosphoric acids* are also diminished, and from the same cause.

The diminution in the excretion of the chief urinary constituents —including, of course, the water—as the disease progresses unfavourably, is well exhibited in a case given by Mosler.

The patient being thirsty, he drank freely :—

| | |
|---|---|
| Ingesta in twenty-four hours . . . . | 4164 |
| Egesta ,, ,, . . . . | 2385 |
| | 1779 |

In three days the body gained, simply from lessened elimination, 11 lbs.

On one day the composition of the urine was as follows :—

| | |
|---|---|
| Urea . . . . . . . . . . | 242 grains. |
| Chlorides . . . . . . . . | 42 ,, |
| Sulphates . . . . . . . . | 20 ,, |
| Phosphates . . . . . . . . | 36 ,, |
| Albumen abundant | |

On the following day the urea was reduced to 126 grains, and the chlorides disappeared.

The mean of the next three days was :—

| | |
|---|---|
| Urea . . . . . . . . . | 143·5 grains |
| Chlorides . . . . . . . . | 17 „ |
| Phosphates . . . . . . . | 26 „ |
| Albumen still increasing. | |

Before death, the cause of which was solely due to the effects produced by obstructed elimination, the urea fell in the twenty-four hours to 55·5 grains.

As recovery sets in, there is, of course, increased elimination. It is singular that the albumen does not decrease to the same extent as the other constituents increase, but is often abundant when recovery is nearly complete.

*Microscopical Characters of the Urine.*

The constituents of which the sedimentary matter deposited from the urine is made up are various.

They consist, first, of various *morphological elements*, derived either from the *kidney* itself, from the *blood* escaped from the renal vessels, or from *pus* formed as the result of acute inflammatory action; as *renal epithelial cells*, *blood* and *pus corpuscles*, sometimes *shreds of fibrine* and *clots of blood*, coloured and decolorized; of *renal casts*, *sanguineous*, *epithelial*, *granular*, and *hyaline*; and of *mucous* and *epithelial* corpuscles and cells proceeding from the genito-urinary mucous surfaces.

These structures and elements may be mixed up more or less with *deposits of certain of the urinary constituents*, especially of the urates and uric acid, and more rarely oxalate of lime.

Of these various constituents the only really characteristic ones are the renal epithelial cells, either separate or aggregated; the fibrinoid renal casts, many of them containing renal epithelial cells; the blood-corpuscles, and the deposits of urates. Occasionally, but not frequently, fat or oil-globules are found in the casts in cases of acute nephritis: they are for the most part due to changes in the effused blood, are not numerous, their occurrence is of short duration, and they are more apt to occur towards the termination of the attack, or after it has continued for two or three weeks.

When, together with the general symptoms previously described, the urine contains these constituents, especially blood-corpuscles and the casts filled with renal cells, and hence called "epithelial casts," the conclusion that the case is one of acute nephritis does not admit of doubt. In place of epithelium more or less altered, the casts sometimes contain only blood, and hence have been called "blood-casts," or both epithelium and blood-corpuscles. Some casts, quite plain, and hence termed "hyaline casts," also occur.

Before proceeding to the microscopical examination of the deposit in the urine presumed to be associated with kidney disease, the observer should make himself well acquainted with the structure and appearances of the several tissues and parts which compose the healthy kidney.

Formerly it was supposed that the presence of the *hyaline* casts was always indicative of disease of the kidneys; it is now known, however, that they generally accompany the presence of albumen in the urine, both in temporary and permanent albuminuria.

These casts, therefore, afford no proof of the existence of renal disease, neither is their absence sufficient evidence that it does not exist, since some cases of renal disease have been observed in which the urine, even to the fatal termination of the malady, was free from both the epithelial and the fibrinoid casts. The majority of such cases resemble in their general character either acute or chronic Bright's disease or waxy degeneration. Dr. Johnston, however, has described them as constituting a separate disease, which may be either acute or chronic, under the name of "*non-desquamative disease of the kidney.*"

In cases of sub-acute Bright's disease, actual kidney structures have been on some occasions met with, as renal tubes, connective fibrous tissue, bloodvessels, and even Malpighian bodies.

### *Condition of Kidneys.*

The kidneys after death are found to be enlarged, and to weigh from five to eight ounces, or even more; the capsule separates readily; the vascularity is usually increased, and commonly sanguineous spots, produced by extravasation, are observed; the vascularity is, however, very variable in degree and extent: sometimes it is considerable and general, at others the surface of the kidneys appears congested in parts only, portions being quite pale, as if from a recent deposit of lymph. In some cases the whole surface appears somewhat pale or anæmic. *On section*, the cortical portion usually is found to be more or less congested, and the same white or yellowish patches are observed as were seen on the surface, as also extravasated spots of blood.

The medullary cones are usually of a dark colour, and their sides appear compressed by the cortical substance lying between them, while their bases spread outwards into the cortex, thus presenting the form of a wheat-sheaf.

## TREATMENT OF ACUTE BRIGHT'S DISEASE.

The chief remedies comprise moderate bloodletting, as by cupping or leeches, the warm bath, counter-irritants, nauseants, diaphoretics, and the non-stimulating diuretics, as digitalis.

When dropsy supervenes, recourse must be had to *hydragogue purgatives*, especially bitartrate of potash, jalap, and elaterium.

When inflammations of serous membranes ensue, *mercury* may sometimes be administered with great benefit, although it must be cautiously employed, since it is apt to occasion rapid salivation; and even a single dose of calomel has been known to give rise to this effect.

*Opium*, especially the compound ipecacuanha powder, will sometimes be found useful in allaying pain and irritability, and in procuring sleep. Its effects on the brain must always be carefully watched, and if contraction of the pupil is noticed, it must be at once omitted.

When the acute stage is passed, occasional warm baths, warm clothing, and general friction to the skin, will prove of much service.

Alkaline remedies, as the *carbonate* and sometimes the *acetate of potash*, exert a most beneficial influence in this disease, by increasing elimination, especially as the more active symptoms subside.

In a case occurring after delivery, in which the urine amounted to only 825 cubic centimetres and the albumen to 52·5 grains in twenty-four hours, after the administration of *bicarbonate of soda* it increased to 1100, 2000, and even 3000 c.c., the albumen gradually disappearing.

Infusion of the leaves of *digitalis* applied as a fomentation in cases of retention or suppression of urine, sometimes increases the amount of urine voided very greatly.

Dr. Parkes has instituted some important experiments with a view to determine the action of gallic acid and tincture of the sesquichloride of iron on the albumen after the acute stage had passed and the dropsy had disappeared. He found, contrary to what might have been anticipated, that *gallic acid* exerted no effect upon the albumen or other constituents of the urine, while *sesquichloride of iron* diminished the albumen considerably, but did not affect the other urinary ingredients.

Lastly, tonics will be found materially to aid recovery, including especially the milder preparations of *iron*, as the citrate of iron, the mistura ferri co., the tincture of the sesquichloride, and the wine of iron.

The *prognosis* in this disease is usually favourable. In most cases, when subjected to early and efficient treatment, it terminates in complete recovery: but occasionally it lays the foundation for the occurrence of chronic Bright's disease.

In some cases of Bright's disease, particularly of the acute form, and when uræmia exists, nitric acid added to urine previously boiled causes the albumen to become first bluish green and then greenish black. These changes are, doubtless, due to the oxidizing action of the acid upon the colouring-matter, and especially on *indican*, which is often present in the urine in considerable amount. Dr. Basham considers that this appearance is of very unfavourable significance. "Experience tells me," he states, "that the development of this pigmentary condition, in combination with albumen in the urine, is of the gravest import. It is always associated with the most advanced stage of renal degeneration; and in every instance in which I have seen it, it has been quickly followed by fatal results. Lehman, in his 'Physiological Chemistry' (vol. i. p. 428), says, as far as his experience goes, it is only when uræmic symptoms have manifested themselves that this peculiarity of the urine is generally observable; and this entirely coincides with my own; or I should rather say that uræmic symptoms always follow or are associated with this change in the colour by nitric acid."

When uræmic symptoms exist, free perspiration should be induced, and the *chlorine mixture* administered, which, according to Frerichs, acts by converting the carbonate of ammonia resulting from the decomposition of the urea in the blood into chloride of ammonium.

Of the urea not excreted by the kidneys, not only is part converted into the volatile carbonate in the blood, but part, as so clearly explained by Dr. Goodfellow, escapes by the stomach and bowels as urea, to be quickly changed into the carbonate.

## CHRONIC BRIGHT'S DISEASE.

Several very distinct forms of renal disease, even if they do not constitute distinct diseases, have been and are still included under the name of chronic Bright's disease; but since they have all much in common, it will be convenient to describe first those symptoms which belong equally to the several forms of chronic kidney disease, and afterwards, so far as they have been determined, those that are distinctive.

The chief forms of non-acute disease of the kidneys are, *chronic inflammation of the kidney*, termed by Johnston *chronic desquamative nephritis*, a result sometimes of the acute disease, and leading to *granular* or *contracted kidney, fatty degeneration*, and *lardaceous, waxy*, or *amyloid degeneration*. Besides these there are, however, some other varieties, which will be described in the proper place.

### *Symptoms.*

The symptoms, are usually, more or less pyrexia, although fever may be even at first absent, since it does not appear that chronic Bright's disease is always attended by an acute inflammatory stage; sense of uneasiness or weight in the lumbar region; diminished excretion of urine, which is permanently albuminous; frequent micturition, nausea, and occasional vomiting; and, as the disease progresses, dyspnœa—at first occasional, and which is sometimes the earliest symptom to attract attention; œdema of the lungs and glottis; chronic bronchitis; local congestions and inflammations; usually dropsy, the face soon becoming puffy, and uræmia, followed by certain cerebral complications. The whole of these symptoms, except the persistence of the albumen in the urine, may be wanting, and yet chronic disease of the kidney exist; the dropsy, even at the last stage, is not unfrequently absent. Hæmorrhage from the nose has been observed to occur in several of the cases recorded of chronic Bright's disease.

Other complications and accompaniments of chronic renal disease are—disease of the liver, especially cirrhosis; severe diarrhœa; chronic rheumatism, first noticed by Dr. Christison; hypertrophy of the heart, usually without, but sometimes with valvular disease; amaurosis; and particularly coma, convulsions, and apoplexy.

The cerebral symptoms resulting from kidney disease are *stupor*, which may be temporary or terminate in death; a combination of *stupor* and *coma; convulsions*, with or without coma; or, as so well described by Dr. Addison, there is "a state of *dulness of intellect, sluggishness of manner*, and *drowsiness*, often preceded with *giddiness, dimness of sight*, and *pain in the head*," and proceeding either to *coma* alone, or to *coma* accompanied by *convulsions*. Further, it should be remembered that the coma bears no constant relation to the quantity of urine voided, which may be large—but more to the amount of urea retained.

It should never be forgotten that these cerebral symptoms come on in the most insidious manner, so that they require to be carefully watched.

In the peculiar rheumatism which sometimes accompanies Bright's disease, the fasciæ would appear to be more affected than the joints, and the pain is in excess of that which might be anticipated from the small extent of the swelling; in fact, it partakes much of the neuralgic character.

Although renal disease produces various pulmonary complications—as œdema, bronchitis, pleurisy, and pneumonia of a low type—it does not predispose to phthisis. Indeed, Dr. Bright was of opinion that the two were opposed. The reverse, however, by no means holds good: the tubercular diathesis and the existence of phthisis do doubtless predispose to disease of the kidneys; thus not unfrequently in phthisis those organs are found to be affected with fatty degeneration, the kidneys not being very much increased in size.

Dr. Johnston describes a form of chronic Bright's disease the chief characteristic of which he states to consist in the absence of renal epithelium, and hence he has termed it "*non-desquamative disease of the kidney*." It may be acute or chronic, or associated with fatty or amyloid degeneration. This absence is explained by Dr. Basham in two ways: "The epithelium decreases from one of two causes, favourable and unfavourable. The first in consequence of the gradual return to the equilibrium of healthy action, by the subsidence of the disturbing cause—just as in catarrhal inflammation of other surfaces, as the balance of the circulation is restored the epithelial exudation diminishes, and at last disappears. The second and unfavourable cause of the absence of epithelium depends chiefly on the disintegration of the cell-structure and its retention in the uriniferous tubes: abortive cells and granular and fatty molecules are seen impacted together, closing up the canals and Malpighian bodies."

Neither of these explanations applies to several of the cases described by Dr. Johnston. In Agar's case, while the epithelium was perfect, appearing only more granular than usual, the canals of the tubules were free; and in the others, the particulars of which are given, the epithelium was equally perfect, the canals for the most part pervious, and the casts, few in number and but seldom met with, were very small, having the exact diameter of the canal when lined with its epithelium.

Dr. Johnston considers that in these cases there is thickening and obstruction of the capillaries, an opinion in which he is corroborated by Dr. Gairdner.

The appearances presented by the kidneys vary according as the disease is acute or chronic; thus, they may be red and congested, or pale and waxy, or even fatty, but they are nearly always increased in size and particularly in density; their surface is smooth and non-granular. The urine is highly albuminous.

### *Characters and Composition of the Urine.*

The urine, as a rule, is scanty, usually pale, but sometimes more deeply coloured than natural, and the solids of all kinds are diminished, the diminution being due mainly to obstructed elimination, arising from mechanical obstacles in the kidney. Hence, in chronic renal disease, the urine is of low specific gravity, from 1008 to 1014, ordinarily about 1012.

The *acidity* of the urine is much less than in health; but there are some exceptions.

The *water*, though usually much reduced in amount, is subject to great variation, some of the causes of which may now be briefly noticed.

To whatever extent or in whatever way the kidneys are diseased, and the passage of the urine through them impeded, they are yet rarely so much so as not to be affected more or less by the same influences which act upon those organs in a state of health, and which determine the amount of urine secreted by them.

Thus, as in health, the urinary water is ordinarily *increased* when a large amount of fluid is drunk; as also by checked cutaneous exhalation, and by diuretics. On the other hand, it is *diminished* by fever, vomiting, diarrhœa, and by dropsical effusion.

Other special causes of variation depend upon disease in the liver, heart, and lungs. Disease of these organs, especially cirrhosis, doubtless affects the circulation through the kidneys and increases the pressure of the blood upon the walls of the renal vessels.

Becquerel explains the diminution of water in this disease in another way. He states that it gives rise to febrile urine, that is, to urine which is dark-coloured and scanty.

Of course, at the very onset of the disease, the urine may be either normal in amount, or only slightly lessened, the diminution increasing as the disease advances, especially when dropsy and uræmia set in; and in some instances it is entirely suppressed towards the fatal termination.

Dr. Parkes has given the quantities of urine passed in 9 cases of kidney disease, together with the condition of the kidneys themselves, as ascertained after death; three of these cases are Frerichs', and the other six his own. In six of these the kidneys were "atrophied," and the amounts of water voided in twenty-four hours were 19½, 23, 33, 34, 35, and 47 ounces: in one it was 59 ounces, the size of the kidneys being nearly normal; in one 33 ounces, the kidneys being of medium size, lardaceous, and weighing 3½ ounces each, but the patient was purged with elaterium: and in the ninth it amounted to as much as 90 ounces, the kidneys being very large, and weighing 10½ and 9½ ounces each.

It is thus rendered obvious that the greatest decrease occurs in connexion with the atrophied kidneys.

Parkes also gives a table of 10 cases of kidney disease, distinguishing between those in which uræmia was present from those in which it was absent; this shows very strikingly not merely the diminution of water during uræmia, but also of the urinary solids generally.

| | Water, 24 hours. | Specific gravity. |
|---|---|---|
| Six cases without uræmia . . | 61½ . . | 1014·3 |
| Four cases with uræmia . . . | 38 . . | 1014·75 |

The decrease is particularly obvious in the urea.

Frerichs gives the range of the urea in 17 analyses, as from 15·17 to 262·17 grains, in the twenty-four hours, and the mean of the whole as 99 grains.

The results of Rosenstein's analyses approximate closely to the above figures. The range of urea was between 16·06 and 249·61 grains, and the mean 112 grains.

The diminution of the urea results, to a great extent, from the same causes as occasion a lessening of the urine excreted, and is due not so much to lessened formation as to retention; the greatest reduction being coincident with marked uræmia.

Sometimes, indeed, in uræmic cases, the urea is absent. In a case of Frerichs', it was only 15 grains, while in one recorded by Schottin the amount discharged in the urine two days before death was 93·04 grains per day.

Usually the diminution of water and urea go together, but this is not always so. The amount of urea may be small in proportion to the water: thus a patient of Dr. Parkes' passed, five weeks before death, 37 ounces of urine, which contained only 134 grains of urea.

Although *the rule* is that the urea is decreased in chronic Bright's disease, some *apparent exceptions* are recorded, these being explicable by reference to the diet, to febrile action, causing increased formation of urea, to absorption of dropsical fluids containing urea, or to increased elimination following retention.

In a case of Parkes, in an advanced stage of the disease, the excretion, being the mean of two days, was of albumen 422·8 grains, and of non-albuminous solids 981 grains.

In a case related by Schottin, in which there was uræmia, only seven days before death 305 grains of urea and 267 grains of albumen were excreted.

In Mosler's case, before referred to under the head of Urea, the mean of three days' excretion was 620 grains of urea.

A very important question in connexion with chronic disease of the kidneys is, whether there is lessened *formation* of urea as well as diminished excretion. Although this point cannot be considered as decided at present, yet there are some circumstances which seem to favour the idea of decreased formation: thus it is obvious that in this class of diseases the nutritive functions, the repair and waste of the tissues, are much at fault; and again, instances are not of unfrequent occurrence in which for a long period the urea discharged with the urine is much below the average; and yet no symptoms of uræmia have arisen, as it might be fairly presumed they must do were an excess of urea retained in the blood.

The *uric acid* is even lessened to a greater extent than the urea, probably from its comparative insolubility; and deposits of the urates are uncommon.

The *extractives* are lessened.

*Sugar* is occasionally present, and this in cases which do not present any diabetic symptoms.

The *pigment* is also generally diminished, and this not merely from retention, but from the impoverished condition of the blood and the smaller number of red corpuscles contained in it, from destruction of which the normal urinary pigment is derived.

In some cases, in which the urine is brownish or reddish-brown, the colour is due not to *normal pigment* but to *hæmatin*.

When boiled with a small quantity of nitric acid, the urine, in many cases of chronic kidney disease, turns of a bluish or violet colour, owing to the presence of *indican*, or, as Heller would say, to his *uroxanthin* and the formation of *uroglaucin*. Occasionally, on exposure to the air for some days, the urine becomes more or less bluish, or a bluish scum forms on its surface: this change is doubtless due to the oxidation of the *indican* and the production of *indigo*.

The *phosphates*, *sulphates*, and *chlorides* are all diminished.

Dr. Parkes points out that in Rosenstein's cases the *chlorine* appeared to be in increased ratio to the albumen. When effusion is occurring, much of the salt escapes with the fluid effused, and when this is reabsorbed, and diuresis occurs, a large excess of the chlorides will be found in the urine.

The amount of *albumen* in the urine of course varies greatly, not only in different cases, but in the same cases on different days: it is greater during the day than at night, owing partly to the movements of the body, and partly, as already noticed, to food. No particular relation can be traced between the quantity of this substance eliminated and that of any of the other urinary constituents. When the albumen is in large amount, it is said that the uric acid and the chlorides are usually much lessened; the urea, however, is sometimes not reduced to the same extent.

In Frerichs' cases the range was between 59 and 286 grains in the twenty-four hours. In Rosenstein's cases it was from 7·72 to 291·81 grains.

The mean of Schmidt's cases was 204 grains, and of those of Gorup-Besanez 237 grains.

In one case Parkes found the enormous quantity of 545 grains in the urine of twenty-four hours.

The amount sometimes approaches, and is even said in some rare cases to exceed, that of the serum of the blood.

The drain of albumen from the blood of course lessens the specific gravity of its serum; from about 1031, the health standard, to 1014, and even 1008.

In a small proportion of cases the albumen disappears from the urine altogether, owing probably to obstruction.

*Fatty* or oily matter is sometimes present in the urine in chronic disease of the kidney, but not often in large quantity, except the urine be chylous, or after large doses of oil. More commonly it is present in very minute amount in the renal cells and tubes, especially in that form of the disease, to be described hereafter, termed fatty degeneration. The amount of oily matter, chiefly *oleine*, found by Kletzinsky, ranged in 5 cases between 37 and 57 hundredths of a grain, and in a sixth case it amounted to 1·93 grains.

Beale succeeded in extracting cholesterine from the fatty matter of the urine in several cases of fatty degeneration of the kidneys.

### *Microscopical Characters.*

It has already been stated that the presence of renal casts in the urine is not always indicative of disease of the kidneys, and also that their absence is no proof that disease of those organs does not exist. Casts are present in the majority of cases of temporary albuminuria, and they are sometimes absent, or nearly so, in cases of permanent albuminuria connected with structural disease of the kidney; indeed, by Johnston, their absence, as previously pointed out, is alleged to be characteristic of a certain form of renal affection which he designates the non-desquamative disease. Mayer states that they may even be present and the urine free from albumen. The epithelium may be absent as well as the casts.

The casts consist of a fibrinoid matter as the basis. In many cases they are entirely composed of this material, and do not enclose epithelium, or other cell or substance; they are then termed "hyaline." These plain casts are met with more or less abundantly in the majority of renal diseases; they occur of two sizes, and hence are called "large" and "small" casts: the former are nearly the width of the renal tubules, and measure about the $\frac{1}{500}$th of an inch in diameter, and the latter only half this size—namely, the $\frac{1}{1000}$th of an inch.

The large casts are considered to be formed in the tubes *denuded* of their epithelium, and the small casts in those which still retain their epithelial lining. Of the large casts two sizes are met with, the one corresponding with the diameter of the convoluted tubes of the kidney, and the other, much larger, with that of the straight tubes: the former have been observed by Dr. Beale to be even enclosed within the latter. We have termed these casts fibrinoid, but their exact composition is undetermined, and probably varies; by some, the material of which they are composed has been compared to the exudation of croupous inflammation; the blood-casts consist, no doubt, mainly of fibrin.

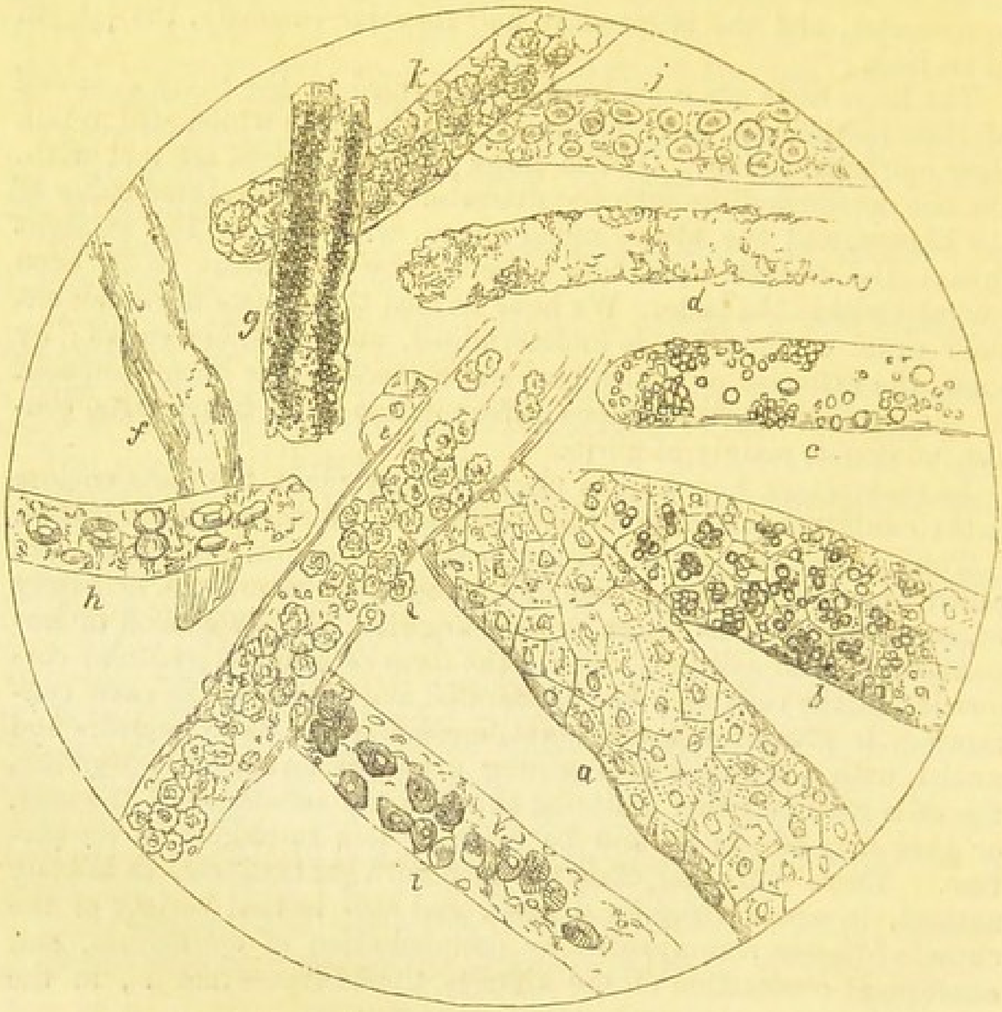
In many cases, however, in place of being plain, the casts enclose in their substance various morphological and other elements and bodies.

Thus sometimes they include renal epithelium, and hence are called "epithelial" casts. The epithelium may be normal, or nearly so, consisting of cells more or less angular: it may consist of imperfectly-formed epithelial cells in the form of rounded granular corpuscles, or the cells may be degenerated and abortive, the casts containing, in greater or less amount, molecular and fatty matters and nuclei, with a few cells approaching a perfect formation. Further, the cells may be either scattered through the substance of the cast, or they may adhere to and be more or less imbedded in its surface. These epithelial casts are met with particularly, as already noticed, in acute Bright's disease, and also in that variety of the chronic disease accompanied by desquamation of epithelium, and consequent contraction of the kidneys themselves—that is, in the chronic desquamative nephritis of Johnston.

In some cases a variety of other elements or structures occur, either in the free state, or enclosed in the casts, as compound nuclear cells, including the large exudation or inflammation, and the smaller pus-corpuscles; free nuclei; crescentic or spherical botryoidal or mulberry bodies, destitute of cell-wall, and apparently made up of aggregations of shining or resplendent nuclei; free fat molecules, or epithelial cells and casts filled with molecules, as in fatty degeneration of the kidneys; and pulverulent or granular matter, free and enclosed in the casts. These several elements do not of course occur alike in every case of renal disease, but some in one and some in another, or they may all be absent. The compound nuclear cells so much larger than pus-corpuscles occur commonly in inflammatory affections of mucous membranes. When the nuclei are numerous, the term glomerulus has been applied to them, and they then appear to correspond with the compound inflammation globules of Gluge.

The cells of renal epithelium, whether normal or diseased, occur

FIG. 71.




RENAL CASTS:—*a. Normal renal tube. b. Tube with epithelium affected with fatty degeneration. c. Casts with droplets of oil. d. Granular cast. e. Altered epithelial cast. f. Hyaline cast. g. Cast with urate. h. Cast with dumb bells of oxalate of lime from a cholera patient. j. Blood cast. k. Pus cast. l. Cast with cells stained with bile.*

in the urine, of course in the free state, as well as enclosed in the casts, and may be either separate or aggregated.

Sometimes the casts, in place of enclosing epithelium, granular or fatty, contain either blood, or more rarely, pus-corpuscles, forming "blood" and "pus" casts, the former of which are usually stained with hæmatin. (Fig. 71.)

At others, they enclose deposits of uric acid, urates, or oxalate of lime, both in the form of octohedra and dumb-bells. These deposits are frequently seen imbedded in the casts thrown off by the tubules in the first few samples of urine passed during recovery from cholera. (Fig. 72, p. 337.)

In addition to the morphological elements proceeding from the kidney, epithelium derived from different parts of the genito-urinary mucous membrane is sometimes met with, the characters of which will be found described under the head of Mucus.

Blood, as evidenced by the presence of blood-corpuscles in the urine, is less frequently found in cases of chronic morbus Brightii than in those of the acute form and in smaller amount.

It is beyond question that by means of the several forms of casts, cells, and other structural elements just noticed, most of the varieties of Bright's disease may be diagnosed; and Dr. Basham affirms not only the perfect practicability of the diagnosis, but asserts that even the progress, whether favourable or unfavourable, of the disease, may be thereby determined.

"Attention," he writes, "to the microscopic character of these casts will at any time enable the practitioner to estimate the nature and intensity of the disease, its advance or decline, its form, and its probable termination. The blood-casts represent the period of active hyperæmia or hæmorrhage; the coarsely granular epithelial cast, with its compound inflammation-corpuscles, and accompanied by amorphous granular flakes stained with hæmatin, the period of inflammatory exudation; the finely granular semi-transparent casts, with scattered epithelial and granule cells, the subsidence of that stage; transparent casts with compound cells, with isolated resplendent molecules and grape-like clusters of granules, represent a stage of chronic subacute disease of grave import; and if these casts become more and more loaded with large and gradually-increasing fat granules, and even oily drops, the progress of fatal fatty degeneration is clearly marked."

It must not be forgotten, however, that these several elements may be absent, and yet disease exist, as in the advanced stage of chronic nephritis, in Johnston's non-desquamative disease, and rarely in fatty degeneration.

Hitherto chronic Bright's disease has been treated of generically, and as one disease: an endeavour will now be made to discriminate between some of its principal forms or varieties; and first, that modification of it may be noticed which Johnston has named chronic desquamative nephritis.

## CHRONIC NEPHRITIS, OR CHRONIC DESQUAMATIVE NEPHRITIS.

This disease is characterized by the long-continued presence in the urine of renal epithelium, either free or entangled in the fibrinoid casts, in a more or less disintegrated condition; by the occurrence of granular and hyaline casts; more or less fatty matter: by a gradual destruction of the epithelial lining of the tubules; by obliteration of the tubules themselves; and finally by a wasting of the substance of the kidneys.

It occasionally, but not very frequently, follows the acute form of the disease; more generally it originates gradually in some derangement of the general health, and especially is often associated with the gouty diathesis; its origin may sometimes be traced to intemperance.

This form of renal disease is usually unattended by dropsy, and is very frequently accompanied by symptoms of cerebral disease from uræmic poisoning.

### *Morbid Appearances of the Kidneys.*

As already noticed, the kidneys, in the advanced stage of the disease, are wasted and sometimes nodulated: this wasting affects at first especially the cortical substance, which is thinner than natural, but subsequently the cones themselves become involved. The lobular markings or divisions, as seen on the surface, become confused and obliterated, and there is general decreased vascularity.

Sometimes there is little or no intra-tubular deposit, in which case the kidneys often become reduced to one-fourth or one-fifth their natural size, and the surface retains in a great degree its smoothness; in general, however, it is more or less white, firm, and corrugated, with patches of vascular engorgement.

In other cases, there is more or less deposit, the kidneys being sometimes nearly their average size: the deposit is not usually distributed equally throughout the tubules, but is most abundant in the convolutions of certain sets of tubules near the surface of the kidney. When the deposit is very abundant, the loss of vascularity is greatest, and when it is recent, the surface of the kidney retains its smoothness, but after a time the deposit contracts, forming white or yellowish, firm *granulations* varying in size from a pin's head to a pea.

The atrophied kidneys are considered by some to represent the third stage of Bright's disease, the first being that of inflammatory engorgement, the second that of effusion with increased weight, and the third that of atrophy and more or less complete disorganization. This view, although plausible, is not consistent with the results of clinical observation; indeed, the peculiarities of this form of renal disease are so great, as shown by the absence of dropsy, the liability to cerebral complication, and its frequent connexion with the gouty diathesis, whence Dr. Todd named the atrophied *the gouty kidney*, as to separate it by well-defined characters from the other forms of Bright's disease.

The disease is often more advanced in one kidney than the other, but usually both organs are affected.

Occasionally patches of a pale colour, not elevated and quite isolated, are observed on the surface of the kidney; these in some cases pass into the fine granulations, but in others they remain in this condition throughout. Rayer has figured this form of deposit in connexion with simple *rheumatic* and *hæmorrhagic* nephritis.

## CROUPOUS DISEASE OF THE KIDNEY.

Dr. Basham describes a form of Bright's disease attended with dropsy, and usually *without tube casts*, in which "the sediment is a flocculent cloud, in which membranous-looking shreds are visible to the unaided eye. These are seen to consist of aggregations of pus-cells, held together in a flaky form; many pus-cells are isolated and free, and mixed with them are these amorphous fibrinous masses stained with hæmatin. This state of the urine is, I think, significant of an inflammatory process different from that which is going on when tube casts are present; it is allied to the *croupous* form of inflammation of other portions of mucous membrane. Eventually it may lead to fatal disorganization. But the renal dropsy in these cases is more tractable and more easily subdued, and the conditions of the patient are more hopeful."

Epithelium from the calyces, pelvis, and ureter were seen in the case recorded by Basham, indicating that those portions of the kidney were to some extent the seat of the inflammation.

## SUPPURATIVE FORM OF BRIGHT'S DISEASE.

This is a somewhat rare form of Bright's disease, distinguished from ordinary pyelitis in its history, in the larger amount of albumen in the urine, and in the presence of dropsy.

As in pyelitis, the urine when passed is milky, and throws down a purulent deposit.

The kidneys in a case the particulars of which are recorded by Dr. Basham, presented the following appearances: they were irregular and lobulated, the capsule non-adherent, the cortical substance was of a madder-red, speckled with numerous groups of yellowish granules. At several points the exudation had undergone purulent softening: from the apex of the cones in both kidneys could be pressed a yellow purulent fluid. Many of the convoluted tubes and Malpighian bodies were found to be filled with pus-cells; indeed, the starting-point appeared to be in these latter bodies.

## ON CYSTIC DISEASE OF THE KIDNEYS.

This disease is usually described as one of the consequences of chronic inflammation and degeneration of the kidney; it is, however, a rare complication of that form of Bright's disease, and since its anatomical characters are so peculiar, it seems advisable that it should be separately described.

Sometimes the substance of one or both kidneys is occupied by vesicles or cysts, which vary greatly in number and size, being in some cases so small as scarcely to be visible with the naked eye, and in others as large as a marble or even a walnut.

The small or microscopic vesicles are filled with fluid, usually serum, but the contents of the larger cysts are various, and they may contain tesselated epithelium, granular cells, oil-globules, uric acid, xanthic oxide (Simon), blood, and a stiff matter like "glue."

A difference of opinion exists as to their origin. Simon thus explains it. As the result of subacute inflammation of the kidney, some of the tubes become blocked up; this obstruction occasions rupture of the tubular membrane, the contents being effused; these containing the germs of cells, become developed until at length vesicles and cysts are formed. In this manner the kidney is changed at first into an aggregation of microscopic vesicles, which either become ruptured or increase in size and destroy its texture.

The above explanation is that which is the more generally received, and which has been confirmed by Rokitansky and Paget. Dr. Johnston, however, ascribes their origin to vesicular dilatations of the tubules, unaccompanied by rupture of the limitary membrane, while Dr. Gairdner regards them as exceptional productions, not essentially connected with the progress of desquamative degeneration, and states that they have all the appearance of being formed *within* the tubules, although they afterwards become separated from them. He is also of opinion that cysts may be formed by the occlusion and isolation of portions of tube, and in one case he observed that the Malpighian capsules were occupied by distinct cysts. Mr. Quekett also found in a case examined by him that the formation of the cysts evidently commenced in the Malpighian bodies beneath the capillary plexus.

Dr. Basham states that cysts are often seen in the kidneys of old people not suspected to be labouring under renal disorder.

There are no symptoms by which the presence of the cysts is indicated during life.

## WAXY DEGENERATION OF THE KIDNEY.

In this form of renal disease, the kidneys are much enlarged, weighing in some instances ten ounces each, and present a marbled, mottled, or pale transparent and waxy appearance. The capsule may usually be readily removed, disclosing a smooth or granulated surface beneath. The capillaries are for the most part rendered impervious, or are even obliterated, while the larger veins, distributed in a stelliform manner, are alone injected; occasionally petechiæ are found. This obliteration of the capillaries is preceded by a high degree of congestion of the kidney, as shown by the enlarged veins on the surface and the occurrence of petechiæ.

In some instances the Author has met with kidneys much enlarged, weighing nine and ten ounces each, and of a liver colour and consistence; the epithelium was perfect, but more granular than natural, and the canals of the tubes free. Kidneys in this condition probably represent the early stage of amyloid or fatty degeneration.

The increase in size is due to the effusion of an unorganized material: of the renal tubules some contain epithelium, which presents an opaque and granular appearance; others are destitute of epithelial lining, and contain large waxy casts, but in the more advanced condition of the disease, the tubular structure appears to be entirely obliterated, and there is a general infiltration of the unorganized material. According to Gairdner, dilatation and thickening of the tubes are characteristic of the extreme stages of waxy degeneration, the dilated tubes being twisted and varicose.

In some cases, while there is considerable enlargement and increased density of the kidney, which presents all the usual outward characters of waxy degeneration, the tubular structure appears but little affected, appearing only more opaque than usual; no effusion can be detected, although the epithelial cells seem to contain more solid contents, but there is great obstruction or obliteration of the capillary vessels. Such cases Johnston includes under his chronic non-desquamative disease: he ascribes the increase of size and weight of the kidney to simple hypertrophy of the glandular tissues.

Virchow states that the coats of the small arteries are usually first affected, the glandular substance becoming subsequently implicated. The walls, especially the muscular coat of the arteries, become thickened by infiltration, their calibre reduced, and thus the circulation through them is arrested. In the kidney, the vessels of the Malpighian bodies and the afferent arteries undergo this change. The cells of the parenchyma lose their granular character, and become homogeneous, being converted into *corpora amylacea*.

This form of degeneration is best detected by brushing a section of the kidney over, first with a solution of iodine, and then with dilute sulphuric acid; on the application of the iodine, red dots and streaks appear, corresponding with the Malpighian bodies and afferent vessels; these, when the acid is used, change to reddish-blue, deep blue, or even black. It appears probable that the so-called corpora amylacea may occur in the urine.

*Corpora Amylacea.*—"Roundish bodies with concentric layers, which give the peculiar violet colour with iodine and sulphuric acid, have been noticed by two or three observers. Whether they indicate the lardaceous or so-called 'amyloid' degeneration of the kidneys is not yet certain, but it is probable." (Parkes.)

Dr. Johnston believes that he can diagnose waxy degeneration during life by the absence in the urine of the renal epithelium, and the occurrence of "the large waxy casts."

"The small waxy casts" are stated by Johnston to occur particularly, although sparingly, in certain cases of what he calls chronic non-desquamative disease of the kidney, but they are met with also in the waxy or amyloid degeneration of the kidney; and it is certain that they are of frequent occurrence in the urine, wholly independent of disease.

In cases of chronic kidney disease, especially those forms of it ending in waxy and fatty degeneration terminating fatally, the structural changes found on post-mortem examination are by no means confined to the kidneys, but extend, more or less, to nearly all the other organs and tissues. The liver particularly is usually found to be affected in the same manner as the kidneys, and when the case is one of fatty degeneration, the muscular fibre of the heart and the coats of the bloodvessels in general are similarly affected.

This degradation of structure is just what might have been expected would be found, when we remember that this disease either originates in a depraved condition of the blood or else quickly occasions its vitiation.

Further, in most forms of chronic Bright's disease, certain white spots are observed on the surface of the heart, termed *maculæ albidæ.*

## FATTY DEGENERATION OF THE KIDNEY.

Fatty degeneration of the kidneys may occur as a sequence of waxy degeneration, and less commonly of acute and chronic nephritis; but usually it would appear to form a special modification, if not disease, having a separate constitutional origin, and, like the waxy or amyloid disease, often, but not constantly, coexisting with a similar disease of other glandular organs, especially fatty degeneration of the liver.

It is diagnosed *during life* by the occurrence in the urine of renal epithelium, either free or enclosed in the fibrinoid casts containing globules of oily matter, and by the occurrence of free oil-globules, as well as casts more or less filled with them.

The existence of this disease must not be inferred from the temporary presence in the urine of a few free oil-globules, or from a few small globules in either the renal cells or casts. We can only safely arrive at the conclusion that fatty degeneration of the kidneys does really exist when the quantity of oil in the cells or casts is considerable, and its presence persistent.

### *Pathological Appearances of the Kidneys.*

The kidneys are usually increased in size and weight, weighing sometimes over ten ounces: they are of a pale colour, and they present a greasy or fatty appearance.

Two forms of fatty kidney have been described—namely, the *granular* and the *mottled* form.

In the *granular* form, the fatty matter is irregularly dispersed throughout the cortical portion of the kidneys, constituting characteristic granulations: if one of these be cut into, and examined with the microscope, the fatty matter will be found to consist of globules, some of which are free; some contained in cells, which are also free, but the germs of which were no doubt originally derived from the ruptured renal tubules; and others aggregated within the canals of the tubules themselves, or in their casts. Much of this oily substance is doubtless derived from a transformation of effused albuminous compounds, as in cases of extensive fatty degeneration occurring in the muscular tissue.

In those portions of the kidney which are less diseased and are not the seat of granular deposit, the tubular structure retains more or less of its normal character, the tubes being lined with epithelium, which, however, is usually more opaque and granular than in the healthy state. Occasionally the canals of the tubules are occupied with the fibrinoid casts.

In the *mottled* form of fatty kidney, which is of less frequent occurrence than that already described, the kidneys are not only enlarged, but they are softer than natural, and œdematous; the surface is smooth, and either uniformly pale, or more usually mottled by the occurrence of patches of congested vessels interspersed amongst the paler fatty deposit; occasionally hæmorrhagic spots are observed. As in most other cases of organic renal disease, the cones retain to a great extent their normal appearance and structure, even to the last. From a kidney affected with this form of fatty degeneration, as much as six per cent. of oil may sometimes be extracted.

The tubes on a microscopic examination are found to be everywhere distended with oily or fatty matter; the epithelial cells, which are usually perfect and adherent to the walls of the tubes, being filled with droplets of oil, in the same manner as are the cells of the liver, when that organ is affected with a similar disease.

## TREATMENT OF CHRONIC BRIGHT'S DISEASE.

In the treatment of the chronic forms of this disease, we should never lose sight of the fact that they are rarely local affections, but frequently have a constitutional origin, which is often the *fons et origo mali.*

Having ascertained that the renal disease has originated in some constitutional derangement or condition, the nature of this should, as far as practicable, be determined, whether it is connected with the scrofulous diathesis, or with a gouty tendency.

We must also endeavour to diagnose the precise form or variety of the disease, whether the case is one of atrophy, of amyloid or fatty degeneration. By repeated and careful microscopical examination of the urine, this point may frequently be determined.

Next we should endeavour to learn the exciting cause of the disease, whether previous attacks of inflammation of the kidney, intemperance or other excesses, typhus, exposure to cold and wet, anxiety, overwork of body or mind, &c.

Having thus become informed as far as possible of the particulars of the case, we are in a position to undertake the treatment with the best chance of success.

The prognosis in all forms of chronic renal disease is not favourable; much, however, depends upon the stage which it has reached, the extent of impairment of the eliminative functions of the kidneys, as ascertained by an examination of the urine, and the extent and nature of the complications—as whether the disease of the kidney is but the evidence of the existence of a similar affection in other organs, as the liver, or whether it coexists with disease of the heart, or is complicated with bronchitis, serous inflammation, dropsy, uræmia, coma, or convulsions.

If the disease is in an early stage, it may possibly be cured: in all cases and stages, much benefit is usually derived from treatment, great relief obtained, and life prolonged.

In nearly all cases it will be necessary to improve the constitutional powers; by generous and carefully regulated diet, by pure air, especially that from the sea, and by the administration of suitable tonics, particularly some of the less stimulating preparations of iron, including the citrate and the sesquichloride of iron. The administration of iron is imperatively demanded, because of the altered state of the blood and paucity of red corpuscles. Amongst the most powerful remedial measures which can be resorted to is a sea voyage.

If the scrofulous diathesis exists, the measures and remedies employed must be such as have been found most suitable for its correction.

If the disease is associated with a gouty tendency, this must be specially treated, the diet must be most carefully regulated, and antacids and tonics, with in some cases colchicum and hydriodate of potash, must be judiciously administered.

In most cases, especially those in which dropsical effusion has occurred, the elimination by the kidneys must be promoted, as this being so defective is the cause of the majority of the secondary complications, as the serous inflammation, dropsy, uræmia, coma, and convulsions.

For this purpose some of the non-stimulating diuretics may be carefully and occasionally administered, as nitrate of potash, digitalis, combined in some cases with blue pill, (the effects of which must be closely watched, however,) infusion of scoparia, &c.

It is an objection to the diuretic alkalies, that while they increase the normal solids, they likewise augment the amount of albumen contained in the urine.

The digitalis may be given in the form not only of tincture, but in that of infusion, in doses of from two to six drachms; or a strong infusion of digitalis made with one ounce of the powdered leaves to a pint of water, may be kept constantly applied to the abdomen, by means of spongio-piline, especially in cases of ascites. This plan is sometimes successful when the internal administration of the remedy fails. It may be applied to the legs in cases of general anasarca.

Care must also be taken to relieve the kidneys by promoting elimination from the bowels and skin.

The bowels must at all times be well regulated, and occasionally, according to the nature of the case and the symptoms, a free purgation with bitartrate of potash and jalap, or elaterium, will often give great relief, while the skin must be kept in action by friction and warm clothing. Cold, damp, and sudden changes of temperature, must be most carefully avoided. Diaphoretics, as citrate of ammonia, given at night, will sometimes be found useful.

The extent to which the eliminative treatment is carried must depend entirely upon the circumstances of each case, upon the quantity and specific gravity of the urine, and upon the general symptoms. Where the quantity is considerable, and the gravity comparatively high, as 1018 or 1020, and where there is an absence of dropsy and uræmia, increased elimination may not be needed at all; and this is often the case in amyloid and fatty degeneration of the kidney—it is in the contracted kidney that it is so essential. It should be remembered that diuretic and purgative remedies are administered in chronic kidney disease on the principle of a choice of evils, and that when they are not absolutely called for by the nature of the case, their administration is positively hurtful.

Sometimes occasional doses of blue pill combined with opium or Dover's powder will be found of much service in checking inflammation of the serous membranes; but counter-irritants must also be employed.

The dropsy is usually general: it is seldom that ascites exists to any great extent, except in those cases in which there is hepatic obstruction and disease as well. For the relief of the anasarca it is sometimes necessary to puncture the legs, and for that of the ascites to tap the abdomen. The punctures should be some half-dozen in number, and it is sufficient if they penetrate into the subcutaneous cellular tissue.

There is one ingredient in the urine in Bright's disease, the amount of which it is very desirable should be lessened—namely, the albumen. The means we possess of accomplishing this object are not very effective, are more general and indirect than special; moreover, in augmenting elimination by the kidneys generally, the remedies employed are apt to increase the albumen as well.

Nevertheless, this object must not be lost sight of, and to some extent our treatment in this respect will be successful.

Gallic acid, given in doses of ten or more grains three or four times daily, will sometimes lessen the albumen.

Tincture of the sesquichloride of iron exerts a more constant effect than even gallic acid.

Infusion of pomegranate, alum, and sulphuric acid, may also be employed for this purpose.

When the facts already adverted to are recalled to mind—namely, that exercise increases the albumen in the urine, and that the amount after food is often much augmented, the necessity for rest in the horizontal position, and particularly after meals, becomes apparent.

It is, however, through diet and suitable tonics, whereby the condition of the blood is improved, that the diminution in the amount of albumen excreted is best effected.

In all cases of renal disease the diet must be regulated with the greatest care, as previously insisted upon: it should be more animal than vegetable, for while the former lessens, the latter increases the albumen. In fatty renal degeneration, it is obvious that the patient should be restricted in the use of oily and fatty food, and as a rule, alcohol should be abstained from in all cases of kidney disease, as tending, while it excites the kidneys, to lessen elimination.

When cerebral complications arise, the treatment should be derivative and eliminative, and should consist of blisters, purgatives, and diuretics.

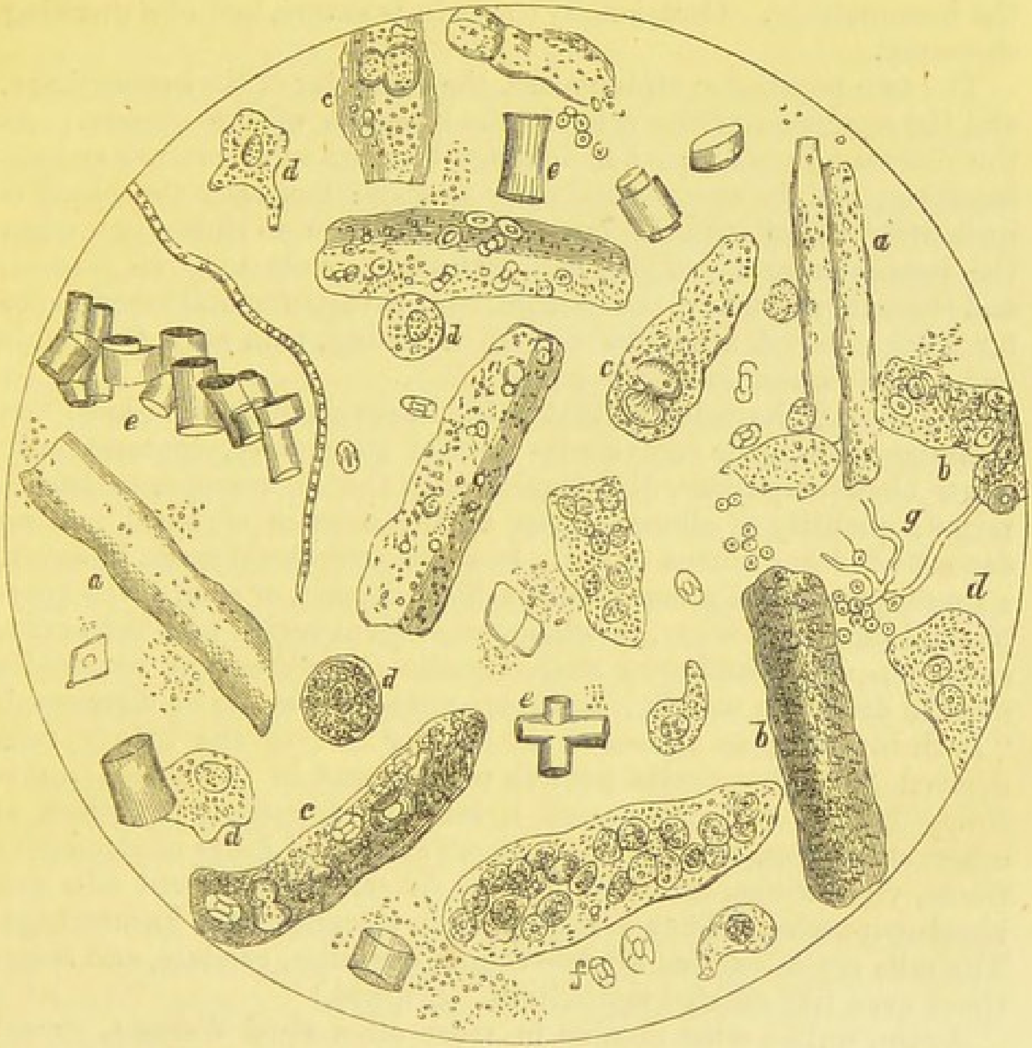
When œdema of the glottis supervenes, the throat should be blistered as quickly as possible, by means of either boiling water or the vinegar of cantharides.

## ON MALIGNANT OR CANCEROUS DISEASE OF THE KIDNEYS AND BLADDER.

Cancerous disease of the kidney, although in some cases difficult to distinguish with certainty, yet presents peculiarities which in general are sufficient to conduct us to a correct diagnosis.

The peculiarities consist, in part, in the absence of symptoms which serve to distinguish some of the renal diseases with which cancer might be confounded, and in part in certain characters which are indicative of malignant disease.

FIG. 72.




*a, a. Fibrinoid casts* of the renal tubules. *b, b. Casts* coloured with *urate.* *c, c.* Casts with *dumb-bell oxalate of lime.* *d, d. Epithelial scales* coloured with *urate.* *e, e.* Crystals of *uric acid.* *f, f. Dumb-bell crystals of oxalate of lime.* *g, g. Sporules* and *thallus of Penicilium glaucum* magnified 220, and *f, f.* 350 diameters. Copied from Report, by the Author, on the Urine of Cholera, General Board of Health, 1854.

Thus, there is usually absence of those sympathetic pains which accompany pyelitis, and especially calculous pyelitis; there may be but little lumbar pain, none referrible to the crest of the ileum, no retraction of the testicles, and usually but little constitutional disturbance. There may, however, be some derangement of digestion, loss of appetite, flatulency, and occasionally nausea and vomiting. In the advanced stage there is emaciation, and the skin assumes the transparent yellow or lemon tint, characteristic of cancerous cachexia; lastly, sometimes there is œdema of the legs, due in part, Roger thinks probable, to coagula in the renal veins and inferior cava, and in part to the watery condition of the blood, the result of the hæmorrhage. Occasionally the pain is severe, and of a gnawing character.

The two peculiar symptoms are, the character of the hæmorrhage, and the condition of the urine in the intervals of the attacks. As the disease advances the hæmorrhage becomes more profuse and exhausting, and it recurs at shorter periods: generally the blood is intimately mixed with the urine, and there are no clots; but when the hæmorrhage is sudden and abundant, clots may be formed, and these may block up the urethra, require instrumental interference for their removal, and give rise to straining, pain over the pubis and at the extremity of the penis.

The second character is, that in the intervals of the attacks of hæmorrhage, the urine recovers its normal appearance, contains only a few blood-corpuscles, discoverable with the microscope, perhaps a minute quantity of albumen even in the absence of blood, and no deposit of either mucus or pus. In some exceptional cases, however, a small quantity of a mucoid or purulent deposit, or even of the encephaloid pulp, may occur, in which, on diligent search with the microscope, suspicious and even characteristic structures and corpuscles may be detected; usually, however, none such are to be discovered. "Both in cancerous disease of the bladder and of the kidney, cells derived from the morbid growth may appear in the urine; sometimes, besides cells, there are isolated or aggregated portions of other structures, such as small bloodvessels and fibres of connective tissue, vegetations, and membranous flakes, with adherent cells and blood-corpuscles. They are frequently attended with hæmorrhage. The cells are of various kinds—round, irregular, caudate, and sometimes even like ciliated epithelium." (Parkes.)

Again, unlike what obtains in most other renal diseases, except during the periods of hæmorrhage, there is no irritability of bladder, and the calls to void the urine are not more frequent than natural.

Further, the diagnosis is sometimes aided by the history of the case, by the condition of other organs, and by the peculiar waxy yellowness of the skin already noticed.

From the different forms of *pyelitis*, cancerous disease of the kidneys is usually distinguished by the absence of purulent deposit, as well as by the character of the pain.

From *Bright's disease*, whether acute or chronic, by the abundance of the hæmorrhage, and by the general absence of albumen in the clear urine, and of dropsy, although this has been occasionally observed in some cases of cancer of the kidneys.

There are, however, diseases with which renal cancer might be confounded, and which, in some instances, it is not easy to diagnose.

One of these is *polypus of the bladder*. In such cases, of course extremely rare, while there is complete absence of all symptoms and sensations pointing to the kidney, others are present referrible to the bladder, and on examination with the sound, the form of the polypus might be determined: again, the blood comes away, not as in renal cancer, equally diffused through the urine, but almost always in clots, which frequently block up the urethra, thereby occasioning great distress and sometimes retention, followed by ammoniacal and fœtid urine.

But cancer is liable to attack the *bladder* and *prostate* as well as the kidneys; and in these cases the diagnosis is still more difficult, owing mainly to the absence of any sympathetic pains or symptoms to characterize the renal disease. There is the same profuse and recurring hæmorrhage as with cancer of the kidneys, only that perhaps a larger proportion of the blood is passed in clots. However, the difficulty is sometimes overcome by the manifestation of symptoms traceable to the bladder or prostate, as pain and tenderness on pressure. Again, on exploration, a tumour may be discovered; in the *ulcerative form of cancer of the bladder* even this means of diagnosis would be wanting.

Lastly, profuse, recurring, and fatal hæmorrhage sometimes takes place from the bladder, of an *idiopathic*, or even a *vicarious* character. The diagnosis of such cases is most difficult, the only particulars to guide us being the absence of tumour and of the cancerous diathesis.

It appears that cancer of the kidneys may occur at any age, from 10 months upwards. Of 35 cases collected by Dr. Walshe, in 16 the cancer affected both kidneys, the right in 13, and the left in 6 only.

In 31 out of 36 cases, "encephaloid, or one of its varieties, was the species of cancer observed; scirrhus in 5 only, 2 of them of doubtful character; while colloid did not in any instance occur in this situation." (Walshe.)

In some cases the form and size of the kidney is but little affected; in others it is nodulated on the surface, and in others it is enormously increased, weighing even four and five pounds, and forming a tumour readily discoverable on external examination.

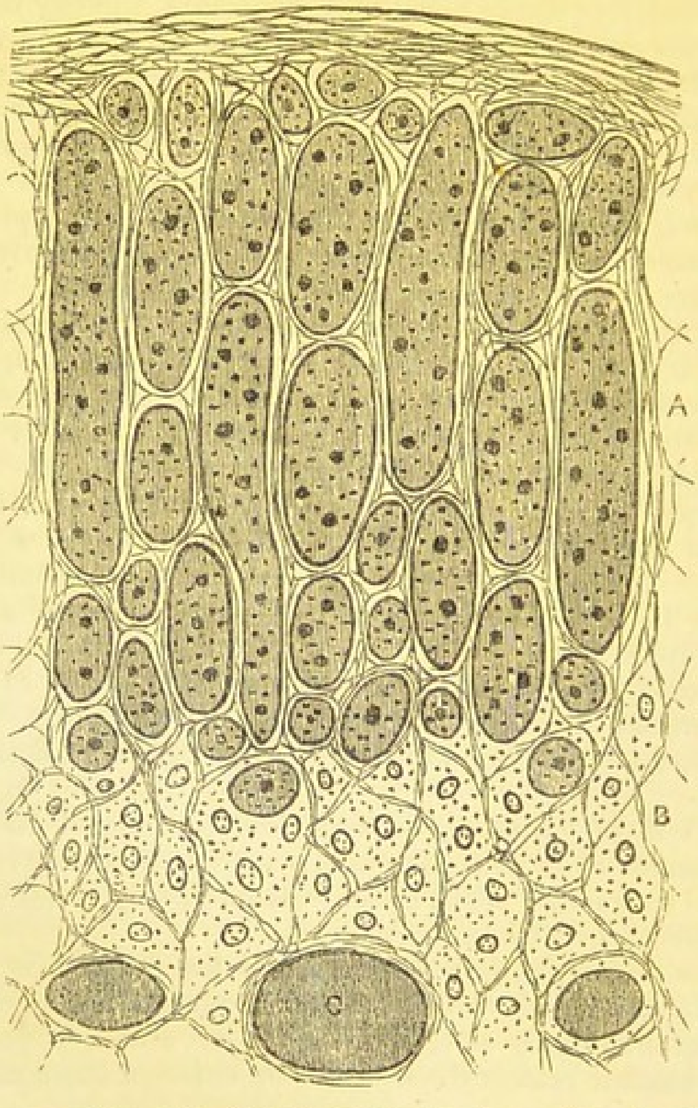
### *Treatment of Renal Cancer.*

The treatment in cases of cancerous disease of the kidneys can, of course, only be palliative: it should consist in the administration of anodynes to relieve pain, and in the free exhibition of astringents to arrest the hæmorrhage, such as sulphuric acid, alum, tincture of the sesquichloride of iron, and gallic acid.

DISEASE OF THE SUPRA-RENAL CAPSULES.

Although no functional relationship has yet been established between the supra-renal capsules and the kidneys, yet being placed in such close connexion therewith, and deriving their names in part

FIG. 73.




Transverse section of a *Human supra-renal capsule.* A. *Cortical,* B. *Medullary substance.* C, C. *Sinuses.* From engraving lent the Author by Dr. Harley.

from those organs, it seems desirable that some account of these bodies should be given in this work.

This course, it is hoped, will at least have the effect of causing them to be more frequently examined, and their condition recorded in autopsies made for the purpose of determining the state of the kidneys.

There are usually two supra-renal capsules, but sometimes one or both may be absent, and at others there are supernumerary capsules of smaller size.

They rest upon, and in fact are, as it were, moulded upon the superior and anterior surface of the kidneys.

They are of a more or less triangular form, and have been compared in shape to a cocked hat; occasionally they are oblong, and even flattened, being spread out in a thin sheet. They are about two inches long by one in diameter, and are stated to weigh from 80 to 180 grains each.

*Structure.*—When cut into, they are seen to consist of two portions, an outer, or cortical, and an inner, or medullary portion.

The *cortical* substance is of a yellowish colour, has a somewhat fibrous appearance, and which, in thin sections examined by the microscope, is seen to be due to its being composed of parallel tubes, or elongated vesicles resembling somewhat those of the kidney; the differences in the length of these are possibly more apparent than real, and may depend upon the direction in which the section is made. (Figs. 73, 74, and 75.)

These tubes on the external surface of the capsule terminate in blind extremities, and are described as having a similar termination internally.

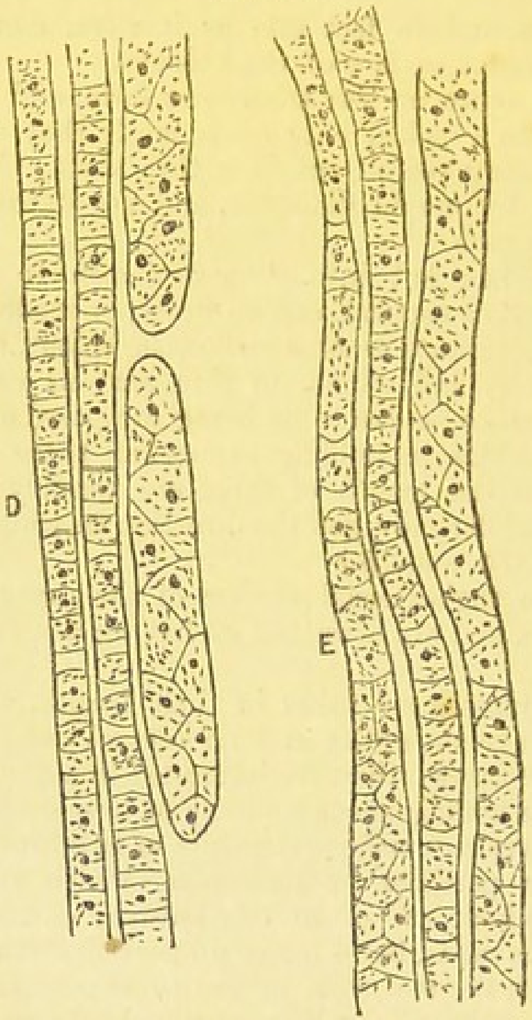
Although they resemble tubes in their length, yet, inasmuch as they appear to have no outlet and no central canal, they certainly do not form true tubes; they are imbedded in a fibrous matrix, and possess a delicate homogeneous limitary or basement membrane.

The tubes or vesicles enclose elements of two kinds; "first, innumerable circular particles or molecules, which reflect the light strongly, and which are of an oily nature; of these the greater part is free in the tubes, but a lesser proportion is enclosed in certain of the cells which are met with in the tubes; second, granular nuclei in large quantities." ("Microscopic Anatomy of the Human Body," by the Author, 1849.) These so-called nuclei are probably really cells, although nuclei are not usually visible. Harley, as will be seen by reference to the woodcut (Fig. 74, p. 342), represents the cells as being sometimes angular, like those of the renal tubules, and with nuclei equally distinct.

The inner, or *medullary* substance, which forms about one-third of the thickness of the capsule, is, before it is freed from blood by washing, of a reddish, and afterwards of a bluish slate colour; traversing its centre are seen large venous sinuses, visible in sections by the round or oval apertures which they present. The cavity which has been described as occupying the centre of each capsule, Dr. Harley, whose researches on the histology and physiology of these organs are well known, considers is produced by rupture of the tissue between the sinuses, either accidentally during the examination, or as the effect of disease.

The medullary substance is described as consisting of fibrous

FIG. 74.




*Columnar cell masses* having the appearance of tubes. From the *Human supra-renal capsule*. D and E, Cells in a single row. From engraving lent the Author by Dr. Harley.

tissue, arranged in a reticulated manner, and the meshes formed by which are occupied with "a number of large pale-coloured cells with round nuclei." (Harley.)

When the Author examined the supra-renal capsule in the adult many years since, he detected in the medullary portion "numerous parent-cells of considerable size, each containing several nuclei, intermingled with, and in part very frequently obscured by, a considerable number of the bright molecules previously referred to;" and he remarked, "It is these cells which impart to sections of the gland the dotted appearance so commonly observed in its medullary portion:" and again he observed, "These cells do not appear to have been hitherto characterized with any degree of precision."—"Microscopic Anatomy." (Fig. 75.)

The cells of the medullary substance have been described by Kölliker and Brown-Séquard as resembling ganglion-corpuscles; but certainly the compound cells filled with oily matter, just described, bear no resemblance to true ganglionic cells, which usually contain but a single well-defined nucleus, the large droplets of oil being alsc absent.

Ecker and Harley describe nuclei surrounded by granular matter, but without distinct cell-walls, as occurring in the medullary substance.

"The vascular distribution in the supra-renal capsule is very simple. On the surface of the organ we have a very beautiful plexus of capillaries, the pentagonal and hexagonal meshes of which lie in the intervals between the extremities of the tubes; in the tubular part, the vessels, both veins and arteries, run in straight lines between the tubules, terminating on the one hand in the plexus on the surface, and on the other in the central plexus." (Op. cit., p. 482, Plate lxxii., Fig. 5.).

The capsule of the supra-renal body in the adult is often laden with fat, which totally obscures the plexus on the surface; indeed, the whole organ frequently abounds in fat, the compound or parent-cells noticed sometimes even closely resembling those of the sebaceous glands.

It is copiously supplied with nerves.

It appears to the Author questionable whether the quasi tubes do not, in an altered form, really extend into the medullary substance.

*Functions.*—Respecting the functions of the supra-renal bodies, in spite of all the skill and labour recently bestowed upon the subject, and so many cruel experiments and operations performed upon some hundreds of poor animals, nothing positive has been ascertained. Dr. Addison believed that they exercised some chromatogenous function, but much evidence has recently been adduced to show that no necessary connexion exists between the disease of those organs and the colour of the cutis.

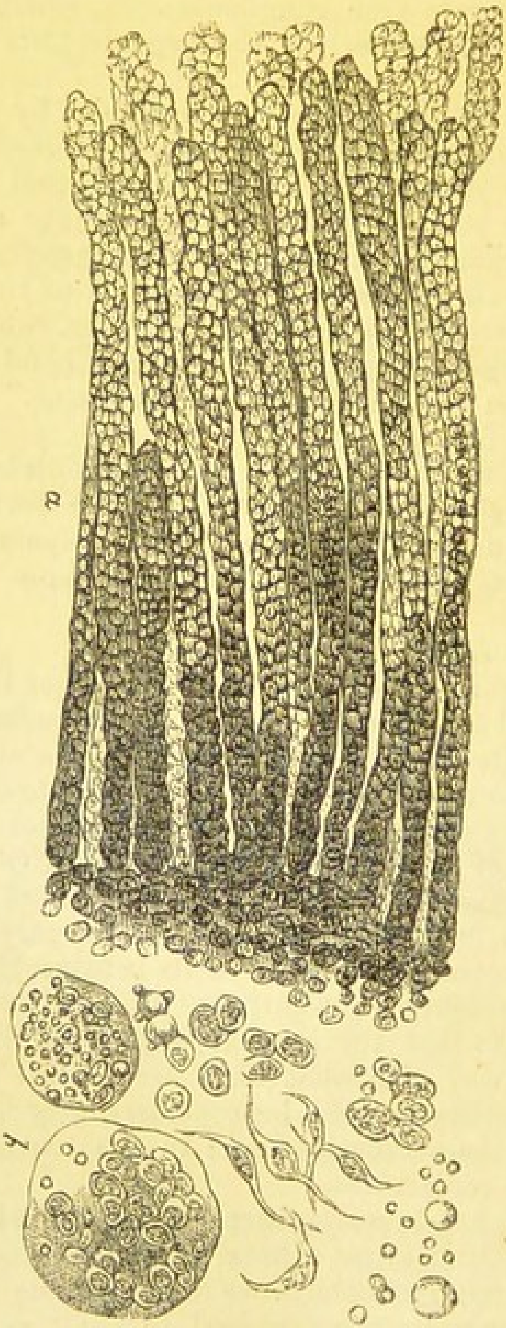
Kölliker thinks that the cortical portion of the capsule is connected in some way with what have been called the blood-glands; while the medullary portion he considers may have some special connexion with the nervous system: these views are, however, little more than mere conjectures.

One particular has, however, been clearly established—namely, that it is not exclusively an organ of fœtal life: since it increases after birth in place of becoming atrophied, we may conclude that its functions, whatever they may be, are exercised in adult as well as in intra-uterine life.

*Pathology.*—From the numerous cases of disease of these organ which have now been recorded, it appears that they are liable to be affected in a variety of ways: with atrophy, tubercle, fatty and amyloid degenerations, and with cancer.

The symptoms described as associated with disease of these bodies are extreme debility, anæmia, feeble action of the heart, irrita-

FIG. 75.




*a.* Tubules of the adult *Human supra-renal capsule*, 90 diameters. *b.* *Cells*, *parent-cells*, *molecules*, and *oil-globules* of the same, 378 diameters. From "The Microscopic Anatomy of the Human Body," by the Author. 1849.

bility of the stomach, emaciation, and especially *bronzing of the skin*, which by Addison was thought to be pathognomonic, not of any one affection, but of all the principal diseases to which they are liable.

It has now been fully proved that there is no invariable or essential connexion between supra-capsular disease and bronzing of the skin; such disease in various forms may exist without bronzing, or this may be present, and the capsules be perfectly healthy. Nevertheless, the two would appear to be associated with remarkable frequency. Discoloration of the skin occurs, however, under such a variety of circumstances, that it seems scarcely reasonable to suppose it to be dependent exclusively upon disease of one particular organ. That disease of the supra-renal capsule is frequently accompanied by profound constitutional disturbance is certain; and it seems probable that this is due less to interruption of its functions than to the effects of the disease on the ganglionic nerves, by which the capsule is so freely supplied, and by which it is surrounded.

It has already been stated that these bodies are sometimes absent; they may be extirpated without apparent injury to health, and Harley records the case of a cat in perfect health, in which both capsules had become replaced by a deposit of carbonate of lime, the remaining portions of the gland containing so much fibrous tissue that their normal structure might be said to have disappeared,—facts which prove, at least, that these organs, whatever their functions may be, are not essential to life.

Frequently other diseases are associated with that of the supra-renal capsules, but patients sometimes die of capsular disease only.

*Treatment.*—The nature and functions of the supra-renal capsule being so little understood, nothing special can be advanced respecting its pathology and the treatment based thereon.

The diseases to which it is liable are, so far as is known, those to which other glandular organs are subject, and which have already been enumerated.

By reference to the symptoms, it will be seen that tonics, including quinine, iron, the mineral acids, and sometimes ammonia, to counteract the debility and depression which exist, are plainly indicated.

## ON FATTY, CHYLOUS, AND SERO-CHYLOUS URINE.

Since the escape of fat, of chyle, or sero-chyle, into the urine may sometimes be connected with an abnormal state or even disease of the kidneys, and since albumen is a constituent of chyle and serum, the description of such cases may be properly included under the head of albuminuria.

Oily or fatty matter, either with or without albumen, occurs in the urine under a variety of circumstances.

Lehmann found *oily matter* in the urine of *tortoises;* Frerichs and Lang commonly in that of *cats.* Rayer and Bernard observed that much *fatty food* occasioned its presence in the urine of *dogs;* and Lang also detected a small amount of fat in *human urine,* especially after the use of fatty food. Mettenheimer has recorded two cases in which fatty matter passed into the urine in large quantities: one was that of a man with cancer of the lungs, who was taking *cod-liver oil;* and the other that of a woman who was recovering from inflammation of the kidneys, and was taking an emulsion of *cannabis indica,* or Indian hemp. Siegmund has ascertained that *cubebs* given to *rabbits* also rendered the urine fatty. It was affirmed by Lehmann to be sometimes present in *human urine,* in diseases attended by *rapid wasting,* or in certain diseases of the *liver,* and in conditions with which *hectic* is associated.

The oily matter sometimes may also be derived from excess of *labial epithelium,* of *mucus* or *pus;* or it may be due to *renal disease* or to *urostealith.*

In the majority of these instances the fat is unaccompanied by albumen, but more frequently it occurs together with albumen and even fibrin.

At a certain stage of digestion, the serum of the blood in some, even healthy, persons, presents a milky appearance, arising from the suspension in it of both fatty and albuminous matter in a molecular condition, but as digestion is completed, it recovers its transparency.

Now, it not unfrequently happens that the urine secreted during the period of opacity of the serum, itself becomes more or less turbid or milky, from the escape of the molecular fat and albumen contained in the serum. It is affirmed that sometimes the opalescence is occasioned solely by albumen. (Buchanan.)

In other cases the urine has been observed to be milky during suckling, and from the same cause—namely, from finely-divided albumen and fat, particularly the latter, a portion of which occurs also in the form of globules.

Whether *casein* is present in such cases, has not been satisfactorily determined.

Here, no doubt, as in the previous class of cases, the condition of the urine is mainly, though not entirely, due to that of the serum, which, during suckling, abounds with fatty and albuminous substances.

But in a third and more important class of cases, the urine contains not only fat and albumen, but fibrin, and even blood, in variable amounts, the presence of the fibrin causing the urine to coagulate spontaneously as it becomes cold.

Sometimes the amount of fibrin is but small, the urine becoming tremulous only; at others it is sufficient to render it firm, like blancmange: the fibrin may even coagulate in the bladder, producing obstruction and giving rise to retention. Its colour also varies according to the quantity of blood and fat present: it may be, either opaque and whitish, or reddish, and even red.

In some of these cases, the presence of the abnormal ingredients is probably due to food (Rayer), while in others the fat is derived from the food, but the albumen and fibrin are probably not so (Bence Jones); while the blood-corpuscles can only proceed from rupture of vessels.

The urine has not been very extensively analysed in these cases, but it is sometimes of high specific gravity, and hence there is probably no great diminution in the amount of its chief constituents. Prout noticed in one case that there was a deficiency of urea *after food;* and this probably occurs in other cases, since part of the albumen of the food escapes from the system without ever having been appropriated by the tissues. From two samples of chylous urine, Bence Jones obtained 8·37 and 7·46, and Beale, from a third sample, 13·9 parts of fat to 1000 of urine. Although the fatty matter is usually in the molecular state, it is sometimes, as in Bence Jones's case, in the form of globules. Again, as in Mr. Gossett's case, recorded by Bird, the fat is sometimes so abundant that it rises to the surface as the urine becomes cold, forming a thick creamy layer, the urine below being perfectly transparent. Mixed with ether in a bottle, and allowed to stand, three layers are sometimes formed—one of fat, a second of fibrin, and the third of clear urine. In Cubitt's case, as shown by Beale, *the clear samples* of urine were entirely free from albumen; in Mr. Gossett's case they were occasionally albuminous; while, lastly, in Bence Jones' case, during complete rest, they were also non-albuminous.

As might be expected, it is usually more fatty after food, and after animal than after vegetable food. The quantity is greatly increased by causes which disturb the circulation—as exercise, standing in the erect position, fatigue, mental or bodily, and anxiety—and produce increased pressure on the walls of the renal bloodvessels, or which augment the amount of fat and albumen in the blood.

It is singular, however, that in Mr. Gossett's case it was generally the urine first voided on rising from bed which was the most milky; and in Mr. Cubitt's case, this was always so, the urine not having been milky even once *during the day.*

In other cases the morning urine is free from fat, and although quite transparent, yet gelatinizes on becoming cold.

The albumen excreted in some cases is considered by some observers to be in a peculiar condition, since it does not coagulate by heat, although it does with nitric acid. Prout termed it "hydrated," and Parkes suggests that "it is not unlikely to be, sometimes at least, in the condition of *peptone* (Lehmann); the *albuminose* of Mialhe, which is characterized by its great diffusive property." (Funke.)

*Pathology of Chylous Urine.*

It is obvious from the remarks already made, that the significance of chylous urine varies greatly. The first distinction to be made in such cases is between those in which the urine contains only fat and albumen, and those in which fibrin and blood are superadded, the latter of course being of more serious import.

The cases in which the urine becomes somewhat milky only during digestion in persons in apparent health, this condition disappearing when that process has been completed, are of but little moment; and the same observation applies to cases of milky urine during suckling: even those in which fibrin coexists with the other ingredients are not generally dangerous. In the more severe cases there is, however, great pain in the back, anæmia, and debility.

While cases of this latter description — that is, of spontaneously coagulable urine — have been occasionally observed in this country, they appear to be of much more frequent occurrence in certain tropical climates, and are even endemic, constituting a disease, which has been named, according to the prevailing character of the urine or the supposed cause of the malady, *diabetes chylosus, diabetes lymphaticus*, and the *hæmaturia* of the Isle of France.

The causes assigned for the occurrence of chyle and sero-chyle in the urine, are *the diffusibility of the albumen* itself, *enlargement of the renal vessels*, and "*varicosity of the renal lymphatics.*" (Gubler.) From the presence of blood in the urine, it is certain that there is *rupture of bloodvessels* in most cases of sero-chylous urine.

*Treatment of Chylous Urine.*

In these cases it is obvious that the diet requires to be carefully regulated, all articles of difficult digestibility being carefully avoided; that rest during digestion should be strictly enjoined; and astringents, such as sulphuric acid and alum, acetate of lead and opium, tincture of the sesquichloride of iron, matico, and especially gallic acid, freely administered. Cantharides have been recommended, and also mangrove bark (*Rhyzophora racemosa*). Stimulants in some cases lessen the milkiness.

## UROSTEALITH.

In 1844 a young man, aged twenty-four, was admitted into the Vienna Hospital, labouring under all the symptoms of stone in the bladder, and who passed several small concretions composed of a peculiar fatty matter, to which Heller gave the name of *urostealith*

These concretions possessed the following characters, physical and general:—When fresh, they were soft, becoming, when dry, hard, yellow, and wax-like, and by transmitted light presenting a greenish-yellow colour: on the application of heat the dry concretions melted, swelled up, ignited, emitting a pungent odour between that of shellac and benzoin, and leaving a voluminous ash. By hot water they were softened, but not dissolved; they were slightly soluble in alcohol, and readily so in ether, the solution leaving a residue which, a gentle heat being applied, assumed a violet colour: they were also dissolved by nitric acid, with slight effervescence.

The only points worthy of record respecting the urine in which they were found were, that it was neutral, had a specific gravity of 1017, was of a light colour, and presented a *whey-like* appearance; it contained 12·63 grains of urea in 1000 grains of urine, much chloride of sodium, but *no* uric acid; and it deposited crystals of triple phosphate mixed with *fat-globules*. Nitric acid did not occasion any precipitate.

More recently these concretions have been identified in two other cases by Dr. Moore of Dublin, who received them from Dr. Robert Adams of the same city, and Dr. Little of Sligo. (*See* the "Dublin Medical Journal," 1854.)

Of the *pathology* of these cases but little is known as yet; their *treatment* is very satisfactory. In Heller's case, as might from the nature of these calculi have been reasonably anticipated, they were dissolved in the bladder by the administration of two drachms of carbonate of potassa daily, and the patient nearly freed from all symptoms in the course of a fortnight.

## FIBRINOUS AND BLOOD CONCRETIONS.

As a sequel to the foregoing remarks on *fatty calculi*, a few words may be bestowed upon fibrinous and blood concretions, simulating calculi.

The *fibrinous calculus* was first described by Dr. Marcet: it had the appearance of yellow wax, and was elastic; it was soluble in potash, from which solution it was precipitated on the addition of an excess of acid; it was insoluble in alcohol and ether, but soluble in acetic acid aided by heat, and was precipitated from the acetous solution by ferrocyanide of potassium.

The "*blood calculi*" were discovered by Dr. Scott Alison in the pelvis and infundibula of the left kidney of a man who died in the Consumption Hospital at Brompton.

The kidney was much wasted and changed. "The black calculi occupied the pelvis, while the infundibula were tenanted with a few calculi of a whitish-grey colour, with one exception small in size, about the magnitude of pear-seeds, and wanting the ordinary physical characters of phosphate of lime. One calculus, which occupied an infundibulum, is the size of a horse-bean, looks somewhat worn and disintegrated, and at one point resembles a piece of decayed wood. At one side it is black, from the presence of altered blood.

It is *very light in weight*, and is composed of blood and phosphate of lime. The black calculi, which form the chief point of interest in the case, were about six in number, and ranged from the size of a coriander-seed to that of a horse-bean. When found, these black calculi were tolerably hard, but being friable, they partly broke asunder in handling. The fractured surface varied a little in colour, in some parts presenting a dark rusty tint." ("Archives of Medicine," vol. i.)

They were soluble in ammonia, and Dr. Owen Rees detected in them what he considered to be the remains of blood-corpuscles.

## KIESTEIN.

When the urine of pregnant women is exposed to the atmosphere, there forms upon it, in a period varying from two to six days, a greasy-looking pellicle, which, as the urine becomes alkaline, breaks up and disappears, sinking to the bottom of the vessel; this was formerly supposed to be of a peculiar character, and to be symptomatic of pregnancy, and has received the names of *kiestein* and *gravidin*.

It was stated that this scum consisted chiefly of *oily matter* and of *casein*, recognised by its cheesy odour during decomposition, and the occurrence of which in the urine was thus explained:—The milk which, in the early months of pregnancy, forms in the breasts, not being required, is reabsorbed into the blood or lymph, from which the oil and casein are separated by the kidneys, and so make their appearance in the urine, the fatty matter rising to the surface on account of its lightness, and carrying with it the casein.

Attention was in the first instance particularly directed some twenty-five years since to this scum by Nauche, and his observations were in 1840 repeated by Dr. Golding Bird, the results of whose investigations in the main confirmed those of the prior observer.

The urine of a woman aged twenty-eight, in the sixth month of pregnancy, on the second day of exposure, "became very much troubled, numerous globules, presenting a fatty or greasy aspect, appeared on its surface; in two days more the urine became completely covered with *a pellicle, very closely resembling that which forms on the surface of mutton-broth in the act of cooling;* on the sixth day of exposure this crust broke up, and fell to the bottom of the vessel." Two other samples of the urine of the same woman presented similar appearances.

Specimens of the urine of thirty different women in from the third to the last month of pregnancy, were now examined, and, with three exceptions, "copious fat-like pellicles" were observed. The three women whose cases appeared to be exceptions to the general rule were all suffering from fever accompanying severe catarrh, and on the disappearance of which the characteristic scum appeared, so that these cases also really confirmed the rule.

Dr. Bird also found the "caseous pellicle" on the urine of two women who had been suckling. In the first case the urine was collected the day after the death of her child, and in the second three days after weaning her child, the breasts being still turgid. In neither case during suckling was the pellicle formed. The same pellicle was also noticed by Dr. Gull in a case of mole pregnancy, the particulars of which were supplied to Dr. Bird.

Dr. Golding Bird next obtained the urine of several *unmarried* women under treatment for amenorrhœa, and in two instances only was any evidence of the presence of the peculiar matter manifested: in one of these pregnancy was strongly suspected, and in the other it was proved by the occurrence of delivery.

These observations, so circumstantial, appear at first sight really conclusive, and the subsequent examination of the scum seemed still further to confirm them.

Thus in several examples the odour of putrescent cheese was remarked, although none of the urines were coagulable by heat, nitric acid, or, "with two or three exceptions, by acetic acid," but this is explained by the statement that the casein in much-diluted milk is not precipitated by the reagent last named.

Again, the pellicle, when placed on a slip of glass, appeared "glistening with a lustre like that of spermaceti," and examined with a half-inch object-glass, "myriads of triangular prisms of triple phosphates were seen imbedded in a mass of granular matter, mixed with which might here and there be seen patches of fat-globules."

By acetic acid the crystals became dissolved, and a white pultaceous mass, consisting of animal matter, resulted; ammonia added to another portion of the crust dissolved this, but did not affect the crystals.

Lehmann, in repeating these observations, separated from the pellicle, by means of ether, a fat which resembled butter; and Dr. Owen Rees detected genuine fat-globules precisely like those found in milk.

Dr. Bird remarks, however, that "the greasy aspect of the pellicle of the so-called *kiestein* arises less from the presence of the fat than from the numerous crystals of triple phosphate which from their brilliancy produced this glistening appearance."

It will be observed that Bird testifies most clearly to the presence in the scum of both fatty matter and an animal substance "closely allied to cheese," and giving off during decomposition a strong cheesy odour; and in respect to the fat, Bird, as we have seen, is confirmed by Lehmann and Rees. Now, if these constituents of milk were constantly present in the pellicle which forms on the urine of pregnant women, it would then form a diagnostic sign of the existence of pregnancy, frequently of the utmost value in practice.

But notwithstanding the apparent conclusiveness and circumstantiality of the observations of Bird and others, the value of this test has been much called in question, and at the present time no reliance whatever is placed upon it: amongst those who doubt its being a sign of pregnancy, the Author has long been numbered.

In a communication read before the Medico-Chirurgical Society, and subsequently published in the "Lancet" for November, 1859, the Author showed that upon feebly acid, neutral, or alkaline urine, or in urine the acidity of which speedily became diminished after emission, there formed on exposure to the air a greasy-looking pellicle, composed in great part of vibriones and crystals of triple phosphate, some of the vibriones being aggregated into roundish masses, which with a half-inch object-glass might readily be mistaken for droplets of oil.

Now, the Author believes that the kiestein of pregnancy is nothing more than this pellicle, the appearance of oil being due to the shining crystals of earthy phosphate, and the animal matter, insoluble in acetic acid, to the vibriones which form so considerable a constituent of the crust.

Its occurrence in the urine of pregnant women he would explain either by the feeble acidity of the urine or the rapidity with which its acidity becomes reduced.

But it is not only in the urine of pregnant women that this scum is formed, but also in that of all persons, both male and female, if it be alkaline or but little acid, or quickly loses its acidity, and also contains mucus or albumen.

If this view be the correct one, the so-called kiestein of the urine has no real significance as a sign of pregnancy.

Even the presence of the fatty matter may be explained on the supposition that it is derived from the animal matter, mucus, and vaginal epithelium, so abundant in the urine of women, and which is often very fatty, owing to the number of sebaceous glands situated in the external organs of generation of women.

In Bird's extremely interesting account of his observations respecting kiestein, reference does not once occur to vibriones, showing it had not entered into his thoughts, that possibly the animal matter of the pellicle might consist of those productions.

In connexion with this view of the nature and formation of the crust, the remark of Bird, that the three pregnant women, out of the thirty examined, in whose urine the crust failed to appear, were labouring under severe catarrh accompanied by fever, and that on the disappearance of the fever the crust appeared, admits of explanation. The fever no doubt rendered the diminished and concentrated urine more acid, and so the vibriones not meeting with the conditions necessary to their development, failed to appear, as also the crystals of triple phosphate.

# CHAPTER XXI.

## ON BLOOD, MUCUS, AND PUS.



### ON BLOOD IN URINE, OR HÆMATURIA.

Blood, when present in urine, may be derived from the kidney itself, or from any portion of the genito-urinary mucous track, both in the male and female.

When it proceeds from the *kidney*, it may depend upon several states or conditions of that organ.

Thus it may be due to congestion and inflammation produced by *acute*, more rarely by *chronic nephritis*, by *variola*, *measles*, and *scarlatina;* or it may result from a *blow*, or from the stimulant action of certain medicines, as *turpentine* or *cantharides*.

It may depend upon the general condition of the blood and solids, as in cases of *purpura* and *scurvy*, *typhus* and *malignant fever*.

It may arise from the presence of a *calculus*.

It may also be due to *abscess*.

Lastly, it may be occasioned by *malignant disease*.

When the hæmorrhage proceeds from the *bladder* or *urethra*, it may arise—

From *acute cystitis*.

From *passive congestion*, as in *adynamic fever*, *purpura*, and *scurvy*.

From *stone in the bladder*.

From *ulceration*.

From *cancerous* or *villoid disease*.

From *stricture* or *gonorrhœa*.

In the *female*, other sources are superadded: it may then be derived from the *vagina* or *uterus*, depending either upon *disease* of those parts, or simply upon *menstruation*.

Whenever blood-corpuscles are present in the urine, they of course indicate rupture of bloodvessels somewhere; but not unfrequently the colouring-matter of the blood, *hæmatin* only, is contained in the renal excretion, it proceeding from the kidney.

The occurrence of blood in the urine implies the presence of something more than the red corpuscles, or colouring matter; the fibrin and albumen of course also escape from the vessels, so that whenever the corpuscles or hæmatin are found, it may be taken for granted that those substances are both present.

The *quantity of blood* in the urine of course varies greatly; in some instances, especially of structural kidney disease, the quantity may be so small as to escape detection by the unaided sight, and to require the microscope for its discovery.

In others it may be somewhat more considerable, but still in amount insufficient to be discovered at first by the eye alone; but after the urine has been allowed to remain at rest for some hours, its presence is clearly indicated by the subsidence of the blood-corpuscles to the bottom of the glass or bottle, where they form a well-defined deep red line resting usually upon the mucus or other deposit which may be contained in the urine.

When the amount is still more considerable, the colour of the urine may be sufficient to determine its presence; this, however, should rarely be wholly relied upon, since blood will often be found to be absent from urine the colour of which would appear to indicate its presence.

Not only is the quantity present very variable, but the colour is not always the same. When the quantity is small and the urine acid, the blood is of a brownish-red colour, and the urine presents the well-known *smoky* appearance; when neutral or alkaline, it is of a much brighter red. In most cases in which the urine presents the dull, smoky hue, the blood will be found to proceed from the kidneys.

The blood-corpuscles are generally in the free state, but sometimes enclosed.

When free, they are usually at first diffused pretty equally throughout the urine, but when confined, they occur enclosed in the fibrinoid casts, forming "blood casts," or else in "clots." The blood-casts are not unfrequently found in the urine in cases of acute nephritis, and after taking turpentine or cantharides. The clots are sometimes long and thin, the blood having become solidified and moulded in its passage along the ureter; sometimes they are pyriform or globular, as when they are formed in the pelvis of the kidney; at others they are of irregular size and shape; and occasionally they are colourless, and consist of nearly pure fibrin, the red corpuscles having been absorbed. This condition occurs as the result of retention of the blood in the bladder.

When the urine first voided is free from blood, and this appears only towards the close of micturition and in the form of clots, it no doubt proceeds from the bladder, and probably from near its neck.

ON THE TREATMENT OF BLOOD IN THE URINE.

The first thing to be done is to determine the *cause* and *source* of the blood: as to its source, whether it proceeds from the *kidney* or the *bladder*, and if from the latter, from what part of the genito-urinary mucous membrane, male or female.

If from the *kidneys*, in most cases symptoms will be present referrible to those organs, as pain in the lumbar region, along the course of the ureters, and extending down the inside of the thigh; there may also be retraction of one or both testicles.

When it has been determined that it proceeds from the kidney, we have still to ascertain the cause, whether it arises from nephritis or other non-malignant disease, from purpura, renal calculus, or from cancer.

The history of the case will generally clear up these points.

The small quantity of blood present, the dull character of the pain, and the absence of retraction of the testicle, sufficiently demonstrate that the case is not one of calculus.

When the pain sets in suddenly, when it follows somewhat the course of the ureter, when there is retraction of the testicle, pain down the thighs, and the hæmorrhage is considerable and to some extent is coincident with the pain, the hæmorrhage is clearly due to *renal calculus.*

If the *bladder* be the source of hæmorrhage, some of the symptoms will usually be referrible to that organ: there may be pain in the bladder, tenderness over the pubic region, especially on pressure, and an aggravation of pain during micturition, and the blood may be voided only with the urine last passed, and it may be in clots more or less moulded in the urethra.

If the case be one of *ulceration of the bladder*, there will generally be more or less purulent matter intermixed with the blood, and pain and tenderness will form more obvious symptoms.

If the hæmorrhage arise from *stone in the bladder*, the pain will be intense, will occur in violent paroxysms, and be increased by micturition, will extend to the extremity of the penis, and there will be a sense of weight in the bladder; in making water there may be a sudden stoppage of the stream, and the hæmorrhage is rarely considerable.

In *malignant disease* of the bladder, the history of the case often affords much useful information: the hæmorrhage is profuse and recurs at intervals, much of the blood escaping in the form of clots, and the pain is great; the complexion is usually sallow and semi-transparent, indicative of a malignant diathesis. Add to these symptoms, that on exploration by the sound no stone is discovered, though sometimes a tumour or thickening may be detected.

In such cases instrumental interference is greatly to be deprecated, as it is nearly always followed by much hæmorrhage, and in other respects aggravates the symptoms.

When the blood contained in the urine is considerable, and equally diffused throughout the urine, judging apart from other symptoms, it probably proceeds from one or other kidney, but when voided in clots, there is some reason to believe that it has its source in the bladder.

Having ascertained the seat and cause of the hæmorrhage, the *treatment* may now be determined.

If the blood proceed from inflammation or other disease of the kidney, the remedies to be employed will depend upon the nature of the affection. What these should consist of has already been considered in connexion with the subject of renal diseases.

If the hæmorrhage be passive, and depend upon a general hæmorrhagic tendency—as when it arises from purpura, scurvy, &c.—then the treatment must be general and constitutional, and consist in the administration of suitable tonics and astringents—as quinine, iron, the mineral acids, &c.—combined with a nourishing diet.

If it arise from renal calculus, the escape and passage of this must be facilitated, and the excruciating pain alleviated by the warm bath, nauseants, and opiates.

If the hæmorrhage is occasioned by malignant disease, then tonics, and particularly astringents, must be employed—as quinine, the mineral acids, tincture of the sesquichloride of iron, alum, gallic acid, and decoction of pomegranate. These remedies should be used in large doses, frequently repeated.

The alum, quinine, and mineral acids may be given together in a mixture; the gallic acid in powder, at suitable intervals; and the decoction of pomegranate may be taken as an occasional drink.

If the bladder be the source of the hæmorrhage, and it proceed either from ulceration or malignant disease, here again regard must be had to the general condition of the patient, and astringents and styptics must be freely exhibited, also anodynes and opiates to alleviate pain.

In cases of passive hæmorrhage, especially from the bladder, copaiba and turpentine cautiously administered will sometimes prove of service when other remedies fail.

When the hæmorrhage depends upon the presence of a stone in the bladder, although the symptoms may be relieved, much good can scarcely be effected until the stone is removed: in the case of phosphatic calculi, this may sometimes be accomplished by the persistent employment of solvent remedies, and in other cases either by crushing the stone or by its removal in the entire state by the ordinary operations.

Cases of hæmorrhage from the kidney and bladder depending upon malignant disease or upon ulceration of the bladder, tax all the resources of the physician, require vigorous treatment, and although life may be prolonged, yet in the end very generally prove fatal.

In some obstinate cases of hæmorrhage from the bladder, astringent injections may be resorted to: these in the female may be easily employed, but in the male subject with more difficulty.

Dr. Prout has recommended that in cases of profuse hæmorrhage from the bladder which cannot be stopped in any other way, an injection containing from twenty to forty grains of alum to the pint should be thrown into the bladder; this remedy, he states, seldom fails to check the bleeding, even when malignant disease is the cause.

When the hæmorrhage is profuse, ice may be applied over the pubis, or even be inserted into the rectum, or ice-cold water may be injected into that intestine.

In some cases, retention has been produced, owing to the large quantity of blood effused into the bladder, and its coagulation while retained. A large-sized catheter with a full eye must then be passed, and an exhausting syringe attached; by this means, aided by the occasional injection of water, the coagula may be removed.

## ON MUCUS AND EPITHELIUM IN THE URINE.

When normal urine has been set aside for some hours, a delicate transparent cloudlike deposit of mucus appears; and if a portion of this be examined under the microscope, it will be found to consist of the well-known granular corpuscles and of epithelial cells or scales mixed up with numerous fibrous threads; if dilute acetic acid be applied to the corpuscles, one or two nuclei will become visible in each, and when liquor potassæ is added to a fresh portion of mucus, viewed under the microscope the granular cells will be seen to swell up and burst.

But mucus not only contains the elements just noticed, but also mucin, a little fat, a very minute quantity of albumen, and certain salts, especially alkaline chlorides and lactates, phosphate of lime, and traces of carbonate of soda.

It is to the mucin that mucus owes its tenacity. This substance is insoluble in pure water, and when mucus is neutralized with dilute acetic acid, and treated with water, it is thrown down as a white coagulum.

Mucus differs from pus chiefly in containing less fatty matter and albumen and fewer granular corpuscles, which, treated with dilute acetic acid, disclose usually but one, and rarely more than two nuclei.

Now this mucus may be derived from any part of the genito-urinary mucous track, and it often becomes of pathological importance to determine its precise source. Fortunately this object can generally be accomplished. The tubes, calyces, and pelvis of the kidney are all lined with epithelium, as also the whole of the urinary and genital mucous membrane; and, further, the characters of this epithelium differ in different localities, so that by its means we are usually enabled to effect the discrimination in question.

The normal epithelium of *the renal tubules* consists of angular flattish cells, of medium size, neatly adapted to each other, so as to form a tessellated membrane, but easily detached. (Fig. 76, *c.*)

That from the *ureters* is *columnar*, some of the cells being spindle-shaped.

That of the *pelvis* of the kidney consists of cells which are triangular or caudate, presenting well-defined nuclei; they adhere together in groups, and are imbricated.

That of the *bladder* consists of thick, roundish, or caudate superimposed cells of considerable size. In the *follicles* the epithelium is columnar. (Fig. 76, *a.*)

That of the lower part of the *urethra, glans penis,* and *vagina* forms an epidermis of large, flattened, nucleated cells, resembling those of the cuticle elsewhere. This kind of epithelium is particularly abundant in the urine of women, being derived from the vagina (Fig. 76, *b.*)

The amount of mucus present in healthy urine is very small, being from ·01 to ·03 in 1000 parts; and it may be easily separated by filtration.

But under circumstances of irritation or inflammation of the mucous membrane of the genito-urinary organs, the quantity passed is often greatly increased, as from deposits of the earthy phosphates, from cystitis, stone, paralysis, stricture, and inflamed or irritable prostate.

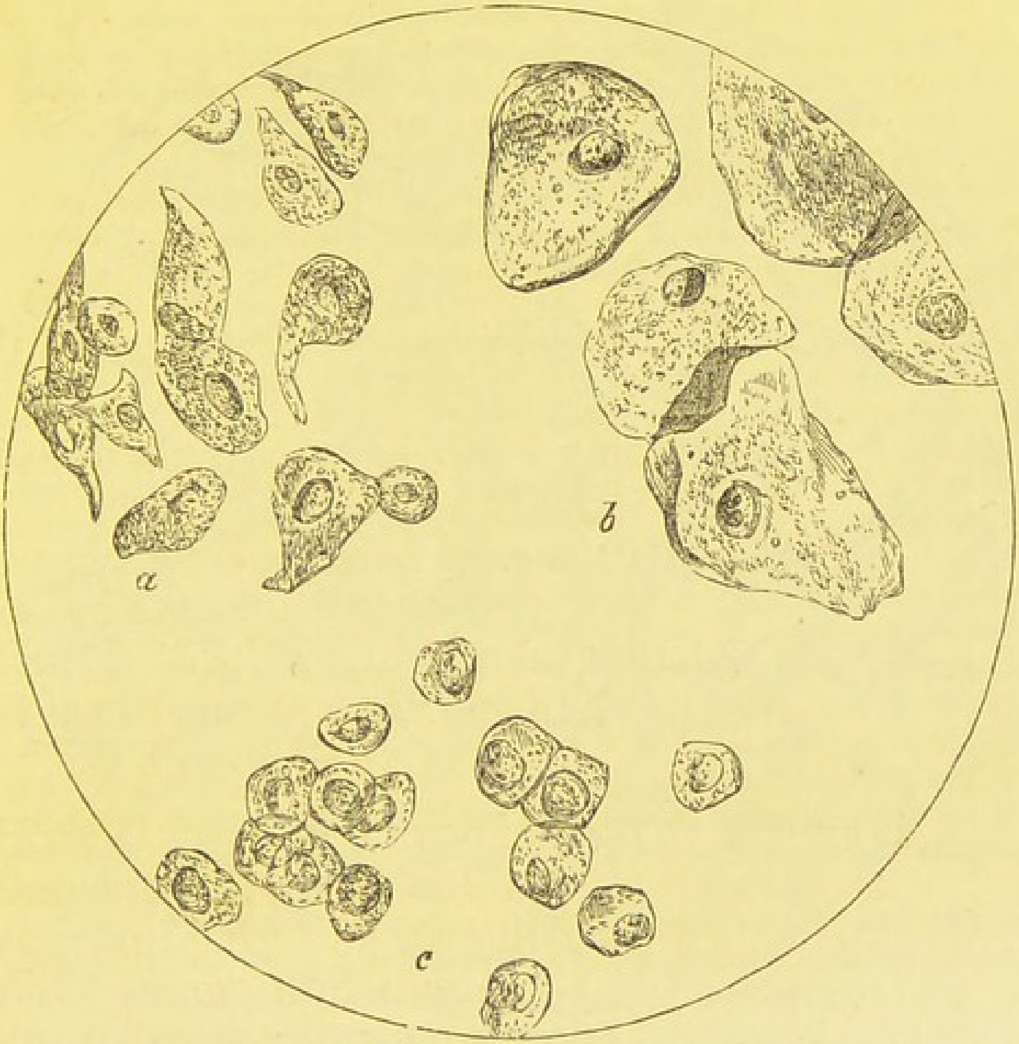
Care must be taken not to confound mucus with the tenacious transparent substance so frequently met with in chronic cystitis or catarrh of the bladder, and which is really composed in great part of pus.

*The fibrous threads* adverted to in the description of mucus, and which were particularly described by the author in the "Lancet" for April, 1858, when carefully examined by the microscope are found to consist of fibrillæ, of variable diameter, usually more or less compound, and presenting the characters represented in Fig. 77. They occur especially in connexion with deposits of oxalate of lime. Dr. Beale is of opinion that they are derived from the seminal tubules of the testis, which is scarcely probable.

The little masses and shreds of mucus often seen in the urine sometimes proceed from the follicles of the prostate: they must not be confounded with the shreds of fibrin sometimes met with in certain cases of Bright's disease, nor with the fibrin of decolorized blood.

Mucus occurs very frequently intermixed with other deposits, as of uric acid, the urates, phosphates, oxalate of lime, renal casts, blood, and especially of the seminal fluid.

FIG. 76.




*a. Vesical Epithelium. b. Urethral* and *Vaginal Epithelium. c. Renal Epithelium.*

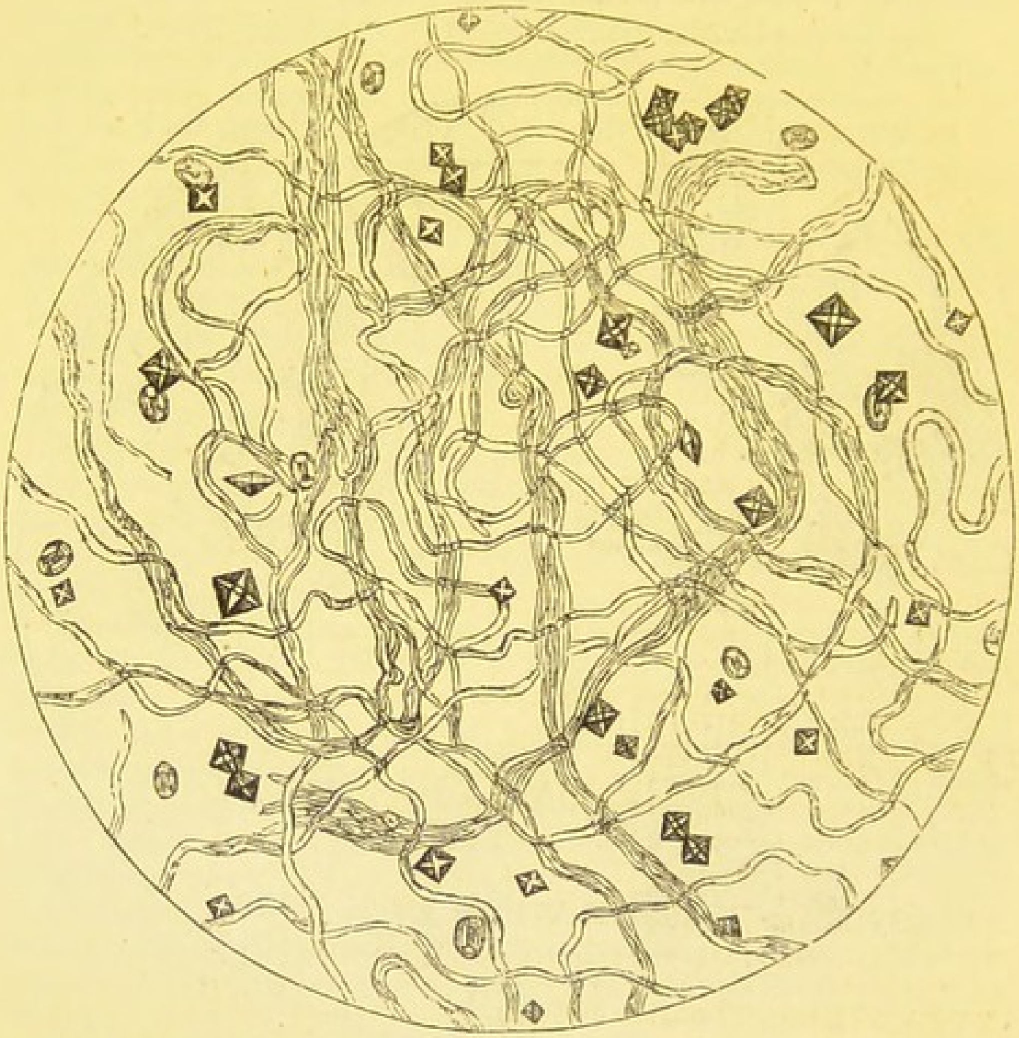
In this place may be described certain corpuscles allied to those of mucus and epithelium, formed for the most part under irritation or inflammation of the mucous membrane of the bladder, and which have occasionally been detected in the mucus of the urine.

Dr. Bird has described two kinds of globules occasionally found in urine, and which he termed " small and large organic globules."

The former, it may be safely concluded, consisted either of altered blood-corpuscles or, more probably, of the sporules of one or other of the fungi formed in urine.

Of *the large organic globules* Dr. Bird wrote: "I know no character by which these bodies can be distinguished from mucus or pus, excepting that they are unaccompanied with the characteristic

FIG. 77.



*Compound fibrillæ* of fibrin, intermixed with octohedral and dumb-bell crystals of *oxalate of lime*. From *Human Urine*, July 6th, 1853.

albuminous or glairy fluid in which the pus and mucus particles respectively float." And in another place this observation is found: "I am not aware whether they are quite identical with what have been termed the exudation or inflammatory globules of Glüge." They are described as being composed of a granular membrane investing a series of transparent nuclei, which become visible on the addition of acetic acid, two nuclei, of a crescentic shape with their concavities opposed, alone being seen in some of the globules.

Dr. Bird met with these large organic corpuscles in several cases of irritation of the bladder, as in the urine of pregnant women during the latter months, and in cases of ardor urinæ; but they occurred in the greatest abundance in the albuminous urine of confirmed morbus Brightii, where they were observed to be so abundant as to cause a drop of the urine to resemble, when microscopically examined, diluted pus.

Dr. Beale has described some corpuscles which appear to be identical with the above, as they were of large size, and contained several transparent bodies within them, which became very distinct upon the addition of acetic acid. They occurred in the case of a patient suffering from rheumatic fever. Some smaller but still large corpuscles, described as being filled with granular matter, were found by the same observer in the urine in a case of chronic bronchitis. These corpuscles seem to differ chiefly in size, and are probably of the same nature.

In a review of Bird's "Urinary Deposits," contained in the "British and Foreign Medico-Chirurgical Review" for July, 1853, some globules or cells were described and figured by the Author, differing certainly from the preceding: they were several times larger than pus and mucus corpuscles, were for the most part of a circular form, and contained usually several very distinct granular nuclei almost as large as ordinary mucus or pus-corpuscles.

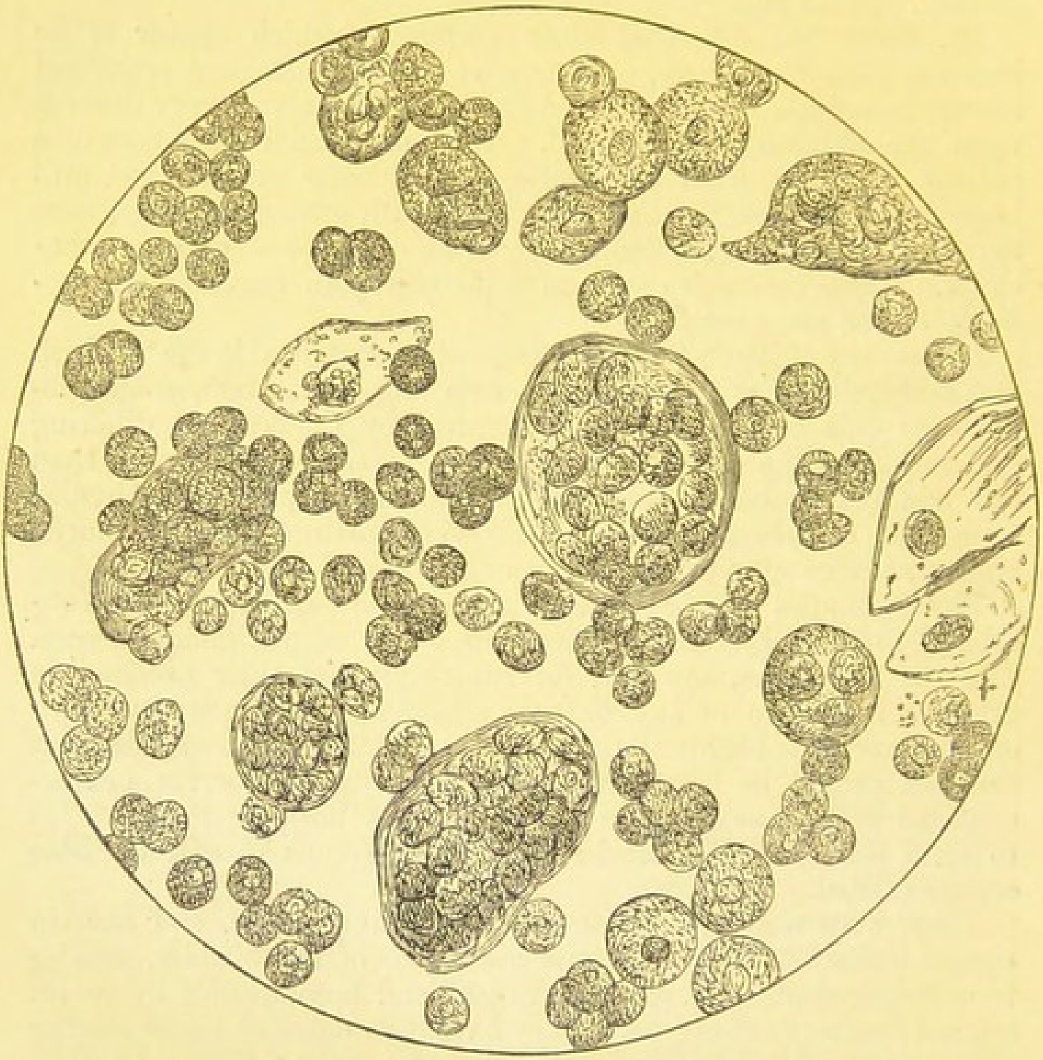
These globules closely resemble the *parent-cells*, which are considered to be characteristic of certain forms of malignant disease. There is no reason, however, for supposing that their presence in urine is indicative of any organic affection of the genito-urinary organs; and it is highly important, in a practical point of view, that this fact should be borne in remembrance. An observer not acquainted with these globules might, on first noticing them, be led to form the erroneous conclusion that cancerous disease of those organs existed.

They were observed in cases of catarrhus vesicæ, and also in simple irritation of the mucous membrane of the bladder, arising from enlarged prostate, or other causes, and accompanied by an increased discharge of mucus. They have been detected under similar circumstances by Henle and Lehmann, who treat of them under the name of "Hassall's Corpuscles."

Another form of corpuscle has been met with by the Author, on several occasions for many years past, in urines containing an abnormal amount of mucus, and especially when they had become somewhat stale: it is of large size, of circular or irregular form, and of granular texture, enclosing two or more *large and perfectly transparent and delicate vesicles*, very different from ordinary granular nuclei, and the appearance of which vesicles the Author suspects is due to incipient decomposition. A corpuscle of this character is figured by Beale.

The *treatment* necessitated by the presence of excess of mucus in the urine resembles that required in cases of purulent urine, and will be found described in the next section, under the head of Pus.

FIG. 78.



*Large Compound Corpuscles*, called by Lehmann "Hassall's Corpuscles." From a case of *Catarrhus vesicæ with enlarged prostate*. Drawn with the camera lucida, and magnified 420 diameters. From Review of Bird's "Urinary Deposits," by the Author, in "British and Foreign Medico-Chirurgical Review" for July, 1853.

## ON PUS IN THE URINE.

### PURULENT NEPHRITIS, PYELITIS, AND CYSTITIS.

Pus, like blood, may proceed from the kidney, or from any portion of the genito-urinary mucous membrane, of either the male or female.

Whenever it occurs in the urine, as in the case of blood, the source must first be determined, and then the cause.

If it proceeds from the kidneys, some symptoms will usually be noticed traceable to those organs; and if from the bladder, urethra, or other part of the genito-urinary track, the symptoms will point to that viscus or portion of the membrane.

When it comes from the *kidney*, it may be formed in the *renal tubules* as the result of inflammatory action, and the pus-corpuscles will then be found in the urine, partly entangled and embedded in the fibrinoid casts, forming what have been termed " pus casts," and partly in the free state. These cases are often rapidly fatal, and are described by Johnston under the name of *suppurative nephritis.*

It may be occasioned by the irritation of a renal calculus, forming *calculous pyelitis,* the purulent discharge continuing in some cases even after the escape of the calculus.

It may proceed from the softening of tubercle in the kidney, constituting *tubercular pyelitis.*

Or it may be caused by inflammation of the *pelvis* of the kidney, the result of severe stricture, and retention of urine—a form which may be termed, for the sake of distinction, *pelvic pyelitis.*

A small quantity of puriform matter is sometimes, but not frequently, present in cases of *carcinomatous disease* of the kidney, but is apt to be overlooked in consequence of the profuse and recurring hæmorrhage which forms so distinctive a character of this disease.

Lastly, the presence of *acephalocyst hydatids* likewise sometimes gives rise to the formation of pus in the kidney, whence, together with some fragments of the hydatids, it may escape into the urine: an occurrence which is, however, extremely rare.

The formation of pus in the kidney, as the result of acute inflammation of its substance, in the healthy subject is rare; but less so in persons of an unhealthy or scrofulous habit.

Tubercular pyelitis is also uncommon; by far the most frequent form being calculous pyelitis, and next in frequency is the milder disorder occasioned by inflammation of the pelvis of the kidney.

*Symptoms of Pyelitis.*

The symptoms of *pyelitis* are pain in the lumbar region, this being sometimes dull but continuous, and at others sharp and darting; it frequently extends to the crest of the ileum or the outside of the thigh, with more or less numbness; sometimes there is retraction of the testicle; there is usually considerable irritation of the bladder, and frequent desire to pass water, giving rise to pain in the perinæum, neck of the bladder, and extremity of the penis, relieved of course on micturition, which is the reverse of what happens in cases of stone in the bladder, in which the pain is greatest after micturition; there may be nausea and vomiting, especially if it be a case of calculous pyelitis, and during the escape of the stone.

It not unfrequently happens, in cases of pyelitis, that all at once the urine voided becomes perfectly clear and free from the smallest deposit of pus. When this occurs, we may infer that one kidney only is affected, and that the escape of the pus has been for a time prevented by the blocking up of the pelvis or ureter, occasioned by an accumulation of thickened pus, or sometimes by the displacement of a renal calculus.

By the symptoms and history of the case, we are generally enabled to determine to which of the causes enumerated the formation of the pus is to be ascribed.

*Calculous Pyelitis.*

The character of the pain, the previous passage of renal calculi, and the frequent deposition in the urine of crystals of either uric or oxalic acid, will generally serve to distinguish calculous pyelitis.

Frequently the calculus is small, more or less rounded, and then its escape is attended with less pain and difficulty. At others it is large, ragged, and even branched; it then often becomes arrested in the pelvis of the kidney, where it increases in size by the constant addition of fresh material, mostly earthy phosphates, to its surface; in such cases its escape is rendered almost physically impossible.

Such an obstruction to the free escape of the pus frequently leads to its accumulation in the kidney, occasioning at length the more or less complete destruction of that organ, and causing it to become dilated so that it may be detected forming a tumour, often nodulated or sacculated, in the lumbar region.

If the obstruction to the escape of the matter be great, the tumour may become of considerable size; adhesions between it and some of the surrounding parts and organs may occur, and ultimately an opening may be formed, either externally or into the colon or peritoneal cavity.

On the escape of the calculus, usually the puriform secretion gradually subsides, and finally ceases; but if much injury has been done to the structure of the kidney, that organ gradually wastes, contracts, and ceases to secrete: if, however, the other kidney be in a sound state, but little inconvenience is felt, and the patient may notwithstanding reach old age.

Now this enlargement and sacculation of the kidney also occurs, but more rarely, in the other forms of pyelitis.

When crystalline uric acid is freely deposited in the kidney, it may give rise to considerable irritation, and be attended with lumbar and sympathetic pains and hæmorrhage. Such cases simulate somewhat calculous pyelitis.

### *Suppurative Nephritis or Pyelitis.*

Suppurative pyelitis may sometimes be traced to a severe attack of *acute nephritis*, especially in an unhealthy subject.

### *Tubercular Pyelitis.*

In tubercular pyelitis there will probably be evidence of tubercular deposit in some other organ or part, as in the lungs and mesenteric glands.

In general no diagnosis can be founded upon the character of the purulent discharge, although cases have been recorded in which matter distinctly tubercular has been found in the urine.

"*Tubercle masses* are described as occurring in the urine in tubercle of the bladder, of the pelvis of the kidneys, or of the kidneys themselves; they are, however, extremely rare. Vogel states that they consist of 'irregular pus-cells, with an undetermined detritus, fragments of cells, unformed nuclei, and an undetermined finely granular mass, with sometimes fragments of cholesterine crystals.'" (Parkes.)

In the pus of tubercular abscess, whether from the lungs or kidneys, there is usually a larger proportion of molecular matter, insoluble in dilute hydrochloric or acetic acid, and the pus-corpuscles are somewhat smaller, the nuclei less compound, and the whole cells less regularly formed than in ordinary pus: these distinctions are, however, too minute and too little defined whereon to found a diagnosis.

Further, while calculous pyelitis usually affects but one kidney, in the tubercular form of the disease both are frequently affected, in which case the urine is never observed to become suddenly quite clear, as sometimes occurs where one of the organs only is diseased.

In tubercular pyelitis, tubercles are also frequently found in the bladder.

The prognosis is, of course, far less favourable than in calculous pyelitis.

Between pyelitis and cystitis the distinction is usually easy. In addition to the absence of symptoms referrible to the kidneys and the presence of others pointing to the bladder, the urine in the two diseases presents very different characters.

In *pyelitis* the pus falls to the bottom as a distinct sediment, leaving the urine above it transparent, of the natural colour, and acid; whereas in cystitis, either acute or chronic, it is usually alkaline, contains triple phosphate, is often offensive, and the animal matter partakes rather of the character of ropy mucus than creamy pus, although pus and epithelial corpuscles are present in it in abundance, and hence it does not form a well-defined deposit.

### *Pelvic Pyelitis.*

When the pus proceeds from the pelvis of the kidney, the discovery of the epithelium which lines that cavity will often determine the diagnosis; the quantity of pus is less, and the symptoms and effects of the disease are altogether of a milder character.

A mild form of pyelitis, leading chiefly to desquamation of the pelvic epithelium, is extremely common in cases of *acute* and *subacute Bright's disease*, and in *cystitis*.

The source of the pus may in many cases be ascertained by the character of the epithelial cells generally present mixed up with the pus in greater or less abundance, and hence both the necessity of being well acquainted with the distinctive characters of the several kinds of renal and genito-urinary epithelium, and the propriety of making diligent search for the cells amongst the pus-corpuscles.

When the pus proceeds from some *cancerous* disease of the kidney or bladder, the quantity is usually very small, and the discrimination may sometimes be effected by means of the microscope, whereby undoubted cancer-cells may be discovered, as well as portions of tissue containing bloodvessels. Care must, however, be observed not to mistake either the fusiform and caudate cells of the vesical epithelium, or the large compound or parent-corpuscles described under the head of mucus, for cancer-cells. Such a mistake would be very serious.

It must be borne in mind that pyelitis may coexist with Bright's disease: this important point should always be determined before expressing an opinion as to the probable termination of the case; if that disease exist, the quantity of albumen in the urine will be much greater than can possibly be derived from the pus, renal casts will be present, and usually some symptoms of dropsy are likewise present. Bright's disease may also coexist with *chronic cystitis*, and may be discovered in the same way.

Again, pyelitis may be associated with *cystitis*; indeed, the former affection is sometimes occasioned by the extension of the irritation and inflammation from the bladder, as in stricture.

When the pus proceeds from the *bladder*,—

It may be due to acute or chronic inflammation of the mucous membrane, constituting *cystitis*.

To the irritation of *stone*, or other urinary deposit, as crystals of *triple phosphate*.

To *malignant disease* in the encephaloid orvillous form, or to *ulceration* of that organ.

When from the *urethra*, it may be due—

To *gonorrhœa* or *gleet*.

To *ulceration*.

To *stricture*.

Or it may proceed from the *prostate*.

When pus is present in the urine of the female,—

It is frequently derived from the mucous membrane of the *uterus* or *vagina*, as in *leucorrhœa*.

In *acute cystitis* there is fever; and as in other febrile diseases, the urine is scanty and high-coloured, is acid, and from it there subsides a white or yellowish deposit, composed of vesical epithelium, exudation and pus-corpuscles, with a few blood-discs.

In *chronic cystitis* the colour of the urine varies: it may be natural or pale, or it may be darker than usual; and in some subacute cases it has a reddish-brown hue, as though it contained hæmatin.

The reaction also varies; at first it is usually acid, but speedily becomes alkaline from the decomposition of urea.

When acid, the deposit is creamy and purulent; but when alkaline, the pus becomes converted into a thick and transparent tenacious substance like mucus: it is then intermixed with crystals of triple phosphate, granular phosphate of lime, and sometimes with pulverulent urate.

Even within the bladder, and when the urine is feebly acid or alkaline, the pus may undergo this change: it may then block up the urethra; or it may be discharged in tough whitish threads, the removal of which has to be assisted.

In *stone* the pus is frequently streaked with blood.

*Stricture* leads to renal disease in this way: the muscular coat of the bladder becomes thickened, the mucous membrane inflamed, and sometimes sacculated; the canals of the ureters dilated and thickened; at length the pelvis, infundibula, and calyces are involved, and pyelitis finally ensues.

The inflammation of the *prostate* may be acute or chronic, and is usually accompanied by more or less urethral inflammation; it is diagnosed by the seat of pain and tenderness, and also sometimes by the presence in the purulent urine of the large *prostatic cylinders*, and little *albuminous masses*, which proceed from the prostatic cells. The cylinders are soluble in acetic acid, and are characterized especially by the presence of yellow or yellowish-green strongly-refracting laminated and calcareous concretions.

### *Quantity of Pus in the Urine.*

The *quantity* of pus contained in the urine of course varies greatly; it may be so small as to be recognisable only in the microscope, or it may amount to ounces in the course of the twenty-four hours, as in many cases of pyelitis and chronic cystitis.

### *Discrimination.*

Even when the quantity is considerable, it will be found a useful precaution never to trust for the discrimination of pus to the unaided eye alone, as deposits of the phosphate and pale urates sometimes closely simulate those of pus, especially as seen in a green glass bottle. It is in all cases safest to pour the contents of the bottle out, so that an opportunity may be afforded for a close examination of the deposit, and if a doubt then remains, to have recourse to the microscope or the action of liquor potassæ; this reagent does not act upon the precipitated phosphates, but it dissolves the urates and converts the opaque cream-like pus into a transparent tenacious substance resembling mucus.

For the discrimination of pus and mucus-corpuscles weak acetic acid may be used; this reagent rarely discloses more than one or two nuclei in mucus-corpuscles, but two, three, four, and even five in those of pus.

### *Physical Characters.*

The physical characters of pus, as already noticed, vary greatly, according to whether the urine is *acid* or *alkaline*.

When acid, the pus, if not coloured with blood, is usually thick, opaque, cream-like, and free from crystals of triple phosphate. When it proceeds direct from the kidney, it usually presents these characters.

When the urine is alkaline, on the contrary, it becomes converted into a transparent, jelly-like, tenacious or ropy substance, and it then contains more or less amorphous phosphate of lime and numerous crystals of triple phosphate.

In many cases of chronic cystitis, the pus discharged presents the above characters; that is, it rather resembles mucus than pus, and hence these cases used formerly to be described under the name of *catarrh* of the *bladder*, the belief being entertained that the substance voided was really mucus and not pus. So tenacious is this altered pus, that it sometimes blocks up the urethra, impedes micturition, and has to be drawn away in long shreds.

Now pus readily undergoes decomposition in men, acid urine rendering it alkaline; this change is thus effected: the decomposing pus acts as a ferment, causing a transformation of the urea of the urine into carbonate of ammonia, so that a purulent urine once voided speedily becomes alkaline, and emits an offensive and ammoniacal odour; the same changes not unfrequently occur even while the pus is still contained in the bladder, and although the urine was at first acid.

By Dr. Rees the alkalinity of the urine is attributed principally to the circumstance that the mucus secreted by the irritated and inflamed mucous membrane of the bladder, being itself alkaline, becomes mixed with the urine, rendering it also alkaline.

Blood-corpuscles are nearly always found in pus more or less abundantly.

## TREATMENT OF DEPOSITS OF PUS.

The treatment will of course vary according to the source and cause of the purulent deposit: these points being determined, the indications at once become obvious.

Irritation and inflammation, wherever existing, must be relieved; when these depend upon the presence of a stone, either in the kidney or bladder, but little actual relief or benefit will ensue until this has been removed.

Anodynes, in many of these cases, must be freely employed, tonics in some; but the class of remedies which will have to be most generally administered are the astringents, amongst which the following may be enumerated.

Sulphate of alum, sulphuric and the other mineral acids, tincture of the sesquichloride of iron, gallic acid, decoctions of uva ursi, and pareira, of the rind of the fruit of pomegranate, and infusion of barosma or buchu.

The fresh fruit of the pomegranate may be eaten.

Of the astringent remedies in the severest cases, two or more may be employed at the same time, including both mineral and vegetable astringents, and their use should be steadily persevered in for a considerable period.

From half a pint to a pint of the infusion of buchu or decoction of pareira should be taken daily, and should be continued for weeks.

In cases of ulceration of the bladder, especially in the female, astringent injections may be resorted to with advantage.

Dr. Prout entertained a high opinion of the value of buchu in cases of so-called *catarrh of the bladder*, provided the remedy was taken for a long period; but Sir Benjamin Brodie gave the preference to pareira brava.

Mr. Henry Thompson has recently published a most favourable report of the effects of an infusion of the root of *triticum repens*, or common bindweed, in irritable conditions of the bladder, and states that it is even superior to buchu. This remedy belongs to the Materia Medica of France, and is considered to possess alterative and diuretic properties. The infusion is thus made: an ounce of the dried root, or rather rhizome, is infused for an hour in a pint of boiling water; the whole pint may be taken in the course of twenty-four hours. Mr. Thompson recommends that the root should be gathered in the spring, before the leaves appear.

Whenever the suppuration is of an unhealthy or scrofulous character, the diet must be nourishing, but unstimulating, and suitable tonics administered; the mineral acids in particular will frequently prove very beneficial.

When the discharge is very profuse, the patient's strength must be kept up in every possible way. This is of the greatest importance; because, in many cases of abscess of the kidney, especially those not of a constitutional origin, if the patient's strength can only be made to hold out a sufficient length of time, the disease will gradually become exhausted, and recovery take place. The Author has had under his care cases in which the hectic and emaciation have been extreme, and which have yet terminated in complete recovery.

In all cases of renal abscess, stimulants should be employed only with great caution.

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# CHAPTER XXII.

## SPERMATORRHŒA AND IMPOTENCE.



UNTIL recently, the medical man, with some few exceptions, from a feeling of false delicacy, thought it beneath his dignity to occupy himself with the treatment of spermatorrhœa, and was too frequently ashamed to avow openly that he paid any attention to this class of cases. This was a great and mischievous mistake, because it left the sufferers from this malady no other alternative than to throw themselves into the hands of quacks and charlatans.

Now, however, this feeling is passing away, and highly qualified physicians and surgeons devote themselves to the treatment of spermatorrhœa.

The charlatans, for their own selfish purposes, too often worked on the fears of their patients, and exaggerated the evil consequences to be anticipated: on the other hand, some of our hospital physicians have fallen into the error of making too light of this affection; and one or two in particular have even gone the length of ignoring its existence altogether. Such a position requires no serious refutation: the affection, though less frequent than quacks would lead us to suppose, is unhappily but too prevalent.

Under the term Spermatorrhœa, are to be included all losses of the seminal fluid not occurring as the result of intercourse.

Before proceeding to treat of the involuntary loss of the fertilizing substance, the semen, which requires for its perfect elaboration all the health and vigour of the best days of manhood, it will be proper to describe briefly the composition and characters, physical, chemical, and microscopical, of that remarkable fluid.

### *Composition and Characters, Physical, Chemical, and Microscopical, of the Seminal Fluid.*

*Composition.*—The seminal fluid, when ejaculated, is composed of the secretions of the testes, of the vesiculæ seminales, of Cowper's and of the prostate glands, together with the mucus and epithelium of the urethra.

According to Dr. Marris Wilson, the amount expelled in health, at each emission, is about half an ounce: the vesiculæ furnishing four-sevenths of the whole; the testes and vasa deferentia about one-seventh; and the prostate, Cowper's glands, and the urethra, the other two-sevenths. These quantities are of course merely approximations, and the total amount as well as the several proportions furnished by each part or organ are liable, even within the limits of health, to very great variation.

That the vesiculæ furnish a large proportion of this fluid is proved by the character and amount of the discharge which takes place in eunuchs and others who have been castrated.

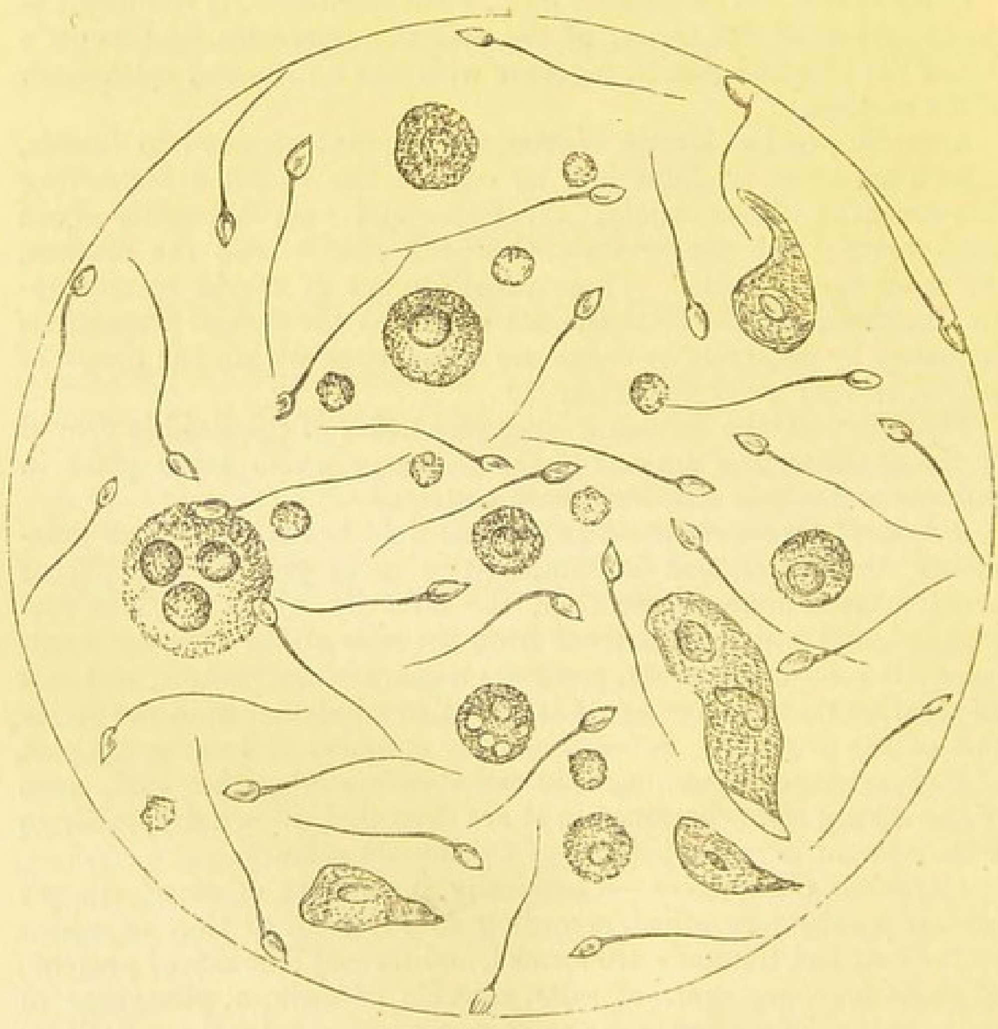
*Physical Characters.*—The seminal fluid has a somewhat gelatinous consistence, and is composed in great part of transparent ovoid masses, more dense than the fluid by which they are surrounded, and which are derived from the cells of the vesiculæ seminales; is semi-transparent, possesses a characteristic odour, and has an alkaline reaction, owing, it is stated, to admixture with the secretion of the prostate. Some time after emission it loses great part of its consistence, becoming thin and watery, while, when cold, some of the earthy salts contained in it are deposited. When dry, it forms a transparent horny substance of a yellowish colour.

*Chemical Characters.*—Chemically, it consists of about six per cent. of a substance allied, according to Frerichs, to that of which epithelium and the nails are formed, and termed binoxide of protein; of about four per cent. of salts, chloride of sodium, phosphate of soda, but chiefly of phosphates of magnesia and lime, and ninety per cent. of water. The presence of the magnesian salt is shown, Lehmann states, by the occurrence in the decomposing semen of well-formed crystals of triple phosphate. It does not become turbid when boiled.

*Microscopical Characters.*—The morphological elements contained in it, detectible with the microscope, consist of a few epithelial cells from the urethra; granular corpuscles of various sizes, some of which are compound, of considerable magnitude, derived from the tubes of the testes, and termed *spermatophori:* but principally of the well-known and easily recognised seminal animalcules or spermatozoa, which are reproduced, as shown by Kölliker, mainly, if not entirely, within the cells denominated spermatophori.

The *spermatozoa* are remarkable in their form and consistence, but particularly in their movements. Their form is too well known to require description. (See Fig. 79.) Their consistence is shown

FIG. 79.



SEMINAL ANIMALCULES, intermixed with *Seminal Corpuscles* and *Epithelial Scales.* Magnified 900 diameters.

by their retaining their form even when boiled, by their remaining uninjured frequently in even putrid urine; and, according to Valentin, when carefully incinerated, by leaving an ash which retains their precise shape.

When the semen is recent and yet warm, the spermatozoa swim about in it with great activity, moving in a zigzag manner, by lashing the tail from side to side; they thus advance in the liquid, but are unable to execute a retrograde movement; they also avoid obstacles as though endowed with volition: if the semen be covered with a piece of thin glass, and its evaporation thus prevented, the movements continue for a long time; as also when it is placed in warm serum, or mucus, and sometimes even in the urine. By water, mucilage, alcohol, and acids, creasote, highly diluted solutions of the metallic salts, and solution of opium, or strychnine, their motions are stopped, the long pointed tail becoming stretched out in a straight line, just as occurs with a true animalcule when killed. On the other hand, by solutions of sugar, urea, glycerine, salicine, and amygdaline, they seem unaffected. When semen is dried upon a piece of glass, or on cloth or linen, and redissolved, even years subsequently, in a weak and tepid solution of albumen, the spermatozoa may be discovered but little changed. This fact, as well as the occurrence of the spermatozoa after coitus in the urine of both the male and female, often afford valuable aid in certain medico-legal inquiries, as in the detection of rape or adultery.

### *Involuntary Seminal Emissions—Nocturnal, Critical, and Diurnal.*

Seminal emissions are either voluntary or involuntary; the latter being termed *nocturnal* or *diurnal,* according to the period of their occurrence. Of the two forms the diurnal are usually the most serious: in some cases the pollutions take place only at night, in others in the daytime as well.

*Involuntary nocturnal emissions* occur during sleep; usually towards the morning, and after five o'clock, and frequently while lying upon the back. Several reasons may be assigned for their happening towards morning: one is that the bladder being by that time more or less full, gives rise to the slight irritation which in some cases of spermatorrhœa is alone necessary to produce an emission; another, that towards morning the fatigue of the previous day has been partially recovered from, and that in consequence there is a natural disposition to erection, which in weakened organs may also produce a similar effect. Again, it is possible that the congestion of the cerebellum which exists in sleep may be favourable to the production of the sexual orgasm.

The circumstances accompanying the seminal discharges vary greatly: ordinarily they are preceded by lascivious and exciting dreams, the sleeper being awakened at the moment of their occurrence, and are attended sometimes with both erection and sensation more or less vigorous, while sometimes the erection is but incomplete and momentary, and the sensation lessened; and at others there is neither erection nor sexual feeling, and then the emissions may occur without consciousness. These, as will be pointed out hereafter, are important circumstances to notice, since they bear upon the prognosis and treatment of this affection.

The frequency with which the seminal losses are repeated also is subject to great variation; the intervals are very irregular: they may happen once a month, once a week, two or three times a week, nightly, and occasionally twice or thrice each night.

When several emissions occur in quick succession on recovery from an illness, they are termed *critical:* their occurrence indicates that the testes are again actively engaged in secretion, and at the same time, that debility exists, rendering the organs incapable of retaining their contents.

*Involuntary diurnal emissions* likewise take place under very different circumstances: usually they occur at stool, without erection or sensation, or with these but little developed, or the seminal fluid escapes with the last drops of urine voided, with slight erection and sensation; or lastly, lascivious thoughts, the slightest touch, friction, or pressure, will occasion them, there then being both erection and sensation more or less imperfect.

The fluid emitted at stool doubtless usually proceeds from the vesiculæ seminales, especially when unattended by any degree of sensation or erection, and by some is stated not to be semen at all, and therefore not to be of the slightest importance. The statements made of the presence of the spermatic animalcules in this fluid are so circumstantial and repeated, that it appears scarcely possible to doubt their occurrence: thus Lallemand affirms, that out of 33 examinations of the fluid of the vesiculæ, he found the spermatozoa in 31; and even Milton, while he denies that they are receptacles for the seminal fluid, yet acknowledges that he detected "a few stray animalcules;" but, even supposing the spermatozoa to be absent, it is not proved that the loss of this vesicular fluid is uninjurious, while it is certain that the impression made on the mind of the patient thereby, exercises a serious effect upon his spirits and health.

### *Varying Characters of the Fluid emitted.*

The *characters of the seminal fluid* discharged differ greatly: when occasionally emitted only, it is thick and glutinous, and abounds in myriads of well-formed animalcules, with granular corpuscles and spermatophori; in fact, it possesses all the characters of the normal seminal fluid. When more frequently discharged, it is thin and watery; it may be very small in amount, be wanting in even the odour of the healthy fluid, and contain but few spermatozoa.

According to Lallemand, these may be small in size and badly formed; the tails even may be absent, the shining heads alone remaining.

When the emissions occur in quick succession, and from abuse, the seminal fluid is sometimes streaked with blood, then inflammation of the testicle, or *orchitis*, followed by alteration and impairment of structure, is apt to ensue.

### *Detection of the Spermatozoa in the Fluid discharged and in the Urine.*

The detection of the animalcules, either in the discharge itself or in the urine, is unattended with difficulty. A minute quantity of the material must be placed upon a slip of glass, and diluted either with a drop or two of tepid water or a little of the white of an egg, the whole being then covered with a circle of thin glass, and subjected to examination with a quarter or eighth-of-an-inch object-glass; if recent, the spermatozoa may be seen in active movement, which, under favourable circumstances, may continue for some time.

After an emission, a drop or two of the liquid still clings to the urethra; if this be pressed out, the animalcules may be detected in it, as also in the sediment of the urine first passed after an emission; and especially in that of the urine of women. Of the escape of semen with the last urine voided, patients are sometimes scarcely or not at all conscious; if this occurrence be suspected, it will be sufficient, after micturition, to press a drop or two of liquid out of the urethra on to a plate of glass, and to subject it to microscopic examination.

The seminal fluid, as already noticed, when exposed to the air, dries up into a transparent gum-like substance, in which the spermatozoa are preserved almost unchanged. By placing, therefore, a drop of the fluid, while moist, upon a slip of glass, covering it with a small disc of thin glass, and allowing it to dry, it may be kept for examination for any length of time.

### *Discrimination of the Discharge of Urethral Gleet, and of the Prostatic and Vesicular Fluids.*

Care must be taken not to confound the discharge of *urethral gleet* with the seminal fluid; the distinction is easy, since the former is distinguished by the absence of the infusoria, by the presence of scaly epithelium, and by the escape being in general continuous. Sometimes the gleety discharge occurs only after sexual excitement, and lasts but for a short time, when of course its character is more apt to be mistaken. The *prostatic fluid* might also be mistaken for semen; in this case the spermatozoa would also be absent, and, in addition, the microscope would reveal in it the presence of the prostatic cylinders, and perhaps also of the peculiar lamellated concretions of phosphate of lime, which are found in the prostate in such numbers. Like the mucus of ordinary gleet, that from the prostate may also be continuous, but more frequently it appears only after violent efforts at defæcation, when a small quantity of matter may be expressed, forming only a drop or two of a thick, stringy, and transparent fluid, which appears at the orifice of the urethra. The prostatic can never be mistaken for the *vesicular fluid*, for this escapes at once as a bulky substance, of the passage of which the person is conscious, even although unaccompanied by any sexual sensation: this fluid, again, possesses physical characters of its own, whereby it may be recognised: thus it abounds in rounded and ovoid masses of mucus, more or less condensed, moulded in the vesicles or cells of the receptacles, and which float in a transparent fluid.

### *Causes of Spermatorrhœa and Impotence.*

The *causes* to which spermatorrhœa may be traced are numerous.

Thus the emissions may be occasioned by *local plethora*, occurring at irregular intervals in the young and robust, and being attended with all the evidences of unimpaired virility.

The discharge taking place under such circumstances is to be regarded rather as salutary than otherwise, and as a natural effort to relieve the engorgement and over-distension of the parts.

It is certain that during the active period of reproduction there is a continuous development of the spermatic fluid; and it is highly probable that in some cases this is not removed by absorption with the same rapidity with which it is generated, and hence that an accumulation occurs rendering an outward escape necessary.

But the foremost and most frequent cause is *abuse:* this acts by producing both general and local debility and irritability.

Another cause is *over-indulgence*, acting in the same manner.

A fourth cause is *local inflammation* and *irritation*. This may be occasioned by *urethritis*, or *blennorrhagia*, specific and non-specific, acute and chronic, by *stricture*, *cystitis*, *inflamed* or *enlarged prostate*, *accumulation* of *sebaceous matter* under the prepuce, *elongated* or *contracted prepuce* producing *phymosis*, and *balanitis*, or *bastard clap*. These several excitants operate by the extension of the inflammation or irritation to the testes, vesiculæ seminales, muscles, and other parts or organs concerned in the formation and ejaculation of the seminal fluid.

*Worms*, particularly *ascarides*, *hæmorrhoids*, *anal fissures*, *cutaneous eruptions* on or near the genitals, are also occasional causes of spermatorrhœa; those which affect the rectum act chiefly by causing a sympathetic and spasmodic contraction of the vesiculæ seminales.

Again, *constipation* may excite spermatorrhœa, especially *vesicular* discharges; this operates partly by producing congestion and irritation in the neighbourhood of the rectum, but chiefly by the compression exerted in the act of defæcation upon the vesiculæ, whereby their contents are forced out.

*Indigestion*, with or without *diarrhœa*, may excite seminal emissions, or they may be aggravated and prolonged thereby.

*Incontinence of urine* in early life also predisposes to them, such cases being often difficult of cure.

*Natural feebleness of constitution*, *debility*, and *irritability*, whether natural or acquired, predispose to spermatorrhœa, and are in some instances its principal causes.

Lastly, disorder or disease of the *brain* may either excite it, or may be the chief cause of its continuance.

Frequently more than one cause is combined, as abuse or over-indulgence, with local inflammation or irritation.

In some cases of spermatorrhœa with general debility, irritability, and dyspepsia, there occur periodically an excitement and plethora of the sexual organs; the testicles enlarge and become painful, the scrotum red, the vas deferens sensitive and enlarged; there is more or less *varicocele*, and a feeling of general distension. These symptoms arise from a determination of blood to the testicles, and a consequent large secretion of seminal fluid. The pain in some cases is extreme, and no relief is experienced until a discharge takes place, while in other milder cases the pain and engorgement cease when the patient assumes for some hours, as when in bed, the recumbent position. Sometimes this condition recurs daily, lasting an hour or two; or it may continue the whole day, and subside during the night, to recur the next morning; or it may continue for several days, and without any emission having occurred; on some extra exertion of either body or mind, or agitation of the feelings, it may suddenly subside, to return, perhaps, in the course of a few days. Such cases are apt to occur in the debilitated, when the brain and sexual organs have been kept in a state of unnatural excitement.

### *Consequences of Spermatorrhœa.*

The *consequences* of spermatorrhœa are even more numerous than the causes, and amongst them may be enumerated debility and irritability, disinclination to exertion of body or mind, timidity, want of memory, confusion of ideas, and despondency; flatulence, sometimes constipation, gastrodynia, and other symptoms of disordered digestion; defective and deranged innervation, as shown by chilliness and various sympathetic nervous sensations and pains; irregular circulation, made manifest by palpitation, sometimes mistaken for disease of the heart; phthisis; cerebral congestion, epilepsy, general paralysis, and insanity; lastly, enfeebled sexual power, and ultimately impotence.

## PROGNOSIS OF SPERMATORRHŒA AND IMPOTENCE.

It has already been stated that an occasional emission occurring in the healthy and robust, and as the result of plethora, is salutary rather than hurtful. The test as to whether it is so or not depends upon the after feelings and consequences: if the system feels relieved and the energies are increased, it is at least evident that it has not exerted any baneful effect.

Writers have gone to the length of asserting that any involuntary discharge occurring oftener than once a month is hurtful. Seeing how much individual health and vigour vary, it is impossible to lay down any merely numerical rule of this kind: what one person bears with perfect impunity, if not with advantage, would exert a most prejudicial effect upon the health of another; whether it is injurious or not, must be judged of, as already stated, by the results. When the emissions, although they may not occur oftener than once a fortnight, produce debility, chilliness, indisposition to mental or bodily exertion, they are too frequent to be compatible with health: this is a safe and unerring test.

Notwithstanding the pitiable effects of long-continued and frequent spermatorrhœa, especially when accompanied by great debility, this affection is one which in nearly every case admits of cure.

The cases themselves vary greatly in severity. When the cause depends upon simple plethora, the cure is easily effected.

It is also more amenable to treatment when it arises from local inflammation and irritation.

But when it results from abuse or over-indulgence, especially long-continued, and the health has in consequence become much impaired, the treatment required is often tedious; but the cases resulting from these causes also differ much from each other in severity.

When the involuntary discharges are nocturnal only, when they awaken the sleeper, and are attended with perfect erection and sensation, the case is amongst the more favourable. When the erections are slight only, and but little sensation accompanies the emission, it is more serious. When the losses occur without erection and consciousness, they are still more difficult of cure; and when, in addition, day pollutions are superadded to those of the night, the case is usually one which taxes the patience and perseverance of both patient and physician.

It has been stated that one of the results induced by spermatorrhœa is enfeebled sexual power, proceeding in the worst cases to *impotence*. Now this condition, when it arises from this cause, is also in the great majority of cases curable; in fact, the spermatorrhœa being cured, the impotence gradually ceases; but the more frequent and long-continued the seminal losses, usually the more severe and lasting is the impotence.

If the person be young, or if of more advanced age, the emissions occur with erotic dreams and awaken the patient, and there are occasional erections, the prognosis is favourable. It is impossible, however, to lay down any strict rule as to the age at which impotence is curable, since the strength and vigour of one person at a given age may exceed that of another some fifteen or twenty years his junior. In general, however, of course the older the individual the less the prospect of his regaining virility.

On the other hand, when impotence is the result of the natural decay of age, or when it proceeds from a wasting or alteration of the structure of the testicles, or from disease of the brain or spinal column, it is of course incurable.

Other occasional and temporary causes of impotence, and therefore usually remediable, are great pain, as that of toothache, dyspepsia, long-continued illness, producing extreme debility, fatigue, and great cerebral excitement.

A symptom of much importance in cases of threatened impotence is a sensation, very troublesome and distressing, not merely of general chilliness, but especially of coldness *in the scrotum*. Whenever this symptom occurs, it should never be neglected.

It is well known that some persons are incapable with certain individuals only; and others, at particular times; thus, some have failed, to their great consternation, on the nuptial night. This is described by some writers as a form of impotence due to nervous agitation and excitement, or as resulting from a want of harmony between the mind and body.

## TREATMENT OF SPERMATORRHŒA AND IMPOTENCE.

The treatment of spermatorrhœa may be divided into *constitutional* and *local*.

Before proceeding to treat a case of this description, we must endeavour to satisfy ourselves as to the cause; and especially we must determine whether there is local inflammation or irritation, whether the disorder is due solely to debility, or whether, as is usually the case with much general weakness, there is also some local implication. In these latter cases the treatment of course must be partly constitutional and partly local.

When the emissions occur only at tolerably long intervals in persons who are healthy and vigorous, and whose powers are not otherwise defective, when, in fact, they are due simply to plethora, the treatment is simple, and consists in abstinence from alcohol in all forms, and from heating and stimulating food; in the occasional administration of cooling aperients, and in moderate sexual indulgence.

When it is due to inflammation of the urethra, specific or nonspecific, or other local irritation, it is sometimes sufficient to limit the treatment to the local affection; the inflammation must be subdued by aperients and nauseants, and when it has reached a more chronic stage, by the stimulating balsams or astringents, as well as by injections. Very frequently the mucous membrane of the urethra is in a state of chronic inflammation or irritation without there being discharge, a condition indicated by tenderness on pressure in the course of the urethra, by more or less scalding of the water, with sometimes redness of the orifice of the urethra; sometimes, also, the prostate is swollen and tender, points which may be ascertained by examination per rectum. These conditions must be removed by recourse to the appropriate remedies.

In the great majority of cases, however, although there may be some degree of tenderness and irritation, it does not amount to inflammation; but there are marked indications of debility, accompanied especially by disorder of the nervous system and derangement of digestion.

The classes of remedies more particularly needed in such cases are *tonics* and *sedatives*.

When, as is frequently the case, the seminal discharges are much affected by weather, when they become more frequent in warm, damp weather, and diminished in frequency in a cold, dry, bracing atmosphere, the administration of tonics is plainly indicated.

Amongst the tonics the most important are the preparations of *quinine* and *iron*. When anæmia exists, iron, either alone or in combination, is indicated.

These remedies require to be watched, however, since, as in other cases of great debility, they sometimes disagree and are too exciting, producing irritability and headache: these effects should not in general be met by abandoning the remedies in question, but by selecting the milder preparations, and by carefully regulating the doses and the time and manner of administration, but especially by combining them with mild aperients.

Mr. Milton writes in very favourable terms of the *tincture of the sesquichloride of iron*. He recommends that it should be given in doses of from twenty to thirty minims, and if at the end of a week no unpleasant symptoms are produced, that the dose should be increased to sixty or even ninety minims three times a day. If, however, the patient has suffered from painful digestion and flatulence, and this is aggravated by even the smaller doses, the remedy should be at once discontinued: if also coldness at the stomach, sickness, nausea, or a feeling of distension and griping come on, the dose is as large as can be borne at the time. When the remedy produces constipation, this of course can be avoided. It sometimes happens that even while drachm doses of the tincture are being taken the spermatorrhœa will suddenly return, in which case the quantity should be increased at once to eighty or ninety minims.

The *mineral acids*, either alone or in combination with bark, quassia, gentian, or some other bitter, will often prove of service, and are less likely to disagree than either quinine or iron.

*Strychnia* is also sometimes useful, especially when there is great want of tone, and in combination with suitable aperients in cases of obstinate constipation.

The sedatives usually resorted to when there is pain or excessive nervousness are preparations of *opium*, *hyoscyamus*, and *digitalis*.

The grains or seeds of the flower of the *hop-plant* have been much recommended by Dr. Sigmund, the dose varying from five to twenty grains; they are both a sedative and tonic.

Two other remedies which have been much vaunted are camphor and ergot of rye.

*Camphor* may be given sometimes with benefit, although its action is somewhat uncertain: it is in the more acute cases that its administration is indicated, it acting as an aphrodisiac, and preventing the priapism or erection which with some precedes the emission. Half a drachm to a drachm of the tincture may be given in water at bedtime, or a few grains of solid camphor may be taken in water, or may be placed between the glans and the prepuce. Lallemand states that in too large doses, or too long continued, it may induce serious and obstinate involuntary discharges.

*Ergot of rye*, like lupulin, has been extolled as a specific; it may be administered in addition to other remedies, especially in cases in which the emissions occur without sensible erection or sensation.

When constipation exists, it may be obviated by enemas, by mild aperients, combined in some cases with minute doses of strychnia.

When fever is present, nitrate of potash and sulphate of magnesia may be given with advantage.

Since the digestive organs are usually, either as cause or effect, so seriously disordered in most cases of spermatorrhœa, a careful regulation of the diet is of very great importance; it should be simple, nourishing, and easily digestible, but not irritating or stimulant. When there is great exhaustion or debility, wine, particularly claret and port, may be allowed in moderation.

Stimulating remedies, including *cantharides*, *phosphorus*, *copaiba*, and *cubebs*, are usually hurtful in spermatorrhœa. The only cases in which they can be used with a prospect of benefit are those attended with atony. In impotence, ergot and the red or amorphous phosphorus may sometimes prove beneficial.

*Smoking* in excess is very injurious in spermatorrhœa accompanied by debility and exhaustion.

A moderate amount of *exercise*, partly in the form of *gymnastics*, if the strength permit, and cheerful *society*, are highly beneficial.

*Fatigue*, both of *body* and *mind*, should be specially avoided.

Of the treatment of those comparatively rare cases of spermatorrhœa arising from worms, fissures in the anus, diarrhœa, cutaneous eruptions, collection of sebaceous matter under the prepuce, stricture, and elongated and contracted prepuce, no detailed remarks are required. It will be sufficient to observe that such cases must be treated upon the ordinary general principles, and with the special object of removing as speedily as possible all sources of irritation likely to affect injuriously the organs of generation.

The *local* measures sometimes called for consist of cauterization, catheterism, injections, blisters, general and topical bathing, and galvanism, on each of which a few observations may now be made.

The operation of *cauterization*, a remedy first suggested by Lallemand, and which in his hands proved so successful, is specially indicated in cases of chronic inflammation or irritation of the urethra: "its results may be considered certain when involuntary discharges follow a common clap or non-contagious gleet. I have also found it successful in many cases where atony or relaxation seemed to predominate, and in a few cases of marked nervous disorder and congenital predisposition. In the latter cases, however, the benefit derived from cauterization has seldom proved permanent, though I believe that, by changing the condition of the tissues, the foundation has been laid for successful treatment by other means." (Lallemand.)

The operation is thus effected. The bladder must be completely emptied, and the length of the urethra determined, a point ascertained by the sudden cessation of the escape of the urine, which occurs at the moment when, on withdrawing the catheter, it enters the canal. The length marked first on the catheter is then measured on the *porte caustique*, the eyes of the catheter, in taking the measure, being applied to the olivary extremity of the former instrument.

The diameter of the olivary body should considerably exceed that of the tube of the instrument, because, although the operator may judge when he is near the neck of the bladder by the nearness of the slide on the stem of the instrument to the glans, still it is proper that he should have a distinct sensation when that point is reached. The passage of the enlarged extremity of the instrument through the sphincter gives this sensation very distinctly. When, on gently withdrawing the instrument, a slight resistance is felt to the re-entrance of the bulb into the urethra, the operator may be certain that the cuvette containing the caustic is in its proper position.

The cuvette should be charged by melting the nitrate of silver into the cavity.

The patient should lie down during the operation. When in proper position, the cuvette is to be very rapidly passed over the inferior surface of the urethra, the stem being slightly rotated; it should then be closed immediately, and slowly withdrawn.

Diluents should now be prescribed, the diet should consist of milk and vegetables only, and rest should be enjoined.

For two or three days, micturition is frequent and painful, accompanied by the passage of a few drops of blood; but these symptoms, if proper care be observed, soon pass off.

The first effect of the operation may be to increase the emissions, and it is only when the inflammation has completely subsided that any opinion can be formed of the amount of benefit derived.

A second operation should be practised only when from any cause the first has failed to produce its usual effects; and when the second application is not followed by any great benefit, it is improbable that a third will be more successful, and recourse ought therefore to be had to other means.

Lallemand thus emphatically expresses his opinion of the beneficial effects of cauterization:—"In conclusion, I may simply record my opinion, that two-thirds of the cases of spermatorrhœa would be beyond the reach of medical assistance, were it not for the beneficial effects produced by the application of nitrate of silver to the prostatic portion of the urethra."

Although probably but few practitioners would feel disposed to go quite the length of M. Lallemand in their estimate of this remedy, yet its great value is undoubted, and has been abundantly confirmed.

In some cases of spermatorrhœa there is great excitability of the nervous system and susceptibility of the genital organs, the slightest excitement, touch, or friction, producing an emission with a very imperfect erection. In cases of this description, Lallemand recommends *catheterism*, or the introduction, at intervals of five or ten days according to circumstances, of a moderate-sized gum-elastic catheter. The passage of the instrument is often attended with much spasm and pain: on the first occasion it should be retained for an hour or so, and subsequently for a longer time.

The introduction of the catheter is followed by inflammation and swelling, which extend to the orifices of the ejaculatory ducts; the disordered nervous action is also modified. The same proceeding may be advantageously adopted in cases of diurnal pollutions attended with excitability, and in those accompanied by simple atony.

Another remedy, somewhat analogous in its action but milder in its effects than cauterization, consists of *injections* of nitrate of silver: these should be used in conjunction with tonics or the other remedies indicated; the injections may vary in strength from five to twenty grains to the ounce.

Mr. Milton, who speaks very highly of the beneficial effects of injections of nitrate of silver, and who prefers them greatly to cauterization, recommends that a syringe with a detached tube should be used, "sufficiently thick from the shoulder to the rings to fill up the urethra, and sloping from the shoulder to the tip. The tube is introduced as far as the membranous part of the urethra; the surgeon grasps the penis firmly low down, and then a syringe, charged with two drachms of the solution of the required strength, the nozzle of which is accurately fitted to the tube, is adjusted, the piston is driven home, and the fluid retained till the patient begins to complain of a strong sense of burning and uneasiness, when it is withdrawn."

The employment of *blisters* has been strongly condemned by Lallemand, on account of the "exasperation affrayante" produced by them, and as strongly recommended by Milton; but much doubtless depends upon the manner of their application and the length of time they are allowed to remain in contact with the part to which they are applied—namely, either the perinæum or the urethra.

*Blistering tissue*, or *the vinegar of cantharides*, may be used, and it may be applied in mild cases for an hour or two, and in severer cases for four or six hours. It is advisable in some instances to sprinkle the surface with camphor, to relieve the chordee which sometimes ensues.

Blistering is, however, at the best, a very disagreeable and painful remedy, and one to which we should resort only when other means have failed. It is in vesicular spermatorrhœa that the employment of blisters appears to be more particularly indicated.

*Bathing*, both general and topical, may now be treated of—a remedy from the use of which frequently great benefit is derived; there are, however, as is well known, many cases in which it proves positively hurtful.

The cases in which cold general bathing is beneficial are those in which the circulation is active, where vigorous reaction follows the bath, and there is no subsequent depression.

It is injurious in those in which the circulation is feeble, where reaction is incomplete, and where the patient feels chilly and weak. Cold bathing, therefore, in spermatorrhœa, as in other disorders, is a remedy which is powerful for both good and evil, and which consequently requires to be carefully watched.

Bathing in salt water is more likely to be beneficial than in fresh water, especially if accompanied by swimming.

Topical is more frequently useful than general bathing, and it is seldom that it is injurious. The patient may sit in a hip-bath, or cold water may be dashed over the genitals, or it may be applied to the loins or perinæum in the form of douches.

Bay, rock, or St. Eube's salt, may be added to the water, and in summer its temperature may be reduced by the addition of certain refrigerating salts, as nitrate of potash and chloride of ammonium in the proportion of two or three ounces of each to a gallon of water.

In inflammation of the urethra or prostate, or when there is painful chordee, cold bathing is contra-indicated, but an occasional hot-bath will be found very beneficial.

Lallemand recommends that cold and hot douches should be alternated, and he states: "I have seen these alternated douches produce a state of priapism even in persons who were perfectly impotent on the previous day."

*Galvanism* has been employed with advantage in cases of extreme atony and relaxation; in those in which inflammation or irritation exists, it is contra-indicated.

Of the barbarous proceeding, termed *acupuncture*, of thrusting needles through the prostate, in the course of the ejaculatory ducts, and even sometimes through the spermatic cord and testicles, little need be said, except in condemnation. This operation is performed with a view to the relief of neuralgic pains, and Lallemand expresses himself in most favourable terms respecting its effects, even remarking: "Acupuncture has unfortunately lately fallen into disrepute. . . . . In cases of spermatorrhœa arising entirely from nervous disorders (which, indeed, are not common), its effects are as prompt and durable as beneficial." Lallemand also considers it to be suitable for those cases in which the pollutions arise from habit.

*Certain mechanical contrivances* may now be treated of, designed either to prevent the escape of the seminal fluid or to arouse the patient in time to prevent an emission.

The first purpose is accomplished by the application of instruments, either through the rectum or to the penis, whereby pressure on the urethra and the temporary closure of its canal is insured. This proceeding is wholly unjustifiable, and is resorted to only by the unscrupulous and the ignorant. It usually seriously aggravates the mischief, and occasions injury to the parts greater than the mischief occasioned by the spermatorrhœa itself: the seminal fluid is still emitted, but in place of escaping externally, it is forced back into the bladder, from which it is discharged with the urine on micturition.

Mr. Milton states that *a leather ring armed with points*, and so fitted on the penis as to produce no uneasiness till erection comes on, is often useful; the patient being then aroused by the pricking, can jump out of bed, and thus avoid an impending emission. Although such a contrivance might prove serviceable in some cases, there are many in which it would be useless, for in some confirmed cases of spermatorrhœa, little or no erection occurs, so that the patient would fail to be aroused.

Although nocturnal emissions occur in some persons while lying upon the side, they take place much more frequently while sleeping on the back; in such cases, as advised by Lallemand, a thin sheet of lead may be applied over the loins, secured in front by a girdle, and having a piece of wood fastened perpendicularly down its centre. With such an arrangement it is impossible for the sleeper to rest on his back.

It is recommended also that the bed should be very hard: it should certainly not be too soft, but in thin and nervous persons a very hard bed will so irritate and disturb as to produce the very evil which it is sought to avoid.

It now remains to be stated, that various as are the causes of spermatorrhœa, and great consequently the differences in the treatment required, yet it is but seldom that either cauterization or blisters are necessary, the majority of cases which come before the physician admitting of cure by the careful regulation of the diet, habits, and conduct, and by the administration of suitable tonics and anodynes.

Many persons entertain the notion that spermatorrhœa is maintained owing to the absence of sexual intercourse: this, when it proceeds from plethora, is no doubt the case, and in such instances moderate indulgence is beneficial, but in the debilitated it will but increase greatly the mischief. It should, however, be remembered, that the generative organs, like all others, may have their energy impaired from prolonged inaction.

In treating spermatorrhœa, the most frequent cause of impotence, we are at the same time adopting the best means of remedying the *impotence* itself. When the latter affection only exists, or is combined with well-marked atonic spermatorrhœa, the use of stimulant measures and remedies may be resorted to with less hesitation, but still with great caution; as cold and hot douches, galvanism, strychnine, iron, ergot, cantharides, capsicum, and the amorphous phosphorus. The diet may then also be both nourishing and stimulant, and alcohol may be allowed in moderate quantity.

Cases of impotence depending upon structural changes in the testes or spinal marrow should always be discriminated, since the treatment proper in the less serious cases might be both hurtful and dangerous if pursued in those that are comparatively incurable.

It may also be necessary to employ the oleo-resins, cubebs and copaiba, in the treatment of those exciting causes of spermatorrhœa, gonorrhœa, and gleet, but injections of nitrate of silver will frequently better answer the purpose.

# CHAPTER XXIII.

## ON THE MEDICAL ORIGIN OF STONE AND STRICTURE.

### *On the Medical Origin, Diagnosis, and Treatment of Stone in the Bladder.*

THE following observations, slightly modified, appeared in the *Lancet* of the 21st of August, 1858, and were subsequently printed in the first edition of this work:—

"The formation of stone in the bladder is not a sudden occurrence—is not the work of a few hours, days, or weeks, but occupies ordinarily months, and even years. Neither is a calculus formed in the bladder without there being a very evident manifestation of the risk and probability of such a catastrophe.

"There is, invariably, a persistent condition of the urine going on for months or years obvious to the unaided sight, and which ought to attract the attention of both patient and physician: that is, for a very long period prior to the formation of a stone, there is a very sensible and obvious deposit in the urine; for it is only those substances, be it remembered, which are but sparingly soluble in the urine, which ever form calculi.

"Now this deposit, in the great majority of cases, although observed by the patient, is allowed to continue and to go on unchecked without his seeking for medical advice; and it is only when symptoms of stone have presented themselves that he is led to seek for aid; but then great mischief is already done, and the physician is called upon to treat not only the condition of the urine which has occasioned the stone, but has to endeavour to act, by his remedies, upon the stone itself. This is generally regarded as a task so difficult that the physician usually abandons it in despair, and the case is handed over to the surgeon, the stone being removed ordinarily by the extreme and heroic remedy of vivisection and forcible extraction.

"In ordinary cases, then, the physician and the patient are alike ignorant of the impending calamity; or if they entertain any suspicion that the condition of the urine is one likely to tend to the formation of stone, they do not usually attach sufficient importance to it to make it the subject of active and immediate treatment. The presence of a stone is usually first determined by the surgeon. Again, when even the calculus is discovered, the physician is rarely called upon to put into operation the resources of his art; but the treatment generally pursued is strictly surgical.

"Now, I contend that the physician ought to take a prominent position in the treatment of stone. The conditions of the urine leading to calculi are chemical, physiological, and pathological, for all which reasons medical treatment is required.

"Further, the medical treatment pursued should not be limited to the period of the actual presence of a stone; for then, although more can be accomplished medically than is usually supposed, the best opportunity for medical treatment has passed. In fact, the treatment should be anticipative and preventive, and not merely palliative and curative. That is, every person whose urine contains an habitual and persistent deposit should seek medical advice, with a view to the correction of that non-natural condition of the urine which predisposes to the formation of calculi.

"The particular nature of the treatment demanded is determined, of course, by the nature and composition of the deposit, and need not here be described; that for persistent deposits of uric acid, the urates, and cystine, has already been fully detailed. We would in this place limit the observations we have to make to some few general particulars relating to the treatment of stone itself when actually formed; and, first, we would treat of solvent and especially alkaline remedies.

"These remedies, as ordinarily employed, are not exhibited to anything like the extent to which they ought to be given. As usually prescribed, they are administered in doses of from ten, twenty, to at the most thirty grains, two or three times a day.

"This fact has been forced particularly upon my attention by the analysis of a quack remedy called '*constitution water*,' and which has acquired some celebrity in the treatment of some forms of stone. It consists of impure carbonate of potash; and the dose is the eighth part of a bottle about the size of a wine bottle, four doses to be taken daily—equal to about 184 grains, or upwards of three drachms of carbonate of potash—a quantity which in some cases may be greatly exceeded with advantage.

"Now, the doses of the other alkalies, alkaline carbonates, citrates, acetates, and tartrates, and indeed of nearly all the solvent remedies employed in the treatment of stone, may be increased in like proportion, and with similar advantage.

"Another very important deficiency in the present mode of treating stone is, that the remedies resorted to, being usually only administered by the mouth, are conveyed to the stone in the bladder by the circuitous route of the circulation: in the blood, of course, these remedies become much diluted, so that they reach the bladder in a greatly weakened form. Again, administered freely, alkaline remedies are apt to disorder the general health, modifying, as they do so materially, the vital and physical properties of the blood, as well as of the various fluids secreted from it.

"Now, these disadvantages may be obviated, by employing the solvent remedies used, in the form of *injection:* these should not only be strong and frequently repeated, but they should be retained in the bladder as long as possible, or should be injected in a continuous stream.

"I am, of course, aware that injections have been tried occasionally in the treatment of stone, with more or less success; but they are not resorted to nearly so frequently as they ought to be, nor have they been employed in the manner most conducive to success.

"I would not be understood as recommending the use of vesical injections, to the exclusion of constitutional treatment; this, of course, should be persevered in as well.

"Again: in some cases, medical may be combined with surgical treatment: that is, the stone having been reduced to fragments by the lithotrite, the solution of the fragments should be attempted by the employment of suitable remedies, both through the medium of the constitution and locally by injection.

"The conditions of the urine tending to the production of stone which call for treatment, are those in which that fluid contains persistent deposits of uric acid, urates, oxalate of lime, cystine, and the earthy phosphates. The calculi ordinarily met with are composed entirely or in part of one or other of these compounds; those composed of uric oxide, silicic acid, and carbonate of lime, are of such rare occurrence that it is scarcely necessary to take them into consideration at all.

"The following figures show the relative frequency of the occurrence of the calculi most commonly met with:—

"Of 1000 calculi, the composition of which has been ascertained, 372 consisted of *uric acid*, alone, or mixed with small quantities of the urates and oxalate or phosphate of lime; 253 of the *earthy phosphates*, chiefly fusible calculi; 233, of varying layers of *uric acid, oxalate of lime*, and *earthy phosphates*; 142 of *oxalate of lime*.

"The urinary deposits and calculi most readily acted upon by solvent remedies are, the several earthy phosphates and cystine; and, therefore, it is in these cases especially that the greatest amount of success is to be anticipated from the treatment here recommended.

"I have now a few remarks to make on the subject of the *diagnosis* of calculi.

"In general, but few attempts are made by the surgeon to determine, either during the existence of a calculus or prior to an operation, the chemical composition of the calculus, and yet the microscope affords a ready and satisfactory means by which this object may generally be accomplished. Thus, the composition of the stone may frequently be determined with considerable accuracy by ascertaining, by means of that instrument, the nature of the ordinary deposit or deposits occurring in several consecutive samples of the same urine. The determination of the composition of the calculus is not, indeed, often a matter of much importance to the surgeon who is about to remove the stone by operation; but to the physician, proposing to treat the case medically, it is a point of the utmost moment, because it is only upon this knowledge that the proper and exact line of treatment to be pursued can be based. There is yet another way in which the composition of calculi may be determined —namely, by a chemical examination of the fragments usually passed after the operation of crushing by the lithotrite.

"Berzelius, in his 'Handbook,' makes these remarks respecting the solution of vesical calculi:—'The attempts which have been made to dissolve concretions in the bladder have not succeeded as we might have expected. However, I am perfectly convinced that they have not been often enough reported to enable us to find out and remedy those obstacles which we are unable to foresee, and which frequently increase the difficulties of their application.'

"An article on the same subject in the *British and Foreign Quarterly Review* contains these words:—'So much has already been done as to hold out every inducement to perseverance, and perseverance must of necessity be crowned with success in a certain proportion of cases.'"

*On the Medical Origin and Treatment of Stricture of the Urethra.*

Stricture of the urethra is usually regarded as a purely surgical affection; we are convinced, however, that this view of its nature is too restricted, and that, like stone, there are certain chemical and medical elements which are more or less concerned in its production and perpetuation.

Many cases of stricture no doubt owe their origin to purely local causes, as urethritis, specific and non-specific; but even in such cases the stricture is aggravated and kept up by the irritating character of the urine continually passing through the urethra.

In other cases the stricture is gradually established without its origin being traceable to local lesion or mischief, and in which its occurrence can only be explained by reference to the condition of the urine.

The composition and characters of that excretion are constantly varying, its reaction especially. In some cases it is abnormally acid, and in others alkaline; in either of these conditions it is rendered more than usually irritating to the mucous membrane over which it passes.

The alkalinity in some instances is due to fixed, and at others to volatile alkali; now few things are more irritating to the skin and mucous membrane than alkalies, even when greatly diluted.

Sometimes the urine is loaded with deposits of uric acid, oxalate of lime, or of the earthy phosphates, and is rendered unusually irritating by their presence.

At others, owing partly to its composition, it is voided more frequently than natural, and in this way, also, the mucous membrane is subjected to continual irritation.

With even these few facts before us, it is impossible to come to any other conclusion than that the condition of the urine has much to do with the origin and continuance of stricture of the urethra.

This being the case, it follows as necessary consequences—

First, that the urine ought to be examined in all cases of stricture of the urethra, and its characters determined.

Second, that being found faulty, the treatment adopted should be partly medical, and based upon the state of the urine.

In very many cases of stricture the health is obviously seriously deranged, and such derangement can scarcely exist without alteration in the characters and composition of the urine.

We believe that the explanation now given of the influence of the urine in occasioning stricture, likewise explains why certain cases of this affection prove so inveterate, and are so apt to recur.

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## CHAPTER XXIV.

## ANALYSIS OF THE URINE.



The methods whereby the different substances and salts, normal and abnormal, found in the urine may be detected and their amount estimated, have already been described separately; it is desirable, however, that a short description should be given of the processes to be followed in making a connected and complete analysis of the urine.

Since the urine varies so greatly at different times of even the same day, the urine of digestion especially differing from that passed during fasting, it is highly desirable, wherever practicable, that the sample analysed should be taken from the mixed urine of the twenty-four hours, as its composition being determined, and the amount of urine voided for the day being known, by a simple calculation the quantity of each constituent daily excreted is readily ascertained.

In many cases the analysis, however complete, of a single sample of urine, voided separately, will afford no useful information, and it may even mislead, as the sample submitted to examination may be an exceptional one: thus albumen or sugar may be present either in the morning urine or in that passed during digestion, and be absent at other times; so that if reliance were placed on the result of a single analysis of a separate sample, an erroneous conclusion would often be formed.

In other cases, however, valuable information is obtained by examining separate urines procured not hap-hazard, but at certain times, during fasting and digestion: thus the urine of inanition may be free from both albumen and sugar, while that of digestion may contain the one or the other; or if the case be one of either Bright's disease or confirmed diabetes, the presence of those substances would be detected in almost every sample of the urine excreted.

In general, therefore, when we desire to make quantitative analyses, we should operate upon a portion of the mixed urine of twenty-four hours, the amount of which excreted has been previously ascertained by measurement.

When any urine is submitted to us for examination, there are certain preliminary particulars which must be noted and determined —such as its physical characters, including its colour, appearance, weight, and reaction.

*Its Colour.*

We must notice, first, whether its colour is deeper or paler than natural; if the former, whether this proceeds from excess of normal pigment urohæmatin, from uroerythrin, hæmatin, or from biliverdin. *Uroerythrin*, when present in excess, is usually accompanied by deposits of urate, the deep pink or crimson stain of which sufficiently reveals the presence of that pigment. *Hæmatin*, when not in sufficient quantity to be identified by the eye alone, may be recognised by the microscope, which will reveal the presence of the blood-corpuscles: and if neither of these colouring-matters is found in the urine, and it is still deeply tinted, we may usually infer that it contains excess of *urohæmatin*. The presence of biliary colouring-matter *biliverdin* is generally sufficiently indicated by the tint of the urine; but if the amount be but small, we must test a few drops of the urine on a piece of white porcelain with nitric acid, as described at page 286.

If the urine be paler than natural, we must test for *indican* with sulphuric acid, in the manner pointed out at page 271; if that substance be absent, or present in but small amount, the inference may be drawn that there is a deficiency of pigment.

### *Its Appearance.*

We must observe whether it is clear or turbid, and if the latter, it must be set aside at rest for some time, so as to allow the substance upon which its turbidity depends to become deposited.

The colour, texture, and other characters of this deposit are frequently, and indeed generally, sufficient to enable a practised observer to determine its nature.

Thus if it be coloured, and of a sandy texture, it is most probably *uric acid.*

If it be more or less coloured, and light and pulverulent, it consists of *urate.*

If it be white or sandy and crystalline, it is composed of some *earthy phosphate.*

If creamy, with a yellowish or greenish tint, it is *pus.*

If transparent, and more or less gelatinous, *mucus.*

If red, it consists of *blood-corpuscles.*

In any case at all doubtful, the microscope may be resorted to; and if this should not set the question at rest in any instance, a few simple reagents may be used, applied, in fact, frequently to the crystals or substance while seen under the object-glass.

Thus if the substance consist of uric acid, it will become dissolved on the application of a strong solution of caustic potash, a soluble urate of potash being formed.

If composed of a urate, a little hot water will dissolve it; or on the addition of a drop or two of either acetic or hydrochloric acid, the uric acid will be separated from its base, and be precipitated in its usual highly characteristic rhomboidal crystals.

If it consist of any of the phosphates, nitrate of silver turns it of a golden yellow colour; and by nitric or hydrochloric acid it is dissolved.

If the precipitate be composed of pus, mucus, blood, semen, or renal casts and cells, the examination by the microscope is conclusive, and reagents are unnecessary.

The forms and other characters of the crystals of the several salts which occur as deposits in the urine are well known to most observers; and since they have already been fully noticed, and figures of them given, any further description in this place is scarcely needed.

### *Its Weight.*

Very important information is furnished by the weight of the urine, taken in conjunction with the daily quantity passed: we thus determine approximately the extent of the waste of the body, and whether the excretory functions of the kidneys are impaired or not.

The weight of the urine being known, and its quantity, we have simply to multiply the last two figures of the specific gravity by Christison's formula, and we are furnished with the number of grains of solid matter contained in 1000 grains of the urine: thus the specific gravity being 10·23, the two last figures multiplied by 2·33 give 53·59 grains as the solid matter contained in that quantity of urine. (See pp. 7 and 8.)

The only exact method, however, of determining the solids of the urine is by the evaporation of a given quantity, first on the water-bath, and then in the vacuum of an air-pump over sulphuric acid. From the total solids thus determined, the amount of *fire-proof salts*—that is, the phosphates, sulphates, and chlorides of soda and potash, lime, and magnesia—may be ascertained by simple incineration.

The gravity may be ascertained by the urinometer, but where accuracy is required, the specific-gravity bottle, which may be made of any size from 100 grains upwards, and the use of which is exceedingly simple, should be employed.

*Its Reaction.*

The acidity and alkalinity of the urine are determined by test-solutions added on the volumetric method.

The *acidity* is ascertained usually by means of a solution of dried or *anhydrous carbonate of soda.*

The solution may be made of any convenient strength, corresponding with the divisions of the alkalimeter, and should be added gradually by means of that instrument, the point of saturation being determined by the aid of delicate litmus-paper, which should be dried on each occasion after being dipped in the urine.

The soda used, by a simple rule-of-three calculation, may be converted into crystallized oxalic acid, in which form the acidity of the urine is now usually represented. The atomic weight of carbonate of soda is 53, and of ordinary crystallized oxalic acid 63: that is, 1 grain of the soda employed corresponds to 1·19 of the acid. Supposing 1000 grains of the urine to require for neutralization 2·3 grains of the soda, this would have to be reduced to the equivalent amount of crystallized oxalic acid, in either of the two following ways:—the atom of the acid, 63, must be multiplied by 2·3, the amount of soda used, and divided by the atom of carbonate of soda, 53; this gives 2·7 grains of crystallized oxalic acid; or the 1·19 may be simply multiplied by 2·3.

In place of the carbonate, *caustic soda*, freshly dissolved and used at once, may be employed; but the carbonate is to be preferred.

All other volumetric calculations are worked out upon the same data, but either of the soda solutions may be made of such strength that a certain quantity, corresponding with the divisions of the burette, is equal to one grain of crystallized oxalic acid, in which case no calculations are necessary.

The *alkalinity*, which is not often measured, may be determined by a dilute solution of *sulphuric acid*, the strength of which is ascertained by the quantity of carbonate of soda it requires for saturation. (See p. 253.)

### *Analysis proper of the Urine.*

We now come to the analysis proper of the urine; this may be either *qualitative* or *quantitative;* the first in some cases is sufficient, but more frequently the latter is required. The tests for the several substances, normal and abnormal, found in the urine, have already been fully described, and it is not, therefore, requisite that the descriptions should now be repeated. The principal abnormal substances which are sought for qualitatively in the urine are bile, albumen, and sugar, the tests for which will be found under the chapters treating of those substances. For the normal ingredients the merely specific tests are needless, since those ingredients are nearly always present in greater or less amounts. In order, therefore, to obtain any useful information, it is requisite that these, as well as most of the abnormal constituents, should be determined quantitatively.

There are two methods upon which the quantitative analysis of the urine is conducted: the one new, the *volumetric,* and the other old, which may be termed the *ponderous* method.

The volumetric method in the determination of certain substances has now, in consequence of the ease and rapidity with which it can be performed, nearly superseded the older method.

Its principle consists in adding to a known quantity of the urine the exact amount of a test liquid required to precipitate the whole of any one ingredient therein contained.

The principle of the more ancient method consists in adding an excess of the test-liquid, and in precipitating the substance in such an insoluble form as to admit of its being subsequently collected, purified, and weighed, the amount of the substance sought for being determined from the weight of the precipitate. Thus, for example, the urine having been acidified, the chlorine is thrown down by means of a solution of nitrate of silver, and chloride of silver is formed; this is collected, washed, ignited, and weighed, and the chlorine thus determined. 1000 grains of the urine furnished 19·4 grains of chloride of silver; the atomic weight of chlorine is 36, of the salt of silver 144; the sum is thus stated: 144 : 36 : : 19·4; the atom of chlorine, 36, is multiplied by 19·4, the quantity of chloride of silver precipitated, and the result divided by 144, the atom of the silver salt; this gives 4·85 grains of chlorine as the amount contained in the 1000 grains of urine.

The volumetric method is usually resorted to only for the determination of the chlorine, urea, phosphoric and sulphuric acids, and sugar, which are amongst the more important constituents of the urine. The amount of chlorine, of phosphoric and sulphuric acids being known, as also the bases with which they are generally united, the latter may be inferentially calculated. Thus, the chlorine is nearly always united to sodium, so that by a simple sum the quantity of the chloride of sodium may be estimated. The atom of chlorine is 36, of chloride of sodium 59, and the amount of chlorine found 4·85 grains; the 36 is multiplied by 4·85, and divided by 59, which gives 7·95 grains of chloride of sodium.

The phosphoric acid of the soluble phosphates is generally in union with soda; that of the earthy phosphates with lime or magnesia, the difference between the atomic weights of which is but small.

Lastly, the sulphuric acid is joined ordinarily to potash. The results of course thus obtained are but approximative, still they are usually near enough for all clinical or practical purposes.

In the following description of the volumetric determination of certain constituents of the urine, we shall endeavour to render the subject as simple as possible; we shall not complicate it by the introduction of the French weights and measures—in fact, we shall omit all figures and calculations that are not strictly necessary, believing that they tend to confuse the mind and to deter any but professed chemists from undertaking the analytical examination of the urine. The array of calculations given in some works descriptive of the volumetric analysis of the urine must be really alarming to those not versed in chemistry, and also in arithmetic.

The operator must remember that the urine to be tested must in all cases be accurately measured, as also the several test-liquors, of known strength, used; further, he must call to mind the purpose for which each solution is employed, and the object which it has to accomplish. Having taken a convenient quantity of the urine, and knowing the strength of his test-fluids, and how much corresponds to a grain, of the substance which he desires to estimate, the analyst may safely be left to determine by his own intelligence the proportions in which he should use them. It will, however, be found very convenient that the measures and burettes should be divided on the centesimal system, and that the strength of the solutions should accord with their divisions as well as with a definite amount of the substance precipitated, a grain being a suitable quantity.

It will be unnecessary to trouble the reader with any lengthened details descriptive of the methods of making the test-liquors —it will be sufficient to point out a few material facts, since these solutions are now regularly prepared by several of the operative chemists, as by Mr. Griffin, Messrs. Lloyd and Bullock, Messrs. Hopkin and Williams, and others.

### *Volumetric Determination of Urea.*

In order to avoid repetition, the reader is referred in the first instance to the remarks made on the estimation of urea, under the head of *Liebig's Process,* at pp. 18 and 19, omitting, however, the last sentence of paragraph five on p. 19.

A convenient quantity of urine to take will be 300 grains, to which half the amount of the baryta solution should be added: two-thirds of the mixture, containing 200 grains of urine, must be separated by filtration, and tested; the mercurial solution is added as long as any precipitate is formed, the point of saturation being determined in the manner pointed out at p. 19.

One grain of urea corresponds to 7·20 grains of the protoxide of mercury; but it is necessary that there should be an excess of oxide, and that the solution should contain 7·74 grains to one of urea.

A correction has now to be made. The first few drops of the mercurial test solution added produced no precipitate, owing to the mercury having combined with the chlorine of the sodium. This deduction has been fixed arbitrarily at an amount of the solution for 200 grains of urine, equal to 3 grains of the protoxide.

The mercurial solution may be thus prepared: crystals of the neutral suboxide of mercury, $Hg_2O,NO_5$, are boiled with nitric acid till vapours of nitrous acid cease to be evolved, and no precipitate occurs, when chloride of sodium is added to a small quantity of the mixture; this is then evaporated to the consistence of a syrup, nitrate of mercury, $HgO,NO_5$, is obtained, and the syrup diluted to the requisite strength.

### *Volumetric Determination of Chlorine.*

The mercurial solution used for the determination of the chlorine is usually much weaker than that employed in the precipitation of the urea, as while 7·74 grains of the protoxide correspond to 1 of urea, 1·84 grains are equivalent to 1 grain of chloride of sodium.

The same quantity of the urine, which should also be first treated with the baryta solution, may be used as in the previous case: indeed, sufficient of the urine may be prepared in the first instance for both determinations; that used for the chlorine must, however, be acidulated with a few drops of nitric acid.

In both cases, before adding the mercurial test, it is necessary to ascertain, which may be done by testing a drop of the urine, whether sufficient of the baryta solution has been added to precipitate all the phosphoric and sulphuric acids: (see p. 243), but for pernitrate read nitrate of mercury, or nitrate of protoxide of mercury, which was formerly called the pernitrate, containing really but one atom of oxide of mercury with one of nitric acid, thus $HgO,NO_5$.

The test-liquor must be added so long as the precipitate formed on the additions of the test is completely redissolved on stirring the mixture.

*Volumetric Determination of Sulphuric Acid.*

One thousand grains of urine, a little hydrochloric acid having been added, are placed in a small flask on a sand-bath until the urine boils.

The test-liquor, consisting of a solution of crystallized *chloride of barium*, is then added as long as the precipitate increases; the flask is then removed, to allow of the deposit subsiding, and a drop or two of the test is added, to ascertain whether more of the solution is required: this operation is repeated until the whole of the sulphuric acid is thrown down. In order to ascertain whether the right quantity of the baryta solution has been used, a drop of a solution of *sulphate of soda* may be added to two or three drops of the mixture in a watch-glass; if a decided precipitate is produced, too much of the test-liquid has been used, and the analysis must be repeated upon a fresh portion of the urine, but if no deposit occurs, more of the test must be added.

3·07 grains of crystallized chloride of barium are equivalent to 1 grain of sulphuric acid. (Refer to page 200 for further particulars.)

*Volumetric Determination of Phosphoric Acid.*

It will be well in the first place to read the observations which will be found on pages 209 and 210.

One thousand grains of the urine may be taken for analysis: to this quantity must be added 100 grains of a solution, composed of 200 grains of acetate of soda, 400 grains of dilute acetic acid, and 1400 grains of water, to prevent the resolution of the phosphate of iron at first precipitated on the addition of the solution of perchloride of iron.

Every 100 grains of the solution contain 10 grains of acetate of soda and 20 grains of acetic acid: now Neubauer has ascertained that for every 1·217 grains of iron, =1·74 grains of peroxide, contained in the test-iron solution employed, about 15 grains of acetate of soda must be added to the urine to be tested, or even a larger proportion if much free acid be present in the test-solution.

The iron combining with the phosphoric acid, hydrochloric acid is set free, which unites with the soda of the acetate, thus liberating the acetic acid, in which the phosphate of iron is insoluble.

The 1000 grains of urine, after the addition of the solution just described, may be divided into two parts, each of which will contain 500 grains of urine; to each of these the iron solution must be added, to one, an amount which is equivalent to one-tenth of a grain of phosphoric acid, and to the other to two-tenths.

After subsidence of the deposit, a small but equal quantity of each portion is filtered into two separate test-tubes, and to each is added a minute quantity of a very weak solution of ferrocyanide of potassium, containing about a grain of the salt to 100 grains of distilled water: if in either, Prussian blue is formed, the analysis is complete; but if not, similar amounts of the iron-test must be added as at first, until, proceeding in the same way, the blue colour is obtained.

It should be understood that the division of the urine into two equal parts is by no means essential, as the analysis may be performed in one operation.

In determining the strength of the test-solution, the iron is estimated as sesquioxide, the atomic weight of which is 80, by adding ammonia, and 1·14 grains of this oxide correspond with one grain of phosphoric acid: or the iron may be more conveniently determined volumetrically by means of a solution of known strength of the crystallized rhombic phosphate of soda, 4·51 grains of which correspond to 1 grain of the sesquioxide of iron.

An inaccuracy, first pointed out to me by Mr. Rodgers, to whom I am indebted for several practical suggestions, and who has verified these calculations with me, occurs in Dr. Beale's description of the strength of the test-solution of perchloride of iron, and which, if not corrected, will necessarily lead to much error and confusion. Dr. Beale gives two processes by which this standard solution can be prepared: one in which a given weight of metallic iron is converted into perchloride; the other in which a solution of the perchloride of iron itself is taken, and the amount of iron contained in a known measure thereof ascertained by analysis. In both cases a solution is finally obtained containing 24·024 grains of iron in 1544·4 grains of water, and which is capable of precipitating, according to his statement, but 15·4 grains of phosphoric acid, whereas that amount of iron would precipitate exactly double the quantity; so that there is an error to the extent of one-half in all analyses which have been made with either of the solutions the methods of preparing which are described by Dr. Beale. Thus, supposing the phosphoric acid to have been estimated in the urine passed by a healthy individual in twenty-four hours, the amount indicated by Dr. Beale's solutions would have been only 32 grains instead of 64 grains, the average quantity.

If we desire to ascertain how much of the phosphoric acid is united to the earths, and how much to the alkalies, we must proceed as follows: the whole of the phosphoric acid must first be determined in one portion of urine; from a second, the earthy phosphates must be precipitated by ammonia, and after filtration and the addition of the solution of acetate of soda, the remaining phosphoric acid must be precipitated as before; the difference in the two amounts gives that which is in union with lime and magnesia.

It is usual to perform a confirmatory analysis; it will, of course, be unnecessary to go through the whole process again, but to add only those quantities of the test-liquor which the first experiment showed approached more or less nearly to the correct amount.

If the analysis be performed in a beaker placed upon white paper, a practised operator will be able to determine when the whole of the phosphoric acid is precipitated, by a change of colour which invariably occurs when this point is arrived at, from the formation of a trifling amount of acetate of iron.

This method furnishes less accurate results than any of the other processes. If the amount of phosphoric acid be small, there may be an error, according to Neubauer, amounting to 10 per cent., or, according to Vogel, to 20 or even 30 per cent., if the mixture be not tested for the excess of iron at once, since the precipitated phosphate of iron gradually absorbs any surplus iron which might have been present in the solution. In order to avoid the trouble and delay of filtration, it is recommended that a piece of bibulous paper should be moistened with the solution of ferrocyanide of potassium, and placed on a piece of porcelain; that a drop of the mixture should be so placed on a second and dry piece of filtering-paper, that it runs through it in a clear state, and falls upon or mixes with the solution in the first paper, giving rise, if sufficient of the liquid has been added, to a blue spot, owing to the formation of Prussian blue.

The solution of the perchloride of iron is made from pure iron-wire dissolved in aqua regia, the mixture being evaporated to dryness in a water-bath; the neutral chloride is dissolved in a definite quantity of distilled water, and diluted to the requisite strength.

### *Volumetric Determination of Sugar.*

Either *Fehling's* or *Barreswil's* modifications of the copper-test may be used, the directions for making which are given at pages 143 and 144, it only being remembered that 2·21 grains of the oxide, or 6·90 of the sulphate of copper, are reduced by 1 grain of anhydrous grape-sugar.

A measured quantity of either of these solutions, containing about as much sulphate of copper as would be reduced by 8 grains of sugar, is to be poured into a porcelain dish, and diluted with several times its bulk of distilled water. Two hundred grains of urine are taken, diluted with from 10 to 20 times its volume of water, and then poured into a burette up to a fixed point or division, which must be noted. The porcelain dish with the test-liquor is now to be placed on a sand-bath, heated by means of a spirit-lamp, and when it nearly boils, the diluted urine is to be added until the blue colour of the test-liquor entirely disappears. In order to ascertain when this occurs, it is necessary to remove the lamp from time to time, that the suboxide of copper formed may become deposited, and the colour of the mixture be more clearly seen.

It is unnecessary that any further details should be given of the quantities of the ingredients to be used in the preparation of the several test-liquors, about which, however, there is really no great mystery or difficulty. If the quantity of the precipitant contained in any of these solutions, which corresponds to a grain of the substance the amount of which it is desired to ascertain, be called to mind (and we have given it in each case), the key is thereby furnished to the necessary strength of the liquid. As before stated, it is not requisite that the practitioner should trouble himself with the compounding of these solutions, since many manufacturing chemists will undertake to supply them and guarantee their accuracy; nevertheless it is advisable that the operator should himself test their strength as a guard against error.

We have now to treat of the quantitative analysis of the urine, as determined by the *weight of the precipitates* resulting from the addition of certain reagents to the urine. Under this head, the remarks we shall have to make will be very brief, as sufficient details will, in most cases, be found in the chapters treating of the substances and salts, normal and abnormal, found in the renal excretion. We shall, in fact, have in this place to do but little more than refer to the pages on which the needful descriptions will be found.

Amongst the substances contained in the urine, and which are frequently determined quantitatively by this method, are urea, uric acid, chlorine, sulphuric and phosphoric acids, the bases combined with these, and sugar.

A nitrate of urea is the salt usually formed, from which the *urea*, by a simple calculation, is estimated. (Refer to p. 16.)

*Uric acid* is generally precipitated by means of hydrochloric acid. (*See* p. 75.)

*Sulphuric acid* is calculated from the precipitated sulphate of baryta, formed on the addition of a solution of chloride of barium or nitrate of baryta to the urine, previously acidulated with nitric or hydrochloric acid (p. 200).

*Phosphoric acid* is usually precipitated by means of a solution of perchloride of iron; acetate of soda and acetic acid having been previously added, in order to prevent the resolution, by the hydrochloric acid set free, of the phosphate of iron first formed (p. 209). The precipitate should be washed with boiling water, dried, ignited in a platinum crucible, with access of air; the residue must be moistened with strong nitric acid, evaporated, and again ignited. Deduct from the weight of the residue that of the sesquioxide of iron contained in the solution used: the difference represents the phosphoric acid.

*Chlorine* is calculated from the chloride of silver formed on the addition of a solution of nitrate of silver, the urine being first well acidulated with nitric acid to redissolve the phosphates, which otherwise would become precipitated (p. 243).

The processes for determining *lime* and *magnesia* are given at p. 210. The oxalate of lime may be carefully incinerated, treated with a solution of carbonate of ammonia or carbonic acid water, and again slightly ignited, and the lime calculated from the carbonate thus formed. The magnesia is estimated from the pyrophosphate of magnesia formed on the ignition of the precipitated phosphate of magnesia and ammonia.

The methods have not hitherto been described for determining the amounts of *soda* and *potash* present in any urine—information required only in special cases. For this purpose, we must proceed as follows: 500 grains of the urine must be evaporated to dryness and then incinerated; the ash treated with distilled water, whereby all soluble salts are dissolved; the phosphoric and sulphuric acids must be removed by means of a solution of acetate of baryta, rendered strongly alkaline with ammonia, an essential part of the process, the precipitate is removed by filtration, the filtrate evaporated to dryness, ignited, and redissolved; ammonia and carbonate of ammonia are now added to remove any excess of baryta; the liquid is again filtered, acidulated with hydrochloric acid, evaporated in a platinum crucible, ignited gently, and weighed; the weight of the combined alkalies, in the form of chlorides of sodium and potassium, is thus obtained. These are to be separated by means of chloride of platinum; the chlorides are to be dissolved in a little water, the platinum solution added in great excess, evaporated nearly to dryness, and digested, with frequent stirring, for some hours, with spirit of specific gravity 8·631; this dissolves out the chloride of sodium and platinum, and leaves the chloride of potassium and platinum, from which the chloride of potassium may be calculated, and the difference between the weight of which and that of the combined chlorides gives the amount of chloride of sodium.

While soda salts abound in the blood, the potash salts occur chiefly in the muscles; and if phosphate of potash be given with the food, the phosphoric acid passes to the soda, and the potash to the chlorine, phosphate of soda and chloride of potassium being formed.

When the *sugar* is determined by the weight of the precipitated suboxide, we proceed as in the volumetric analysis, only that in this case an excess of the test-solution may be used (*see* p. 143). One grain of anhydrous grape-sugar reduces 2·21 grains of the oxide, and, according to Neubauer, 2·016 grains of the suboxide of copper.

The various processes have now been described, whereby the principal compounds and salts, normal and abnormal, contained in the urine may be recognised and their amounts determined. Although numerous other substances are occasionally found in disease in the renal excretion, it is not necessary to repeat the description of the methods, given in other parts of the work, by which they are discriminated and their amounts ascertained. The reader is therefore referred to the chapters in which the subjects in respect to which the information is required are discussed.

The following *Table of Equivalents* will be found useful in calculating analyses of the urine, and will save the time and trouble of referring to other works—

TABLE OF EQUIVALENTS.

| | | | |
|---|---|---|---|
| Ammonium | 18 | Ammonia | 26 |
| Argentum | 108 | Oxide of silver | 116 |
| Barium | 68·60 | Baryta | 76·6 |
| Calcium | 20 | Lime | 28 |
| Ferrum | 28 | Peroxide of iron | 80 |
| Magnesium | 12 | Magnesia | 20 |
| Hydrargyrum | 100 | Oxide of mercury | 108 |
| Platinum | 99 | Suboxide of copper | 71·36 |
| Potassium | 39 | Protoxide of copper | 39·68 |
| Sodium | 23 | Potassa | 47 |
| | | Soda | 31 |
| | | Caustic soda | 40 |
| Carbonic acid | 22 | | |
| Chlorine | 35·46 | | |
| Hydrochloric acid | 36·46 | Urea | 60 |
| Nitric acid | 54 | Basic uric acid | 84 |
| Anhydrous oxalic acid | 36 | Anhydrous grape-sugar | 180 |
| Crystallized oxalic acid | 63 | Crystallized grape-sugar | 198 |
| Phosphoric acid | 71·36 | Urea and protoxide of mercury | 492 |
| Sulphuric acid | 40 | | |

| | |
|---|---|
| Crystallized sulphate of copper | 124·68 |
| Phosphate of lime | 155·36 |
| Pyrophosphate of magnesia | 111·36 |
| Bichloride of potassium and platinum | 247 |
| Perphosphate of iron | 151·36 |
| Crystallized chloride of barium | 122·06 |
| Crystallized rhombic phosphate of soda | 361 |

| | |
|---|---|
| 1 gramme | = 15·44 grains. |
| 1 cubic centimetre | = 15·44 grs. of water. |
| 1 decem | = 10 fluid grains. |
| 1 litre | = 1000 cubic centimetres. |
| 1 ounce troy | = 480 grains. |
| 1 ounce avoirdupois | = 437·5 „ |
| 1 pound troy | = 5·760·0 „ |
| 1 pound avoirdupois | = 7·000·0 „ |
| 1 fluid ounce | = 437·5 „ |
| 1 pint | = 8·750·0 „ |
| 1 imperial gallon | =70·000 „ |
| 1 millilitre, or cubic centimetre | = 16·9 minims. |

By dividing c. c. by 28·4—a number obtained by dividing 437·5 by 15·44, or 480 by 16·9—we are furnished with the amount in imperial or fluid ounces at 62° Fah., and the weight nearly (if it were pure water) in avoirdupois ounces.—*Extract from Letter by Dr. Parkes.*

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## PROPOSED NEW METHOD OF DETERMINING THE EXTRACTIVES.

*Extract from a Letter by* E. A. PARKES, M.D.

"FOR a good many years I have been acquainted with a curious reaction of urine, which want of time has prevented me from properly following out. If starch be added to urine, and a standard solution of iodine in iodide of potassium, such as is used for the determination of hyposulphites or hydrosulphuric acid, is dropped in, the blue colour at first given is immediately destroyed, and this continues until a considerable amount of iodine has been added. I give two examinations in two perfectly healthy young men as an instance of the amount. The strength of the iodine solution was one-twentieth of an equivalent of iodine dissolved by a little iodide of potassium in 1 litre of water (6·34 grammes of iodine in 1000 c. c. of water).

"In one of these cases the average number of cubic centimetres of the iodine solution which had to be added to 100 c. c. of urine before the permanent blue colour was given, was 14 on a mean of 17 days. It varied from 28 c. c. to 8 c. c. for 100 c. c. of urine. Reckoned for the whole quantity of urine of twenty-four hours, the number of c. c. of iodine solution required for the blue tint varied from 597·8 c. c. (containing 3·79 grammes, or 58½ grains, of iodine) which was required for 2120 c. c. of urine, to 125 c. c. (containing 0·79 grammes, or 12 grains, of iodine), which was required for 1005 c. c. of urine.

"In the second case the numbers of c. c. of iodine solution required to give the blue tint with 100 c. c. of urine averaged 17·78 c. c. on a mean of 7 days; the total quantity which would have been required for the whole quantity of urine passed on any one day varied from 204 c. c. (required for 1020 c. c. of urine) to 149 c. c. of iodine solution (required for 1070 c. c. of urine).

"I have found the reaction most strongly marked in a case of diabetes, and in some other diseases.

"At present I have not succeeded in definitely determining what ingredient of the urine has this curious effect on iodine, nor whether the non-production of the blue colour is owing to the formation of hydriodic acid, as in the reaction with hydrosulphuric acid. Urea and uric acid apparently do not give it; and though I have not tried the various salts, it seems impossible that it can be owing to them. In this state of uncertainty I should have hesitated in saying anything about this point, had I not chanced to see, a few weeks ago, in Schmidt's *Jahrb.*, Oct. 1862, p. 123, a notice of some experiments made by Kletzinsky, of Vienna, in 1859, but only just published.

"Kletzinsky has noticed this reaction, and considers that it is owing to the action of 'extractives;' and he proposes it as a means of quantitative determination of them. By the term 'extractives' he implies pigment chiefly. He does not, as I have done, add the starch, and then the iodide solution from a burette, but mixes the starch and iodine together, and then adds it from a burette. The strength of the 'iodine-dextrin' is unfortunately not given; but it is said that 1 centigramme of extractive matter will about decolorize 1 c. c. of the iodine starch-solution which he uses.

"I have not happened to meet with any similar observation, and I see no reference made to a test of the kind in the last (fourth) edition of Neubauer and Vogel's 'Anleitung zur Analyse des Harns,' just published.

"Without prejudging the question whether Kletzinsky is right or not in thinking he has found a measure of the pigment, it seems probable that the further examination of this reaction will be of interest."

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## ADDITIONS,

### CHIEFLY FROM SUGGESTIONS BY DR. PARKES.

Exercise (p. 32).—From experiments on a dog Voit has denied that urea is increased.—*Unters. über den Einfluss des Kochsalzes, des Kaffen, und der Muskelbewegungen auf den Stoffwechsel, von Carl Voit,* 1860, p. 148 et seq.

Speck, from renewed experiments on men, has reaffirmed the statement he formerly made, that the urea is increased, though in a much less proportion than the carbonic acid. He also believes that some of the nitrogen passes off in other ways.—*Archiv der Versins für wiss. Heilk.*, Band vi. p. 161. 1862.

Nitrogen and Urea (p. 33).—The experiments of Johannes Ranke, lately conducted with great care in Pettenkofer's carbonic-acid room at Munich, seem to prove that in *his* case, during perfect rest, *all* the *nitrogen* is contained in the urine, and that the urea holds nearly all of it, none escaping by the skin or lungs.

Urea in Scarlet Fever (p. 35).—In scarlet fever, it would appear, from Ringer's late observations, that the urea is *not* in relation to temperature; whether this is owing to some condition of the kidney is not clear.—*Medico-Chirurgical Transactions*, 1862.

Composition of the Urates (p. 60).—Bence Jones has published, in the *Journal of the Chemical Society for* 1862, three analyses of the urates of healthy urine; the bases were potassa, soda, and ammonia, the first in much the larger amount: these results confirm in the main the prior analyses of Scherer.

| | *First Analysis.* | *Second Analysis.* | *Third Analysis.* |
|---|---|---|---|
| Uric Acid | 94·36 | 91·06 | 92·11 |
| Potassium | 3 15 | 3·78 | 5·06 |
| Ammonium | 1·36 | 3·36 | 1·61 |
| Sodium | 1·11 | 1·87 | 1·20 |

The first sample was dried at the temperature of the air, the second, to avoid loss of ammonia by drying, was, when washed with alcohol, mixed with dilute acetic acid, and the third, after having been washed with alcohol, was treated with hydrochloric acid. In none of the samples was uric acid present in the free state. It appears from these analyses, that the urates are very unstable combinations, being usually decomposed in part, and a portion of the uric acid set free by simple washing on a filter with hot and even cold water; further, the uric acid is frequently in excess of the amount necessary to form acid urates, forming even quadrurates.

Sugar in Normal Urine (p. 152).—The presence of sugar in small amount in normal urine may now be considered to have been fully established; thus Brucke has proved it to be a constituent of healthy urine; Bence Jones has confirmed Brucke's statement (*Journal of the Chemical Society*, 1861); as also Winogradoffe, who, however, did not find it to be always present (*Virchow, Archiv*, 1862).

Brucke's process, adopted by Jones, is as follows. The urine is precipitated, first with neutral and then with basic acetate of lead; after filtration, ammonia is added, the precipitate occasioned by which contains the principal part of the sugar present; the precipitate is then treated with either a solution of oxalic acid or with sulphuretted hydrogen, to remove the lead. The filtrate is now sufficiently pure to be tested in the usual manner with the copper or other test. By this process one-seventh of a grain of sugar in 3000 grains of urine may be readily detected, and two-thirds of the sugar added recovered.

Bile-Acids (p. 287).—"The statements of Kühne have been called in question by Neukomm (*Archiv für Anat. und Phys.*, 1860, p. 364), who, after injection of bile-acids into the circulation, found only an extremely small quantity in the urine in some experiments, while in the majority they were absent. Neukomm, indeed, thinks his experiments support the views of Frerichs that bile-acids *may* form colouring-matters. Hoppe (*Virchow's Archiv*, 1862, Band xxiv. p. 1), on the other hand, after re-examination of the subject, supports Kühne. He does really seem to bring forward indisputable evidence, that a small quantity of a substance derived from the bile-acid is present in icteric urine. The substance obtained in more than thirty cases of icterus was, both from its elementary composition and its polarizing action on light, cholonic acid ($C_{52}H_{41}NO_{10}$), a derivative of cholalic acid. Hoppe states that when injected into the blood, the bile-acids are in part eliminated, but this occurs very slowly, going on even for days."—*Parkes, in Letter.*

Sediments of Xanthine.—Bence Jones has detected in the urine of a boy aged nine and a half years, a sediment of xanthine in lozenge-shaped crystals, and which was at first taken for uric acid. The deposit disappeared on boiling the urine; it was soluble in water, alkalies, and hydrochloric acid, also in nitric acid, without effervescence, leaving on evaporation a yellow residue.

In June, 1861, the boy, having had hæmaturia three years previously, caught a slight cold, and was delirious one night: the urine was generally thick, and contained some albumen, but no blood-cells or casts, and was of high specific gravity. At the end of July, Dr. Jones received two samples of the urine: they were thick and deep-coloured, and contained the deposit in question. Subsequently, many samples of the urine and of its deposits were examined, but the latter were found to consist of uric acid, urates, with sometimes oxalate of lime, and on no other occasions was xanthine discovered.

Process for Determining the Total Amount of Nitrogen.—This process, devised by Voit, is simply the decomposition of a certain amount

—say, 100 grains—of undried urine by means of soda-lime, and the reception of the ammonia into sulphuric acid of known strength, as in the ordinary determination of Nitrogen. The urine not being evaporated to dryness, all fallacies arising from previous decomposition of the urea are avoided.—(*Neubauer and Vogel,* 4th Edition, 1863, p. 184.)

Mohr's Process for the Determination of Chlorine.—The urine, if acid, must be rendered neutral or faintly alkaline only, by the addition of carbonate of soda, and the test-solution must also be neutral. The chlorine is precipitated by means of a graduated solution of nitrate of silver, the point of saturation being determined by the formation of the highly characteristic crimson chromate of silver, a minute quantity of a solution of chromate of potassa having been previously added.

One grain of chlorine corresponds to 4·79 grains of nitrate of silver.

This is a very easy plan, though not so accurate as the nitrate of mercury process. Neubauer found the result always too high, owing to the presence of other matters, as pigment and extractives, in the urine, and gives a plan for destroying the organic matters by ignition with nitre; but this makes the process (though still easy) somewhat long for medical men.—For further particulars, see p. 137 of Neubauer's 4th Edition.

Determination of Phosphoric Acid by Precipitation as Phosphate of Uranium, with Ferrocyanide of Potassium as Indicator.—This method, devised nearly simultaneously by Sutton and Neubauer, appears to be the best hitherto employed. It is based on the fact that when nitrate or acetate of uranium is added to a solution of tribasic phosphoric acid, containing acetate of ammonia and free acetic acid, the whole of the phosphoric acid is thrown down as double phosphate of uranium and ammonia, $Ur_2O_3,NH_4O,PO_5+Aq$. "When this precipitate is washed with hot water, dried, and burned, the ammonia is entirely dissipated, leaving phosphate of uranium ($Ur_2O_3,PO_5$), and contains in 100 parts 80·09 of sesquioxide of uranium and 19·91 of phosphoric acid." (Sutton.)

This method may of course be employed volumetrically: 500 grains of the clear filtered urine are to be measured into a flask, 30 or 40 grains of ammonia (specific gravity 0·96) added, and the precipitate redissolved with an excess of acetic acid; the mixture is then warmed, and the uranium solution added, with stirring as long as a precipitate occurs; a drop of the mixture is then added to a drop of a solution of ferrocyanide of potassium, placed on a piece of white porcelain until, a few moments having been allowed to elapse, the slightest indication of a chocolate-brown colour is perceived. So long as this fails to appear, the addition of the uranium solution must be continued; if too much of this test-liquid has been accidentally used, a small additional quantity of urine may be added.—For further details the reader is referred to Sutton's *Volumetric Analysis.*

The advantages of this process are, that the compound of uranium and phosphoric acid is definite, and that the mixture does not require filtration.

The uranium solution is made by dissolving the crystals of nitrate of uranium in distilled water; but since these readily lose a portion of their water of crystallization, it becomes necessary to determine the exact strength of the test-liquor, an object effected by means of a standard solution of crystallized phosphate of soda, powdered, and freed from superfluous moisture by pressure between folds of blotting-paper. 5·02 grains of this phosphate correspond to 4·02 of sesquioxide of uranium, equivalent to 1 grain of phosphoric acid.

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THE END.



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