A Course of Lectures ON URINE, URINARY DEPOSITS, AND CALCULI.

DELIVERED AT THE PATHOLOGICAL LABORATORY,
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BY
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LECTURE V.

URINE IN DISEASE. SOLUBLE SUBSTANCES PRESENT IN URINE IN DISEASE WHICH DO NOT EXIST IN THE HEALTHY SECRETION. ALBUMEN. *Of Detecting the Presence of Albumen; Tests; Nitric Acid; Heat; Anomalous Results in Employing these Tests; Apparent Presence of Albumen in Urine which contains none; Phosphate resembling Albumen; Uric Acid resembling Albumen; Cases. Apparent Absence of Albumen in Urine which contains a large Quantity; Cases. Cause of the Precipitation of Albumen by Heat being prevented by a Trace of Nitric Acid. Other Tests for Albumen. On Estimating the Quantity of Albumen. Peculiar Substance in Urine allied to Albumen. Of the Importance of Albumen in Urine in a Clinical point of view. Dropsy in Disease of the Kidney. BILE. Tests. Nitric Acid. Heller's Test. Pettenkofer's Test. Yellow Colour of the Cells, etc., in the Urinary Deposit. SUGAR. General Characters of the Urine in Diabetes. Diabetic Sugar. Tests for Diabetic Sugar; Moore's Test; Trommer's Test; Barreswill's and other Solutions. On Testing for Sugar when only Traces are present. Circumstances interfering with the Action of Trommer's Test. Of the Yeast Test. Maumené's or the Perchloride of Tin Test. Bismuth Test. Of Estimating the Quantity of Sugar; volumetrically; by Fermentation; by Dr. Garrod's Method; by the Polarising Saccharimeter. Circumstances under which Sugar is excreted in the Urine. Analyses of Urine in Diabetes. OTHER SOLUBLE SUBSTANCES WHICH ARE NOT PRESENT IN HEALTH. LEUCINE. TYROSINE. INOSITE. ACETONE. CYSTINE.*

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Sugar is not present in healthy urine. Occasionally, however, traces of this substance are met with in the urine of persons who are not suffering from any particular symptoms. It may be excreted for days, or even for a few weeks at a time, in small proportion. It does not follow that all such cases are to pass into confirmed diabetes, but they should be carefully watched by the practitioner. Sometimes, after abstinence from food for some hours, a meal, consisting entirely of starchy matter, will cause sugar to appear in the urine, and if a person, under these circumstances, take a quantity of cane-sugar, a temporary diabetic condition will almost certainly be produced. Instances, in which sugar has been detected in the urine daily for several weeks, and recovery taken place, have occurred. Diabetes may last for many years, but generally it causes death in from one to four years. Although much light has been thrown upon the production of sugar in the animal body of late, no satisfactory explanation of these cases has yet been offered, nor do we know anything of the condition of the system which precedes and ushers in the fatal form of diabetes.

Two kinds of diabetes have been described—*diabetes mellitus* and *diabetes insipidus*. I have already had occasion to allude to the latter, and have mentioned that in this condition large quantities of pale urine, containing little solid matter, and, it need scarcely be repeated, no sugar, are passed, it is therefore quite unnecessary to describe this condition as a distinct disease; the term *diabetes* should never be applied to it. Diabetes is sometimes called *mellituria* or *glucosuria*.

Diabetic urine is usually of a very pale colour, and possesses a peculiar odour, which has been compared to that of violets, apples, new hay, whey, horses' urine, musk, and sour milk. Such comparisons serve only to show how difficult it is to define, in words, a particular odour. No doubt all of you are well acquainted with this peculiar smell, which it is useless to attempt to describe.

Specific Gravity—Reaction. The specific gravity of diabetic urine is very high, almost always above 1030, and it sometimes reaches 1050. In some cases, however, the specific gravity does not differ from the healthy standard. Its reaction is generally acid, and sometimes its surface is covered with a whitish film, owing to the rapid development of the sugar fungus or torula. It has a sweet taste, and often attracts a great number of flies. This last circumstance is sometimes the first thing that directs the patient's attention to his water.

Deposits are not often met with in diabetic urine; those which have come most frequently under my own notice are deposits of the *phosphates*, and deposits of *uric acid*. The fixed salts are generally present in small quantity, and chloride of sodium is often altogether absent. The urea and extractive matters are, as a general rule, relatively much diminished in quantity; but in some cases they exist in considerable proportion. Lehmann states that diabetic urine always contains hippuric acid, but Dr. Garrod fails to confirm his observations. The quantity of urine secreted by patients suffering from this malady is sometimes enormous, and in many cases this is the first point to attract attention to the disease. Some patients have passed as much as twenty pints of urine *per diem*, and P. Frank mentions a case in which the enormous quantity of fifty-two pounds were discharged in twenty-four hours. The proportion of solid matter varies greatly in different cases; it not unfrequently exceeds two pounds, the greater part of which is composed of sugar.

Diabetic sugar is easily obtained from the urine when but little urea and extractive matter are present. If some of the urine of specific gravity 1050, from a bad case, be allowed to evaporate at a temperature of 100°, small warty masses, of a rounded form, soon make their appearance. Under the microscope, these are seen to be composed of very beautiful crystalline plates. When a considerable quantity of the sugar has crystallised, it may be washed with ice-cold water, well pressed between folds of bibulous paper, and dried over sulphuric acid. It is now, in many cases, nearly colourless, and, after two or three crystallisations, from distilled water, it becomes nearly pure. In fig. 6 some beautiful crystals of grape-sugar

Fig. 6.—Crystals of Diabetic Sugar from Diabetic Urine containing very little Urea.

are represented. These were obtained by allowing a few drops of diabetic urine, containing a mere trace of urea and salts, to evaporate spontaneously on a glass slide. Similar crystals were obtained from the tears of the patient (case reported by Dr. Gibb, in *Archives of Medicine*, vol. i, page 250). Lately, I have obtained crystals from several specimens of diabetic urine. These crystals are very beautiful objects when examined by polarised light. I am not aware that they have been figured before.

TESTS FOR DIABETIC SUGAR.

The presence of grape sugar in urine is readily ascertained by the application of certain tests, and if moderate care be taken in the examination, the detection of this substance is not open to many fallacies.

Moore's test for grape-sugar consists in adding, to the urine suspected to contain it, about half its bulk of liquor potassæ. If sugar be present, the mixture becomes of a rich brown colour upon boiling, which increases in intensity if the boiling be prolonged. The brown colour of the solution is owing to the formation of mellassic or sacchulmic acid; glucic acid is also produced in the decomposition. This test, however, cannot

be depended upon for detecting the presence of small quantities of sugar, because there are some other substances besides sugar which will cause the development of the colour in a slight degree.

Trommer's test. Of all the tests which have yet been proposed, that originally suggested by Trommer, or some slight modification of it, will be found of the greatest practical value for showing the presence of sugar in diabetic urine, in clinical investigations. Trommer's test is applied as follows:—A small quantity of the urine, placed in a test tube, is to be treated with solution of potash, and a drop or two of a solution of sulphate of copper is to be dropped into the mixture. If sugar be present in any quantity, the precipitate at first formed will be redissolved, and the solution will be of a dark blue colour. If only traces of sugar are suspected to be present, one drop of the sulphate of copper solution will be sufficient. The dark blue solution is now to be heated to the boiling point, and if sugar be present, a pale reddish brown precipitate of suboxide of copper is immediately thrown down. Instead of boiling the mixture, it may be allowed to stand for some time, when a similar deposit will gradually subside. If the suboxide is only reduced after prolonged boiling, this cannot be taken as good evidence of the presence of sugar, for under these circumstances there are some other substances which will cause the reduction of the oxide of copper. Again, if the solution simply change colour by boiling, without the occurrence of a distinct precipitate, we must not infer that the change is necessarily due to the presence of sugar, for almost all specimens of urine exhibit this change. A flocculent precipitate of earthy phosphate, which always takes place, cannot be mistaken for the suboxide, as it is quite colourless, or of a pale greenish tinge. The reaction alone characteristic is the production of a brown or yellowish precipitate (varying in quantity according to the amount of sugar the urine contains), either after the mixture has stood for some time, or upon boiling it not longer than for a minute.

Modifications of Trommer's test have been proposed by Barreswil, and others, the most applicable, however, according to Lehmann, being that of Fehling (Lehmann's *Physiological Chemistry*, by Day, vol. i, p. 288. Cavendish Society). As this test is more easily applied than the sulphate of copper and potash, it may be well to mention its composition,—69 grains of sulphate of copper are to be dissolved in 345 grains of distilled water; to this solution a concentrated solution of 268 grains of tartrate of potash, and then a solution composed of 80 grains of carbonate of soda in an ounce of distilled water are to be added; the mixture may be poured into a 1000 grain measure, and filled up with water.

Barreswil's solution is composed of the following constituents:—

Cream of tartar	. . .	96 grains
Crystallised carbonate of soda	. . .	96 "
Sulphate of copper	. . .	32 "
Caustic potash	. . .	64 "
Water	. . .	2 fluidounces.

In using these tests, it is only necessary to add about an equal bulk to the urine in a test tube, and then to boil the mixture. If sugar be present, the precipitate of suboxide occurs immediately. The application of this solution to the quantitative determination of sugar, will be considered under *volumetric analysis*. Trommer's, or one of the above mentioned modifications, will be found the most delicate test which can be used, when only small quantities of sugar are suspected to be present, and the tartrate of copper solution is applied as easily as the liquor potassæ test, while the results obtained from it are far more to be depended upon. If albumen be present, the reduction of the oxide of copper does not take place, so that in using the copper test we must ascertain that this substance is absent. Ammonia also dissolves suboxide of copper.

It has been shown that allantoin, creatine, and creatinine, have the power of producing a precipitate of suboxide of copper, like grape-sugar, and more recently, M. Berlin has proved that uric acid possesses to some extent the same property.

Sometime since I endeavoured to ascertain the cause of certain anomalous results, which were sometimes met with in employing this test; and as these to some extent explain the discrepancies of different authorities with reference to the presence or absence of sugar in the urine in certain cases, it is well to allude to them here. The following results were obtained.

1. The precipitate of suboxide of copper was readily dissolved by acetic, hydrochloric, and nitric acids. It was also dissolved by ammonia.

2. The precipitate was insoluble in a solution of chloride of sodium, but was readily dissolved by a weak solution of chloride of ammonium.

3. The addition of a few drops of chloride of ammonium previous to boiling, entirely prevented the precipitation of the suboxide, the mixture retaining its greenish colour. Upon adding some solution of potash, however, the precipitate of suboxide was produced, and ammoniacal fumes were given off at the same time. If a moderate quantity of solution of chloride of ammonium was present, the precipitate did not occur upon the addition of potash, even after very prolonged boiling.

4. If a drop of a very dilute solution of the chloride of ammonium was added to a pretty strong solution of sugar, and, after the addition of the tartrate, the mixture was boiled, no precipitate took place, but the solution became of a pale brown tint; the suboxide being immediately thrown down upon the addition of a few drops of a solution of potash, with the development of ammoniacal fumes. In the above cases in which no precipitate took place, it was ascertained that there was the usual excess of alkali present in the test solution.

5. A solution of oxalate of ammonia also prevented the precipitation of the suboxide, but a greater quantity of this salt than of the chloride of ammonium was required.

6. A neutral solution of urate of ammonia (artificially prepared) also prevented the reduction of the suboxide, and dissolved the precipitate if added to it. On carrying out this experiment further, it was found that the precipitate of suboxide of copper was dissolved by urine containing an excess of urate of ammonia.

7. A solution of grape-sugar in water was prepared, and by a preliminary experiment it was ascertained that, upon being boiled with the tartrate test, an abundant precipitation of suboxide took place.

To a portion of the precipitate of suboxide produced in this way, about a drachm of healthy urine, immediately after it was passed, and while yet warm, was added, and the reddish precipitate was instantly dissolved, forming a perfectly clear solution. Upon further boiling, a slight precipitate of phosphate took place. The suboxide, however, could not be precipitated by the further addition of potash and prolonged boiling.

8. Upon mixing a small quantity of grape-sugar with the same specimen of healthy urine, and boiling the mixture with the tartrate test, no precipitate, except a little phosphate, was produced. About half an ounce of the same mixture of urine and grape sugar was placed in a test tube, mixed with six drops of yeast, and inverted over mercury. The whole was then placed in a temperature from 70° to 100° for about twelve hours, at the end of which time the tube was found quite filled with gas, and all the liquid was expelled into the vessel in which it had been placed. The specimen of urine with which the above experiments were tried, was allowed to stand in a still place; and when it had become quite cold, an abundant precipitate of urate of ammonia was found to be present.

9. A portion of the aqueous solution of grape-sugar was mixed with a strong solution of urate of ammonia (artificially prepared), and then a certain quantity of the tartrate solution was added, and the mixture boiled. The characteristic precipitate, or opalescence, was not produced, but the mixture became of a pale fawn colour. In a weak solution of urate of ammonia, the characteristic precipitate appeared after boiling the mixture for some minutes. So that, although much sugar is present, the colour of the mixture may be merely changed to brown, and no precipitate whatever may take place.

10. A solution of grape-sugar was treated with a drop of a dilute solution of chloride of ammonium, and boiled with the tartrate solution. The mixture became of a brown colour, but no precipitate occurred. Upon the addition of a few drops of solution of potash, the precipitate of suboxide was produced.

A solution of grape-sugar, treated with Trommer's test, according to the usual method, behaved in the same way, in the presence of chloride of ammonium, as when treated with the tartrate of copper solution; but in this case a greater quantity of the chloride was necessary, for when only traces were present, ammoniacal vapours were given off, and the precipitate of suboxide subsided, as before remarked.

From the results of the above experiments, the following conclusions with reference to the practical application of Trom-

mer's test, and Fehling and Barreswil's solutions, and other modifications of the copper test, may be drawn* :—

1. That if the urine contain chloride of ammonium (even in very small 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.

2. That unless there be a considerable quantity of one of the above salts present (in which case the blue colour will remain), the mixture will change to a brownish hue upon boiling, but no opalescence or *precipitate* of suboxide of copper will occur. When only a moderate amount of sugar is present, I have been unable to obtain a precipitate, under these circumstances, by the addition of potash to the solution, and prolonged boiling. By observation 8, it appears that a specimen of urine exhibiting this reaction may contain a large quantity of sugar, as ascertained by the yeast test.

3. That in many cases in which the precipitation of the suboxide is prevented by the presence of ammoniacal salts, the addition of potash to the solution, and subsequent boiling, will cause the production of a precipitate with the evolution of ammoniacal fumes. Hence care should always be taken that there is a considerable excess of free alkali present.

4. When only small quantities of sugar are present in the urine, and the precipitate of suboxide of copper is not decided, the fermentation test should be resorted to.

Upon treating different specimens of diabetic urine with Trommer's test, or its modifications, it has often been noticed that in one case the precipitate is produced as soon as the mixture reaches the boiling point, or even before; while in other instances it is necessary to keep it in active ebullition for some minutes, before any precipitate is produced. This circumstance receives explanation from the facts above detailed with reference to the presence of ammoniacal salts; and other anomalous results, which must have occurred to many in the habit of employing this test, become explained.

As a test for diabetic or grape-sugar, if proper precautions be observed, much greater dependance can be placed on this test than by simply boiling with liquor potassæ. Specimens of urine in which sugar is suspected to be present, and no decided precipitate of suboxide (which must be carefully distinguished from phosphate +) occurs, should be carefully fermented with yeast before any conclusion is arrived at.

On Testing for Sugar when only Traces are Present. In fluids which are suspected to contain only mere traces of sugar, it is necessary to separate some of the other constituents before applying the test. The plan recommended by M. Leconte is the following:—Excess of acetate of lead is added, and the precipitate separated by filtration. The solution is concentrated by evaporation, treated with ammonia, and again filtered. The copper test is then applied. The objections to applying the reduction test to solutions containing ammonia has been already discussed. It is better to employ carbonate of potash, or soda, instead of ammonia. The excess of lead salt may also be removed from the filtered solution by passing sulphuretted hydrogen. The precipitate of sulphuret of lead is removed by filtration, and the liquid, after evaporation to a small bulk, may be tested.

Another plan recommended by M. Leconte is to treat the urine with acetic acid, and evaporate it to about the fifth of its bulk; it is then treated with alcohol, and after filtration from the salts, etc., the alcoholic solution is evaporated and tested. This plan is free from the objection that ammonia may cause the destruction of the sugar where only traces are present.

The Yeast Test. This is one of the most satisfactory tests for the presence of sugar, and if employed with proper care can hardly fail in its results. Two test tubes, of the same form, and of equal size, are to be taken. One is nearly filled with water, and into the other a corresponding quantity of the urine is to be poured. An equal amount of yeast is now to be added to the liquids in the tubes, and after pouring in just sufficient fluid to fill the tubes, the thumb is to be carefully placed over the opening, and the tube inverted in a small cup of mercury. The best plan, however, is to cut out a little india-rubber pad, slightly larger than the upper extremity of the tube. When the tubes have been filled up to the brim with a little water, the pad is allowed to float on the surface; next a little cup or

beaker is inverted, and carefully placed over the end of the tube. The india-rubber being pressed against the open end, the fluid is prevented from escaping. The whole may be inverted, and a little mercury having been poured into the beaker, the india-rubber may be removed, with forceps, without any escape of the fluid. The tubes may be supported in position by a wire stand. Both tubes are then to be exposed, for a few hours, to a temperature of from 80° to 90°, and the comparative size of the bubble of gas in the upper part of each may then be noted. If an appreciable quantity of sugar be present, the bubble of gas in the tube containing the urine will be many times larger than that in the tube which contains the yeast and water. In the latter tube the bubble of gas merely arises from the small quantities of air previously mixed with the yeast, becoming disengaged, and floating to the surface. Fermentation, when carefully performed, is positive evidence of the presence of sugar, although it does not indicate the kind of sugar present.

Maumend's Test. A little woollen rag, as merino, is cut into strips, and soaked for four or five minutes in a solution of perchloride of tin (one part of the perchloride to two parts of water). The slips are then dried over the water bath. A drop of the urine suspected to contain sugar is allowed to fall on a small slip of the prepared merino, which is then dried, and exposed to the dull red heat of a spirit lamp. If a trace of sugar be present, a black spot is produced.

Bismuth Test. Bottger has lately proposed a new test for sugar. This consists in adding first of all potash, then a small quantity of subnitrate of bismuth; lastly, the mixture is boiled. If sugar is present, the oxide is reduced to metallic bismuth, which is precipitated in the form of a black powder. It has been asserted that sulphuret of bismuth is formed, but this seems not to be the case. Brücke shows that this test is more delicate than Trommer's (or the modification of it by Fehling); and he finds that the black precipitate is produced to some extent in specimens of healthy urine. The bismuth test may be also applied thus. A solution of carbonate of soda (crystallised carbonate 1 part, water 3 parts) is prepared, and a certain quantity added to an equal amount of the urine. A little basic nitrate of bismuth is then added, and the mixture heated to the boiling point. If sugar be present, a black precipitate is produced.

[To be continued.]

Original Communications.

A CASE OF SUDDEN DEATH, WITHOUT ANY ADEQUATE POST MORTEM APPEARANCES.

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On the 24th of April, the housemaid in a medical man's family was sent out to fetch the beer, when, within ten minutes afterwards, she was found by the cook lying apparently dead in the scullery. I saw her myself in about another quarter of an hour. There was no action of the heart, no breathing, no sensibility; the body was still warm; the face livid and swollen. The only symptoms observed during life were that, for about a week before her death, she suffered from earache, appeared unusually indolent and stupid, and at times complained of faintness.

POST MORTEM EXAMINATION, about twenty-two hours after death. The body was large, finely developed, very fat. Cadaveric rigidity was strongly marked in the limbs, and the firmly clenched lower jaw. The left ventricle of the heart was filled with dark fluid blood, and was firmly contracted; the right was flaccid and collapsed, containing but a very small clot. The muscular substance was apparently normal. The heart was altogether small in proportion to the body. The lungs were slightly congested. Between the two openings of the stomach was an oblong patch of fine punctiform florid injection in the lines of the rugæ. It contained an undigested meal of some stewed steak, of which the patient had partaken shortly before death. No poison of any kind was found in a careful analysis instituted by Mr. Rodgers, at the request of the jury. The intestines were not opened; their peritoneal coat was covered with congested veins, but in no very marked degree. The

* Professor Brücke has recently drawn attention to the action of ammonia in preventing the precipitation of the suboxide of copper, and other points connected with this subject. Probably he had not seen the results just given, which were obtained in 1852. (Med.-Chir. Review, Jan. 1853, vol. xi, p. 113.)

+ The precipitate of suboxide may be distinguished from phosphate by its solubility in ammonia.