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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Of Estimating the Quantity of Sugar. The quantity of sugar is easily determined, though not with absolute accuracy, by fermentation. The quantity of carbonic acid formed may be measured, weighed directly, or its weight may be determined by ascertaining the loss of weight the urine has sustained from fermentation.

Fermentation. If the carbonic acid is to be measured, the mixture of yeast and urine must be placed in a graduated tube inverted over mercury. When the fermentation is complete, which is generally the case in from six to twelve hours, at a temperature of 100°, the volume of gas may be read off, and, after correction for temperature and pressure (Miller's *Elements of Chemistry*, vol. i, pp. 48, 180), the amount of sugar calculated. One grain of sugar corresponds to nearly one cubic inch of carbonic acid.

The carbonic acid may be weighed by causing it to pass through a solution of liquor potassæ, specific gravity 1250, in an ordinary Liebig's potash tube. One grain of carbonic acid corresponds to about two grains of grape-sugar. The urine (about 500 grains) with the yeast may be placed in a small retort, to the end of which is adapted a chloride of calcium tube, or a tube containing pumice stone moistened with sulphuric acid, for the purpose of drying the gas. To the extremity of the drying tube the potash apparatus is connected. This is weighed just before and immediately after the fermentation, which should be allowed to proceed at a temperature of from 80° to 100° for twelve hours. The increase of weight is due to dry carbonic acid. Or, lastly, about 200 grains of urine with a little yeast are placed in a flask, to the mouth of which a small drying tube is adapted, as shown in fig. 7. The apparatus is to be carefully weighed before and after the experiment, and the loss indicates carbonic acid.

The results afforded by fermentation are not so accurate as

those obtained by the volumetric process of analysis, which I shall describe in my last lecture.

Fig. 7.—Flask containing the urine and yeast. The disengaged carbonic acid passes through the little tube containing chloride of calcium or fragments of pumice-stone moistened with strong sulphuric acid.

Determination of Sugar by the Polarising Saccharimeter. Biot, many years ago, proposed a plan for estimating the proportion of sugar in fluids, depending upon the influence which the solution of sugar exerted upon a ray of polarised light made to pass through a thick stratum. Under these circumstances, a succession of colours is produced in the following order: yellow, green, blue, violet, red. If, in order to produce this series of changes, the hand must be turned towards the right, the solution is said to divert the plane of polarisation to the right, or to exhibit *right-handed polarisation*; but if to the left, *left-handed polarisation*. Cane-sugar and diabetic sugar have the first property; the sugar of fruits the second. The amount of rotation varies according to the quantity of sugar present. Two or three different forms of apparatus have been made. Mitscherlich's and Soleil's are the best. A modification of Mitscherlich's, made for me by Mr. Becker, of the firm of

Fig. 8.—Polarising saccharimeter made by Mr. Becker.

Elliott, brothers, Strand, is represented in fig. 8. The urine or saccharine fluid is placed in the long tube. At the end near the lamp is a prism of Iceland spar, the *polariser*; and at the other extremity another prism, the *analyser*. The latter crystal is connected with a moveable bar, which can be rotated with the hand, and the arc through which it is carried can be accurately measured on the graduated circle with the aid of a vernier. The instrument is placed with the posterior aperture about two inches from a homogeneous light,* and the prisms adapted to zero, which is found by arranging the posterior prism so that, the tube being empty, when the arm stands at zero, the little spectrum is quite dark. It is then ready for use. The tube is filled with the solution carefully filtered; and if dark coloured, it is to be decolorised in the first instance by animal charcoal. Upon moving the arm towards the right, it will be found that, after it has passed through a certain number of degrees, the colour of the spectrum becomes blue, and gradually violet and red. Now, the exact degree at which the colour passes from the violet to the red is to be noted; and the number will vary according to the quantity of sugar. The

* The best light is a very good argand or Leslie's burner, with a white porcelain reflector having a dull surface behind; or a piece of thin ground glass, or semi-opaque white glass, may be placed in front of the lamp.

value of each degree is ascertained by examining in the first instance a few solutions having known quantities of sugar dissolved. Supposing that 50 grains of sugar, dissolved in a certain quantity of water, require a rotation of 20° , 100 grains in the same quantity of fluid would require a rotation of 40° before the violet colour would appear. This method is very simple and accurate.

M. Clerget (*Annales de Chimie*, III, xxvi, 175) used Soleil's instrument, which was also employed by Dr. Bence Jones for determining the quantity of sugar in wines and in diabetic urine. (*Med. Times and Gazette*, vol. xxv, 1852, p. 102.) The apparatus consists of a polariser and an analyser, made of Iceland spar. The light, which should be bright, white, and homogeneous, is placed behind the polariser. Between the polariser and analyser is placed the tube containing the saccharine solution, as in the other apparatus. Before reaching the saccharine solution, the rays of light pass through a circular plate of quartz "composed of two half circles possessing equal and opposite rotatory power". The colour of the two plates will be the same before placing in the sugar, but afterwards the colour varies much; and by moving the compensator, composed of two wedges of quartz, which can be slipped over each other, the colour will be equalised. The amount of movement required, or the thickness of the quartz, varies according to the amount of sugar present; and thus the proportion may be determined.

Dr. Garrod's Plan of Estimating the Quantity of Sugar. Dr. Garrod has lately devised an instrument for estimating the quantity of sugar in urine, founded on the principle that the alteration of colour caused by boiling a mixture of diabetic sugar and carbonate of potash varies in intensity according to the quantity of sugar present. A standard solution is prepared of the colour produced by a solution containing half a grain of sugar to the fluidounce. This is placed in a clear glass tube of about half an inch in diameter. The solution of carbonate of potash is prepared by dissolving four ounces of the carbonate in six ounces of water, and the solution filtered.

In the first place, Moore's test is applied; and if the colour produced after boiling for a few minutes be deeper than an amber red, it is necessary to dilute the urine before making the quantitative determination. The darker the colour produced, the more the urine is diluted. An equal bulk, twice or three times its bulk, of water being added, according to circumstances; the exact proportion of water added must, of course, be carefully noted.

Thirty minims, by measure, of the urine, diluted or not, as the case may be, are mixed with an equal quantity of the carbonate of potash solution, and poured into a small flask. The measure is to be washed out with about a drachm and a half of water, which is also to be mixed with the solution. Next, the whole is to be boiled over a spirit-lamp for five minutes. When cool, the mixture is transferred to a graduated tube of the same calibre as that which contains the standard solution, and diluted with water until its tint is exactly the same as that of the standard solution. By a simple calculation, the quantity of sugar is easily found. Suppose it has been necessary to make the urine by dilution, forty times its original bulk, in order to obtain the exact tint, it will contain forty half-grains of sugar per ounce, or twenty grains of sugar. From these data, the proportion passed in the twenty-four hours is easily calculated. The apparatus was made by Messrs. Coxeter.

Circumstances under which Sugar is excreted in the Urine. Although of late years many new and important facts connected with the formation and destruction of sugar in the healthy organism have been discovered by Bernard, and verified by many observers, the pathology of diabetes is still obscure. There can, however, be little doubt that the sugar is formed in the liver, principally from albuminous substances; but whether its excretion in such large quantity depends upon increased activity of the actions concerned in its production, or arises from the cessation of the destructive changes which occur in a normal state, has not been determined. Neither can we say how far the affection may be influenced by the state of the nervous system. Nevertheless, very much has been done by physiologists in this direction; and I think we are justified in feeling sanguine that in a few years the nature of this wonderful and fatal disease will be revealed.

I do not propose to enter upon the subject of the treatment of diabetes, although we may consider some of the circumstances which cause an increase or diminution in the quantity of sugar excreted. Diabetes is often only of temporary duration, and we know that many persons for a time pass small quantities of sugar

in the urine without even being aware of the occurrence. In other instances, diabetes may persist for some time, and then pass off. In many cases, the diabetic condition lasts for a certain time, passes off, and after an interval reappears. The disease may continue for many years, or may carry off the patient in a few months. The urine is, as before remarked, usually of high specific gravity; but sometimes urine containing sugar is not more than 1015. The reaction is generally acid, often excessively so. The quantity of urea varies much in different cases; usually it is diminished, but a large quantity of this substance, as well as sugar, is sometimes excreted. In one of Dr. Garrod's patients, as much as 1085 grains of urea and 3500 grains of sugar were eliminated in twenty-four hours. The observation of Lehmann, that diabetic urine does not contain uric acid, is undoubtedly erroneous; for, in this country at least, it is not uncommon to meet with an abundant deposit of this substance. Dr. Prout regarded the presence of uric acid as a favourable sign. Hippuric acid is said to be present in diabetic urine (Lehmann and others); but in some specimens of urine, in which Dr. Garrod sought for it, he failed to detect it. (*Gulstonian Lectures*, BRIT. MED. JOURNAL, 1857.)

The highly important and interesting observation lately made by M. Hohl, in a case of diabetes where inositol was passed in large quantities, and seemed to take the place of the urea and sugar, must not be passed over. I shall have occasion to recur to this very shortly.

The quantity of sugar, as you know, is much influenced by the quantity and nature of the food. It increases shortly after a meal, and it is undoubtedly augmented when much starch is taken. A meat diet, with bran or gluten bread, always causes a diminution of the sugar. Total abstinence from food, and rest, diminish the proportion; and it is increased by exercise, and favoured by a large quantity of food. As much as two pounds of sugar may be excreted daily; but about one pound is the more usual quantity. I have now under my care a girl, aged 19, who excretes daily about one pound and a half of sugar.

The dry harsh skin, the intense hunger and thirst, the emaciation, the tendency to the formation of tubercle in the lungs and other organs, are familiar to all who are acquainted with the clinical history of this disease. Dr. Garrod observes, that oedema of the legs is always present in diabetes. Although in some cases it is very slight, he states that it is always to be detected.

In extreme cases of phthisis, sugar is occasionally detected in the urine; and towards the close of many exhausting diseases, a meal of starch is followed by the excretion of saccharine urine. It has also been detected in severe disease of the respiratory organs, as pneumonia and bronchitis. I have proved the presence of a considerable quantity of sugar in the sputum, in a case of acute pneumonia, just before the patient's death. It has been asserted by some observers, that sugar can always be detected in the urine after anaesthesia produced by chloroform, and in cases of bronchitis and emphysema. I have carefully tested for sugar in the urine of several patients who had taken chloroform, but did not succeed in detecting it in a single instance. The presence of the sugar is accounted for under these circumstances, on the supposition that in disease of the pulmonary organs the sugar is not further oxidised, and carried off as carbonic acid. But Bernard has shewn that this theory has no foundation, and has proved that the condition of temporary diabetes produced by irritation of the floor of the fourth ventricle, close to origin of the pneumogastric nerves, is not due to the impaired action of the respiratory organs, as Reynoso and others have supposed.

Bernard has brought forward various facts which militate against the above view; as, for instance, no sugar appears in the urine after complete section of the pneumogastric nerves, and in many other conditions where the respiratory function is impaired. Nevertheless, Reynoso (*Comptes Rendus*, t. xxxiii, xxxiv) states that sugar is present in the urine of persons who have been placed under the influence of chloroform, bichloride and iodide of mercury, salts of antimony, opium and narcotics generally, quinine, and carbonate of iron. He also states that in pleurisy, asthma, and chronic bronchitis, hysteria, and epilepsy, he discovered sugar in the urine. The test employed, it is very important to observe, was Barreswill's solution; but, before applying it, the extractive matters were removed. About 1500 grains of the urine to be tested were treated with a solution of subacetate of lead. The precipitate was collected on a filter, and the excess of lead salt in the filtrate was decomposed by chloride of sodium; and the solution was again filtered. The clear fluid, after being concentrated, was treated

with the copper solution. To another portion the yeast test was applied.

Michèa, who, it should be observed, employed Moore's test, failed to confirm the above conclusions. Déchambre (*Gazette Médicale*, 1852) found sugar in specimens of urine obtained from several old people. The test employed was the same as Reynoso used, except that the excess of acetate of lead was decomposed with carbonate of soda instead of chloride of sodium. Dr. Bence Jones obtained "slight but distinct" evidence of the presence of sugar in the urine of a patient who had been twenty-four hours under the influence of chloroform. The urine was examined according to Reynoso's directions. M. Blot also confirms Reynoso's observations to a great extent. He found sugar in the urine of pregnant women, and in those who are suckling children as soon as the milk was secreted. It is possible that affections of the respiratory organs may be instrumental in producing the diabetic condition; but this may be due to the excitation of the peripheral extremities of the pneumogastrics, depending upon the altered state of the pulmonary membrane, being propagated along the trunks of nerves to that particular part of the medulla oblongata the artificial irritation of which in animals is known to induce diabetes. There are many facts which support the doctrine that the processes concerned in the production of the sugar are capable of being excited in a reflex manner, and they may therefore be included in the excito-secretory actions.

These observations of Reynoso and others seemed to be so important that it was very desirable to repeat them. I therefore tried numerous experiments, but was unable to confirm the results. I often found the fluid change to a brown colour when heated with the copper solution; but, as I have shown, this is not a proof of the presence of sugar. I never conclude that sugar is present in a specimen of urine, unless a decided precipitate of the suboxide of copper is produced. Though this precipitate be very slight, it is characteristic. If it only amount to an opalescence, as I have before stated, it is sufficient; but a change of colour even to a dark brown, the solution still remaining clear, does not, I believe, indicate the presence of sugar.

These negative results led me to institute the experiments upon the action of Barreswill's and Fehling's solutions, and different forms of the copper test, which have been already described.

[To be continued.]

Illustrations OF HOSPITAL PRACTICE: METROPOLITAN AND PROVINCIAL.

BIRMINGHAM EYE INFIRMARY.

THE SURGICAL TREATMENT OF SHORT SIGHT.

OUR associate Mr. J. V. Solomon has hit upon an operation by which the focal range of short-sighted persons, whose corneæ are not conical, may be doubled in length. He has found the plan equally successful, whether the eyes are prominent or small, the aqueous chambers deep or shallow. He has tested the operation on cases varying from the age of 12 to 45 years. A man of the latter age, who had worn double concave glasses of immense depth (No. 16) for a great number of years, and, unaided by lenses, could see with clearness the features of a person to know them at a distance of nine feet only, obtained at once by the operation an increase of seven feet in his focal range. In a child of 12 years of age, the operation increased the reading distance from four to eight inches, and the power of identifying persons' features from twenty to forty yards; and in one of 16 years, the effect was still more remarkable.

These results have been obtained by dividing in a transverse direction some fibres of the muscle of the lens—the ciliary muscle. Mr. Solomon does not consider it material which part of the muscle is selected for division, but generally prefers either the upper or the lower part of the circle. Supposing the latter situation to be selected, and the patient to be seated in a chair, the operator stands behind, and fixes the globe with the left fingers, as in extraction, holding a cataract-knife in his right hand; with the flat of the blade directed upwards, he pushes the point in succession through the corneo-sclerotic

union, the pillars of the iris, and the ciliary muscle. The direction given to the instrument is obliquely downwards and outwards. Care is taken that the incision in the muscle is of the same length as the puncture of entrance; namely, about two lines or two lines and a half in diameter. In some cases, Mr. Solomon has found that the power of adapting the eye to distant objects has been increased by practice and lapse of time.

In a young man who had been myopic from his childhood, and had suffered for the last three years from congestion of the retina, the visual power and focus have been so much increased that the outline of large buildings at a distance of a mile and a half can now (six weeks after operation) be distinctly made out; whereas, before the ciliary muscles were divided, they appeared as mist.

On another occasion, we shall draw the attention of our readers to Mr. Hancock's operation for glaucoma, and point out wherein it differs from the procedure adopted by Mr. Solomon; also to the latter gentleman's theory of the curative action in glaucoma of Gräfe's and Hancock's operation.

Original Communications.

ON THE INFLUENCE OF BELLADONNA ON THE PNEUMOGASTRIC NERVE.

By RICHARD HUGHES, M.R.C.S., and L.R.C.P.Ed. (Exam.),
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DRYNESS of the throat and dysphagia are two of the earliest and most invariable symptoms of the influence of belladonna. On what do they depend?

The pneumogastric nerve appears to preside over alike the muscular fibre and the secreting apparatus of the alimentary canal from the fauces to the stomach. Claude Bernard has ascertained the result of its division upon the stomach. "The section was made during the free flow of gastric juice (through a cannula previously introduced into the stomach), excited by the presence of an alimentary bolus. The flow immediately ceased, and the mucous membrane, which had been tense and turgid the moment before, became withered and pale. On introducing the finger into the stomach itself, the walls were perceived to be perfectly flaccid, and there was no longer the gentle pressure which had been previously felt" (Carpenter's *Human Physiology*, 5th ed., p. 87). It stands to reason that, if such be the effect of loss of pneumogastric influence on the stomach, similar phenomena—check of secretion and diminished muscular power—higher up in the alimentary canal, must be referred to depression of the influence of the same nerve. Consequently, the dryness of throat and dysphagia caused by belladonna must result from a depressant influence exercised by it on the pneumogastric nerve.

That belladonna has such an influence will farther appear from a consideration of its effects on disease. Hooping-cough and asthma are admittedly spasmodic affections, in which irritation of the pneumogastric nerve is at the bottom of the phenomena: and both of these affections are singularly under the control of belladonna and its congeners. Stramonium is the favourite remedy in asthma; and the use of belladonna in hooping-cough is becoming more and more general. In the former case, we have the evidence of direct experiment for our theory. Galvanisation of the pneumogastric has been found by Valentin to produce constriction of the trachea and bronchial tubes; while on the other hand, in animals poisoned by belladonna and stramonium, these tubes have been found lax, and have refused to contract under the strongest stimuli (Watson's *Lectures on Physic*, 4th ed., vol. ii, p. 358, 363). Lately, moreover, an enterprising French surgeon has attempted and (apparently) achieved the cure of asthma by injecting a solution of atropine upon the pneumogastric nerve in the neck (*Medical Times and Gazette*, Nov. 26, 1859). Another affection in which belladonna has been found very beneficial, and in which the pneumogastric is the seat of irritation, is obstinate spasmodic vomiting. A patient was suffering from cancer of the pylorus; the usual incessant vomiting took place. Belladonna was given, and it ceased. After death the stomach was found lax and enormously distended. Mr. Amesbury tells me he once had a case of obstinate vomiting in pregnancy. All the usual remedies failed; at length he tried belladonna, with complete success. Here again, as the pneumogastric is the motor nerve of the muscular coat of the stomach, a sedative influence exercised by the belladonna upon this nerve will explain the phenomena.