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THE SIGNIFICANCE AND DETECTION OF Traces of SUGAR IN THE URINE,

WITH SOME REFERENCE TO

LIFE INSURANCE.

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THE SIGNIFICANCE AND DETECTION OF Traces of SUGAR IN THE URINE,

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The materials introduced into the body for its maintenance are the albuminoids, carbo-hydrates, hydro-carbons, salts, water, and oxygen. The substances which, under physiological conditions, appear in the excretions are, practically speaking, urea, salts, carbonic acid, and water. The albuminous matters serve their purpose, and, being non-diffusible, are converted into the crystaloid urea in order to be gotten rid of. The carbo-hydrates and hydro-carbons, having a great affinity for oxygen, are by this agent converted into water and carbonic acid; while the remaining proximate principles, the mineral salts and water, being very diffusible and little prone to change, are excreted under their own forms. Thus, theoretically, at the start it appears that, under normal conditions, the urine should contain none of the organic ingredients

of the food, nor any of their immediate derivatives [Albumen, peptone, paraglobulin, metalbumen, glucose, maltose, chyle.]

On the other hand, various observers have for many years held that sugar is a natural ingredient of the urine [Bince Jones, Brücke, Brodecker, Gubler, Pavy], while as many equally reliable ones have failed to satisfy themselves of its presence. [Lehman: "Physiological Chemistry," Phila., 1855, Vol. 1, p. 257; Kulz, Malay, Seegen, Gorup-Besanez.] Thus has arisen a controversy which I think, however, is now about concluded. Those who maintain the affirmative of this question have either been obliged to employ large quantities of urine, concentrate it by evaporation, and bring to bear profound chemical knowledge in order to demonstrate a trace of sugar, or they have depended upon the reducing properties which normal urine possesses when treated with some of the standard tests for glucose. Now, normal urine which will respond to the reduction tests, will not undergo the alcoholic fermentation in the presence of yeast. And it is generally acknowledged by those who consider sugar to be a normal consituent, that urine contains something else capable of reducing cupric oxide. Uric acid has long been known to possess this property, and Dr. Pavy ["Med. Chir. Soc. Trans.," Vol. 63, p. 222] expresses his side of the question when he says that the re-

ducing action (on cupric oxide) which normal urine exerts is due, one-fourth to uric acid and three-fourths to the small amount of sugar naturally present in the urine.* He further adds that it is doubtful if there is any other body worthy of consideration which has any reducing effect. Our own experiments on this point have convinced us that after the removal of the uric acid from normal urine by lead acetate, the urine still contains something capable of reducing cupric oxide and picric acid, yet inactive to the yeast test, even when concentrated by evaporation; and our conclusion was that this something is not sugar. Therefore our belief has been, and still is, that the urine from a person who is free from disease or functional disorder, and who has not recently ingested an excess of starchy or saccharine food, will be found to be free from sugar.

This view has been recently verified by the researches of Mr. George S. Johnson, M. R. C. S., F.C.S., etc. ["Proc. Royal Soc.," Vol. 42]. In a word, Mr. Johnson has discovered that, besides uric acid, which, agreeing with Pavy, represents one-fourth the reducing action of normal urine, there is another body, not sugar, which answers for the other three-fourths, namely, kreatinin. And that when both the kreatinin

*Dr. George Johnson, in an analysis of 300 specimens of urine, found a reducing substance which reacted with copper and picric acid, but not with yeast.—*Lancet*, June, 1883.

and uric acid are removed, the final filtrate has no reducing effect either with cupric oxide or picric acid. And as uric acid does not reduce picric acid, Mr. Johnson has discovered that it is kreatinin which causes all urines to react with this test.

The conclusions of this observer are that "cupric oxide will be reduced by the normal urine in quantities equivalent to the reduction effected by 0.43 to 0.51 grains of glucose per 1 fluid ounce. The total reduction effected by normal urine is accounted for by the uric acid and kreatinin which it contains."* And Dr. George Johnson, basing his faith upon his son's researches, says ["Brit. Med. Jour.," Jan. 8, 1887] that it is conclusively proven

1st, That not a trace of sugar is to be found in normal urine.

2d, That as uric acid has no reducing action on picric acid, the chief, if not the sole, constituent of normal urine which reduces picric acid in the presence of potash is kreatinin.

From what we have said regarding our position on the question as to the presence of sugar in normal urine, it is evident that the researches and conclusions

*Mr. Johnson mentions that "uric acid and kreatinin together are credited by Prof. E. Salkowski ["Cent. f. d. Med. Wiss'sch'n," March, 1886] with one-sixth to one-fifth of the total reducing action of normal urine, the remainder being due to "other substances, and very probably to compounds of glycuronic acid [Glykuronsäuereverbindingen]."

just described were of great interest to us, and we immediately set to work to repeat the experiments.

The result is that we are perfectly satisfied as to their correctness, and feel justified in believing that the verdict must stand: Normal urine contains no sugar.

Hence the presence of sugar in the urine in any amount must have some significance, and it behooves us to familiarize ourselves with all possible conditions with which it is associated, in order to determine its import.

To begin with, we would have the distinction between glycosuria and diabetes mellitus constantly borne in mind. Too many writers confound the terms. We may have glycosuria without the diabetic element, as we may have diabetes without the glycosuric feature. Without going into the complicated and unsettled pathology of glycosuria, with or without diabetes, we will state that our understanding and belief is that diabetes mellitus is the result of a central lesion of the nervous system, while glycosuria is caused by direct irritation of the hepatic vessels by toxic constituents of the blood. [Pavy, Harley, Ralf.]

We believe that Prout ["Stomach and Renal Diseases," Phila., 1843, p. 43] was the first to describe cases of glycosuria without diabetes, occurring in gout, dyspepsia and in the aged. He also points out the fact

that a low specific gravity of the urine is no certain indication of the absence of sugar. The extremes of specific gravity which he encountered ranged from 1020 to 1050, and once or twice he had seen it at 1013; and in a note he records an instance where it was 1010 and distinctly and rapidly underwent the vinous fermentation. Seegen and others, ourselves included, have since frequently found sugar in urines of low specific gravity.

Dr. Wm. Ord ["St. Thomas' Hosp. Report," Vol. XII., p. 1] in a paper on "Some Clinical Aspects of Glycosuria," narrates a series of cases wherein the urine contained sugar in variable amounts, unassociated with the diabetic element. Many proved to be of a serious nature, and at times the presence of sugar was difficult to detect. His list, which excludes temporary glycosuria "from certain passing provocations," consists of twenty-two cases, ranging from fifty to eighty-four years of age, and includes only two women. There were twenty cases of nervous disorders; gout, eight; errors of diet, over-eating and drinking, three; albuminuria, ten. There were two cases of syphilis in young persons, with variable amounts of sugar. The conditions found to exist and symptoms complained of were nervousness, excessive mental work, anxiety, insanity, apoplexy, locomotor-ataxia, hypochondriasis, tinitus, shingles, hysteria,

headache, loss of memory, numbness in limbs, sciatica, and angina pectoris, two cases.

We have notes of twelve cases bearing upon this subject, of which the following four are good examples:

1. L. W., age 35, upholsterer. Has felt ill for a year. Lost flesh. Is depressed and indisposed to work. Has occipital headache. Bowels regular. Appetite fair. Does not drink to excess. Looks pale and tired. Has backache. Voids the normal amount of urine Drinks very little water. No cause for these symptoms could be discovered by physical examination, until we came to the urine. Sp. gr. 1020. No deposit. Careful manipulation detected decided trace of sugar. Ordered mineral acids and calomel, and to avoid sweets and starches. At the expiration of three weeks the sugar permanently disappeared, and the patient ceased to complain.

This was a case of faulty tissue metabolism, and he could not tolerate sugar.

2. H., broker in Wall street. Single; 40; 150 pounds; 5 feet 6½ inches. High liver. Drinks to excess. Well until recently, when his head began to trouble him. Could not apply himself to business. Insomnia. Pain in occiput. Restless and apprehensive. Does not void an excess of urine. Urine, dark amber. Sp. gr. 1015. No albumen Sugar, a trace.

Advised a regular life, abstinence in eating and drinking, vacation in the mountains. A month afterwards he was feeling slightly better, but albumen and renal epithelium had appeared in the urine. This case has gradually gone on to chronic Bright's.

3. B., 36, 135 pounds, 5 feet 7 inches. Tutor in college. Applied for life insurance. Feeling perfectly well. Rarely ill. The urine was sent to me for analysis. Daily quantity, 50 ℥. Sp. gr. 1025. A marked trace of sugar. A second specimen two weeks later showed sp. gr. 1035, and gave unmistakable evidence of sugar with the copper test, but not with fermentation. A third specimen two weeks later showed sp. gr. 1030, and same chemical reactions as the others. The subsequent history of the case I have not been able to learn.

4. Mr. X., 35, 5 feet 10½ inches, 180 pounds. Family history excellent. This is a very wealthy gentleman, who carries a large line of life insurance, and desired to increase it. He has scarcely ever known a sick day, is genial, and in appearance is in perfect health. He had never encountered any difficulty in being accepted by any company until last winter, when his urine, being examined by a very competent physician for an out-of-town company, showed a sp. gr. of 1026, and with Fehling's solution it gave a prompt and copious deposit of cuprous oxide This discovery surprised the physician and startled the gentleman. The risk was postponed, and Mr. X. was unable to obtain the additional insurance which he desired.

The case was referred to the writer. No other evidence of disease could be found. The patient felt perfectly well, and was not aware of an ache or pain. The only thing observed about him was an intense and nervous manner. Nine specimens of his urine were examined, voided at various times of day, and under conditions both of abstinence and while indulging in an excess of sweets. The daily quantity was never excessive, but the specific gravity always ranged be-

tween .1025 and 1030, and in every instance unmistakable evidences of sugar were present. These facts were stated to the various life insurance companies with whom the gentleman wished to insure, and the result was that some declined, while others accepted him for large amounts. So far as known he continues to enjoy good health.

Now, enough has been said to indicate the points which we wish to make prominent regarding the significance of small amounts of sugar in the urine. Of course, we do not mean those instances familiar to us all as being insignificant, which are associated with what Dr. Ord calls "passing causes," and constituting temporary glycosuria. Such conditions are easily produced by the rapid absorption of an excess of starchy or saccharine food, slight nervous derangements, physical exercise, etc. We speak of cases where a trace of sugar is either constantly or intermittently found in a given urine, unassociated with the diabetic element, and associated or not with ascertainable bodily ills. The life insurance companies are not agreed whether to accept such lives. Formerly they would not have considered them for a moment; now, however, influenced by a more liberal standard, and under the stress of competition, some of the best institutions do not hesitate to insure them.

Of course we do not consider it proved that every

case of even long-standing glycosuria indicates an incurable derangement. For we have seen how often it is a part of the general disorders which we call gout, dyspepsia, neurasthenia, etc. Yet we do hold that we should bear in mind its equally frequent connection with serious and fatal affections of the brain, the kidneys and the heart. As it is not true that every case of albuminuria means Bright's disease, so traces of sugar in the urine do not indicate diabetes mellitus. Yet, as the discovery of a trace of albumen in the urine means look out! so the finding of a small quantity of sugar indicates danger. The thought often occurs to us whether the heavy mortality which life companies often experience among those whose applications present the cleanest records of personal health and family history may not, in part at least, be due to the failure of the examining physician either to appreciate the significance of the subject which we are discussing, or to be able to apply the proper tests to discover it.

A man who has a serious chronic disease, as a rule suddenly develops an insatiable desire to have his life insured. Agents whom hitherto he would not recognize even in church, and against whose approaches he had always provided an impregnable barricade, now become his bosom friends and confidential advisers. They get at his symptoms with a skill all their own. They find that the disease is glycosuria, for instance.

The patient is immediately advised to live strictly according to orders as to diet, etc., and is shown how to submit his urine to the specific gravity test and Fehling's solution every morning. Pretty soon a specimen is encountered which is not suspicious, and with this in his pocket application for insurance is made to some company known to be not over-skillful in their examinations. That such risks frequently pass we very well know.

Although it is a simple matter to demonstrate the presence of sugar in the urine of a case of established diabetes mellitus, it is not so easy to detect a trace in instances where the diabetic element is absent. In the former case the urine is highly diluted with water and loaded with sugar, while in the latter the proportions of the normal constituents of this fluid are very little, if at all, altered. On several other occasions we have drawn attention to the fallacies and interferences which the natural urine offers towards the usual tests for sugar, especially if present in minute proportions. ["Detection of Sugar in Urine," *N. Y. Med. Jour.*, Sept., 1872; "Note on the Detection of Sugar in Urine," *N. Y. Med. Record*, May 2, 1885.]

Of all the tests which are known to possess characteristic reactions with glucose, a few only are applicable to the urine under conditions convenient, satisfactory and comprehensive to the practising phy-

sician. These are Fermentation, Trommer's (or Fehling's modification), and the Bismuth test.

The most convenient method for the application of the fermentation test is Einhorn's saccharometer,* which is probably familiar to most of us. It consists of a tube bent upon itself, one arm being short and dilated so as to form a bulb. The upright tube collects the gas, and is graduated so as to read from ¼ to 1 per cent., or from 1 to 5 C. C. In experimenting with this apparatus with solutions of glucose of known strength the amount of gas collected did not agree with the graduations, and were different for the same solution with different trials. Hence we cannot depend very much on fermentation, and this instrument especially, for an accurate quantitative analysis of saccharine solutions. This is especially true when we are dealing with organic fluids. The urine, for instance, will absorb its own volume of carbonic acid gas at the ordinary temperature, and will vary in this regard according to the degree of its alkalinity or acidity. We have frequently discovered an appreciable amount of sugar by the copper test in urine, which failed to evolve a bubble of gas when treated with yeast. Then, again, sugar in contact with nitrogenous substances, at an elevated temperature, is apt to be

*Can be obtained at Eimer & Amend's, Third Avenue and Eighteenth Street, and directions accompany it.

converted into lactic acid, and thus disappear. The fermentation test is, therefore, not a very delicate one, failing in my hands to demonstrate one-tenth of one per cent. of sugar, and, consequently, must not be relied upon where great delicacy is demanded. It is, however, very useful and simple under ordinary circumstances.

When it is desired to detect minute proportions of sugar with Fehling's solution, the urine should be filtered through animal charcoal (a paste being made) by which decoloration is effected, and the Fehling should be deprived of its intense blue color by dilution, about one-half, with distilled water; with these conditions small degrees of reduction become visible. After boiling, which should be only for a moment, it is important to set the test-tube aside for an hour, and then scrutinize the bottom of it for any granules of red copper oxide which may not have been seen in suspension, but which have now settled down.

Another metal whose salts suffer spontaneous reduction by glucose, in a boiling alkaline solution, is bismuth. A solution analogous to Fehling's is thus made:

10% Sol. Sodium Carb.	100.
Bismuth Subuit.	2.
Rochelle Salts.	4.

M

Use one part of this to ten of urine; boil, and, if

sugar is present, the whole assumes a gray or black appearance, due to the reduction above spoken of.

The conclusions which we would submit are the following:

1. Normal urine contains no sugar.

2. The reducing power of normal urine upon cupric oxide and picric acid is due to uric acid ¼ and kreatinin ¾. Both these bodies are removed by adding to the unconcentrated urine one-twentieth its volume of a cold saturated solution of sodic acetate, and then one-fourth its volume of a cold saturated solution of mercuric chloride, after the manner described by Johnson.

3. Any reduction of either cupric oxide or picric acid after this manipulation is due to the presence of sugar.

4. Sugar may persist in traces, unaccompanied by the diabetic element.

5. Diabetes may be warded off by recognition of the first appearance of sugar as a persistent ingredient of the urine.

6. The importance of this subject to life insurance companies, in view of the facts above stated.

7. The detection of traces of sugar in the urine requires special skill and care, and a low specific gravity should not be considered conclusive evidence of the absence of sugar.