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Contributors

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Glycosuria in Connection with
Appendicitis :

DIABETES MELLITUS.

*A Clinical Lecture delivered at the Phila-
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BY

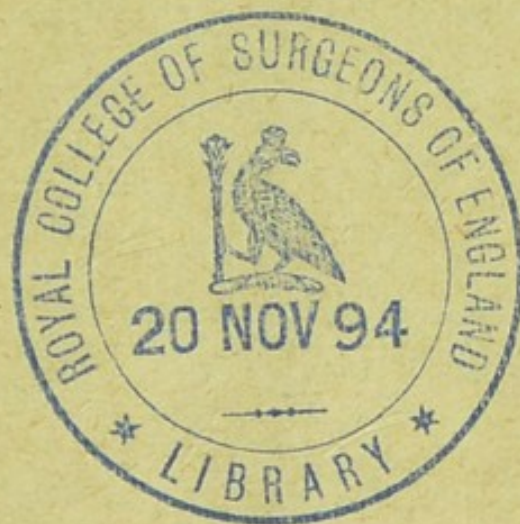
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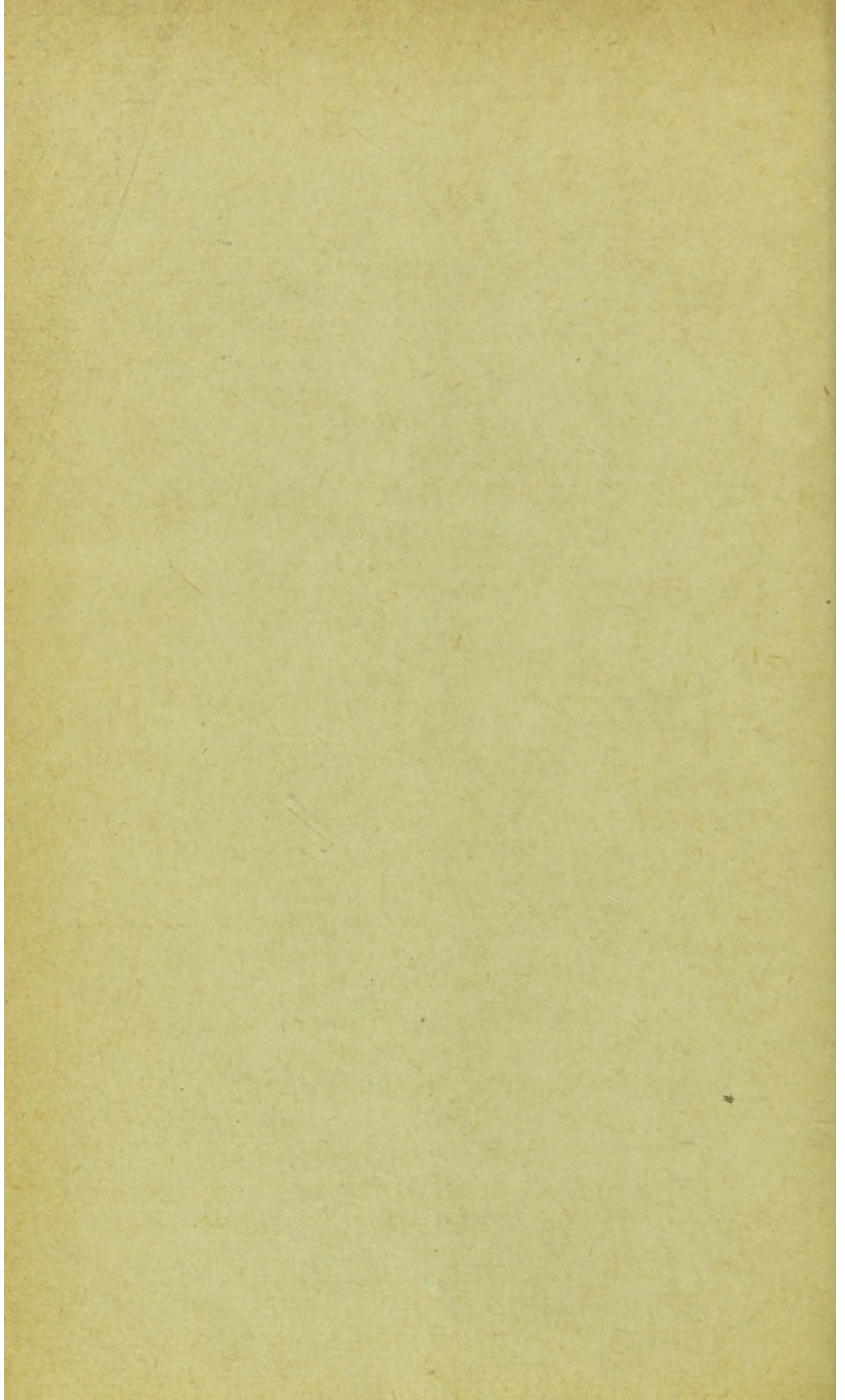
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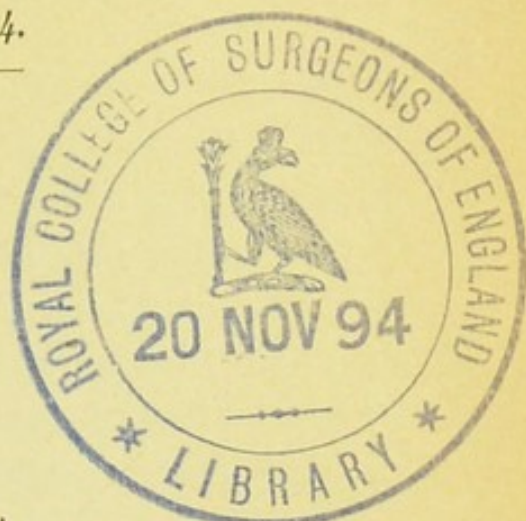
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GLYCOSURIA
IN CONNECTION WITH APPENDICITIS :
DIABETES MELLITUS.

A CLINICAL LECTURE DELIVERED AT THE PHILADELPHIA POLYCLINIC,
February 16, 1894.

BY SOLOMON SOLIS-COHEN, A. M., M. D.,
PROFESSOR OF CLINICAL MEDICINE AND THERAPEUTICS, ETC.

GENTLEMEN : By a curious coincidence, having promised to speak to you to-day concerning diabetes mellitus, I have just received a copy of the *International Clinics* for January of this year, in which is reported a lecture on the Treatment of Diabetes that I delivered here quite a long while ago, November 21, 1892—the delay in publication being my own fault—when three patients were exhibited before the class, among them Mrs. McB., who is here to-day, and Mrs. M., to whom, as we had not seen or heard from her for some time, our chief of clinic, Dr. Riesman, wrote asking her to come and report. Before reading the answer received from Mrs. M.'s son, I will read you something that was said concerning her in the lecture referred to :

“There is present in the left mamma, as a gradual growth of two years' duration, a hard mass, which my col-

league, Professor T. S. K. Morton, believes to be carcinoma. Operation is deemed inadvisable because of the presence of sugar in the urine." It is the view of many surgeons of the greatest experience and soundest judgment that persons having diabetes mellitus should not, as a rule, be operated upon, except in an emergency, to save life which would be lost certainly if the operation were not attempted. Other surgeons do not go so far as this, but lay down certain indications and counter-indications for operation upon diabetic patients which we will speak of later. In a disease like carcinoma, however, in which there is no certainty of cure by the operation, and the worst that can happen to the patient is to die in the course of time by the carcinoma, operation is entirely counter-indicated in cases in which sugar is found in the urine.

As stated, we wrote to Mrs. M., asking her to come to the clinic to-day. She is not here, and we have received the following letter from her son:

"DEAR SIR: MRS. M., who formerly visited your clinic, has been dead since November 21, 1893, having undergone an operation for cancer in the breast."

The operation was declined here on account of the presence of sugar in the urine. Some one rashly undertook it and the result was just what should have been expected.

The patient, Louis G., who is here to-day, is an illustration of the same point. He is referred to this clinic by my colleague, Professor T. S. K. Morton. Briefly, his case may be stated as one of chronic appendicitis. Dr. Morton explained that part of the diagnosis to you, so that I need not now enter into it.

The patient having come into the house for operation, if operation should be found advisable, the invariable rule of this hospital, both in its medical and surgical wards and clinics, was carried out, and his urine was examined. Sugar

being found therein, Dr. Morton declined operation,* just as he did in the case of Mrs. M., because he believes that operation is not usually advisable in the case of patients with sugar in their urine, unless there is an emergency which can not otherwise be met.

At present this man, Louis G., seems to be doing fairly well. Should acute symptoms recur, so that his life is threatened by them, surgical intervention would be perfectly justifiable; because, under the circumstances, he would have a fair chance of surviving the operation, and he would have little chance of surviving the condition for the cure of which the operation was undertaken. The balance of probabilities would be in his favor.

The conditions in this case are not like those in carcinoma, in which an operation could only be palliative in any event; in this case the operation would be curative. It would add nothing to first risks, because without the operation he would be in great danger, and he would have at the worst one chance in two of survival from the operation, while he would not have one chance in a dozen of survival without the operation. Therefore, if at any time the threatening conditions should recur, I would strongly advise this man to undergo operation; but I would not operate upon him while he remains so comfortable as he appears to be at present.

We now inquire concerning his apparent diabetes. This is our first opportunity to question him.

Q. Did you know when you came here that you had sugar in your water? A. No.

Q. Tell us your name, age, occupation, and nationality? A. (through interpreter). Name, Louis G.; age,

* Some later experience in which sugar was found in the urine of patients with appendicitis and disappeared after operation has led Dr. Morton to modify this opinion as to the class of cases in question.

forty-five years; occupation, laborer; a native of Posen in Poland.

As he speaks poor English, we shall have some difficulty in communicating with him, and will leave mere routine details to be supplemented later by the clinical assistants.

He says that his health had been fair until the present trouble began some five months ago. He then noticed soreness in the right iliac fossa, but paid no attention to it for some time. The trouble increasing, he applied to a hospital, where operation was advised, but was refused by him. His pains subsided until a day or two ago, when he was advised to enter this hospital for operation. Dr. Morton diagnosticated subacute appendicitis. You can still feel a sausage-like mass in the iliac region. The patient was put to bed and his bowels kept open by salines. One to two per cent. of sugar was found in the urine, but no albumin. The operation was postponed, and the man now comes before us for treatment.

First let us inquire whether this man had any symptoms pointing to the presence of sugar in the urine, because I think that, just as in the case of Mrs. McB., he has a lesson for us to the effect that persons frequently suffer from diabetes without being at all conscious of it, or without offering any symptoms that would lead the physician to suspect the condition unless he was very much on the alert for cases of diabetes through having seen many of them. It is not a common disease, although we usually have two or three cases a year at this clinic. We seem now to be enjoying a "run" of them, but in a majority of clinics diabetes is one of the very rarest of diseases.

Now, let us see about his symptoms. Mrs. McB., when she came here, did not know that she had diabetes, but came complaining of pruritus.

Q. Have you any itching? A. No.

Q. Do you ever have boils? A. No.

Q. Do you pass a great deal of water? A. Three times a day.

Q. Do you have to get up at night to pass water?
A. No.

Q. What is the record since he has been in the house?
A. He passes about sixteen ounces a day.

Then, with such small quantities of water, the case can not be called one of diabetes; it is a case of *glycosuria*. Diabetes implies increased urination. Thus we have *diabetes insipidus*, or *polyuria*, in which are passed large quantities of water which does not contain sugar; or *diabetes mellitus*, in which the increased amount of urinary water contains an abnormal quantity of sugar. This is a case of glycosuria or saccharine urine, without diabetes. We must look a little more carefully into the subject, and may perhaps find reason to modify our view as to the advisability of a surgical procedure.

When scanty urine occurs in conjunction with high specific gravity, there is a liability to mistake uric acid and urates for sugar when the test is made with Fehling's solution. This mistake has not happened, however, in the present case. Professor Leffmann has supplemented the house analysis by polariscopic and chemical tests. The matter is simply suggested to me by the scantiness of the urine.

Q. What is the specific gravity? A. 1.016.

A low specific gravity. This is still more unusual—to have a low specific gravity in connection with sugar, and, moreover, with small quantities of urine. This case requires some special study. Apparently there is an hepatic and perhaps a renal failure. The amount of urea passed is below normal and the kidneys are not stimulated to their work. Hepatic disease, pylephlebitis, and abscess may re-

sult through portal infection following appendicitis. We have no evidence of it here, but it must be borne in mind.

Q. Are you thirsty? *A.* Sometimes.

Dr. Moore says he is thirsty—wants a great deal of water.

Q. Do you sweat? *A.* Sometimes he sweats, but not as a general rule.

If a patient sweats a great deal, as a matter of course the quantity of urinary water will be diminished. And then again we have been treating this man with salines and drawing off large quantities of fluid by the bowels, so that the patient is actually passing more water, though not by the kidneys, than at first sight appears.

On casual inspection, he exhibits some of the symptoms of vaso-motor ataxia. This and diabetes are very often associated, and in such cases there is frequently a gouty diathesis. We have no special record as to the urates or uric acid in this man's secretions.

Q. Do you feel weak? *A.* Yes.

Q. When did you first begin to feel weak? *A.* Only for about two weeks.

Q. Before that you felt pretty strong? *A.* Yes.

In this case, then, there is no history of gradual weakness, which is one of the very early symptoms of ordinary cases of diabetes. The patient will complain of languor and disinclination to work long before sugar can be found in the urine.

Q. Have you indigestion? *A.* For five or six months he has complained of a sense of discomfort in the epigastrium and palpitation of the heart; had nausea some weeks ago.

This may have been due to his appendicitis; it is difficult to decide.

Q. Do you have vertigo? *A.* Four or five weeks ago he complained of vertigo.

That, too, we must throw out, as it is subsequent to the onset of the appendicitis.

Q. Are you strong? *A.* Not now.

Let us see how the knee-jerks are. Right and left both good; a little lively, if anything. In cases of long, progressive diabetes diminution or loss of the knee-jerks is quite common—a symptom attributable to neuritis, multiple neuritis being one of the conditions which the presence of sugar in the blood, like that of alcohol, lead, arsenic, and other toxic agents, gives rise to. Sometimes the symptoms are sensory only—neuralgic rather than neuritic.

Q. Are you very hungry? *A.* He used to eat one meal a day.

He certainly has not exhibited bulimia if he has been satisfied with one meal a day.

Q. How many do you eat now? *A.* Sometimes two meals a day while here in the hospital. Before coming here, only one meal a day for about three or four months. Sometimes he takes one meal; sometimes two. When he takes two, he does not feel so well; he has symptoms of indigestion.

Q. Did you eat more than usual; did you have craving for food all the time? *A.* He has not at any time had an abnormal craving for food. He often has a desire for some special thing.

Q. Are you very fond of sweet things? *A.* He is not overfond of sugar and sweet things.

This error of metabolism, then, is not due, as in some persons, to the over-consumption of sweet things, because he has not a special craving for them and takes sugar only occasionally. To sum up, he has not had bulimia or, as it is sometimes called, polyphagia; he has not had polydip-

sia, and does not at this moment exhibit polyuria. There is some feebleness and there is a degree of emaciation, but the chronic indigestion and the acute inflammation, with the history of restricted diet, sufficiently account for these symptoms. Thus far we have established a case of glycosuria and not a case of diabetes. But let us be perfectly satisfied as to the quantity of water passed before we discuss the probable cause of the glycosuria.

Q. Please make sure of this point: Did he pass more water before his entrance to the hospital than he is now passing? A. He is sure he passed much more water before admission.

Q. How much more did he pass in twenty-four hours before he came here than now? A. About twice as much. That is, about a normal quantity.

Q. Is he passing large quantities of water by stool? A. Rather large, because of the salines.

This may account, then, for the diminution of water.

Examination of the lungs and heart shows nothing abnormal. The thyroid gland is apparently normal. In the abdomen we find only the conditions already described. The coated tongue and dyspeptic symptoms prove nothing; he tells us that he has no more difficulty in digesting fats than with other foods. No fat has been found in his stools while here. There is no history of jaundice, no symptom or sign pointing to liver or pancreas; as to the nervous system, we have noted only slight vaso-motor signs and some exaggeration of reflexes; this indicates a neurotic condition but no definite disease.

Probably there is a reflex or mechanical disturbance of the solar plexus, which in a predisposed subject produces this symptom.

We have therefore established simply a case of glyco-

suria, for which we have found no cause other than the appendicitis; and we fail to find diabetes. At the same time, the mere fact that there is sugar in his urine makes us pause as to the advisability of operation, on account of the indisposition of wounded surfaces to heal when that condition is present. Nevertheless, this case does not present the same contraindication of operation as though we had all the symptoms of diabetes.* We shall study this man's urine for a week, uninterfered with by medication, before we arrive at a positive conclusion concerning him; we shall have his eye ground examined and note the digestive conditions more carefully; but I believe our present opinion will only be confirmed by the more exact data we shall obtain.

Do not misunderstand me that all operative procedures turn out badly in the subjects of diabetes. Surgeons have

* Bad symptoms recurred and an operation was urged, but at first declined. The following letter from Dr. Morton gives the subsequent history:

"Our patient with appendicitis complicated by glycosuria finally consented to operation on April 4th, when reduced to an extreme degree of septicæmia and exhaustion. A three-inch incision was made into the tumor mass in the right iliac region and an abscess at once entered. This contained about half a pint of exceedingly foul pus. As the patient was in such poor physical condition, and as I did not know how the peritonæum would react in presence of glycosuria, I contented myself with simply irrigating the pus cavity and gently packing it with iodoform gauze. I here departed, for the reasons given, from my almost invariable custom of securing the appendix when operating for appendicitis. A specimen of urine submitted to Dr. Henry Leffmann two days after the operation was still reported to contain a large amount of glucose. But from that on, although repeatedly searched for, the presence of sugar was not again demonstrated. He rapidly gained in weight and strength, and in five weeks returned to his home and occupation apparently in perfect health. The wound closed solidly by granulation in three weeks."

collated statistics showing that the majority of diabetics submitted to various operations for various conditions recovered. Nevertheless, it must be remembered that diabetes mellitus is among the conditions interfering with the ability to recover from ether or chloroform narcosis, as well as with the recuperative power in general, and thus adds to the gravity of operation in every case. The general condition of the individual patient must be considered. The nature of the condition demanding interference, and the character of that interference, also must have weight. Operation must not be done unless necessary to save or prolong life, and unless the patient has preserved a fair degree of vigor, nor should it be done unless the chances of good result, apart from the diabetes, are sufficiently promising to compensate for the increased risk of death.

Now we will look at our other patient.

CASE II.—Mrs. McB.'s urine, which she brings to-day, has a specific gravity of only 1.010. No albumin is found; and while the Fehling solution is colored green, there is no deposit of the red precipitate which would indicate positively the presence of sugar. For further assurance, we will ferment the urine. Very small quantities of sugar sometimes turn Fehling's solution only green, and not red. We are sure that our Fehling's solution is good, and is not spoiled by keeping, from the fact that we keep the copper solution and solution of alkaline tartrates in separate phials, and admix them as occasion requires.

This patient came to us November 24, 1892, for relief of backache. I will not read her previous history in full. The principal points were complaint of pruritus vulvæ, and of the vaso-motor symptoms connected with the menopause.

Q. Have you finished the change of life now? A. No, sir; still in same condition.

Although a local condition, cervicitis with acrid dis-

charge, seemed to account for the itching of the genitalia, we were not satisfied until we had made an examination of the urine, which disclosed the presence of sugar. I want to mention this again to insist upon the necessity of examining for sugar in every case that comes to you, whether of backache or headache or toeache, and also to impress upon you the great significance of pruritus—pruritus vulvæ in the female, pruritus of the urinary organs in the male, and in both sexes, pruritus ani, or sometimes general pruritus.

Q. How much water do you pass now? *A.* Two quarts and half a pint.

This is a slight reduction.

From the published record it appears that this case was treated with levulose and strontium bromide. Levulose was given as a food, strontium bromide as a medicament. Levulose or fruit sugar was formerly supposed to be an isomeric form of dextrose, and to differ from the latter merely in its behavior toward polarized light. Its name was, indeed, derived from the fact that it deflected the polarized ray to the left, while glucose, as it is commonly called, turned the polarized ray to the right, and hence received the name of dextrose. More recent investigations have shown that the chemical composition of levulose differs fundamentally from that of dextrose, notwithstanding the identity of their empiric formulæ. Dextrose belongs to the aldehydes, while levulose is classified among the group of ketones, and this difference of chemical relation probably accounts for their different behavior in the system. It would appear, in other words, that the fault of metabolism by which the organism in cases of diabetes fails to assimilate amyloids and aldehydes does not extend to ketones, and thus the patient is able to take the latter form of carbohydrates. As a mixed dietary is necessary to good

health, and as the craving for sweet things is satisfied by levulose, it will be seen what a boon this substance is to diabetics. The great drawback to its extensive use is its high cost. I have given it in quantities as high as four ounces a day. Dr. Leffmann has made careful chemical analyses of the urine of these patients for prolonged periods, and in no case has he found the secretion of sugar increased. He finds neither levulose nor an increased quantity of dextrose secreted by patients who are taking levulose. The importance of this, let me repeat, lies in the fact that we can give patients like Mrs. McB. sugar which they can use *ad libitum*, and thereby satisfy a craving for sweets which is natural; but the advantage of the drug is more particularly marked in the case of those patients who are suffering from the more severe forms of diabetes, in which the nutrition suffers in the first place from the disease, and in the second place from the withholding of a form of aliment which is necessary to the production of heat and of adipose tissue. It is true that we endeavor to supplement this loss in the case of the class of patients to whom we refer by the increased administration of oils and fats; but that does not altogether answer the purpose. And, having in levulose a carbohydrate the empirical formula of which is exactly identical with that of dextrose, though its rational formula differs from the latter, we are able to give the patient a carbohydrate aliment absolutely unobjectionable, from which he can evolve heat and which goes to the building up of his tissues. That it is assimilated, that it does go to the production of heat and to the forming of tissue, is shown by the fact that we are unable to recover it either in the fæces or in the urine. Therefore it is used in the economy; the proof is definite. Levulose is unfortunately sold under a trade name, but I never prescribe it under the trade name. The druggists to

whom my patients go buy levulose where and under what name they choose, but they dispense it upon prescription under its proper name. The manufacturers, it is true, make no secret of its composition, but I entirely disapprove of specialized trade names and drug monopolies. They are opposed to science and to progress and open the door to serious abuses.

Stout patients are permitted to take levulose in such doses as they see fit; lean patients are told to use it for all sweetening purposes, and in addition to take about two drachms after each meal so as to make the whole quantity *per diem* not less than one ounce. One patient, a woman also, but of quite an opposite type to Mrs. McB.—a thin, nervous, excitable person—increased in weight very remarkably under the treatment with levulose. All other forms of carbohydrate were excluded from the diet, with occasional exceptions in favor of bread and potatoes. You will never find a patient that will get along without bread. Even if one tells you that he is doing without bread, he will eat it on the sly; and it is all right that he should do so; we have to face facts and not theories. All gluten bread is “n. g.”—that sums up the whole question. Soya bread I have tried to have made and found it impossible. I once got a lot of soya flour, but none of the patients could use it. I also imported some soya biscuit, but under our unwise tariff legislation it cost so much to get it through the custom house that I could not afford to repeat the experiment. As soya beans grow only in Japan, and no one in America makes the biscuit, I fail to see who benefits by this prohibitive duty. We are for the present thrown back upon ordinary bread in restricted amounts. Let your patient take not more than six small slices of bread—about three ounces—a day; if it can be cut down to less, so much the better, but let that be the maximum; and

once in a while let the patient have a big roasted mealy potato. The patient will relish that, and if you let him have a feast of one potato in this form once or twice a week, being careful to abstain therefrom the rest of the time, no harm will be done.

Most writers on the subject of diabetes prohibit the use of milk. I think this very unwise; I allow my patients to drink all they want. I would rather have them take milk than too large quantities of meat. With such patients as Mrs. McB., and most of the stout patients, little meat should be given, because in most of these cases there is a uric-acid diathesis, and lithæmia is a provocative to diabetes. How, I don't know; probably, I think, by the irritation of the vaso-motor centers. I believe that that will prove to be the explanation of the connection between lithæmia, vaso-motor ataxia, and diabetes—that the uric acid or some associated toxine irritates the vaso-motor centers, and they in turn give rise to a disturbance of hepatic circulation which is represented by diabetes. But be that as it may, the practical effect is that if you can diminish the uric-acid formation in your patient you diminish the amount of sugar in his urine. Butcher's meat is, above all things, the article of diet which mostly gives rise to uric acid, especially when the patient does not take sufficient exercise; and I think that milk, although it contains lactose, is far preferable to meat as forming the bulk of the diet. Indeed, I have found some diabetics able to dispose of lactose itself, one or two ounces daily, without increase of glycosuria and without recovery of lactose in the urine; so that, instead of restricting milk, I encourage the patient to take it. The fat of the cream is also helpful. Fish is entirely unobjectionable; and eggs, where there is not too much uric acid, are usually unobjectionable. I cut off sugar absolutely—ordinary cane sugar and all malted preparations—anything that contains.

any form of dextrose. Levulose is admitted in this class of patients. Saccharin is not given, because, although it has a sweet taste, it has no nutritive value, and it often tends to impair digestion, producing dyspepsia. Green vegetables should also be given—lettuce, cabbage, sorrel, spinach, cresses, onions (especially the green shoots, but also the bulbs), etc. Although they do contain small amounts of starch, the amount of other vegetable products which they contain so far overbalances the starch that the advantage lies on their side. They are also advantageous from the fact that they contain certain salts of alkaline bases—the organic acids and the alkaline bases being necessary to keep the blood in a pure condition and alkaline. This brings us to a point upon which special stress should be placed in the medicinal treatment of all classes of cases, both stout and lean: *keep the blood alkaline*. Keep the urine at least neutral; do not let it become acid. To promote this I prefer strontium bromide to any other of the agents I have used, because it interferes less with nutrition than salts of potassium or sodium. Sometimes I give lithium salts or so-called lithia waters. Occasionally these patients will develop rheumatic pains. I use the word “rheumatic” here in the general, and perhaps often incorrect, sense. Sodium salicylate should then be given. This is used by some as a specific remedy in diabetes. That is not my own experience; but I do find it useful occasionally under the conditions I have named, when it may be given in large doses, such as forty or fifty grains a day; or small doses—as small as fifteen grains a day—according to circumstances. I now give it in capsule, because that overcomes the objection of some to its taste, the capsule being followed with a large draught of water.

I do not restrict the amount of water taken by diabetic patients. Let them drink all the water they want; it helps

to wash out the uric acid and other *débris*, and supplies to some extent the loss of water incident to the disease. And when patients with diabetes are inclined to take small quantities of water, I encourage them to take larger quantities, because it is necessary.

Besides the general management of the case, there are in individual cases special lesions or symptoms that need watching, and sometimes therapeutic intervention. Mrs. McB. has a tendency to constipation, and her heart is dilated—two points that need especial care. We must question her a little.

Q. Mrs. McB., can you tell me what your special complaint is just now? A. I did not feel well before my sickness came on, Saturday; was feeling very miserable; was sick for two days, but feel better now.

Q. Have you lost or gained flesh? A. I think I am gaining.

Q. I do not care especially about your gaining; do you feel strong? A. Not extra strong.

Q. Do you feel stronger than you did? A. I think so; but the last few days my head has been swimming again. I have been compelled to rest Saturday and Sunday and Monday.

Let me hear how her heart is acting to-day. Some months ago she had an attack of vertigo, almost syncope with great prostration, due to weakness of the heart, for which we put her to bed and treated her with digitalis. That is one of the incidents and accidents which sometimes occur in cases of diabetes. The heart seems to be doing its duty pretty well to-day; but remembering what she has said as to recent weakness, I think that the best thing she can do is to go home and go to bed—stay in bed for three or four days, and then let me see her again. Mrs. McB. has likewise been complaining of constipation. Never allow diabetic pa-

tients to become constipated, because constipation is often the precursor of coma, perhaps through the production of toxæmia, even a cause of coma, and coma is the great danger that threatens these patients. You will find that sodium phosphate in drachm doses, thrice daily, is one of the best remedies to guard against constipation. The dose and frequency are to be gradually lessened. Mrs. McB. now finds that by taking a full dose only once a day the bowels are opened three or four times. We will therefore reduce the dose to half a drachm before breakfast. In hepatic cases I find this drug useful, quite apart from its laxative effect; and in cases of temporary glycosuria due to hepatic disturbance in stout persons, sodium phosphate sometimes brings about an entire disappearance of sugar from the urine. In cases presenting the characteristics of Mrs. McB.'s—cases which sometimes run on for twenty years or more—we do not aim to secure the disappearance of sugar. In fact, patients usually feel better when they are passing a little sugar; and we must look out for squalls if sugar is entirely absent. The prognosis as to life, in these cases, is very favorable, as you perhaps gather from what I have said. The prognosis as to comfort is likewise good, provided the physician is not too anxious to experiment upon the patient with new drugs. In such cases the duty of the physician is to watch the patient, guard the diet, not give too much medicine, but to carefully look out against the accidents that might occur in the course of the disease.

