

## THE DIFFERENTIAL DIAGNOSIS BETWEEN DIABETIC AND NONDIABETIC GLYCOSURIAS IN PREGNANCY\*

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THE necessity of distinguishing between diabetes mellitus and the more harmless glycosurias is always definite, and especially in pregnancy, where the possibilities for misfortune are so great in the event of diabetes not being recognized. During pregnancy, this distinction is sometimes very difficult. It was hoped that perhaps more information could be gained by reviewing cases of glycosuria of all origins, after a final classification. It is admitted that the final decision was not made in all cases without the lapse of time, in some instances not until after a succeeding pregnancy. The proved series is not large, but it may well form the basis for future work. Out of a total of 24 cases of glycosuria there were obtained for study, eight cases of diabetes and seven of glycosuria.

The diabetic cases usually offered less trouble in recognition than the nondiabetic glycosurias and are presented not only as a datum point to the consideration of the others, but also as having interest as examples of diabetes complicating pregnancy. As there is a possibility that the reader, applying his own criteria, may not agree with the final diagnosis, the cases are given in some detail.

The *first* diabetic patient was thirty-nine years old, at term in her seventh pregnancy. All previous pregnancies and deliveries had been normal. She was seen on March 20, 1921, the day after delivery, which had occurred about a month prematurely. She gave a history of edema of the legs for some days before labor, and for

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a day or two, nausea and vomiting. On March 13, glycosuria had been found. On March 20, there was marked glycosuria, with a positive ferric chloride reaction in the urine. The patient had livid lips and finger tips, and was hyperpneic. Alveolar CO<sub>2</sub> tension (Marriott) was 35 mm. Treatment was largely by forced intake of fluids and low carbohydrate diet. On March 28, after the acidosis had subsided, the blood sugar was 109 mg. per 100 c.c., one and a half hours after breakfast. The patient went home April 3, in good condition, on appropriate diet.

On March 19, 1923, the patient was readmitted in coma. She was given the 100 units of insulin available and restored to consciousness. Lobar pneumonia was then discovered. The patient lapsed again into coma, after a few hours, and died.

The *second* case was that of a woman of thirty, seen on February 28, 1922. Quickening had occurred on October 17, 1921. Sugar was found in the urine on February 28. Her mother and one brother had died of diabetes. Previous to the present pregnancy, in January, 1921, glycosuria was observed. Three previous pregnancies had ended in miscarriage. The patient was grossly overweight before the present pregnancy.

She was given a low carbohydrate diet and it was decided that, if pregnancy continued until the eighth month, to induce labor, as the surest method of getting a living baby.

On March 2, the urine showed a positive ferric chloride test, with alveolar CO<sub>2</sub> tension of 35 mm. Labor was induced on March 3, with resulting normal delivery. On March 7, the fasting blood sugar was 112 mg. On March 14, the blood sugar, one and a half hours after breakfast, was 122 mg., and, on March 23, 130 mg. In March, 1926, the patient was in good condition, taking care with her diet. The baby was doing well.

The *third* case occurred in an enormously fat woman of twenty-four, seen on April 18, 1924, because of pruritus vulvae and threatened abortion. In 1917 and 1918 glycosuria had been found. She had aborted at two months in 1917. In 1921, she had been delivered of a stillborn, full-term fetus. Since then, she had had four miscarriages. When seen, there was slight vaginal bleeding, with about a two months' pregnancy. On April 19, the fasting blood sugar was 204 mg. The patient aborted on April 19. Up to October, 1924, on restricted diet, she was free from glycosuria, and lost some weight, but another miscarriage occurred then.

The *fourth* diabetic case was that of a woman of twenty-seven, admitted on November 17, 1924, because of glycosuria. For eight years she had had pruritus vulvae. She had lost 25 pounds of weight during the year. She had been pregnant nine times, with four children living. She had had two miscarriages and one stillbirth. There was no family history of diabetes.

The patient was three and one-half months pregnant. Glycosuria without ketonuria was found, after admittance. The fasting blood sugar was 200 mg. After instruction as to diet, the use of insulin and the testing of urine, the patient was discharged to Out-Patient observation on December 3, 1924. Readmission occurred on February 2, 1925, because of marked glycosuria and weakness, following a heavy cold. At this time, the fasting blood sugar was 370 mg. During this period of observation it was noted that diacetic acid was apt to be found in the urine, although sugar was absent. On February 11, 1925, she was discharged to the Out-Patient department.

Final admission on March 9. No glycosuria. The fasting blood sugar was 113 mg. A steadily increasing ketonuria was present, not controllable by increase of carbohydrate in the diet and greater dosage of insulin. On March 19, the fasting



blood sugar was 101 mg., and 94 mg. on April 2. On April 10, labor was induced, about a month before term, because of apparently impending fetal death. As a preliminary to labor, rectal instillations of glucose solution, with appropriate amounts of insulin were given subcutaneously. Labor was normal, and after delivery, ketonuria disappeared rapidly, and food tolerance rose greatly. Mother and baby were discharged in good condition on April 24, 1925.

The *fifth* case occurred in a primigravida of twenty-eight, admitted on May 23, 1923, because of glycosuria. There had been no symptoms suggesting complications. Blood sugar, three hours after breakfast, was 168 mg. On appropriate diet, the glycosuria disappeared, and on May 25, the fasting blood sugar was 98 mg. The patient was discharged to follow the diet at home. When readmitted in labor on August 8, she stated that glycosuria had been found frequently. She was delivered of twins on August 9. On discharge, she was sugar free. On April 3, 1924, she was readmitted to the medical service with the history of a gradual loss of weight over three months, and polyuria and thirst for one month. There had been no restriction of diet. Sugar had been found in the urine two days before admission. The subsequent course of this patient has been that of a diabetic, requiring a moderate amount of insulin to utilize carbohydrates, with two attacks of acidosis, induced by acute respiratory infections.

The *sixth* case of this group occurred in a woman of thirty-three, admitted on December 26, 1924, two and a half months pregnant. She had been pregnant three times before, the third pregnancy ending in a stillbirth, in August, 1921. Glycosuria had been found immediately after this delivery. Four months before admission, pruritus vulvae had developed, but had been relieved by diet. Her father had died of diabetes mellitus. Glycosuria was found after admission. The fasting blood sugar was 160 mg. After treatment and instruction, the patient was discharged on January 6, 1925.

She was readmitted on February 5, with vaginal bleeding, which had begun two hours before. She stated that she had found sugar in the urine on only two days since discharge. During this stay, no glycosuria was detected, and on February 12, the fasting blood sugar was 84 mg. She was again discharged on February 14.

On June 16, she was admitted in labor and was delivered normally. Her food tolerance increased after delivery, and for three months she was able to nurse her baby. Since weaning the child, she has been able to get along quite well without insulin.

The *seventh* diabetic case was in a woman of twenty-eight, pregnant at term for the third time, seen on January 21, 1920. The two previous pregnancies had been entirely normal. The patient's mother and two of her mother's sisters were diabetic. The patient was delivered on the day of admission, after precipitous labor. Glycosuria was absent on admission and on the following day, but was found on January 23. A glucose tolerance test on January 24, gave this result: Blood sugar, fasting, 180 mg.; one hour after taking 75 gm. glucose, 540 mg.; two hours after glucose, 320 mg.

After instituting diet, the patient remained sugar free until discharge on February 10. On March 5, blood sugar two and a half hours after a meal was 240 mg. After further readjustment of diet, no sugar was found in the urine until May 4. The patient then dropped from sight.

The *last* diabetic case, a primigravida of twenty-seven, was admitted on January 17, 1921, about eight months pregnant. Menstruation always irregular, with intervals varying from six weeks to four months. She was apt to have severe nosebleeds during the longer periods of amenorrhoea. The patient was somewhat obese, with a

florid complexion. Blood pressure was 180/114. Glycosuria was present. The blood total nonprotein nitrogen was 36 mg., and blood sugar, fasting, 125 mg. After treatment and instruction, she went home.

Readmission on February 17. The patient then looked ill. Blood pressure was 170/108; the heart sounds were weak. There was marked edema of the legs; also retinal edema. About two hours after admission, she sustained a short clonic convulsion, so that delivery was promptly undertaken. The fetus was dead. Following delivery, the patient recovered so that by March 4, the day of discharge, the blood pressure was 134/90. Sugar occurred in the urine on February 28, only.

The later history of this patient is that as long as she kept to her diet, no glycosuria appeared. A miscarriage at six weeks took place in December, 1921. In November, 1922, she had not lost weight. Her blood pressure was 182/110, and blood sugar one and a half hours after a meal was 150 mg.

The next series of cases is made up of the nondiabetic group, of which the *first* occurred in a woman of twenty-six, pregnant for the fifth time, admitted on December 14, 1921. Three children were living. She had had no miscarriage. No glycosuria during these pregnancies. On December 12, glycosuria had been found by the Out-Patient staff. She had no thirst, polyuria, or increased appetite. On full diet, the glycosuria test varied (over several days) from none to a heavy reduction. On December 17, the fasting blood sugar was 169 mg., and 250 mg., two hours after breakfast. On December 20, with reduced diet, the blood sugar was 162 mg. She was discharged on a restricted diet, on December 21. On February 3, 1922, she was readmitted in labor, and was delivered and recovered normally, except that in two days, a slight sugar reduction was found.

On December 8, 1925, the patient was again admitted, pregnant, with blood pressure 195/130, with edema of the feet, albuminuria, and with hyaline casts in the urine. The blood nonprotein nitrogen was 29 mg., and the fasting blood sugar, 64 mg. on December 10. Glycosuria had not been found during antenatal observation. Spontaneous delivery took place on December 22. Discharge was on January 5, 1926, with blood pressure 130/80. Glycosuria did not appear throughout this period of observation.

The *second* case of glycosuria was that of a single woman of twenty-four, admitted in labor after her first pregnancy on January 3, 1922. She had no knowledge of previous glycosuria. The pregnancy had been normal. The blood Wassermann was strongly positive. Glycosuria was found on admission. Labor was long, and the fetus stillborn and premature. On January 7, blood sugar one hour and a half after breakfast was 175 mg. After January 4, when glycosuria was found for the second time, no sugar was detected in the urine up to discharge on January 22. In April, 1925, the patient was quite well, and putting on much weight, it is stated by her doctor.

The *third* glycosuria case occurred in a woman of twenty-seven, admitted in labor at term of her second pregnancy, on June 9, 1923. The first pregnancy had been normal. At the fifth month of the second pregnancy abortion was threatened. Shortly after this, glycosuria had appeared. The fasting blood sugar had been determined then as 95 mg. Delivery of a dead fetus was accomplished on June 9. No glycosuria was found during the puerperium. The patient was discharged on June 29.

In 1924, she suffered considerably from maxillary disease. In March, 1926, delivery occurred, after her third pregnancy, which had been normal to within five days before delivery. At this time, blood pressure had risen to 180/110, and, as no improvement in symptoms occurred under treatment, labor was induced. After deliv-



ery, recovery was rapid. No glycosuria was found during this period of observation nor, it should be stated, during the time between the second and third pregnancies.

The *fourth* case was that of a woman of thirty-eight, pregnant for the first time, admitted on March 22, 1923. Quickening had occurred November 30, 1922. Some seventeen years before, she had had much upper respiratory trouble and otitis media, with albuminuria.

The patient complained of headache; there was edema of the feet and hands. The heart was not enlarged, but was rapid (100). An aortic systolic murmur was present. Retinal edema was noted. The urine was negative.

On March 30, glycosuria was found, and frequently but not constantly thereafter, until April 8. After April 8 until discharge on May 10, no glycosuria appeared. On April 6, the fasting blood sugar was 139 mg. The patient was delivered by cesarean section, because of the cardiac condition on April 30. The baby died. On July 24, and August 14, no sugar was present in the urine.

On September 25, 1924, the patient was again delivered by cesarean section. During this pregnancy and puerperium, no glycosuria occurred.

The *fifth* case of nondiabetic glycosuria was very interesting. The patient, thirty-eight years old, was admitted in her third pregnancy on May 27, 1924, because of glycosuria. Her two other pregnancies had been normal. Three weeks before entry, pain over the pubes developed; increased frequency of urination with burning and pain had been present throughout pregnancy. About the seventh week of this pregnancy, the patient had had several furuncles on her back. These healed rapidly and did not recur. Epistaxis had been frequent during this pregnancy. For some weeks before admission, the patient had been salivated. Quickening was felt May 13.

The ptyalism was marked. Three examinations of urine on the day of admission showed sugar. Glycosuria was present also the next day but, except on June 5 and 8, was absent until discharge on June 11. On May 28, the fasting blood sugar was 83 mg.; on May 29, 69 mg. The patient had been given atropin (grain  $\frac{1}{100}$ ) three times on May 28. This drug was then given twice each day from May 29 until June 2, on which day but one dose was given. On June 6, fasting blood sugar was 80 mg. Salivation had ceased on discharge.

Later observation showed that on liberal diet, there was no glycosuria, up to August 5. The effect of ptyalism on food intake may have had some influence in this case.

The *sixth* case was a primigravida of thirty-three, admitted on April 10, 1921. Quickening noted on December 18, 1920. There had been much vomiting throughout pregnancy. Edema of the legs present during the later months. No abnormal urinary findings. Normal delivery April 10. On April 12, glycosuria was detected, persisting till April 15, after which none appeared. On April 13, fasting blood sugar was 120 mg. Discharged April 15.

A normal delivery in July, 1922, after a pregnancy characterized by marked edema. During the pregnancy, no glycosuria was found, but on the fifth day of this puerperium, a slight sugar reduction was noted. After this, there was no urinary abnormality up to March, 1926.

The *last* of the glycosuria cases was a woman of thirty-three, admitted in her first pregnancy on November 21, 1922. Term was estimated as January 13, 1923. Pregnancy had been normal until two days before entry, when the patient had vomited. She had been thirsty for some days and had noticed pruritus vulvae.

A heavy glycosuria was found upon admission. On November 14, the fasting

blood sugar was 45 mg., and 68 mg., one and a half hours after breakfast. The urine, however, was negative on November 14, and remained so until discharge on December 29.

A comparison of these two groups of cases shows very definitely that it is impossible to divide sharply the diabetic from the non-diabetic patient, whether by history, physical status or blood-sugar reactions. The passing of time seems to be the final diagnostic factor.

Included in the second group are examples of nondiabetic glycosuria, with a temporarily (at least) high blood sugar, and of glycosuria with low blood sugar. It may be that the type with hyperglycemia is not very familiarly known, for the literature reviewed includes but one mention<sup>1</sup> of this.

It is obvious, as Schenck remarks, that extreme caution must be used in the treatment of these cases, and that it is wisest to treat them as diabetic, until observation shows them to be nondiabetic.

Hypoglycemia seems to be harmless, yet there is a certain deceiving sound of finality to the expression "renal glycosuria." Since, as a matter of fact, we know little about the origin of this type, "of unknown origin" would seem to be a better characterization. At least, a confession of ignorance may tend toward carefulness.

NOTE.—It is the habit to subject urine, found for the first time to contain sugar, to both fermentation and phenylhydrazine tests. In all the cases under present discussion, glucose was found as the reducing body.

#### REFERENCE

<sup>1</sup>Schenck, S. B.: AM. JOUR. OBST. AND GYNEC., October, 1924, viii, 457.

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