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**THE CLINICAL SIGNIFICANCE OF GLYCOSURIA IN PREGNANT
WOMEN.**

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I KNOW of no complication of pregnancy the significance of which is more variously interpreted than the presence of sugar in the urine of pregnant women. Certain writers regard it as a harmless almost physiological phenomenon, while others hold that it is always indicative of the existence of diabetes. Thus, Charrin, Brocard, Leduc, Salémi, and Bar state that a larger or smaller quantity of glucose can be demonstrated in the urine of from 40 to 66 per cent. of all pregnant women, and is, therefore, of no clinical significance. On the other hand Eshner, in 1907, collected the histories of 35 cases of diabetes complicating pregnancy, with a gross maternal mortality of 54 per cent. Moreover, it sometimes happens that the same case may be interpreted as a harmless and transient glycosuria, or as a mild case of diabetes, according to the point of view of the writer.

This divergence of opinion is in great part due to the influence exerted upon medical thought by a paper upon puerperal diabetes, which J. Matthews Duncan read before the London Obstetrical Society in 1882. At that time he collected from his own experience and the literature the histories of 22 pregnancies occurring in 16 women who had become pregnant while suffering from diabetes, or who had developed the disease during the course of pregnancy. Four died in coma or collapse within a few days after delivery and 7 others perished from diabetes or tuberculosis within the following two years, while 47 per cent. of the children were lost. He therefore

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concluded that diabetes constituted one of the most serious complications of pregnancy, and his views were accepted without question, so that the practitioner, and even the obstetrical specialist, has come to regard the presence of sugar in the urine of pregnant women as of most serious prognostic import.

During the last five years I have seen a number of cases of glycosuria complicating pregnancy, and desire upon this occasion to call attention to my experience, and, after reviewing the literature upon the subject, to draw certain conclusions which I hope may be of practical value.

CASE I.—*Lactosuria in Pregnancy.* Mrs. H. J. B., aged thirty years, pregnant for the fourth time. Definite reduction with Fehling's solution occurred in the seventh lunar month, continued at intervals until the birth of the child, and disappeared entirely after the tenth day of the puerperium. The sugar varied between 1 and 2 per cent. in amount and did not undergo fermentation. At no time were any untoward symptoms noticed. An 8½-pound child was born after an operative labor; the puerperium was normal. Sugar did not reappear in the course of the following two years.

CASE II.—*Transient Glycosuria in Pregnancy.* Mrs. J. M. K., aged twenty-five years, pregnant for the first time. Three months before labor sugar appeared in the urine, and was demonstrated repeatedly during a period of three weeks, after which it disappeared spontaneously and did not return. It varied from 0.5 to 1 per cent. in amount, and readily underwent fermentation. There were no symptoms and the daily output of urine varied between 1200 and 1800 c.c. An 8½-pound child was delivered after an easy low-forceps operation; the puerperium was normal. Sugar did not reappear in a subsequent pregnancy three years later.

CASE III.—*Transient Glycosuria in Pregnancy.* Mrs. G. D. P., aged forty-three years, a stout woman, pregnant for the sixth time. Specimens of urine examined during the fourth and fifth months were normal. About the middle of the sixth month she began to complain of considerable thirst, and stated that her appetite was abnormally large as compared with that noted in previous pregnancies. The urinary output varied between 1500 and 2000 c.c. and contained from 1.3 to 2 per cent. of glucose on ordinary diet. Upon placing her upon an antidiabetic diet the sugar did not entirely disappear, but decreased to about 0.125 per cent., becoming abundant whenever a more liberal diet was permitted. The symptoms gradually subsided, although traces of glucose could be detected up to the time of labor, but disappeared permanently during the puerperium, being entirely absent from a specimen examined on the tenth day. The labor and puerperium were normal and the child weighed 8¾ pounds.

CASE IV.—*Alimentary Glycosuria in Pregnancy.* Mrs. D. K. B. (a) The patient when first seen was twenty-four years of age and in

her second pregnancy. Two months before labor the presence of sugar was demonstrated upon repeated occasions, and, after persisting for six weeks, passed off spontaneously. There were no symptoms, and the daily output of urine varied from 1500 to 2000 c.c. The sugar varied between 0.25 and 1 per cent. in amount, and consisted of a mixture of glucose and lactose; as positive results were obtained both by the polariscope and by fermentation, the former indicating a much larger quantity of sugar than the latter. After a spontaneous labor she gave birth to a live child weighing $8\frac{1}{4}$ pounds, and had no further trouble until the next pregnancy. (b) Three years later she became pregnant for the third time and sugar made its appearance during the seventh lunar month, persisting in varying quantities up to the birth of the child. She presented no symptoms and passed in twenty-four hours from 2000 to 2500 c.c. of urine, which contained from 0.25 to 1 per cent. of glucose. Its quantity remained unchanged no matter whether she was upon an ordinary or a carbohydrate-free diet. On discussing the matter with the patient I found that she had suffered from constipation for years and used senna prunes for its relief. These were prepared by stewing one pound of prunes in a decoction of a handful of senna leaves in a quart of water, to which one pound of sugar was added, which was then evaporated down to a thick syrup. Each night she took one-half dozen or more of prunes with considerable quantity of the syrup. It occurred to me that the glycosuria might possibly be due to the fact that she was unable to assimilate this extra amount of sugar. This supposition was found to be correct, as all trace of sugar disappeared from the urine upon replacing the prunes by a simple purgative, but it would promptly reappear as soon as their use was resumed. In this instance it appeared that the patient was intolerant of sugar administered in this form and suffered from alimentary glycosuria whenever it was used, but at the same time was able to assimilate the carbohydrates in her ordinary diet. She gave birth to an $8\frac{1}{4}$ -pound child after a normal labor, and no trace of sugar could be found after the puerperium.

CASE V.—*Recurrent Glycosuria during Pregnancy.* Mrs. J. T. H. (a) She became pregnant for the first time when twenty-nine years of age. The pregnancy was perfectly normal up to the seventh month when glycosuria appeared and continued until the time of labor, but gave rise to no symptoms. The amount of glucose varied from a mere trace to 0.5 per cent. and was uninfluenced by diet. A well-developed child was born after a normal labor and no trace of sugar could be detected during lactation. (b) The second pregnancy began eleven months after the birth of the first child. Sugar was detected at the second month and persisted in varying quantities until the time of labor. It varied from a mere trace to 1 per cent. and was definitely shown to be glucose. The glycosuria was not influenced by diet and gave rise to no symptoms. Pregnancy and

labor were uneventful and the sugar disappeared immediately after the latter. (c) Her third pregnancy occurred four years after the birth of the second child. Repeated examination showed that the urine was free from sugar up to the sixth month, at which period it made its appearance and persisted up to the time of delivery. Chemical examination showed that it was definitely glucose, and ordinarily varied between 0.25 and 0.5 per cent. The glycosuria was not influenced by carbohydrate-free diet, and gave rise to no symptoms; acetone bodies were at no time present. The patient passed through a normal pregnancy, labor, and puerperium, and no trace of sugar could be found later.

CASE VI.—*Mild Diabetes complicating Pregnancy.* Mrs. L. W., aged twenty-nine years, came to the hospital in the seventh month of her second pregnancy, her physician having discovered the existence of glycosuria a few weeks previously. She complained of frequent micturition and stated that she was obliged to drink large quantities of water on account of excessive thirst, but had observed no other symptoms. On the day of admission she passed 1000 c.c. of urine which contained 2.5 per cent. of glucose. The glycosuria disappeared entirely upon a milk diet, but reappeared when she was placed upon a restricted ward diet, the urine containing 0.46 to 0.50 grams of glucose per liter. After remaining in the hospital for two weeks she was dismissed in good condition with instructions as to diet. Her physician has kindly informed me that she remained in good condition during the rest of her pregnancy upon a restricted diet, and had a normal labor at term. Six months later her urine contained 3 per cent. of glucose with a specific gravity of 1044. She presented no symptoms and would have been unaware of her condition were it not for the fact that she was kept under constant supervision and upon a restricted diet.]

The histories which I have briefly given serve as examples of the various conditions in which sugar may be observed in the urine of pregnant women. Thus in Case I we had to deal with simple lactosuria, in Cases II and III with transient glycosuria, in Case IV with alimentary glycosuria, in Case V with recurrent glycosuria, and in Case VI with mild diabetes. With the exception of the latter, all of the cases were observed in private practice.

By way of comparison I have gone over the urinary records of 0300 consecutive patients in the Obstetrical Department of the Johns Hopkins Hospital. In this series the urine was examined as a matter of routine by the assistant or student on duty at weekly intervals, except for a catheterized specimen obtained immediately after labor, and the presence of sugar was recorded only when a definite reduction was obtained with Fehling's solution. Judged by this criterion, sugar was demonstrated in 167 patients during pregnancy, labor, or the puerperium, a frequency of 5.57 per cent.

The incidence in the several periods was as follows: Pregnancy alone, 24 cases (0.8 per cent.); puerperium alone, 137 cases (4.57 per cent.); and in both pregnancy and puerperium, 6 cases (0.2 per cent.).

Upon analyzing the cases in which the presence of sugar was demonstrated only during pregnancy, it is found that it was noted in 12 instances two weeks before labor, in 6 instances between two and four weeks before labor, in 4 instances between four and eight weeks before labor, and in 2 instances during the sixth and seventh months of pregnancy, respectively. The last 2 cases were examples of definite glycosuria, one being the case of diabetes whose history was given above (Case VI); while unfortunately no particulars can be given concerning the other, as she insisted upon leaving the hospital after a stay of only a few days, and has not been heard from since. It may be assumed that the majority of the other 22 cases were examples of lactosuria, as in no instance in which the nature of the sugar was determined was it found to be glucose. Moreover, its appearance so late in pregnancy would indicate that it was associated with premature mammary activity. Likewise, in all probability, we had to deal with lactosuria in the six cases in which a reduction was obtained both in pregnancy and the puerperium, as in each instance sugar appeared only shortly before labor, but unfortunately its exact nature was not determined.

In all of the 137 cases in which the presence of sugar was demonstrated only during the puerperium, we presumably had to deal with lactose. This belief is based upon the fact that the condition was usually associated with abnormalities in the mammary secretion, and furthermore that fermentation failed to occur in any of the cases subjected to that test, although of course it is possible that occasionally it may have been combined with glucose; but positive statements cannot be made in this regard, as in no instance were the characteristic osazones isolated.

Naturally, the 167 cases here mentioned do not represent the actual incidence of the presence of sugar in the urine during the last weeks of pregnancy and the first two weeks of the puerperium, for the reason that the examinations were made only once a week and a positive result recorded only when a definite reduction was obtained with Fehling's solution. Doubtless, a much greater incidence would have been indicated had daily examinations been made with more delicate reagents.

I shall now turn to the literature upon the subject and shall consider separately each of the following conditions: (a) Lactosuria; (b) transient glycosuria; (c) alimentary glycosuria; (d) recurrent glycosuria; and (e) diabetes.

Lactosuria. Although the presence of sugar in the urine of puerperal women was mentioned by Heller in 1849, it was first brought prominently to the attention of the profession in 1856, by Blot, who

stated that he had been able to demonstrate it in amounts varying between 1 and 2 grams per liter in 45 consecutive women who suckled their children. He held that its presence was dependent upon the functioning of the breasts and that its quantity served as an index of the abundance of the milk supply. Moreover, he stated that sugar could be found in the urine of about 50 per cent. of women in the last weeks of pregnancy. Unfortunately, he designated the condition as "physiological glycosuria," but did not attempt to determine whether the sugar in question was glucose or lactose. This communication aroused great interest and gave rise to a discussion which has extended to the present time.

Blot's statements were promptly tested by a number of investigators, some of whom absolutely denied their correctness and attributed his results to faulty technique, while others confirmed them more or less fully. Thus, Wiederhold, Leconte, Capezzuoli, Riedel, Iwanoff, and others stated that sugar was not present under such circumstances and that the reduction of the copper solution, which had been attributed to it, was due to the presence in the urine of mucus, uric acid, creatinin, or other substances. On the other hand, De Moulins, Kirsten, Brücke, Lecoq, Chailly, Louvet, Hempel, De Sinéty, Gubler, and Johannovsky demonstrated the presence of sugar in the urine of a varying proportion of puerperal women.

It is interesting to note that De Moulins, Wiederhold, Lecoq, and others suggested that the sugar in question might be lactose, while De Sinéty demonstrated that it disappeared in animals upon amputating the breasts and failed to appear after subsequent labors. Moreover, all investigators who obtained positive results were united in stating that the largest quantities of sugar were noted in women who did not suckle their children or in whom the breasts had become engorged from one cause or another, and accordingly attributed it to resorption. Consequently they concluded that Blot's contention was erroneous concerning the value of the condition as an index of mammary activity.

In 1877 and 1879 Hofmeister and Kaltenbach, respectively, isolated the sugar in question and definitely showed that it was lactose, thereby conclusively demonstrating that the condition was one of lactosuria, and that the term glycosuria was a misnomer. They held that the condition in all probability was due to the resorption of lactose from the milk in the more or less engorged breasts, and was, therefore, associated with their imperfect functioning. The suggestion of Luther that milk sugar, which thus gained access to the blood current, did not pass through the portal system, as well as the demonstration by Moritz and Voit that it was excreted unchanged through the kidneys when injected directly into the circulation, whereas it was utilized for metabolic purposes when administered by the mouth, afforded a thoroughly satisfactory explanation for the production of the phenomenon.

Notwithstanding the demonstration of the nature of the sugar in these cases, the majority of subsequent writers failed to make use of the term "puerperal lactosuria," but continued to designate the condition as glycosuria, puerperal diabetes, or resorption diabetes, as the case might be, and thereby materially retarded the general recognition of its true significance. Following the establishment of the mode of production of puerperal lactosuria, all investigators, who have made daily examinations of the catheterized urine of puerperal women, have been able in most cases to demonstrate the presence of traces of lactose at some time during the first few days of the puerperium, as well as considerable quantities whenever the breasts became engorged or the child was weaned. Observations of this character have been made by McDonald, Davenport, Ney, McCann and Turner, Lemaire, Keim, Leduc, Queirel and Domergue, Commandeur and Porcher, and others.

In view of these findings, the existence of slight degrees of lactosuria (0.5 to 1 gram per liter) in the early days of the puerperium may be regarded as perfectly physiological, while the presence of larger quantities (10 to 30 grams per liter) may be expected whenever the breasts become engorged or the child is weaned. The fact that sugar was found in only 143 out of 3000 puerperal urines in my service should not be regarded as invalidating this statement, for two reasons: In the first place, as our urines were examined only once a week, such a transient phenomenon occurring between the second and fourth days would frequently escape detection; and, secondly, as the examinations merely formed a part of the routine duties of the assistant on duty, it is highly probable that only such cases would be reported which presented a perfectly typical reduction with Fehling's solution, which is not observed unless at least 1 per cent. of sugar is present.

In this connection it is important to direct attention to the diagnostic significance of lactosuria accompanying the process of weaning the child, as in such cases the quantity of sugar may rise as high as 3 or 4 per cent. and persist until the secretion has been checked and the breasts have become soft and flabby. For this reason, the detection of sugar in the urine of a nursing woman who has just weaned her child in order to enter a hospital, for example, should not lead to the diagnosis of diabetes until the nature of the sugar has been definitely determined: as it may readily happen that failure in this regard may lead to the postponement of a necessary operation or to erroneous conclusions concerning the prognostic significance of diabetes complicating surgical procedures. Attention was first directed to this fact by Sir W. J. Sinclair as early as 1886.

Lactosuria of Pregnancy. The observations of Bar, Brocard, Bürgers, Commandeur and Porcher, Ludwig, Naunyn, and others have clearly shown that by appropriate means slight degrees of lactosuria may also be detected during the last weeks of pregnancy

and is usually associated with premature mammary activity. Thus, Ludwig noted it in 46 per cent. of 82 women in the last weeks of pregnancy, while in 10 per cent. more of his patients lactose alternated with glucose. Commandeur and Porcher found lactosuria in 30 consecutive cases, although in 8 instances it was associated with glycosuria. In the latter event they believe that the condition is due to the fact that the breasts are not sufficiently active to convert into lactose all of the glucose which is brought to them by the blood, as they hold that such a transformation usually occurs as soon as the breasts begin to function. Moreover, they consider that both they and Bert have adduced experimental evidence in support of such a transformation by finding that the urine of recently delivered goats, whose breasts had been amputated just before conception, contains considerable quantities of glucose in place of the lactose which is usually present.

In 22 of the 24 cases in which sugar was present during pregnancy in the urine of 3000 consecutive patients in my service, it is probable that we had to do with lactosuria, as in none of them was the presence of sugar demonstrated prior to the last six weeks of pregnancy and usually only during the two weeks immediately preceding delivery. Moreover, only lactose was found in the cases in which the nature of the sugar was differentiated. On the other hand, Case I clearly shows that lactosuria does not occur exclusively in the last weeks of pregnancy, as in this instance milk sugar was definitely demonstrated during the course of the seventh month, and doubtless many similar cases have occurred in the experience of others.

In consideration of the facts just adduced, I feel that one is justified in stating that moderate degrees of lactosuria occurring either during pregnancy or the puerperium may be regarded as physiological and, therefore, of no prognostic significance. The practical importance of the condition lies in the fact that an incautious observer may confound it with glycosuria and, believing that the latter is indicative of the existence of diabetes, may express a sombre prognosis, which is usually not justifiable.

Transient Glycosuria. Leaving out of consideration the minute amounts of glucose which have been shown by the observations of Brücke, Ivanoff, Abeles, Pavy, Luther, Moritz, Lemaire, and others to be present in the urine of normal men and women, certain authors also state that appreciable quantities of glucose may be demonstrated in the urine during the second half of pregnancy and particularly during its last few weeks. The following authors make varying statements concerning its incidence: Keim, 10 per cent.; Ludwig, 12 per cent.; Ney, 16.6 per cent.; Commandeur and Porcher, 26 per cent.; Charrin, 40 per cent.; Bar, 43 per cent.; Brocard, 45 per cent.; Leduc, 60 per cent.; Salémi, 66 per cent; while Rudaux holds that its presence is practically universal, and Brocard and Bar state

that glycosuria is observed much more frequently in multiparous than primiparous women.

Manifestly, in such cases the amount of glucose is very small, varying from 1 to 2 or 3 grams per liter, and consequently must be tested for by delicate reagents, as the presence of at least 1 per cent. is necessary in order to give a characteristic reduction with Fehling's solution. On the other hand, it not infrequently happens that larger quantities may be observed during pregnancy and yet have no connection with diabetes. This is clearly demonstrated by the histories of Cases II and III, as well as by many other instances which might be adduced from the literature. Exceptionally, the amount of sugar may rise as high as 3 or 4 per cent., and even give rise to slight symptoms, such as pruritus, increased thirst, and frequent urination, although subjective manifestations are usually absent. In either event, the glycosuria may disappear spontaneously after a longer or shorter period, or may persist throughout the balance of the pregnancy to disappear definitely after the birth of the child. It would appear that many physicians, being ignorant of the possibility of such an occurrence, have described cases of this character as examples of true diabetes, and it would seem that the cases described as such by Partridge, Taylor, Durieux, and others might be placed in this category.

Unfortunately, it is frequently impossible in a given case to determine immediately whether the presence of sugar is merely an evidence of transient glycosuria or of mild diabetes, and in many instances an assured diagnosis can be made only after the conclusion of pregnancy. If the condition is merely transient glycosuria, all traces of sugar promptly disappear after delivery and there are no further symptoms; whereas in diabetes the glycosuria persists and in many instances the symptoms become aggravated. The importance of recognizing the existence of transient glycosuria and of not confusing it with diabetes has been strongly insisted upon by Naunyn, Senator and Kamminer, Salus, Brook, and others. Very exceptionally the condition may still further simulate diabetes, particularly as it is sometimes associated with hydramnios, as in the cases reported by Rossa in which the maternal urine contained 0.92 per cent. of glucose, while 0.345 per cent. was present in the amniotic fluid.

On inquiring as to the significance of transient glycosuria, it may be said that the milder degrees (1 to 2 grams per liter) should be regarded as practically physiological, while, on the other hand, the occurrence of larger quantities must be considered abnormal, although as far as our knowledge at present goes, not necessarily of clinical significance.

The most important practical point in connection with this condition, however, is to realize that it does occur, and that it is even quite common. Therefore, when the presence of glucose is demonstrated in the urine of pregnant women, diabetes should not be

diagnosicated, unless the sugar is present in large amounts and is accompanied by definite symptoms. Unfortunately, as has already been indicated, it is frequently impossible to differentiate between the two conditions until after delivery, as was clearly demonstrated in Cases III and IV. In both instances 2 per cent. of glucose was observed during the course of pregnancy and gave rise to no symptoms. In Case III the sugar disappeared immediately after delivery, while in Case IV it did not, but actually increased in amount, thus indicating that the former was an example of transient glycosuria and the latter of mild diabetes. The mode of production of this variety of glycosuria will be taken up under the following heading:

Alimentary Glycosuria. In 1895 Lanz and von Jaksch pointed out that women were less tolerant of sugar during pregnancy than at other times, and that transient glycosuria frequently followed the ingestion of an amount of glucose which would have been thoroughly assimilated by a non-pregnant woman. Investigations upon similar lines have since been undertaken by Keim, Brocard, Payer, Ludwig, Combemale and Oui, Charrin and Guillemonat, Schroeder, Rudaux and Bar, all of whom, with the exception of Ludwig, have more or less fully confirmed the findings of Lanz and von Jaksch. Thus Brocard administered to 17 pregnant women varying quantities of glucose before breakfast, and was able to demonstrate its presence in the urine in a varying proportion of cases within the course of the following two hours. He also found that alimentary glycosuria sometimes occurred in non-pregnant women, but far less frequently. The following table gives an idea of the varying effect of increasing doses of sugar in the two conditions:

	Per cent. of pregnant women.	Per cent. of non-pregnant women.
50 grams caused glycosuria in	50	11
80 grams caused glycosuria in	70	15
100 grams caused glycosuria in	70	16
150 grams caused glycosuria in	88	19
200 grams caused glycosuria in	100	29

Payer likewise experimented upon 45 pregnant women, 35 of whom manifested alimentary glycosuria, the average amount of glucose necessary to give rise to the phenomenon being 130 grams in pregnant, as compared to 200 grams in non-pregnant women. Schroeder, in 1905, performed similar experiments with levulose, and after a dose of 150 grams administered before breakfast obtained positive results in 17 out of 95 women. Moreover, it is important to note that all but 2 of his positive cases presented moderate degrees of albuminuria, which was of a very high grade whenever the levulosuria was marked. Combemale and Oui, and Bar have also observed more or less similar results following the administration of

cane sugar. Bar, who conducted a most careful series of experiments, calculated the amount which could be assimilated for each kilogram of the patient's weight, and found that the power of assimilation was greatly reduced during pregnancy; his experiments showed that glycosuria would follow the administration of 6 to 8 grams of sugar per kilo of body weight in pregnant as compared to 12 or 13 grams in non-pregnant individuals.

There is no doubt that alimentary glycosuria occurs comparatively frequently in practice and has occasionally been described as diabetes. Case IV was a striking example of this condition, and in it the glycosuria could be made to appear or disappear according as senna prunes were used as a laxative or not.

Numerous theories have been advanced in explanation of this phenomenon, and, while none of them are entirely satisfactory, we are obliged to reckon with the fact that the pregnant woman is less tolerant of sugar than at other times, and that, therefore, the practitioner will occasionally have to deal with cases of alimentary glycosuria. Moreover, it is quite possible that the same factors which are concerned in its production apply equally well to transient glycosuria.

Keim and others have advanced the theory that glycosuria in pregnancy is merely a manifestation of a toxemia. They hold that the latter is associated with disturbed function of the liver, by which the conversion of glucose into glycogen may be interfered with, thus leading to the production of glycemia and consequent glycosuria. Schroeder takes a somewhat similar view, which is based upon the fact that albuminuria was present in 15 out of 17 cases in which he was able to produce alimentary levulosuria. As he believes that the albuminuria of pregnancy is associated with abnormalities in the function of the thyroid gland, he is inclined to attribute the lessened power of assimilation of sugar to some similar derangement, although his view has not been accepted by most writers upon the subject. Brocard, on the other hand, holds that glycosuria is merely an expression of a diminished necessity for the consumption of carbohydrates during pregnancy, while Bar contends that it is a manifestation of a diminished power of assimilation. It is apparent, however, that these explanations are of but little value, as they throw no light upon the ultimate factors underlying the disturbed metabolism.

Rudaux, and Commandeur and Porcher associated the production of glycosuria with the mammary function. Rudaux believes that large quantities of glycogen are stored up in the liver and other organs in anticipation of lactation. Consequently, when this has been accomplished beyond a certain extent it becomes impossible for the usual amounts of glucose to be transformed into glycogen and thus be removed from the circulation, so that it becomes necessary for the excess to be excreted through the kidneys. Commandeur and Porcher, on the other hand, attribute the condition to lack of function

on the part of the breasts; they believe that during lactation the latter convert into lactose large quantities of glucose brought to them by the blood, and that normally this function becomes inaugurated in the last weeks of pregnancy. In connection with these theories, the observations of Charrin and Guillemonat are of interest, as they have apparently definitely shown that the liver cells of pregnant guinea-pigs contain far more glycogen than usual. They attribute this to lessened consumption, and hold that the overloaded cells are unable to take up the usual quantity of glucose from the blood and consequently glycemia and subsequent glycosuria must result.

Hofbauer, in his important recent contribution to our knowledge of the toxemias of pregnancy, studied the livers of several perfectly normal pregnant women who died from traumatism, and in each instance discovered characteristic changes in the liver cells, which he believes are normally associated with pregnancy. These consist in more or less fatty degeneration of the peripheral portions of the lobules, associated with a marked diminution in the glycogen content. If his observations hold good, it would appear that the cause of glycosuria must be sought in some abnormal condition of the liver cells resulting from pregnancy which interferes with the storage of glycogen in the ordinary quantities, so that the portion of sugar which should be so transformed must of necessity circulate in the blood and be excreted through the urine. It is interesting to note that Cristalli advanced a somewhat similar explanation in 1900.

Notwithstanding the large amount of work which has been done upon the subject, it is apparent that we are as yet unable to give a satisfactory explanation for the production of either transient or alimentary glycosuria, but at the same time it must be admitted that their occurrence is a fact which must be reckoned with and is of great diagnostic importance. In the present stage of our knowledge it would seem permissible to diagnosticate alimentary glycosuria in any case in which the sugar disappeared from the urine upon removing excessive quantities of sugar from the diet, while not restricting other forms of carbohydrate food.

Recurrent Glycosuria. Case V is a typical example of this condition. The patient presented glycosuria in three consecutive pregnancies, which varied in amount from a fraction of 1 to 2 per cent.; it gave rise to no symptoms, was not influenced by diet, disappeared after labor, and reappeared in each subsequent pregnancy.

It is interesting to note that two of the earliest cases described as diabetes in pregnant women were presumably of the same character, namely, those reported by Bennowitz and Lever in 1826 and 1847, respectively. Matthews Duncan was acquainted with the condition and drew from it the conclusion that "diabetes may occur only during pregnancy, being absent at other times." Likewise, Partridge, in 1895, in describing what he considered to be a case of diabetes complicating pregnancy, but which was probably only

an example of transient glycosuria, stated among other conclusions, that "diabetes may originate during pregnancy, persist throughout its course, and disappear on its completion to reappear in a subsequent pregnancy." Somewhat similar cases have been reported by Ruoff and Tate. In the former case 4 to 7 per cent. of sugar was present in the second, fourth, and fifth pregnancies, but disappeared during the puerperium in each instance. In Tate's case sugar was present in the second and third pregnancies and disappeared after the birth of the child.

It is difficult to speak positively concerning the significance of such cases. In those described by Bennowitz and Ruoff, the patients presented definite diabetic symptoms during pregnancy, and excreted large amounts of sugar, but the fact that the condition cleared up immediately after delivery and gave no further trouble until the occurrence of a subsequent pregnancy, would strongly militate against its diabetic nature. On the other hand, in the case reported by Tate, as well as in my Case VI, there were no symptoms and the condition was discovered simply on account of the routine examination of the urine. Whatever may be thought of the first group of cases, it seems clear that the latter group cannot be classified as diabetes, and is best described as recurrent glycosuria. At the same time it is probable that they should be regarded as of a more serious nature than ordinary transient or alimentary glycosuria, in that they probably indicate the existence of a more profound and continuous disturbance of metabolism.

Diabetes. Our knowledge upon this subject practically began with Duncan's paper in 1882, which was based upon the study of 22 pregnancies occurring in 16 women. Four of these died in coma or collapse at the time of labor, and 7 others perished from diabetes or tuberculosis in the course of the following two years, while 47 per cent. of the children were either born dead, succumbed during labor, or died early in the puerperium. As the result of his investigations he held that the association of pregnancy and diabetes was a most serious complication and formulated the following conclusions: (1) "Diabetes may come on during pregnancy." (2) "Diabetes may occur only during pregnancy, being absent at other times." (3) "Diabetes may cease with the termination of pregnancy, recurring some time afterward." (4) "Diabetes may come on soon after parturition." (5) "Diabetes may not return in a pregnancy occurring after its cure." (6) "Pregnancy may occur during diabetes." (7) "Pregnancy and parturition may be apparently unaffected in its healthy progress by diabetes." (8) "Pregnancy is very likely to be interrupted in its course and probably always by the death of the foetus."

Considering these conclusions in the light of our present knowledge, it would appear that the conditions described under conclusions 2 and 5 probably possessed no points in common with diabetes,

except the presence of sugar in the urine, and were merely examples of transient, alimentary, or recurrent glycosuria. Moreover, as will be shown farther on, Duncan apparently took a somewhat too serious view of the dangers of true diabetes when associated with pregnancy.

Such a point of view can be readily understood, when it is remembered that at the time at which he wrote very few physicians were in the habit of examining the urine of apparently normal pregnant women at frequent and regular intervals, and made such examinations only in the presence of more or less serious symptoms. Consequently the majority of the cases of simple glycosuria must have escaped detection, and practically only the more serious forms of true diabetes were diagnosticated. That this interpretation is justifiable is shown by the fact that none of the six cases reported in this article would have been recognized had the frequent examination of the urine not formed part of the routine care of all pregnant women. On the other hand, as has already been indicated, Duncan's series of cases included several examples of non-diabetic glycosuria, which were probably more or less accidentally discovered and described as diabetes in the absence of more precise information. Indeed it may be said that all statistics upon the subject have suffered from this defect, as the authors in their anxiety to collect a large series of cases have included a number of questionable significance.

From my own experience and a study of the literature I feel that the significance of diabetes associated with pregnancy may be profitably discussed under following headings: (*a*) Pregnancy may occur in definitely diabetic women. (*b*) Diabetes may be first recognized during pregnancy and persist afterward. (*c*) Diabetes may first appear during pregnancy and disappear afterward. (*d*) Diabetes may recur in each pregnancy and disappear after each delivery. (*e*) Diabetes may exist before and after pregnancy, but disappear during its course.

There can be no doubt as to the significance of the conditions described under the headings *a* and *b*, as in them the existence of diabetes can be readily established. The same may be said of group *e*, although the case described by Stengel is at present the only one belonging in the category. On the other hand, the diabetic nature of the conditions included in groups *c* and *d* is open to discussion, as they probably merely represent exaggerated examples of transient, recurrent, or alimentary glycosuria. Skepticism in this regard is justified by our conception of diabetes as a chronic, practically incurable disease, in which glucose is never long absent from the urine; therefore it would not appear permissible to describe as such, conditions in which the sugar permanently disappears.

One of the great merits of Duncan's work was that it clearly proved that pregnancy might occur in women suffering from diabetes, and thus did away with the old view that they were absolutely sterile.

At the same time it is generally admitted that the probability of conception becomes markedly diminished in such cases, partly because the disease usually occurs after the menopause, but more especially as the researches of Loeb, Hofmeier, Nebel, Seegen, Lecorché, and others have shown that it may be associated with profound changes in the internal genitalia. These may vary from a simple endometritis to marked atrophic processes in the ovaries or in the uterus, by which the ova are destroyed in situ or the uterus rendered unfit for their proper implantation and nutrition.

It is probably in great part due to partial persistence of the older view that most writers state that diabetes occurs much more frequently as a complication of pregnancy than that conception takes place in diabetic women. Thus Eshner, in 1907, stated that the latter occurred in only 8 out of 33 cases. On the other hand, I am inclined to hold that such a belief is erroneous and is based upon incorrect interpretation. The mere fact that the presence of sugar was first detected during the course of pregnancy by no means proves that it had not been present previously, but merely indicates that the condition was not accompanied by symptoms sufficiently severe to make it necessary for the patient to consult a physician. In such cases a diagnosis would not have been made had not the occurrence of pregnancy lead to the examination of the urine, just as it frequently happens that the existence of diabetes is unexpectedly discovered in men applying for life insurance, who had previously believed that they were in perfect health.

The accompanying table, which is based upon the histories of 66 definite cases of diabetes in pregnant women which I have collected from the literature, shows that in 55 instances the disease was present before the occurrence of the pregnancy in question, while in the remaining 9 it made its first appearance after conception. In this series no case was classified as diabetes unless the characteristic urinary changes persisted after the puerperium, for had the ordinary cases of glycosuria been included it is quite probable that the relationship would have been reversed. At the same time I do not desire to claim that my figures are beyond peradventure, but they at least clearly indicate that diabetes may exist anterior to conception in a much larger proportion of cases than is generally believed.

Upon reviewing the literature upon the subject, it is apparent that diabetes must be regarded as a serious condition no matter whether occurring primarily or as a complication of pregnancy, as is shown by the following figures: Thus, Chapiet, Stengel, Ruoff, and Vinay reported a maternal mortality of 25, 26, 46, and 55 per cent., respectively, in four tabulations which included 68, 19, 28, and 34 cases. My own statistics, which are based upon 66 cases collected from the literature, show an immediate maternal mortality of 27 per cent., while an additional 23 per cent. of the patients died within the following two years.

Generally speaking the patients do comparatively well for the first seven or eight months of pregnancy, although they may suffer considerably from pruritus, increased thirst, ravenous appetite, and frequent micturition. Exceptionally coma may supervene in the latter part of pregnancy, and the patient may die undelivered or shortly after the birth of the child, as reported by Born, Hofmeier, and others; although occasionally, as in the case reported by Offergeld, she may rally from the comatose condition and die weeks or months later. More usually, however, symptoms do not appear until the time of labor, and in such cases the patient may die either in coma or collapse within a few hours after the birth of the child; but even at this time coma is not necessarily fatal, as recovery has been reported and the patients have lived for some time afterward.

On the other hand, in a considerable proportion of cases, labor and the puerperium go on normally, while the diabetes pursues its usual course and leads to death in coma or from tuberculosis months or even years later. Moreover, it is a well-established fact that certain subjects may repeatedly give birth to children with comparative impunity. This occurred in Case VI, and was strikingly exemplified by the experience of Lecorché and Lop. The former reported that uncomplicated pregnancy and labor had occurred in seven of his patients, while the latter stated that four women under his care had gone through 6, 3, 2, and 1 normal labors respectively, after the diagnosis of diabetes had been definitely established.

I have included among the diabetic cases only such patients as died with characteristic symptoms, or in whose urine the presence of glucose was repeatedly demonstrated after childbirth. If this precaution be not taken many cases, which are merely examples of some of the other forms of glycosuria, will be improperly placed in this category. In order to illustrate this point I have included in Section "C" of my table 10 cases which are usually described as diabetic by other writers, but from whose urine all trace of sugar disappeared immediately after delivery. These ten women had twelve children with no maternal mortality and but two foetal deaths, a result which is so striking as to cast grave doubt upon the correctness of the diagnosis.

The deleterious effects of diabetes whether existing before conception or appearing during the course of pregnancy are not limited to the mother, as a review of the literature shows that the child suffers equally severely. Thus abortion and premature labor occur more frequently than usual, and even if the pregnancy goes on to term it is not unusual for the child to die shortly before the onset of labor and to be born in a more or less macerated condition. Moreover it seems that the condition frequently predisposes to excessive development on the part of the child, which may give rise to serious dystocia and lead to its death during delivery.

Some idea of the increased danger to the child may be gained from

the tabulations of Chapiet, Duncan, Vinay, Stengel, and Ruoff, according to which the foetal mortality was 27, 47, 48, 50, and 53 per cent. respectively. Chapiet's figures are based upon the largest series of cases: 103 pregnancies occurring in 68 women.

One of the interesting complications associated with the condition is hydramnios, with its serious effect upon the development of the child and its tendency toward the production of premature labor. I have been able to collect from the literature twelve examples of this condition, namely, the cases reported by Duncan, Reid, Husband, Warner, Hehir, Ludwig, Rossa, Lop, Herman, Liepmann, Hofmeier, and Offergeld. Moreover, it is interesting to note that the amniotic fluid frequently contains sugar, its presence having been demonstrated chemically in more than one-half the cases, while in some of the earlier ones its presence was indicated by the sweet taste and sticky consistency of the fluid. In the observations of Ludwig, Rossa, Herman, Hofmeier, and Offergeld quantitative determinations were also made and the amount of sugar was found to vary from 0.165 to 0.7 per cent. The fact that it disappeared from the urine of Rossa's patient shortly after delivery would apparently indicate that it was not a case of true diabetes, and accordingly it may be concluded that sugar may be present in the amniotic fluid in simple glycosuria as well as in diabetes.

Observations of this character are of interest not only in themselves, but also because they at one time seemed adapted to throw some light upon the vexed question of the origin of the amniotic fluid. At first they apparently indicated that it must be a transudate from the maternal blood, as the absence of sugar from the foetal urine in several instances, as well as the fact that several other children were born in a macerated condition, indicated that their urinary secretion could not have contributed to the formation of the amniotic fluid. Unfortunately the observations of Chamberlent and Offergeld have shown that such conclusions are untenable, as the former demonstrated the existence of glycosuria in a child born of a diabetic mother, and the latter showed that both the blood and urine of an unborn child contained glucose, thereby raising the question whether the latter had been transmitted through the placenta or indicated the existence of foetal diabetes.

DIAGNOSIS. From what has already been said it is apparent that the mere reduction of Fehling's solution, upon which the practitioner ordinarily bases the diagnosis of diabetes, is open to many interpretations in the pregnant woman. Leaving out of consideration all substances other than sugar which may give rise to such a reaction, it may be obtained in as radically different conditions as lactosuria, the several varieties of glycosuria, and true diabetes. Accordingly the mere detection of the presence of sugar is of but little diagnostic or prognostic value, and as far as my experience goes has been pro-

ductive of quite as much harm as good, in that it frequently leads the incautious practitioner to diagnosticate the existence of diabetes with its comparatively sombre prognosis in patients who present a harmless lactosuria or glycosuria. That this is the case is shown by the fact that each year I receive letters from physicians in different parts of the country asking for advice in cases of supposed diabetes complicating pregnancy, which upon closer investigation have nearly always proved to be examples of transient glycosuria or lactosuria.

Therefore, whenever the presence of sugar is demonstrated in the urine of a pregnant woman, the first essential is to determine whether it occurs in the form of glucose or lactose. For practical purposes this is readily ascertained by the use of the fermentation saccharometer, as glucose ferments readily while lactose does not. If more accurate information is desired the characteristic glucosazone or lactosazone must be isolated, but unfortunately this latter procedure cannot be employed if quantitative results are desired. Moreover, it should be borne in mind that both glucose and lactose may occur together, and such a combination should be suspected whenever there is a discrepancy between the readings obtained by titration with Fehling's solution and by the use of the saccharometer, or when the polarimeter indicates the presence of a greater amount than the saccharometer.

If the sugar is definitely shown to be lactose, the condition must be regarded as lactosuria and may be dismissed from consideration as of no practical significance. On the other hand, if the presence of glucose is demonstrated the matter is not so simple, as it is then desirable to determine whether the patient is suffering from true diabetes or merely from transient or alimentary glycosuria. Unfortunately such a differentiation is by no means easy and frequently cannot be made without prolonged observation or knowledge of the previous history of the patient. If it be known that the glycosuria existed before conception the diagnosis of diabetes is assured, but if it were first detected during the course of pregnancy the interpretation is not so clear.

Generally speaking it may be said that a tentative diagnosis of diabetes is permissible whenever large amounts of glucose are present, or the patient presents characteristic symptoms; whereas transient or alimentary glycosuria should be suspected if the percentage of sugar is low and symptoms are absent. Such rules, however, are not absolute, as it sometimes happens that in the first class of cases the sugar and symptoms may permanently disappear after the delivery, while in the second the glycosuria may persist after labor and the characteristic symptoms of diabetes sooner or later may become manifest. This was clearly shown in Case VI, which was considered as transient glycosuria during pregnancy, and yet was shown to be true diabetes by the subsequent course of events.

Likewise the persistence or disappearance of sugar under dietetic treatment does not necessarily afford accurate information concerning the nature of the condition, as it sometimes happens, on the one hand, that cases of glycosuria will be uninfluenced by a carbohydrate-free diet, while, on the other hand, in true diabetes all trace of sugar may disappear temporarily under a plain milk diet, as was demonstrated in Cases II and III and Case VI, respectively.

The existence of alimentary glycosuria should be suspected in any case in which the sugar disappears from the urine upon the removal from the diet of certain saccharine substances, but without restricting the use of other carbohydrates. In view, however, of what has been said concerning the common factors in the etiology of transient glycosuria, it is manifest that it frequently will be impossible to differentiate between the two conditions.

PROGNOSIS AND TREATMENT. Unless the condition can be demonstrated to be either lactosuria or definite alimentary glycosuria, the presence of sugar in the urine of a pregnant woman should be regarded as a danger signal, and as an indication for continuous and careful observation. If diabetes be definitely diagnosed from the previous history of the patient, the condition should be regarded as serious but by no means hopeless for either the mother or child, for as long as the patient presents no serious symptoms, acetone bodies are absent, and the output of sugar can be controlled by dietetic means, the prognosis may be regarded as favorable as far as the present pregnancy is concerned, and all that is necessary will be careful supervision. If, however, serious symptoms supervene, acetone bodies appear in the urine, or the output of sugar cannot be controlled by dietetic means, the condition should be considered as alarming and the pregnancy should be ended at once by the most appropriate means, as its continuance will add to the danger of the mother, while the child's prospects are so poor that they are not entitled to consideration. It is of course understood that the interruption of pregnancy will not cure the underlying disease, but it may nevertheless temporarily relieve the disordered metabolism from such a degree of strain as to enable nature to reassert herself and thus allow the patient to live for several years.

Most writers upon the subject advocate the induction of premature labor under the conditions just mentioned, although Vinay and Kleinwächter are absolutely opposed to it, while Graefe and Lesse believe that it is indicated only when the diabetes is complicated by hydramnios. Fellner, Schauta, and Senator and Kamminer hold that abortion is indicated in the early months provided the diagnosis is assured. Likewise the same line of treatment is indicated even if the existence of diabetes is not absolutely certain, but is rendered probable by the presence of large amounts of sugar or by the onset of threatening symptoms.

TABULATION OF CASES OF DIABETES COMPLICATING PREGNANCY.
A. *Pregnancy Occurring in Diabetic Patients.*

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
1. Husband	1874	26	III	Uncertain.	5.5	?	Spontaneous.	None.	Very small, lived several days.	Died 8 months later from tuberculosis.
2. Newman (a)	1876	36	II	Several years.	4.0	Uneventful.	"	"	Normal.	Diabetes continued.
3. Newman (b)	1876	36	III	Same patient as case (a).	4.0	"	Premature, sixth month.	"	Dead.	Died in coma third day.
4. Newman (a)	1878	32	m.p.	Same patient as case (a).	?	"	Spontaneous.	"	Normal.	Diabetes continued.
5. Newman (b)	1880	34	m.p.	Previous pregnancy.	?	"	"	"	"	Died in coma 2 years later.
6. Duncan	1879	35	XI	Several years.	Large.	Great thirst.	"	"	"	Died comatose 8 months later.
7. Reid	1880	32	II	Several years.	10.0	Thirst and diuresis	"	Hydramnios, fluid sticky.	Large, macerated.	Typical diabetes 2 years later.
8. Williams (a)	1880	?	I	Same patient as case (a).	?	Uneventful.	"	None.	Normal.	Sugar afterward.
9. Williams (b)	1881	?	II	Same patient as case (a).	2.0	"	"	Hydramnios, no sugar.	"	Diabetes continued.
10. Williams (c)	1881	?	III	Same patient as cases (a) and (b).	5.0	"	"	None.	"	Died 6 weeks later in coma.
11. Williams	1882	36	VI	Uncertain.	Large am't	Thirst and diuresis	"	"	Macerated.	Died in coma 4 months later.
12. Duncan	1882	30	V	Several years.	3.0	Uneventful.	Low forceps.	"	"
13. Lecorché (a)	1885	?	?	Before pregnancy.	?	Spontaneous.	Normal.	Died third day after delivery in collapse.
14. Lecorché (b)	1885	?	?	"	?	"	"	Diabetes continued.
15. Lecorché (c)	1885	?	?	"	?	"	"	"
16. Lecorché (d)	1885	?	?	"	?	"	"	"
17. Lecorché (e)	1885	?	?	"	?	"	Premature rupture membranes Eighth month.	Died second day.	"
18. Lecorché	1885	?	?	"	?	"	Normal.	"
19. Lecorché	1885	?	?	"	?	Premature.	"	"
20. Tarnier and Budin	1886	?	?	"	Slight.	None.	Spontaneous.	None.	"	"
21. Tarnier and Budin	1886	?	?	"	5.0	Symptoms.	Premature at six months.	Dead.	Died in coma 3 hours later.
22. Warner (a)	1886	32	II	Second pregnancy	Definite.	"	Spontaneous.	None.	Large, macerated.	Diabetes persists.
23. Warner (b)	1886	?	III	"	"	"	"	Hydramnios.	"	"
24. Warner (c)	1886	?	IV	"	"	"	"	None.	"	"
25. Warner (d)	1886	?	V	"	"	"	"	"	"
26. Packard	1889	41	m.p.	For years.	4.06	"	Repeated abortions.	Abortion.	"

	1899	1890	1892	1893	1893	1893	1895	1897	1898	1899	1899	1899	1901	1903	1905	1906	1906	1907	1907
27. Gaudard	44	m.p.	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
28. Demelin	32	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
29. Hehr	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
30. Seegen (a)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
31. Seegen (b)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
32. Seegen (c)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
33. Seegen (a)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
34. Seegen (b)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
35. Seegen (c)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
36. Ludwig	42	IX	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
37. Graefe	37	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
38. Kleinwächter	25	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
39. Lop (a)	?	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
40. Lop (b)	?	VII	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
41. Lop (c)	?	VIII	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
42. Lop (d)	?	IX	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
43. Lop (e)	?	X	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
44. Lop (f)	?	XI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
45. Lop (g)	?	IV	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
46. Lop (h)	?	V	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
47. Lop (c)	?	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
48. Lop (a)	?	II	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
49. Lop (b)	?	III	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
50. Lop	?	III	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
51. Chamberlent	31	IV	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
52. Liepmann	30	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
53. Fels	24	III	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
54. Hofmeier	33	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
55. Offergeld	34	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
56. Eshner	37	II	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
57. Chapiet	?	VI	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?

57 pregnancies in 34 women: gross mortality, 24.58%; during labor and puerperium, 12.29%; children alive, 50.88%; born dead, 36.88%; aborted, 12.24%.

B. Diabetes Developing during Pregnancy.

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
58. Duncan	1871	30	III	Early in pregnancy.	Large.	Emaciation, amaurosis, Normal.	Accouchment force. Slow.	Macerated.	Died in coma third day
59. Winckel	1874	?	?	Day of labor.	"	Normal.		Hydramnios.	Normal.	Sugar on discharge thirteenth day.
60. Loeb	1881	22	?	Second month.	4.0	Symptoms.	Abortion at six months.	Dead.	Died 1 month later.
61. Davidson	1882	38	IV	Middle of pregnancy.	10.0	Thirst, emaciation	Spontaneous, premature.	None.	Died 13 hours.	Died in coma 4 months later.
62. Frerichs	1882	36	X	Eighth month.	?	Normal.	Normal.	"	Normal.	Death 15 months later, phthisis, brain tumor.
63. Fry	1891	31	II	Fourth month.	3.0 to 6.0	Symptoms.	Premature.	"	Macerated.	Died in coma 3 days later
64. Born	1892	24	I	Seventh month.	8.5	"	Died in coma undelivered at seven months.	Dead.	Died in coma.
65. Taylor	1897	31	II	Sixth month.	8.5	No symptoms.	Normal.	None.	Normal.	Diabetes persists.
66. Herman	1902	30	VII	Third month.	2.0 to 3.0	Comatose.	Premature.	Hydramnios.	Macerated.	Died ninth day, sarcoma of lung.

9 pregnancies in 9 women: 78% maternal mortality; 45% in first ten days; 33% one to fifteen months later; 66.67% fetal mortality.

C. Doubtful Cases of Diabetes Complicating Pregnancy. Sugar Disappeared after Delivery.

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
67. Bennowitz (a)	1826	22	IV	This pregnancy.	?	Intense thirst.	Spontaneous.	None.	Normal.	Sugar disappeared.
68. Bennowitz (b)	1826	?	V	Early.	12.0	"	Operation.	Threatened coma.	Dead, 12 lbs.	Perfect recovery.
69. Bennowitz (c)	1826	?	II?	?	"	Spontaneous.	None.	Normal.	"
70. Williams	1882	33	VII?	Consid'able	Emaciation.	Face, forceps.	Perineal tear.	"	"
71. Marcus	1892	27	I	Puerperium.	0.7	None.	Forceps.	Decubitus.	"	Sugar disappeared 5
72. Trouillard	1893	28	III	Early in pregnancy.	?	Thirst, somnolence	Abortion.	Twins at five months.	Dead.	Disappeared in 6 weeks.
73. Partridge	1895	20	I	Fourth month.	3.0	Marked symptoms	Spontaneous.	Albuminuria.	Normal.	No sugar for next 2 years
74. Taylor	1897	39	m.p.	Seventh month.	0.75	No symptoms.	"	None.	Normal.	No sugar after labor.
75. Rouff (a)	1903	25	II	This pregnancy.	4.0	Pruritis.	Version.	Hydrannios.	Lived 12 hours.	Gradually disappeared.
76. Rouff (b)	1903	25	IV	Fourth month.	?	Slight symptoms.	Forceps.	Dead.	Disappeared after delivery.
77. Rouff (c)	1903	25	V	Onset of pregnancy.	5.0 to 7.0	Marked symptoms	Induced labor at eight months.	Lived 3 months.	Disappeared permanently
78. Stengel	1904	33	II	Sixth month.	5.0	Hunger and thirst	Spontaneous.	None.	Normal.	"
79. Durieux	1905	37	III	Seventh month.	Large am't	Intense thirst.	"	Rigorous diet.	"	"
80. Tate (a)	1906	33	II	Third month.	Consid'able	Pruritis, thirst.	Abortion at four months.	Dead.	Disappeared 4 weeks later.
81. Tate (b)	1906	35	III	second pregnancy.	Present.	"	Spontaneous.	None.	Normal.	Disappeared later.

15 pregnancies in 10 women: no maternal deaths; 12 labors at term; 1 premature labor; 2 abortions; 10 live children (75 per cent.).

On the other hand, it should be remembered that in the vast majority of cases the presence of sugar is not indicative of the existence of diabetes, but merely of transient or alimentary glycosuria, and the latter diagnosis should be made tentatively whenever the amount of glucose does not exceed 2 or 3 per cent. and symptoms are absent or only slightly marked. In such cases the urine should be examined at frequent intervals and the amount of sugar excreted in the twenty-four hours definitely determined. As long as it remains stationary or can be controlled by dietetic measures, the prognosis should be regarded as favorable and there should be no thought of interfering with the pregnancy.

In view of the fact that many cases of mild diabetes have no deleterious effect upon the course of pregnancy and labor, such an outcome should not be taken to indicate that the condition is merely simple glycosuria; but the urine should be examined at varying intervals following delivery and diabetes should be diagnosed if sugar is persistently present, whereas if repeated examinations show that it has disappeared, such a diagnosis is not justified no matter what its percentage may have been during pregnancy or by what symptoms it may have been accompanied.

CONCLUSIONS. 1. A positive reaction with Fehling's solution during pregnancy does not necessarily indicate the existence of diabetes, but is usually due to lactosuria or to transient, alimentary, or recurrent glycosuria.

2. In such cases it is imperative to determine whether the sugar occurs as lactose or glucose, as lactosuria is without clinical significance and is probably associated with premature activity of the breasts.

3. The significance of glycosuria is not so clear. If alimentary in character it may be regarded with impunity. Otherwise it may be of the transient or recurrent variety, or may indicate the existence of true diabetes.

4. If the glycosuria appears late in pregnancy, does not exceed 2 per cent. in amount and is not accompanied by symptoms, it is probably transient and may disappear spontaneously at any time or persist until the end of pregnancy. In either event it is usually of slight clinical significance, and merely indicates that the patient should be carefully watched.

5. If the sugar appears early in pregnancy and in large amounts the condition is more serious, as it may be impossible to make a positive diagnosis until after delivery, when the condition disappears in glycosuric but persists in diabetic cases.

6. Pregnancy may occur in diabetic women or diabetes may become manifest during pregnancy. Either is a serious complication, although the prognosis is not so alarming as is frequently stated; many patients do perfectly well, while a smaller proportion die in coma or collapse at the end of pregnancy, or during or shortly after labor.

7. If the output of sugar is large and cannot be controlled, or at least markedly diminished by suitable dietetic and medicinal treatment, the induction of abortion or premature labor is indicated even in the absence of serious symptoms, and much more so when they are present.

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