Presentation
C.B., a 24-year-old woman, came to our clinic for a diabetes consultation after being referred by her mother, who is one of our regular patients and has type 1 diabetes herself. The older woman’s diagnosis was made elsewhere 7 years before she sought care with our office and had been based on her lean frame (5% below ideal body weight [IBW] based on height) at presentation and relatively normal insulin sensitivity (insulin requirements have always been <0.5 U/kg/day). No antibody studies or C-peptide levels were done at the time of diagnosis.

Her daughter, C.B., was diagnosed with type 2 diabetes at a community clinic in a rural area near Seattle 3 weeks before her visit with us. The diagnosis was based on her lack of ketones at presentation, “low” presenting blood glucose of 254 mg/dl, and age at diagnosis.

Oral agents were suggested for C.B., but her mother insisted on insulin therapy. Her primary care provider was concerned about this, noting that insulin is rarely the best first-line treatment in patients with type 2 diabetes, but prescribed a temporary regimen for her to use until her appointment with me. At bedtime, she was told to take 2–4 U of NPH, depending on her bedtime blood glucose level, as obtained with home blood glucose monitoring. She was also given a sliding scale for lispro to be taken before eating, depending on her blood glucose readings. If her blood glucose value was <150 mg/dl, she was instructed to take no supplemental lispro.

C.B. received no nutrition information, but her mother taught her carbohydrate counting. They were told that metformin was the treatment choice but would not be started until our office suggested it.

Besides being 3 weeks late with her menstrual period and having some breast tenderness, C.B. had no other symptoms of pregnancy. Her mother was the only family member with diabetes of any type. C.B. and her husband had been trying to conceive for the past 3 months.

On exam, C.B. was a pleasant young woman with a weight of 67 kg and a height of 147 cm (IBW = 65 kg, therefore only 3% over IBW). Except for mild bilateral thyromegally, her physical exam was normal. Her home blood glucose monitoring data were well ordered but revealed chaotic fluctuations, with several readings above 400 mg/dl in the mornings and below 100 mg/dl at midday. Her HbA1c was 9.2% (normal 4.0–6.0 %). A serum pregnancy test was positive.

Questions
1. How certain is the diagnosis of type 2 diabetes in this patient?
2. What course of action is indicated in patients presenting with hyperglycemia when pregnancy is diagnosed?
3. How should C.B. be counseled as to her risk of congenital anomalies if she decides to continue the pregnancy?
4. What methods should be used to screen for pregnancy in women with diabetes?

Commentary
Patients with type 2 diabetes are almost always obese (>20% over IBW). As discussed in a previous issue of Clinical Diabetes by Hansen et al., obesity and family history of obesity are present in virtually all patients with type 2 diabetes. This is perhaps the most important risk indicator when considering the diagnosis. Patients with type 2 diabetes not only have a strong family history of the disease, but also frequently have family members with a preponderance of macrovascular conditions.

People with type 1 diabetes are not usually obese and typically do not present with a clear family history of the disease. Often, there is weight loss at diagnosis, which is seldom a feature of type 2 diabetes. Insulin sensitivity is spared, so small doses of insulin produce potent hypoglycemic results. Though not measured in this case, the presence of certain specific antibodies, such as islet cell antibody (ICA) or anti–glutamic acid decarboxylase antibody (anti-GAD64) are common at diagnosis and even diagnostic when hyperglycemia is evident.

C.B. was lean and was aware of no overweight relatives. She and her mother were the only family members with diabetes. Although she did not present with ketones, this is a notoriously bad diagnostic marker. Patients with type 2 diabetes can present with ketones if they have fasted or are seriously ill. Age at diagnosis also is not a reliable marker for either disease, since both types of diabetes can occur in young or older people. Although she had not
and miscarriage is an important, and sometimes grave, necessity. Women who have had poor preconception control of their diabetes are at greater risk of spontaneous miscarriage, and those with sustained hyperglycemia during the first trimester have a higher rate of major malformations. Brown et al. at the University of Washington Medical Center have observed specific risk relationships between presenting HbA1c level and the risk of poor outcomes. Their preliminary unpublished data, presented in Fig. 1 with permission of the investigators, graphically illustrate the profound effect of hyperglycemia at the time of conception.

Clinical Pearls
1. Obesity and family history of type 2 diabetes are present in virtually all patients with the disease. They are strong markers. Age, the presence of ketones at diagnosis, and presenting serum glucose are poor indicators.
2. Every woman with diabetes who is of reproductive age must be counseled about contraception and family planning and asked if there is even the slightest chance she could be pregnant. This should be a part of the interview every time she visits your office.
3. All women with diabetes who are of reproductive age should be counseled before they are pregnant about the need to optimize metabolic control and plan pregnancy and the risks of spontaneous abortion and birth defects associated with poor metabolic control.
4. In diabetes, the risks of spontaneous abortion and fetal anomalies are directly related to metabolic control at the time of conception as well as throughout the pregnancy. Hyperglycemia is most destructive to fetal development during the first trimester of gestation.

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Case Study: A 36-Year-Old Woman With Type 2 Diabetes and Pregnancy

Diane M. Karl, MD

Presentation
C.M. is a 36-year-old Spanish-speaking Mexican-American woman with a 3-year history of type 2 diabetes. She was seen in her primary physician’s office because of a missed menstrual period; a pregnancy test was positive. Her past obstetrical history included five vaginal deliveries and six miscarriages. All of her previous pregnancies occurred before the diagnosis of diabetes. Her previous medical care was in Mexico. She was never told of any glucose problem during her pregnancies, and she does not know the birth weights of her children. At the time of referral, she was 8 weeks pregnant and taking glyburide 10 mg twice daily. She was checking her blood glucose once daily in the morning with typical readings between 180 and 220 mg/dl on a plasma-referenced meter. Family history was positive for diabetes in her mother.

Her height was 62 inches, and her weight was 198 lb. Other than mild acanthosis nigricans and obesity, her physical examination was normal. She had no retinopathy and no evidence of neuropathy. Her glycosylated hemoglobin (HbA1c) level was 10.5% (normal <6.0%), and an office capillary blood glucose 4 h after lunch was 201 mg/dl.

She was started on insulin immediately and her glyburide was discontinued. She began monitoring her glucose before and after each meal, making daily adjustments in insulin. She received nutrition education with an appropriate calorie intake plus an emphasis on frequent smaller meals and limited carbohydrate intake. Within 1 week, her plasma glucose values were in the target range for pregnancy, but in the following week she had a spontaneous miscarriage. After her miscarriage, she discontinued insulin on her own and resumed taking glyburide 10 mg twice daily.

Questions
1. Is there a relationship between C.M.’s diabetes and her adverse obstetrical history?
2. What should have been done before her recent pregnancy to increase the odds of a favorable outcome?
3. What considerations affect the choice of therapy for her diabetes now?

Commentary
In the past, most diabetic women who conceived had type 1 diabetes. Today, however, we see an increasing number of women who have preconception type 2 diabetes. One reason is the tendency for many women to delay pregnancy until a later age. Another important factor, however, is the increasing number of children and young adults, especially in minority groups, who are developing type 2 diabetes.1

The presence of diabetes in a woman of childbearing years is a special challenge. Blood glucose control during the first 2 months of pregnancy is critical to normal organ development. Commonly, however, women do not seek medical attention until after this period of early fetal development. Many women do not yet realize they are pregnant during this important period, especially if the pregnancy is not planned, which is the situation in well over half of all pregnancies. For this reason, preconception counseling must be an important aspect of management in all diabetic women of childbearing years, regardless of whether there is an expressed desire to conceive.2,3

Even though C.M.’s diabetes was diagnosed 3 years ago, the fact that she is already poorly controlled on maximal sulfonylurea treatment suggests a longer duration of diabetes. This supports the possibility that her poor obstetrical history may have been related to undiagnosed (and, therefore, uncontrolled) diabetes. Certainly during her most recent pregnancy, C.M. was poorly controlled during the critical period of organ development, possibly leading to an anomaly incompatible with fetal viability.

Comprehensive preconception counseling is now indicated for C.M. Oral diabetic medications have not been adequately studied for safety during pregnancy. Therefore, a woman who is taking oral medication and who wishes to conceive should be switched to insulin, and control should be established before she becomes pregnant. If C.M. plans another pregnancy or if she is not actively using birth control, she needs to resume insulin treatment.

Even patients whose diabetes is well controlled with diet and exercise are almost certain to require insulin during the later stages of gestation, when insulin resistance increases markedly. Preparing patients for this likelihood and teaching insulin administration as part of preconception counseling is advisable. Before pregnancy occurs is the ideal time to address any patient fears and misconceptions about insulin treatment.

For a woman of childbearing age who does not wish to become pregnant, choice of therapy can be important. Insulin resistance, almost universally present in type 2 diabetes, may be associated with decreased fertility. This is most clearly evident in polycystic ovary syndrome.4 Oral diabetic medications that reduce insulin resistance, such as metformin and thiazolidinediones,5 may also restore fertility. Thus, a previously
infertile patient with type 2 diabetes may become unexpectedly pregnant after starting an insulin-sensitizing medication unless she is counseled regarding the need for birth control.

Clinical Pearls
1. Preconception counseling is important for all women with diabetes, type 1 or type 2, who are in their childbearing years, since many pregnancies are not planned and poor glucose control early in pregnancy is associated with a higher incidence of major congenital defects.
2. Especially in minority populations, increasing numbers of women with type 2 diabetes who are treated with oral medications may be in their childbearing years. There are not adequate safety data to recommend the use of oral diabetic medications during pregnancy.
3. Oral diabetic medications that reduce insulin resistance may increase fertility in women previously unable to conceive.

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Case Study: Complicated Gestational Diabetes Results in Emergency Delivery

Ginny Lewis, ARNP, FNP, CDE

Presentation
A.R. is a 33-year-old caucasian woman initially diagnosed with diabetes during a recent pregnancy. The routine glucose challenge test performed between 28 and 29 weeks gestation was elevated at 662 mg/dl. A random glucose completed 1–2 days later was also elevated at 500 mg/dl. A follow-up HbA1c was elevated at 11.6%. Additional symptoms included a 23-lb weight loss over the past 3–4 weeks with ongoing “flu-like” symptoms, including fatigue, nausea, polyuria, and polydypsia.

A.R. had contacted her obstetrician’s office when her symptoms first appeared and was told to contact her primary care provider for the “flu” symptoms. She had called a nurse triage line several times over the previous 2–3 weeks with ongoing symptoms and was told to rest and take fluids.

She presented to her primary care provider 3 days after the HbA1c was drawn for ongoing evaluation of hyperglycemia. At that time, she was symptomatic for diabetic ketoacidosis. She was hospitalized and started on an insulin drip.

A.R.’s hospitalization was further complicated with gram-negative sepsis, adult respiratory distress syndrome, and Crohn’s disease with a new rectovaginal fistula. She was intubated as her respiratory status continued to decline and was transferred to a tertiary medical center for ongoing management. She required an emergency Caesarian section at 30 1/7 weeks gestation due to increased fetal distress.

A.R. had no family history of diabetes with the exception of one sister who had been diagnosed with gestational diabetes. Her medical history was significant for Crohn’s disease diagnosed in 1998 with no reoccurrence until this hospitalization. Her prepregnancy weight was 114–120 lb. She had gained 25 lb during her pregnancy and lost 23 lb just before diagnosis.

A.R.’s blood glucose levels improved postpartum, and the insulin drip was gradually discontinued. She was discharged on no medications.

At her 2-week postpartum visit, home blood glucose monitoring indicated that values were ranging from 72 to 328 mg/dl, with the majority of values in the 200–300 mg/dl range. A repeat HbA1c was 8.7%. She was restarted on insulin.

Questions
1. What is the differential diagnosis of gestational diabetes versus type 1 diabetes?
Commentary
Gestational diabetes is defined as “any degree of carbohydrate intolerance with onset first recognized during pregnancy. This definition applies whether insulin is used for treatment and whether or not the condition persists after pregnancy.”1 Risk assessment is done early in the pregnancy, with average-risk women being tested at 24–28 weeks’ gestation and low-risk women requiring no additional testing.1,2 A.R. met the criteria for average risk based on age and a first-degree family member with a history of gestational diabetes.

Screening criteria for diagnosing diabetes include 1) symptoms of diabetes plus casual plasma glucose >200 mg/dl (11.1 mmol/l), or 2) fasting plasma glucose >126 mg/dl (7.0 mmol/l), or 3) 2-h plasma glucose >200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT).1 For women who do not meet the first two criteria, a glucose challenge test (GCT) measuring a 1-h plasma glucose following a 50-g oral glucose load is acceptable. For those women who fail the initial screen, practitioners can then proceed with the OGTT.1

In A.R.’s case, she most likely would have met the first criterion if a casual blood glucose had been measured. She had classic symptoms with weight loss, fatigue, polyuria, and polydypsia. Her 1-h plasma glucose following the glucose challenge was >600 mg/dl, which suggests that her casual glucose would also have been quite high.

Medical nutrition therapy (MNT) is certainly a major part of diabetes management. However, with this degree of hyperglycemia, MNT would not be adequate as monotherapy. Treatment for gestational diabetes includes the use of insulin if fasting blood glucose levels are >95 mg/dl (5.3 mmol/l) or 2-h postprandial values are >120 mg/dl (6.7 mmol/l).1

Several days passed from the time of A.R.’s initial elevated blood glucose value and the initiation of insulin therapy. While HbA1c values cannot be used for diagnostic purposes, in this case they further confirmed the significant degree of hyperglycemia.

Plasma blood glucose values initially improved in the immediate postpartum period. A.R. was sent home without medications but instructed to continue home glucose monitoring.

At her 2-week postpartum visit, whole blood glucose values were again indicating progressive hyperglycemia, and insulin was restarted. A.R.’s postpartum weight was 104 lb—well below her usual pre-pregnancy weight of 114–120 lb. Based on her ethnic background, weight loss, abrupt presentation with classic diabetes symptoms, and limited family history, she was reclassified as having type 1 diabetes.

In immune-mediated, or type 1, diabetes, β-cell destruction can be variable, with a slower destruction sometimes seen in adults.3 Presentation of type 1 diabetes can also vary with modest fasting hyperglycemia that can quickly change to severe hyperglycemia and/or ketoacidosis in the presence of infection or other stress.3 A.R. may have had mild hyperglycemia pre-pregnancy that increased in severity as the pregnancy progressed.

The final issue is communication among multiple health care providers. A.R. was part of a system that uses primary care providers, specialists, and triage nurses. She accessed all of these providers as instructed. However, the information did not seem to be clearly communicated among these different types of providers. A.R. called triage nurses several times with her concerns of increased fatigue, nausea, and weight loss. The specialist performed her glucose challenge with follow-up through the primary care office. It seems that if all of these providers had the full information about this case, the diagnosis could have been made more easily, and insulin could have been initiated more quickly.

Clinical Pearls
1. Hyperglycemia diagnosed during pregnancy is considered to be gestational diabetes until it is reclassified in the postpartum period. Immune-mediated diabetes can cause mild hyperglycemia that is intensified with the increased counterregulatory hormone response during pregnancy.
2. Insulin therapy needs to be instituted quickly for cases in which MNT alone is inadequate.
3. The GCT is an appropriate screening test for an average-risk woman with no symptoms of diabetes. In the face of classic symptoms of diabetes, a casual plasma glucose test can eliminate the need for the glucose challenge.
4. As part of the health care industry, we need to continue to work on information systems to track patient data and share data among multiple providers. Patients can become lost in an ever-expanding system that relies on “protocols” and does not always allow for individual differences or for cases with unusual presentation.

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