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DIABETES Under Control

CE 3 HOURS
Continuing Education

Identifying and Treating Gestational Diabetes Mellitus

Advances in screening and current interventions.

One of the most common complications of pregnancy, gestational diabetes mellitus affects about 7% of all pregnant women in the United States—more than 200,000 cases annually—according to the American Diabetes Association (ADA). In some populations, the prevalence may be as low as 1% or as high as 14% of pregnancies. In 90% of cases there is no diabetes prior to pregnancy; in 10% of cases there is preexisting type 1 or type 2 diabetes.[1] The Centers for Disease Control and Prevention (CDC) says that approximately 1.85 million American women between 18 and 44 years old have diabetes and about 500,000 cases are undiagnosed. According to the CDC's *Diabetes and Women's Health Across the Life Stages,* "women with gestational diabetes have up to a 45% risk of recurrence with the next pregnancy and up to a 63% risk of developing type 2 diabetes later in life."[2]

Although such risk factors as sedentariness and poor diet can adversely affect blood glucose levels and contribute to the onset of diabetes mellitus, a woman can't cause gestational diabetes mellitus. Hormones that the placenta produces to support a healthy pregnancy, including human placental lactogen, progesterone, and estrogen, increase the mobilization of glucose, decrease insulin sensitivity, and create insulin resistance, thereby necessitating additional insulin secretion.[3] These conditions contribute to the development of gestational diabetes mellitus, defined as any degree of abnormal glucose tolerance beginning or first recognized in pregnancy.[4] This definition applies whether insulin treatment is initiated or the condition persists after pregnancy. The majority of cases resolve after childbirth.

Several studies have established an association between maternal hyperglycemia, the hallmark of diabetes mellitus, and unfavorable maternal and fetal outcomes, but technologic advances have improved outcomes[5-8] (see *Maternal and Fetal Complications,* page 67). Unger shares Coustan's belief that "Intensive diabetes management during pregnancy, combined with aggressive fetal surveillance and perinatal care, produces outcomes nearly identical to those in the nondiabetic population."[9]

Education is crucial in helping women with gestational diabetes achieve glycemic control. Although some women receiving a diagnosis of gestational diabetes mellitus may view it as an opportunity to learn and adopt certain changes in eating and physical activity habits, this may not be other patients' first reaction. That's why it's important for nurses to begin with a frank discussion of the patient's feelings about the diagnosis and beliefs about the disease.

Diabetes care involves daily management, including blood glucose self-monitoring, physical activity, carbohydrate counting, and—often, but not always—insulin administration. Instruction and information on nutrition, physical activity, and stress management can help prevent maternal and fetal complications and may prevent or delay the onset of type 2 diabetes.

RISK FACTORS

Although any woman can develop gestational diabetes mellitus, there are certain clinical characteristics that intensify risk. The American College of Obstetricians and Gynecologists issued evidence-based recommendations in 2001, according to which, "it is appropriate to screen all pregnant

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DIABETES Under Control

TABLE 1. Determining Risk When Screening

Risk Category	Recommendations for Screening
High risk (has 1 or more of the following) • family history of type 2 diabetes • previous history of gestational diabetes mellitus • body mass index greater than 25 • previous infant weighing 9 lbs. or more at birth • history of poor outcome of pregnancy • glycosuria • polycystic ovary syndrome	Screen as soon as possible (at first prenatal visit). Repeat at 24 to 28 weeks' gestation if first screening is negative.
Average risk patients who don't fit into the high-risk or low-risk category	Screen between 24 and 28 weeks' gestation.
Low risk (must have *all* of the following) • no known history of abnormal glucose tolerance • age less than 25 years • body mass index less than 25 • no diabetes in a first-degree relative • not a member of a high-risk racial or ethnic group (Hispanics, African Americans, Native Americans, Pacific Islanders) • no prior poor outcome of pregnancy	Screening not required.

American Diabetes Association. *Diabetes Care* 2004;27 Suppl 1:S88-90; Biastre S. Gestational diabetes. In: Franz MJ, et al., editors. *A core curriculum for diabetes education.* 4th ed. Chicago: American Association of Diabetes Educators; 2001. p. 73-97; Metzger BE, Coustan DR. *Diabetes Care* 1998;21 Suppl 2:B161-7; Dunaif A, Thomas A. *Annu Rev Med* 2001;52:401-19.

women for [gestational diabetes mellitus], whether by patient history, clinical risk factors for [gestational diabetes mellitus], or a laboratory test to determine blood glucose levels."[10] Therefore, at the first prenatal visit, a pregnant woman's risk of developing abnormal glucose tolerance should be assessed. (See Table 1, above.)

Obesity. More than half of U.S. adults, women in particular, are overweight or obese.[11] In adults, overweight is defined as a body mass index (BMI) of 25 or greater, obesity as a BMI of 30 or greater, and extreme obesity as a BMI of 40 or greater. These definitions are consistent with those of the National Heart, Lung, and Blood Institute and the World Health Organization. (BMI is calculated by dividing weight in pounds by the square of height in inches, then multiplying that number by 703. For example, a woman who weighs 150 lbs. and is 5′ 2″ [62 in.] tall has a BMI of 27.5. For more on calculating BMI, go to www.cdc.gov/nccdphp/dnpa/bmi/bmi-adult-formula.htm.)

Obesity is a very strong risk factor for developing both gestational and type 2 diabetes.[1] Also, the correlation between gestational diabetes, obesity, and polycystic ovary syndrome has recently become more apparent.

Polycystic ovary syndrome (known as PCOS) is among the most common endocrine disorders in women. It usually begins at 15 to 30 years of age, and its etiology is unknown. Characteristics include menstrual disturbance (cycles that last 35 days or longer, or fewer than eight cycles per year) and increased androgen production resulting in acne, hirsutism, alopecia, and acanthosis nigricans.[12] Until recently, this syndrome was considered a reproductive disorder because it often led to infertility. Research has now shown a significant metabolic component associated with insulin resistance.[13] Knockenhauer and colleagues found that the prevalence of polycystic ovary syndrome among women of reproductive age was approximately 4.6%; but depending on the criteria used, their estimate ranged between 3.5% and 11.2%.[14] Women who have polycystic ovary syndrome are at higher risk for developing gestational diabetes mellitus as well as type 2 diabetes later in life.[15]

SCREENING

The diagnostic criteria for gestational diabetes are not the same as those for diabetes in the general population,[16] but it's also important to note that there has been considerable debate over the appro-

priate diagnostic criteria for gestational diabetes mellitus.[1] There are two different methods of screening, but the one used almost exclusively in the United States involves a two-step process.

Step one, a glucose challenge test, measures the plasma glucose level one hour after ingestion of a 50-g oral glucose load. The glucose load is given without regard to time of last meal or time of day. Evaluating the results of this test using a 140-mg/dL threshold identifies approximately 80% of women who have gestational diabetes mellitus; using a threshold of 130 mg/dL identifies approximately 90%. Although more women have to undergo step two of the diagnostic process—the three-hour 100-g glucose tolerance test—if the lower threshold is used, the inconvenience and added cost are offset by the increase in the percentage of cases detected.[1] But different institutions use different standards.

If the glucose level on the 50-g glucose challenge test is 139 mg/dL or lower, the result is considered negative and no further testing is required. If the result is between 140 mg/dL and 184 mg/dL, a three-hour, 100-g glucose tolerance test is warranted. According to Carpenter and Coustan, when the glucose threshold exceeds 185 mg/dL on the 50-g glucose challenge test, a diagnosis of gestational diabetes mellitus is given and no further testing is required.[17] (See Table 2, page 68.)

Step two, a three-hour, 100-g oral glucose tolerance test, confirms diagnosis when any two or more glucose values (fasting level and one-hour, two-hour, and three-hour postprandial levels) either meet or exceed the glucose threshold. (See Table 3, page 68.)

TREATMENT

Food, stress, and hormones elevate blood glucose levels, and exercise and insulin lower them.[18, 19] It's important to instruct women in both the nonpharmacologic and pharmacologic interventions that maintain euglycemia (also known as normoglycemia) throughout pregnancy.

Blood glucose self-monitoring is essential in managing gestational diabetes mellitus. It provides immediate feedback that helps both patient and provider tailor management strategies, including dietary changes, stress management, physical activity, and insulin therapy. For example, if a patient walks for 15 minutes after dinner one day, she may notice that her blood glucose level is lower than on a day she doesn't do so. This kind of information complements patient education and permits patients to direct the management of their condition.

It's recommended that women with gestational diabetes mellitus monitor blood glucose levels four times daily, first obtaining a "fasting" level (before eating the first meal of the day) followed by three "postprandial" levels (one hour after the start of each meal).[20]

Problems of definition. There's disagreement among experts in the field, as well as among professional organizations that promulgate standards, over several issues concerning the management of gestational diabetes mellitus. In addition to the fact that there aren't universally accepted blood glucose target ranges, there's confusion as to whether the one-hour or two-hour postprandial glucose level has the greatest impact on fetal growth and development. And some clinicians recommend that women monitor blood glucose one hour after the start of the meal and others, one hour after the end of the meal—another source of confusion

Maternal and Fetal Complications

Maternal complications of gestational diabetes mellitus include
- pregnancy-induced hypertension.
- preeclampsia.
- polyhydramnios (an excess of amniotic fluid).
- cesarean section.
- an increased risk of gestational diabetes mellitus in subsequent pregnancies.
- an increased risk of type 2 diabetes in later life.

Fetal complications of gestational diabetes mellitus include
- macrosomia.
- shoulder dystocia.
- traumatic delivery resulting from cephalopelvic disproportion.
- hypoglycemia.
- hypocalcemia.
- polycythemia.
- hyperbilirubinemia.

Fetuses exposed to hyperglycemia in the first trimester are at increased risk for spontaneous abortion and congenital anomalies, most often those involving the cardiovascular, central nervous, and skeletal systems.

Hyperglycemia exposure in the third trimester is associated with respiratory distress syndrome and stillbirth, as well as a risk of obesity, impaired glucose tolerance, and diabetes in childhood.

Coustan DR, Carpenter MW. *Diabetes Care* 1998;21 Suppl 2:B5-8; Sweet Success (California Diabetes and Pregnancy Program). Sacramento: Department of Health Services, State of California; 1998; American Diabetes Association, *Diabetes Care* 2004;27 Suppl 1:S88-90.

TABLE 2. Diagnostic Criteria for 50-g Glucose Challenge Test

If results of the 50-g glucose challenge test shows a glucose plasma level of

- 139 mg/dL or less, a negative result has been obtained and no further testing is required.
- 140 mg/dL to 184 mg/dL, a positive result has been obtained and a 3-hour, 100-g oral glucose tolerance test is required.
- 185 mg/dL or greater, a test result that is diagnostic of gestational diabetes mellitus has been obtained and no further testing is required.

Carpenter MW, Coustan DR. *Am J Obstet Gynecol* 1982;144(7):768-73.

TABLE 3. Diagnosis of Gestational Diabetes Mellitus Using a 3-Hour 100-g Oral Glucose Load Test

If any 2 of the following blood glucose levels are found (or are higher), a diagnosis of gestational diabetes mellitus is given.

- a fasting blood glucose level of 95 mg/dL
- a 1-hour postprandial blood glucose level of 180 mg/dL
- a 2-hour postprandial blood glucose level of 155 mg/dL
- a 3-hour postprandial blood glucose level of 140 mg/dL

The test should be administered in the morning after a fast of 8 to 14 hours and after at least 3 days on an unrestricted diet (including 150 g or more of carbohydrates per day) and unlimited physical activity. The subject should remain seated and should not smoke during the test.

Adapted with permission from American Diabetes Association, *Diabetes Care* 2004;27 Suppl 1:S88-90.

for providers and patients. Some charts showing blood glucose levels don't even specify the times at which glucose should be monitored. And the level of hyperglycemia that might adversely affect maternal and fetal well-being is disputed.[1, 18, 21]

In addition to these concerns, there are two types of blood glucose meters (whole-blood meters and plasma-referenced meters), and they analyze blood samples differently; they therefore yield different readings. The whole-blood meter is the older of the two and has largely been replaced by the plasma-referenced meter. However, published target glucose values often don't distinguish between the two types of meters and results. Older sources give values obtained by the whole-blood meter, without explicitly stating so, because they were published before the introduction of the newer technology. Whole-blood meters typically yield glucose values 10% to 15% lower than the plasma-referenced meters do.[22, 23] But since the introduction of plasma-referenced meters, the ADA has revised the suggested blood glucose treatment goals to distinguish between whole-blood and plasma-referenced values.[18, 21, 24] Clinicians should note that subsequent position statements of the ADA may not give target values for both types of blood meter.

According to Jovanovic, the blood glucose level at one hour after beginning a meal is the best predictor of subsequent fetal macrosomia.[21] Following recommendations by Unger, our center uses a fasting blood glucose target level of 90 mg/dL or less and a one-hour postprandial target level of 140 mg/dL.[9] (Others use a one-hour postprandial target level of 120 mg/dL.) To promote consistency, all of our patients use plasma-referenced meters; it should be noted, however, that, despite improvements in self-monitoring technology in recent years, these meters are not diagnostic tools.

Medical nutrition therapy promotes euglycemia throughout pregnancy and ensures adequate caloric intake for fetal growth while preventing maternal ketosis.[23] The carbohydrates eaten have the greatest impact on the postprandial glucose level, so it's important for women to learn about the sources of carbohydrates in their diets. Milk and milk products such as yogurt, fruit, starchy vegetables (such as potatoes, corn, and peas), grains, and sweets contain significant amounts of carbohydrates.[23] Nonstarchy vegetables like lettuce, celery, and broccoli contain water and fiber, primarily, and don't significantly affect the postprandial glucose level. Many people with diabetes plan meals by counting carbohydrates and keeping track of the carbohydrates they consume in a food diary. (Some people also keep track, in the food diary, of their blood glucose levels, to show the association between those levels and the foods they eat.)[25] This method allows for more flexibility in the diet. (See *Sample Menu for Women with Gestational Diabetes Mellitus,* page 69.)

The ideal carbohydrate intake isn't known, but most guidelines suggest that carbohydrates account for 40% to 45% of total daily calories.[19, 26] Carbohydrate servings should be distributed throughout the day in three main meals and two to four snacks (with fewer carbohydrates eaten as snacks).[19] Because the fetus constantly draws glucose, it's recommended that pregnant women take regular meals and snacks to avoid developing hypoglycemia.[23] During pregnancy, higher levels of cortisol and growth hormone diminish carbohydrate tolerance in the morning; carbohydrates are toler-

ated better at the later meals.[26] In our practice, patients often tolerate only 30 g or less of carbohydrates at breakfast but can tolerate greater amounts at lunch and dinner.

Morning urine ketone testing can help to determine the adequacy of caloric intake.[1, 19, 26] The presence of ketones in the urine may indicate that a pregnant woman is consuming insufficient calories or carbohydrates, resulting in accelerated fat breakdown.[27] It has been postulated that continued fetal exposure to ketones affects neurologic development.[28] If the patient is spilling ketones in morning urine, increase the size of the bedtime snack (blood sugar permitting) or move the snack time to later at night so that the snack lasts longer.

The importance of making healthful dietary choices and getting a moderate amount of unsaturated fat and lean protein during pregnancy are explained as part of the initial counseling session. We don't have patients count fats or weigh their protein portions (protein intake generally doesn't increase postprandial glucose levels[19]). Self-monitoring of blood glucose levels, results of urine ketone testing, weight gain, and appetite assessment guide nutrition therapy at follow-up sessions.[23] Adjustments to carbohydrate distribution can be made once the food diary and blood glucose results are reviewed. Protein and fat needs are discussed in detail and tailored to the woman's needs. If insulin therapy is initiated, the patient is told to eat consistent amounts of carbohydrates at meals and in snacks to help with insulin adjustment.[19]

Physical activity increases insulin receptor sensitivity by counteracting the hormonal changes that accompany pregnancy. Women who don't have contraindicating medical or obstetrical complications should be encouraged to participate in exercise programs approved for pregnancy.[1] Performing 15 to 20 minutes of armchair exercises daily can help a pregnant woman reduce hyperglycemia without increasing the risk of inducing uterine contractions. Such exercises can be performed during routine sedentary activities, such as watching television or reading.

Stress management. Although stress can significantly raise blood glucose levels, it's usually the least addressed factor. Managing gestational diabetes mellitus can be time consuming. It's important to assess a woman's feelings about her diagnosis as well as her support system. Nurses can also educate women on coping techniques such as deep breathing and keeping a journal and encourage them to engage in activities that they find enjoyable.

Sample Menu for Women with Gestational Diabetes

Breakfast
- 1 to 2 scrambled eggs
- 1 to 2 slices whole-wheat toast (15 to 30 g carbohydrates)
- Decaffeinated tea or coffee

Midmorning snack
- 1 small apple (15 g carbohydrates)
- 1 oz. cheddar cheese
- Flavored seltzer (without added sugar)

Lunch
- 3 oz. turkey on a roll (30 g carbohydrates) with tomato* and mayonnaise
- Tossed salad* with oil and vinegar
- 8 oz. milk (13 g carbohydrates)

Afternoon snack
- Yogurt with less than 25 g carbohydrates per serving, with sliced almonds

Dinner
- 5 oz. grilled salmon with lemon
- 2 medium baked sweet potatoes (30 g carbohydrates)
- Broccoli*
- 8 oz. milk (13 g carbohydrates)
- 1 small pear (15 g carbohydrates)

Bedtime Snack
- 2 tablespoons peanut butter on 6 whole-wheat crackers (22 g carbohydrates)
- Flavored seltzer (without added sugar)

*Nonstarchy vegetables are not counted.

Pharmacologic therapy. If euglycemia isn't achieved by medical nutrition therapy and exercise within 10 days, then insulin therapy is initiated. Pregnant women need three to four times the amount of insulin that a woman who isn't pregnant needs. In some women, the pancreas is unable to produce enough endogenous insulin to meet the demands of a healthy placenta. Insulin is the pharmacologic therapy that has shown the most consistent reduction in fetal morbidity when used in conjunction with medical nutrition therapy. Approximately 60% of the women we counsel require insulin therapy, most commonly one injection of neutral protamine Hagedorn (NPH) insulin at bedtime. Human minimally antigenic insulin should be used when insulin is prescribed, and blood glucose

self-monitoring should guide the doses and timing of the insulin regimen.[29] Although insulin analogs are not currently approved by the Food and Drug Administration (FDA) for use in pregnancy, several studies have documented their effectiveness in pregnant women.[30, 31] We substitute rapid-acting analogs, such as insulin aspart recombinant (NovoLog) or insulin lispro recombinant (Humalog), for regular insulin and have been successful in achieving optimal glycemic control. Because the onset of action is rapid in these analogs, the peak effect of the insulin corresponds more closely with the digestion of the meal. Note that, in accordance with the prescribing information that comes with the medication, insulin glargine (Lantus), a popular once-daily insulin analog used in the management of diabetes, isn't recommended for use by pregnant women.

Oral glucose-lowering agents also aren't generally recommended during pregnancy. But according to an ADA position statement, *Gestational Diabetes Mellitus*,

> one randomized, unblinded clinical trial compared the use of insulin and glyburide in women with [gestational diabetes mellitus] who were not able to meet glycemic goals on [medical nutrition therapy]. Treatment with either agent resulted in similar perinatal outcomes. All patients were beyond the first trimester of pregnancy at the initiation of therapy. Glyburide is not FDA approved for the treatment of [gestational diabetes] and further studies are needed in a larger patient population to establish its safety.[1, 32]

Postpartum follow-up. The same ADA statement also recommends that maternal glycemic status be reevaluated at least six weeks after delivery using a two-hour, 75-g glucose tolerance test. Further reassessment should be conducted every three years in women who have normal postpartum glucose levels. Women who have postpartum impaired fasting glucose levels (known as IFG—meaning their fasting level is elevated) or postpartum impaired glucose tolerance (known as IGT—meaning they have elevated blood glucose levels at any time) "should be tested for diabetes annually . . . receive intensive [medical nutrition therapy], and . . . be placed on an individualized exercise program because of their very high risk for development of diabetes."[1] According to Hicks, they should also be informed of the need for family planning to assure optimal glycemic regulation from the start of any subsequent pregnancy.[3]

When a woman is diagnosed with gestational diabetes mellitus, it's a window into her future; it's an opportunity to educate her on diet, weight loss, and exercise, all of which can help to delay or prevent the onset of type 2 diabetes.[33] t

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LEARNING OBJECTIVES: After reading the two previous articles and taking the test on the next page, you will be able to

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- discuss the etiology, incidence, and risks associated with gestational diabetes.
- outline the current diagnostic protocols for gestational diabetes.

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