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## 3. Screening and Diagnosis of Diabetes

### Types of Diabetes

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#### *How is diabetes classified?*

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Patients with any form of diabetes may require insulin treatment at some stage of their disease. The use of insulin, in itself, does not classify the type of diabetes.

#### Type 1 Diabetes Mellitus

Type 1 diabetes is characterized by a beta cell destructive process that is either autoimmune or idiopathic and may eventually lead to absolute insulin deficiency. Although not widely appreciated, type 1 diabetes can occur at any age. Multiple studies have shown that the clinical onset of type 1 diabetes occurs more frequently in adults than in children and that it is not unusual for patients to present in their 60s, 70s, and 80s.

Presentation of type 1 diabetes is usually acute or subacute. Classic symptoms are:

- Polyuria
- Polydipsia
- Polyphagia
- Weight loss
- Visual disturbance
- Recurrent vaginal or urinary tract infections
- Fatigue and malaise

In older adults, type 1 diabetes may present in a more subacute or chronic manner and may mimic type 2 diabetes. This form of type 1 diabetes is often referred to as *latent autoimmune diabetes of adults* and is characterized by a

slower progression of beta cell loss secondary to autoimmune destruction of the islets.

More than 90% of cases of type 1 diabetes are autoimmune in nature, characterized by insulinitis and the presence of autoantibodies against components of the beta cell or insulin itself (e.g., anti-insulin antibodies, glutamic acid decarboxylase antibodies, or islet cell–associated antigen antibodies). These antibodies are frequently present years before the clinical onset of diabetes, and patients ultimately become insulinopenic and dependent on insulin therapy for survival. Approximately 20% of those with type 1 diabetes develop other organ-specific autoimmune diseases, such as celiac disease, Graves' disease, hypothyroidism, Addison's disease, pernicious anemia, and vitiligo. For a discussion of less common autoimmune syndromes, see *Type 1 Diabetes—Learning from Uncommon Diseases*.

The diagnosis of type 1 diabetes is not excluded by age or by the presence of obesity, which usually indicates type 2 diabetes. Depending on the population, 5% to 20% of patients categorized as having type 2 diabetes are actually autoantibody positive, which suggests that they have type 1 diabetes.

Early after diagnosis, patients with type 1 diabetes may go through what is termed the *honeymoon period*, during which they require little insulin for weeks, months, or sometimes even years. During this time, some can control blood sugars by diet and physical activity or by using type 2 diabetes oral medications. The reason for the honeymoon period lies in the remarkable degree of reserves the pancreas has for producing insulin; insulin insufficiency may only become apparent in the setting of additional stresses such as infection or trauma. However, as the autoimmune destruction continues, the honeymoon period eventually ends and the patient requires daily insulin.

## Type 1 Diabetes—Learning from Uncommon Diseases

Some understanding of the pathogenesis of immune-mediated diabetes has come from the identification of monogenic forms of diabetes associated with multiorgan autoimmune syndromes. In particular, two rare syndromes have been identified.

APS-I syndrome (autoimmune polyendocrine syndrome type 1, also called *autoimmune polyendocrinopathy candidiasis ectodermal dystrophy* or *APECED*) results from mutations of the autoimmune regulator gene (AIRE). AIRE is a transcription factor that is important in the thymic expression of a number of peripheral antigens, including insulin. This expression is important for the central deletion of autoreactive T cells. About 18% of affected patients go on to develop type 1 diabetes.

The IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy, X-linked; also called *X-linked polyendocrinopathy, immune dysfunction, and diarrhea syndrome (XPID)*) results from mutations of the foxP3 gene. This gene is important for the development of regulatory T cells responsible for peripheral tolerance. Most affected children manifest neonatal diabetes. These “experiments of nature” have aided investigators in understanding (at least in a preliminary way) the roles of both central and peripheral tolerance in the development of autoimmune diabetes.

Because the honeymoon period occurs so early after diagnosis, some patients may view the normalization of blood glucose readings as a sign that the diagnosis was a mistake or that they do not really have diabetes. The end of this period can be particularly devastating for these patients, who must then adjust again to the reality of the diagnosis. It is important, therefore, to prepare patients for this possibility and assess their emotional response during and after this phase of the disease.

### Type 2 Diabetes Mellitus

Type 2 diabetes is characterized by a combination of insulin resistance and a beta-cell secretory defect. The disease may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance. With time, progressive beta-cell dysfunction can develop, leading to absolute insulin deficiency (see *Understanding Type 2 Diabetes*).

Most patients with type 2 diabetes are obese or at least have abdominal obesity (high waist-to-hip ratio). Presentation may range from an

asymptomatic one to the classic symptoms listed above for type 1 diabetes. The presence of ketoacidosis does *not* exclude the diagnosis of type 2 diabetes, particularly in non-white populations.

Approximately 20% of patients with newly diagnosed type 2 diabetes have established chronic microvascular complications of the disease at presentation; an even higher percentage may have coronary artery disease or peripheral vascular disease at presentation. Indeed, in a prospective study of patients with acute coronary syndromes, 57% were found to have impaired glucose tolerance, and 66% of those who met the criteria for diabetes did not have a previous diagnosis or were not treated.

### Diabetes of Defined Etiology

A subset of patients with diabetes have a known genetic defect, syndrome, or environmental insult leading to disease. Some of the causes include:

- Genetic defects of beta cell function (e.g., maturity-onset diabetes of the young [MODY]—see below)

## Understanding Type 2 Diabetes

In type 2 diabetes, the plasma insulin concentration (both fasting and meal-stimulated) is usually initially increased, although only relative to the severity of insulin resistance. Early in the disease, patients may even develop compensatory islet hypertrophy, but eventually, the plasma insulin concentration is insufficient to maintain normal glucose homeostasis. Frequently, there is a delay or loss of early-phase insulin release in response to oral glucose. With time, progressive beta-cell dysfunction can develop, leading to absolute insulin deficiency.

The obesity often associated with type 2 diabetes may directly contribute to insulin resistance. Adipose tissue may influence insulin action through release of free fatty acids and by secretion of such adipose-derived proinflammatory peptides as TNF- $\alpha$ , IL-6, and TGF- $\beta$  and by modulation of hormones, including adiponectin, leptin, and resistin.

Numerous in vitro experiments have demonstrated profound insulin resistance in tissues from obese patients with type 2 diabetes; we are starting to understand the tissue and cellular defects leading to this insulin resistance. Type 2 diabetes also appears to involve numerous downstream defects in insulin receptor signaling, including abnormalities in phosphorylation of the insulin receptor substrate family of proteins. Similarly, PI 3-kinase activity in skeletal muscle is reduced, which correlates with a decrease in whole body glucose disposal.

- Genetic defects in insulin action (e.g., leprechaunism)
- Uncommon forms of immune-mediated diabetes (e.g., stiff-man syndrome)
- Other genetic syndromes (e.g., Wolfram's syndrome)
- Diseases of the exocrine pancreas (e.g., pancreatitis)
- Endocrinopathies (e.g., Cushing's syndrome)
- Drug- or chemical-induced causes (e.g., glucocorticoids)
- Infection (e.g., congenital rubella)

Based on the underlying etiology, the presentation and treatment of type 1 and type 2 diabetes may be similar. Some of these forms of diabetes may be reversible with correction of the underlying problem—for example, a growth hormone abnormality or cortisol excess.

An estimated 5% of persons with diabetes in the United States have an autosomal dominant form of the disease known as *MODY*. Presentation is generally before age 25 but can occur at

any age. The cause is diminished insulin secretory capacity due to mutations in the gene for glucokinase, the rate-limiting enzyme in the glycolytic pathway (*MODY 2*), or in genes for transcription factors involved in regulating the insulin gene (*MODY 1, 3, 4, 5, and 6*).

## Gestational Diabetes

Gestational diabetes is defined as diabetes developing or discovered during pregnancy. Associated with an increased risk of perinatal morbidity and mortality, an increased rate of cesarean delivery, and chronic hypertension in the mother, gestational diabetes is usually asymptomatic and is diagnosed through routine screening during pregnancy.

Women with gestational diabetes carry a high risk for type 2 diabetes—nearly 50% develop type 2 diabetes within 5 years after diagnosis of gestational diabetes (see *Gestational Diabetes, Predictor for Subsequent Diabetes*). A small subset of women with gestational diabetes have positive islet cell antibodies, indicating that they have type 1 diabetes.

## Gestational Diabetes, Predictor for Subsequent Diabetes

Because insulin binding during pregnancy is unchanged, increases in insulin resistance during pregnancy are believed to be secondary to postreceptor factors. Defects in glucose transport may also play a role, as GLUT4 transporter numbers are reduced in adipose tissue later in pregnancy. In addition to increased insulin resistance, insulin clearance may increase moderately as the placenta actively degrades insulin. Even in women without gestational diabetes, insulin secretion in the third trimester in response to glucose is 1.5 to 2.5 times greater than that seen in the nongravid state and is accompanied by islet cell hyperplasia.

During the latter half of pregnancy, circulating levels of estrogen, progesterone, and prolactin, as well as the placenta-derived factors human chorionic somatomammotropin and placental growth hormone variant, all increase. The combined effect of these and other hormonal changes is to oppose insulin at peripheral and hepatic sites while at the same time increasing insulin secretion. Gestational diabetes may develop, particularly in women with coexisting defects in insulin secretion or utilization. This is likely why women who develop gestational diabetes are at higher risk to subsequently develop type 2 diabetes.

## Diagnosing Diabetes

### *How is diabetes diagnosed?*

Diabetes can be diagnosed in one of three ways:

- Symptoms of diabetes (polyuria, polydipsia, unexplained weight loss) and a casual plasma glucose (any time of day, regardless of fasting status) of  $\geq 200$  mg/dL;
- Fasting plasma glucose (after 8 hours or longer of fasting) that is  $\geq 126$  mg/dL;
- Plasma glucose  $\geq 200$  mg/dL 2 hours after ingestion of 75-g oral glucose (2-hour oral glucose tolerance test).

The American Diabetes Association (ADA) criteria for the diagnosis of diabetes recommends that whichever test is used, it must be repeated on another day to confirm the diagnosis. Practically, if a patient does not seem likely to return to the office for a confirmatory blood glucose test, a single positive fasting or random blood glucose level may be used to initiate diabetes education and referral for medical nutrition therapy. Likewise, if the diagnosis of diabetes is uncertain, management should include education about prediabetes and counseling for

exercise and weight loss to prevent or delay the actual onset of diabetes.

### *What are the differences among the tests used for diagnosing diabetes?*

Fasting plasma glucose and the oral glucose tolerance test (OGTT) are the two most commonly used tests for the diagnosis of diabetes.

#### **Fasting Plasma Glucose**

Fasting plasma glucose is used commonly in clinical practice because of its ease of use and low cost. It is currently the ADA preferred test for screening and diagnosis. However, data from the Third National Health and Nutrition Examination Survey (NHANES III) indicate that the test loses sensitivity in older populations characterized by a disproportionate prevalence of postchallenge hyperglycemia.

#### **Oral Glucose Tolerance Test**

The glucose load used in the OGTT varies depending on the setting.

- Nonpregnant adults: 75-g load
- Screening for gestational diabetes: 50-g load

- Diagnosis of gestational diabetes: 100-g load

OGTT is not recommended by the ADA as a first choice for diagnosing type 2 diabetes. Although this test identifies more people at increased risk of developing macrovascular disease (especially coronary artery disease), it remains poorly reproducible and cumbersome to perform. OGTT should be performed under the following conditions:

- If diabetes is strongly suspected and other test results are equivocal
- When the fasting glucose concentration is in range for impaired fasting glucose (100–125 mg/dL)

Proper preparation is important for the accuracy of the OGTT. A high-carbohydrate (150–200 g) diet should be followed for 3 days prior to testing.

### Hemoglobin A1C

Hemoglobin A1C is widely accepted as a measure of glycemia and is used in monitoring patients with diabetes; however, its use as a diagnostic test is controversial. Although not recommended as a diagnostic test, many clinicians use A1C for screening because of its ease of administration. Several studies have found high sensitivity and specificity for the diagnosis of diabetes, but other studies have found sensitivity and specificity to be inadequate. If the A1C value is to be used for screening, usually a value of 5.8 to 6.0 (depending on the laboratory normal range and sensitivity and specificity desired) is used as a cut-off followed by OGTT for diagnosis.

The advantages of hemoglobin A1C as a screening test are that it can be performed at any time of day without special preparations and that it may provide a more accurate reflection of glycemic status because it includes both fasting and postprandial components. Unfortunately, hemoglobin A1C assays are not yet standardized worldwide, and many conditions, such as hemoglobinopathies, can render A1C results unreliable. Because of this, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus recommends against their use for the diagnosis of diabetes.

- If A1C is used for screening, it should be remembered that results may fluctuate widely when different testing products are used.
- Elderly patients have a higher risk of post-meal hyperglycemia and may have high A1C results with normal fasting glucose levels. OGTT can confirm the diagnosis in these patients.

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### What is prediabetes?

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Patients with glucose levels that are elevated but do not meet the diagnostic criteria for diabetes have prediabetes. The term *prediabetes* was adopted to highlight the significantly higher risk these patients have of progressing to diabetes. Impaired glucose tolerance (IGT) is associated with a 2-fold increase in risk for cardiovascular disease and mortality. Although patients with prediabetes usually have no symptoms of hyperglycemia, it is now recognized that approximately 10% of them may develop microvascular complications of retinopathy, neuropathy, and nephropathy before meeting diagnostic criteria for diabetes.

A patient with prediabetes may have impaired fasting glucose (IFG), based on results of fasting glucose level, or IGT, based on results of a 2-hour OGTT. The diagnosis of diabetes and prediabetes based on interpretation of fasting plasma glucose and 2-hour OGTT results is shown in **Table 3-1**.

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### What educational issues should I discuss with patients with prediabetes?

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Patients who have a high risk of developing diabetes should be educated about the effectiveness of regular physical activity and modest weight loss in slowing the progression to diabetes. More information on counseling patients about nutrition, exercise, and goal-setting strategies can be found in Chapter 2 (Patient Engagement and Self-Management), Chapter 4 (Preventing

Table 3-1. Diagnosis of Diabetes and Prediabetes

Diagnosis	Fasting Plasma Glucose	2-Hour Oral Glucose Tolerance Test
No diabetes	<100 mg/dL	<140 mg/dL
Prediabetes	100–125 mg/dL	140–199 mg/dL
Diabetes	≥126 mg/dL	≥200 mg/dL

Data from Benjamin SM, Valdez R, Geiss LS, Rolka DB, Narayan KM. Estimated number of adults with prediabetes in the US in 2000: opportunities for prevention. *Diabetes Care*. 2003;26:645-9.

Diabetes), and Chapter 5 (Helping Patients Make Lifestyle Changes).

- Never tell patients that they have “a little bit of diabetes” or “borderline diabetes.” Patients need to know that they have prediabetes, which already has an increased risk of mortality, but that they can do specific things to prevent progression to diabetes.
- Discuss the importance of smoking cessation as a strategy for helping to prevent cardiovascular complications (see Chapter 12, Complications of Diabetes).
- Stress that incremental changes are more long-lasting and effective than sudden, drastic changes in eating and exercise behaviors.
- Ask patients to choose a behavioral goal at the end of your discussion; for example: “Will you do anything between now and our next visit to help lower your risk for diabetes?”
- Refer for education and/or medical nutrition therapy. Some, but not all, insurance plans and managed care organizations offer reimbursement for education and medical nutrition counseling for the prevention of diabetes. Being prepared by first clarifying reimbursement with the diabetes educator or common insurance plans in your area will facilitate referral.

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*What educational issues should I discuss with patients with a new diagnosis of diabetes?*

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Diabetes education in newly diagnosed patients can relieve the anxiety associated with misconceptions and fears about the disease. Provide patients with resources for learning more about diabetes and referral for diabetes education and medical nutrition therapy. Of particular importance is a discussion about the patient’s role in managing his or her own disease. Ongoing counseling and self-management support with a diabetes educator, dietitian, or the patient’s primary care team is important for success.

- At the time of diagnosis, patients with diabetes (type 1 or type 2) experience much distress. These patients report feeling shocked, guilty, angry, anxious, depressed, and helpless. It is important to ask patients how they feel about their diagnosis, what their concerns and fears are, what questions they have, and how you can be of help.
- Provide factual but hopeful messages. For example: “Diabetes is a serious disease, but it can be managed. It is important for you to understand that most of the day-to-day care is up to you. It is common to feel overwhelmed, angry, or frustrated at times, but I am going to do all I can to help you, and we are going to work together to make sure you get the information and help that you need.”
- Regardless of the age of the person with diabetes, the diagnosis affects the entire family. If possible, talk with the family members and address their fears, concerns, and questions; encourage them to learn all that they can about the disease as well.

## Screening for Diabetes

### Who should be screened for diabetes?

Screening for diabetes (as opposed to the diagnosis of diabetes) consists of testing asymptomatic persons who may be at increased risk of the disease. Although screening is best when carried out as part of a health-care office visit, community screening may help identify patients who do not have maintenance health care. Screening is performed to identify those with type 2 diabetes and, in pregnant women, gestational diabetes.

Type 2 diabetes has a prodromal stage during which the patient is asymptomatic but has an increased risk of diabetes-related complications. The onset of diabetes in this population is estimated to occur approximately 4 to 7 years before the clinical diagnosis. For this reason, and because a large proportion of patients with type 2 diabetes have complications at the time of diagnosis, the ADA recommends screening for type 2 diabetes in all asymptomatic people 45 years or older (**Table 3-2**). If screening is negative for diabetes, testing should be repeated at 3-year intervals. In persons with additional risk factors for developing diabetes, screening should begin at a younger age and/or should be performed more frequently.

A recent study has shown that higher fasting glucose levels that are still within the normal glycemic range (i.e., below 100 mg/dL) may act as an independent risk factor for type 2 diabetes among young men. These results underline the importance of screening asymptomatic patients for type 2 diabetes and closely monitoring high-risk patients.

The incidence of type 2 diabetes is increasing in children and adolescents. Starting at age 10 years or at the onset of puberty (whichever is earlier), children at high risk of type 2 diabetes (**Table 3-3**) should be screened by fasting plasma glucose level. As with adults, a positive result (fasting glucose values  $\geq 126$  mg/dL)

Table 3-2. Criteria for Screening for Type 2 Diabetes in Adults

1. All asymptomatic adults 45 years and older should be screened every 3 years.
2. Adults with a body mass index  $\geq 25$  ( $\geq 23$  for Asian Americans, according to the International Diabetes Federation and World Health Organization) and with any of the following additional risk factors should be screened more frequently and screening should be started at a younger age:
  - Sedentary lifestyle
  - First-degree relative with diabetes
  - Member of an ethnic group with a high prevalence of diabetes (Hispanic, Asian, American Indian, African American, Pacific Islander origin)
  - History of gestational diabetes or have delivered a baby weighing more than 9 pounds
  - History of impaired glucose tolerance or impaired fasting glucose
  - Hypertension
  - Dyslipidemia (HDL cholesterol level  $< 35$  mg/dL and/or triglyceride levels  $> 250$  mg/dL)
  - History of vascular disease
  - Polycystic ovary syndrome
  - Signs of insulin resistance (e.g., acanthosis nigricans)

Adapted from: American Diabetes Association. Standards of medical care in diabetes—2006. *Diabetes Care*. 2006;29 Suppl 1:S4-42.

should be repeated on another day to confirm the diagnosis of diabetes. Screening should be repeated every 2 years in patients who do not meet the criteria for diabetes.

Type 1 diabetes causes significant symptoms at onset and thus generally does not require screening. In addition, measurement of autoantibodies related to type 1 diabetes is not recommended for screening outside of research studies owing to the lack to knowledge regarding how to interpret and follow up abnormal results.

## Gestational Diabetes

### Who should be screened for gestational diabetes?

Whether or not a woman should be screened for gestational diabetes depends on her level of risk, which should be determined at the first prenatal visit.

**Low risk:** Women with *all* of the following features are at low risk of gestational diabetes and do not require screening:

- Age  $< 25$  years

Table 3-3. Criteria for Screening for Type 2 Diabetes in Children

<p>1. Obesity as defined by body mass index &gt;85th percentile for age and sex or weight &gt;120% of ideal for height</p> <p><i>Plus</i></p> <p>2. Any two of the following risk factors:</p> <ul style="list-style-type: none"> <li>• Family history of type 2 diabetes in first- or second-degree relative</li> <li>• At-risk race/ethnicity (American Indian, African-American, Hispanic, Asian/Pacific Islander)</li> <li>• Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome)</li> </ul>
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Adapted with permission from: American Diabetes Association. Type 2 diabetes in children and adolescents. *Diabetes Care*. 2000;23:381-9.

- Normal body weight
- No family history of diabetes
- No personal history of glucose intolerance
- No history of poor obstetrical outcome
- Not a member of an ethnic group with a high prevalence of diabetes (Hispanic, African American, Asian, Native American, Pacific Islander)

**High risk:** Women with *any one* of the following features are at high risk of gestational diabetes and should be tested as soon as possible and retested (if initial results are negative) at 24 to 28 weeks' gestation:

- High body mass index
- Personal history of gestational diabetes
- Family history of diabetes
- Glycosuria

**Average risk:** Women at average risk do not meet the criteria for either low risk or high risk. These women do not need to be screened for gestational diabetes until 24 to 28 weeks' gestation.

Protocols for screening for gestational diabetes follow either a one- or two-step approach (Table 3-4).

### *How is gestational diabetes managed?*

Women who have gestational diabetes and women with diabetes who are pregnant should

Table 3-4. Protocols for Screening for Gestational Diabetes

<p><b>One-step approach:</b> Perform 100-g oral glucose tolerance test (OGTT) test directly on all patients who require screening.</p> <p><b>Two-step approach:</b> Perform initial screening test with 50-g oral glucose load. In patients with a glucose concentration &gt;140 mg/dL 1 hour after glucose load, perform 100-g OGTT test.</p> <p><b>Criteria for diagnosis:</b> The OGTT test is performed in the morning after an overnight fast of 8 to 14 hours. The criteria for diagnosis after 100-g OGTT are as follows:</p> <table border="1"> <tr> <td>Fasting</td> <td>≥105 mg/dL</td> </tr> <tr> <td>1 hour after load</td> <td>≥190 mg/dL</td> </tr> <tr> <td>2 hours after load</td> <td>≥165 mg/dL</td> </tr> <tr> <td>3 hours after load</td> <td>≥145 mg/dL</td> </tr> </table> <p>Two or more of the plasma glucose values must be met or exceeded for a positive diagnosis of gestational diabetes.</p>	Fasting	≥105 mg/dL	1 hour after load	≥190 mg/dL	2 hours after load	≥165 mg/dL	3 hours after load	≥145 mg/dL
Fasting	≥105 mg/dL							
1 hour after load	≥190 mg/dL							
2 hours after load	≥165 mg/dL							
3 hours after load	≥145 mg/dL							

Data from: American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2006;29 Suppl 1:S43-8.

be followed closely with the help of a diabetes educator, a diabetologist, an obstetrician familiar with diabetes management, a nutritionist, and a social worker to prevent poor outcomes (see Chapter 13). Insulin is the treatment of choice to control blood glucose in pregnant women. Oral hypoglycemic agents, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and cholesterol-lowering agents should be stopped as soon as possible, and blood pressure medications should be changed to drugs known to be safe during pregnancy. Evaluation and management of complications of diabetes should be performed before or as soon as possible after the onset of pregnancy. Women with a diagnosis of gestational diabetes should be screened for diabetes 6 weeks postpartum and periodically thereafter.

### *What educational issues should I discuss with women with gestational diabetes?*

All women with gestational diabetes should be referred for diabetes self-management education and medical nutrition therapy, which are covered benefits under most insurance plans. Important areas to discuss with patients include:

- The importance of near-normal blood glucose levels to prevent complications to the baby

- Meal planning to manage blood glucose levels, not to lose weight
- Blood glucose monitoring and how to use the results
- Therapies: lifestyle, then insulin—no oral drugs during pregnancy (Most women are able to stop insulin postpartum because diabetes goes away; in some women, however, the diabetes does not resolve.)
- Increased risk for type 2 diabetes in the future (Patients should be screened periodically for type 2 diabetes and for gestational diabetes early in subsequent pregnancies.)
- Postpartum preventive strategies, such as exercise and returning to prepregnancy weight
- Pre-conception counseling if type 2 diabetes continues

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