As the prevalence of type 2 diabetes mellitus (T2DM) continues to rise worldwide, so does the incidence of gestational diabetes mellitus (GDM), ranging from 1% to 14% in direct proportion to the prevalence of T2DM in that given population or ethnic group.¹

Identifying and managing gestational diabetes
GDM is commonly defined as glucose and carbohydrate intolerance that first becomes apparent during pregnancy. This condition is worth monitoring and treating, since it has been demonstrated that good metabolic control maintained throughout gestation can reduce maternal and fetal complications.5

Several studies have identified that there is an increase in the incidence of GDM, which is fueled by advancing maternal age, racial and ethnic shifts in childbearing and increasing incidence of obesity.3 New studies that have expanded our knowledge about gestational diabetes include the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study,4 the Australian Carbohydrate Intolerance in Pregnancy (ACHOIS) randomized trial5 and the Metformin in Gestational Diabetes (MiG) randomized trial.6 Each of these studies has elucidated several diagnostic and therapeutic issues.

Screening for GDM
The American Diabetes Association (ADA) recommends screening for GDM at pregnancy determination if any of the following risk factors are present:
- severe obesity
- prior history of GDM or delivery of a newborn that is large for gestational age
- glycosuria
- polycystic ovarian syndrome
- family history of T2DM.7

Women not screened early in pregnancy should undergo diabetes screening at 24 to 28 weeks gestation if any of the following are present:
- age >25 years
- overweight before pregnancy
- nonwhite race and ethnicity
- family history of diabetes or history of abnormal results at glucose tolerance testing.7

The American College of Obstetricians and Gynecologists (ACOG) has similar recommendations.8 In contrast, the World Health Organization recommends universal screening of all women for GDM at 24 to 28 weeks gestation.9 (See Table 1 for various screening tests for GDM that have been proposed.)

Glucose levels and adverse outcomes
Adverse outcomes increase continuously with glucose levels. The National Institutes of Health sponsored the HAPO study to resolve the controversy over whether maternal hyperglycemia that is less severe than in T2DM is still associated with an increased risk of adverse pregnancy outcomes.4

In the HAPO study, 25,505 pregnant women at 15 centers in nine countries underwent 75-g oral glucose tolerance testing at 24 to 32 weeks of gestation. Women with particularly elevated levels of glucose were “unblinded” and treated. The final cohort consisted only of women whose glucose values had an uncertain risk of adverse outcomes. Even in this group there was a continuous relationship between maternal glucose levels and neonatal adiposity. These results indicate strong continuous associations of increased maternal glucose levels below those diagnostic of diabetes, with increased birthweight and increased cord-blood serum C-peptide levels. So the risk of future diabetes may be affected even while in utero. When assessing perinatal outcome measures, some primary considerations include the following:
- birthweight above the 90th percentile for gestational age
- cesarean delivery
- clinical neonatal hypoglycemia
- cord-blood serum C-peptide values above the 90th percentile.

Risks of GDM with obesity
In recent years, increased attention has been paid to the substantial overlap in complications of GDM and obesity during pregnancy.10 Complications associated with GDM may be, at least in part, explained by the increased body mass index (BMI) of women with GDM. The Pregnancy Risk Assessment Monitoring System, a surveillance project of the Centers for Disease Control and Prevention, revealed that the proportion of GDM cases attributable to overweight and obese women totaled 46% in a population-based study of more than 20,000 subjects from seven states. More than 70% of the women with GDM had a pre-pregnancy BMI of at least 25 kg/m2, compared with 44.9% who did not have GDM during pregnancy.11 In addition, if a woman’s pre-pregnancy BMI is >25 kg/m2, that woman has more than double the risk of developing GDM.12

Other GDM risks
Women with GDM are at increased risk for many other health concerns with short- and long-term implications for both mother and child. Women with GDM are at higher risk for glucose-mediated macrosomia, hypertension, adverse pregnancy outcomes (stillbirth, birth trauma, cesarean section, pre-eclampsia,
Managing GDM

The strategies and techniques for managing GDM during pregnancy have greatly improved in the past two decades. Newer insulin therapies and delivery mechanisms are now available. Self-monitoring of blood glucose, exercise and adherence to dietary restrictions are now central to management plans of women with GDM. This really begins with preconception care of women with diabetes or those deemed at increased risk. However, this discussion is beyond the scope of this article, which is focusing on diabetes and women who are now pregnant.

The value of identifying and treating GDM has been well established with two large randomized trials: one conducted in the United States through the Maternal Fetal Network and the ACHOIS study conducted in Australia. The Maternal Fetal Network Study demonstrated the benefits of a collaborative management program effectively delivered by a team of providers, including nutritionists and diabetes educators. This program’s model is similar to that of chronic diabetes education, and it offers the best chance of healthy outcomes.

The ACHOIS study helped to confirm adverse perinatal outcomes in pregnancies complicated by mild, untreated gestational diabetes. Specifically, the rate of serious adverse perinatal outcomes including stillbirth, neonatal death, shoulder dystocia, bone fracture and nerve palsy were three-times higher in the control group than in the treatment group (4.4% vs. 1.4%). There were fewer infants, large for gestational age, born to the intervention group (13.4%) than to the control group (21.9%).

Weight gain and pregnancy

Guidelines for weight gain during pregnancy have been a moving target because of increasing rates of obesity and glucose intolerance during pregnancy. In 2010, the Institute of Medicine revised its guidelines for weight gain and monitoring during pregnancy, which are illustrated in Table 2.

In general, normal women should gain 25 to 35 pounds in pregnancy. This recommendation is reduced by 10 pounds in women who are overweight and by 15 pounds in obese women.
Treatments options

Diet is the mainstay of treatment in GDM, whether or not pharmacologic therapy is introduced. Dietary control should include a reduction of fat intake and the substitution of complex carbohydrates for refined carbohydrates to achieve and maintain the essential maternal blood glucose profile during gestation. The ADA also recommends nutritional counseling where the efficacy of the team approach is best used to individualize the nutrition plan based on height and weight. 

The ADA has also endorsed exercise as “a helpful adjunctive therapy” for GDM when euglycemia is not achieved by diet alone. New studies indicate that exercise—which affects insulin resistance—in the absence of either medical or obstetrical complications, is certainly a suitable intervention for GDM women with GDM.

Pharmacotherapy recommendations

If women are not able to achieve glycemic goals with diet and exercise alone, pharmacotherapy with insulin has been widely recommended and used. The gold standard has been neutral protamine Hagedorn or regular insulin for basal injections two to four times daily.

The starting insulin dose is often calculated based on the patient’s weight. Doses of 0.8 U/kg can be initiated in overweight women and 0.9-1.0 U/kg in obese women. In pregnant patients who have diabetes, the rationale for insulin therapy is based on mimicking the normal physiology of insulin secretion.

Conventionally there are two methods for administering insulin: subcutaneous multiple daily injections and continuous subcutaneous insulin infusion via a pump. The basal insulin is supplied by the administration of NPH, or neutral protamine Hagedorn, insulin at bedtime or both before breakfast and at bedtime. An insulin pump can also deliver continuous infusion of a rapid-acting insulin analog, such as insulin lispro or insulin aspart, for motivated patients who are able to check their blood glucose levels and use glucose monitoring devices frequently.

The meal-time administration of insulin includes insulin lispro or insulin aspart before meals by means of subcutaneous injection or with an insulin pump (0 to 15 minutes) or regular insulin given subcutaneously before meals (30 to 45 minutes).

This basal bolus algorithm characterizes intensified therapy (multiple injections daily vs conventional therapy (one or two injections daily). If after three to seven days the patient with GDM does not achieve the desired level of glycemic control, the total insulin dose should increase from 10% to 20% and thereafter should be adjusted when needed.

Theoretically, the use of oral agents is appealing in that subcutaneous injections can be avoided, leading to subsequent improvement in glucose levels, as well as patient satisfaction. Although use in the T2DM community is common, oral sulfonylureas, including glyburide, have not yet been endorsed by the ADA and ACOG because of concerns about impact on perinatal outcomes. The MiG trial revealed that 46% of women randomly assigned to receive metformin eventually required the addition of insulin, although the adverse outcome rate was not higher in the metformin group.

Postpartum concerns

Women who have GDM are at higher risk of developing T2DM in the future. This risk has been shown to be as high as 50% for future T2DM risk. The ADA recommends that all women with GDM be screened at six to 12 weeks after delivery for persistent diabetes and then every three years thereafter.

Those women who integrate regular

Table 2

Institute of Medicine Guidelines for Monitoring and Weight Gain

<table>
<thead>
<tr>
<th>Monitoring</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During pregnancy</strong></td>
<td></td>
</tr>
<tr>
<td>Glucose level targets (whole blood)</td>
<td>If BMI &lt;18.5 kg/m²,</td>
</tr>
<tr>
<td>Fasting ≤95 mg/dL</td>
<td>28-40 lbs recommended,</td>
</tr>
<tr>
<td>1-hour ≤130-140 mg/dL</td>
<td>with 1.0-1.3 lbs/week</td>
</tr>
<tr>
<td>2-hour ≤120 mg/dL</td>
<td>in 2nd/3rd trimesters</td>
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<tr>
<td>Self-monitoring of kick counts</td>
<td></td>
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<tr>
<td>during the last 8-10 weeks of pregnancy</td>
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<tr>
<td><strong>Fetal Nonstress Testing (NST)</strong></td>
<td></td>
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<tr>
<td>At 32-37 weeks, followed by contraction stress testing, Doppler evaluation of the umbilical artery, and/or biophysical testing if NST equivocal Fetal ultrasound for assessment of congenital malformations and estimates of fetal weight</td>
<td></td>
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<tr>
<td><strong>After pregnancy</strong></td>
<td></td>
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<tr>
<td>Postpartum screening consisting of fasting glucose alone</td>
<td>If BMI ≥30 kg/m²,</td>
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<tr>
<td>OR</td>
<td>11-20 lbs recommended,</td>
</tr>
<tr>
<td>2-hour 75 g oral glucose tolerance test</td>
<td>with 0.4-0.6 lbs/week</td>
</tr>
<tr>
<td>Glucose level targets (plasma)</td>
<td>in 2nd/3rd trimesters</td>
</tr>
<tr>
<td>fasting ≤100 mg/dL</td>
<td></td>
</tr>
<tr>
<td>2-hour ≤140 mg/dL after a 75 g challenge</td>
<td>BMI &lt;25 kg/m²</td>
</tr>
</tbody>
</table>

physical activity and moderate weight loss can reduce the future diagnosis of diabetes by nearly 50%. Further, the thiazolidinediones (TZDs) have shown a protective effect in women who take them after having gestational diabetes. The Troglitazone in Prevention of Diabetes (TRIPOD) and Pioglitazone in Prevention of Diabetes (PIPOD) trials demonstrated that the risk for future diabetes can be significantly reduced and last longer than the treatment duration.

Final notes
If recent HAPO recommendations for diagnosis are adopted, GDM is poised to become one of the most common co-morbidities of pregnancy. Even if current diagnostic criteria remain unchanged, the prevalence of GDM will continue to increase as obesity rates rise. Close attention to these risks, early active intervention by physicians, effective use of nutritionists with diabetic educators and appropriate use of pharmacologic therapy can help GDM patients complete a healthy pregnancy and have fewer long-term morbidities.

References