

# Gestational Diabetes Mellitus

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**G**estational diabetes mellitus (GDM) is defined as glucose intolerance that begins or is first detected during pregnancy.<sup>1-3</sup> GDM affects ~ 7% of all pregnancies, resulting in > 200,000 cases per year.<sup>2</sup> Depending on the population sample and diagnostic criteria, the prevalence may range from 1 to 14%.<sup>1,2</sup> Of all pregnancies complicated by diabetes, GDM accounts for ~ 90%.<sup>1</sup>

## DIAGNOSTIC CRITERIA

The oral glucose tolerance test (OGTT) most commonly used to diagnose GDM in the United States is the 3-hour, 100-g OGTT. According to diagnostic criteria recommended by the American Diabetes Association (ADA), GDM is diagnosed if two or more plasma glucose levels meet or exceed the following thresholds: fasting glucose concentration of 95 mg/dl, 1-hour glucose concentration of 180 mg/dl, 2-hour glucose concentration of 155 mg/dl, or 3-hour glucose concentration of 140 mg/dl.<sup>1,2,4</sup> These values are lower than the thresholds recommended by the National Diabetes Data Group and are based on the Carpenter and Coustan modification.<sup>5</sup> The ADA recommendations also include the use of a 2-hour 75-g OGTT with the same glucose thresholds listed for fasting, 1-hour, and 2-hour values.<sup>1,2</sup>

The World Health Organization (WHO) diagnostic criteria, which are used in many countries outside of North America, are based on a 2-hour 75-g OGTT. GDM is diagnosed by WHO criteria if either the fasting glucose is > 126 mg/dl or the 2-hour glucose is > 140 mg/dl. Table 1 summa-

**Table 1. ADA and WHO Criteria for the Diagnosis of GDM<sup>2,6</sup>**

	ADA 100-g OGTT	ADA 75-g OGTT	WHO 75-g OGTT
<b>Fasting (mg/dl)</b>	95	95	126
<b>1-hour (mg/dl)</b>	180	180	—
<b>2-hour (mg/dl)</b>	155	155	140
<b>3-hour (mg/dl)</b>	140	—	—

For the ADA criteria, two or more of the values from either the 100- or 75-g OGTT must be met or exceeded to make the diagnosis of GDM. For the WHO criteria, one of the two values from the 75-g OGTT must be met or exceeded to make the diagnosis of GDM.

rizes ADA and WHO criteria for the diagnosis of GDM.

The Brazilian Gestational Diabetes Study evaluated the ADA and WHO diagnostic criteria against pregnancy outcomes in an observational cohort study of nearly 5,000 women. Using the 2-hour 75-g OGTT criteria proposed by the ADA, the incidence of GDM was 2.4% (95% CI 2.0–2.9). The incidence of GDM using the WHO criteria was 7.2% (6.5–7.9). Both the ADA and WHO criteria predicted an increased risk of macrosomia, preeclampsia, and perinatal death. However, this increase was not statistically significant for macrosomia by the ADA criteria or for perinatal death by the WHO criteria. This study concluded that, although the WHO criteria identified more cases of GDM, both the ADA and WHO criteria are valid options for the diagnosis of GDM and the prediction of adverse pregnancy outcomes.<sup>6</sup>

## PATHOGENESIS

Pregnancy is a diabetogenic condition characterized by insulin resistance with a compensatory increase in  $\beta$ -cell response and hyperinsulinemia. Insulin resistance usually begins in the second trimester and progresses throughout the remainder of the pregnancy. Insulin sensitivity is reduced by as much as 80%. Placental secretion of hormones, such as progesterone, cortisol, placental lactogen, prolactin, and growth hormone, is a major contributor to the insulin-resistant state seen in pregnancy. The insulin resistance likely plays a role in ensuring that the fetus has an adequate supply of glucose by changing the maternal energy metabolism from carbohydrates to lipids.<sup>7</sup>

Women with GDM have a greater severity of insulin resistance compared

## IN BRIEF

Gestational diabetes mellitus (GDM) is a common condition affecting ~ 7% of all pregnancies. The detection of GDM is important because of its associated maternal and fetal complications. Treatment with medical nutrition therapy, close monitoring of glucose levels, and insulin therapy if glucose levels are above goal can help to reduce these complications.

to the insulin resistance seen in normal pregnancies. They also have an impairment of the compensatory increase in insulin secretion, particularly first-phase insulin secretion. This decrease in first-phase insulin release may be a marker for deterioration of  $\beta$ -cell function.<sup>7</sup> Xiang et al.<sup>8</sup> found that Latino women with GDM had increased resistance to the effects of insulin on glucose clearance and production compared with normal pregnant women. In addition, they found that the women with GDM had a 67% reduction in their  $\beta$ -cell compensation compared with normal pregnant control subjects.

There is also a subset of women with GDM who have evidence of islet cell autoimmunity. The reported prevalence of islet cell antibodies in women with GDM ranges from 1.6 to 38%. The prevalence of other islet autoantibodies, including insulin autoantibodies and glutamic acid decarboxylase antibodies, has also been variable. These women may be at risk for developing an autoimmune form of diabetes later in life.<sup>9</sup> Finally, in ~5% of all cases of GDM, the  $\beta$ -cell's inability to compensate for the insulin resistance is the result of a defect in the  $\beta$ -cell, such as a mutation in glucokinase.<sup>7</sup>

## COMPLICATIONS

There are both fetal and maternal complications associated with GDM. Fetal complications include macrosomia, neonatal hypoglycemia, perinatal mortality, congenital malformation, hyperbilirubinemia, polycythemia, hypocalcemia, and respiratory distress syndrome.<sup>1-3,10-19</sup> Macrosomia, defined as birth weight > 4,000 g,<sup>7</sup> occurs in ~20–30% of infants whose mothers have GDM.<sup>10</sup> Maternal factors associated with an increased incidence of macrosomia include hyperglycemia,<sup>3,10,11</sup> high BMI,<sup>7,10-12</sup> older age,<sup>11</sup> and multiparity.<sup>7,11</sup> This excess in fetal growth can lead to increased fetal morbidity at delivery, such as shoulder dystocia,<sup>11</sup> and an increased rate of cesarean deliveries.<sup>11,13</sup>

Neonatal hypoglycemia can occur within a few hours of delivery. This results from maternal hyperglycemia causing fetal hyperinsulinemia.<sup>7</sup>

The association between GDM and perinatal mortality has been more controversial. Several studies have concluded that the rate of perinatal mortality (including stillbirths and neonatal deaths) was increased in women with GDM in the past.<sup>14-16</sup> However, recent studies have shown that, with the combination of increased antepartum monitoring, medical nutrition therapy (MNT), and insulin therapy if needed, this difference in perinatal mortality rates is potentially avoidable.<sup>17,18</sup>

Another controversial association is that between GDM and congenital malformations. The incidence of a major malformation in an infant whose mother does not have any history of diabetes is 1–3%. In women with a history of diabetes before pregnancy, this risk is increased three to eight times.<sup>19</sup> In women with GDM, an increased incidence of malformations occurs when the mother also has fasting hyperglycemia.<sup>19,20</sup>

Long-term complications to the offspring include an increased risk of glucose intolerance, diabetes, and obesity.<sup>2</sup>

Maternal complications associated with GDM include hypertension, preeclampsia, and an increased risk of cesarean delivery.<sup>6,11</sup> The hypertension may be related to insulin resistance. Therefore, interventions that improve insulin sensitivity may help prevent this complication.<sup>21</sup> In addition, women with a history of GDM have an increased risk of developing diabetes after pregnancy compared to the general population, with a conversion rate of up to 3% per year.<sup>7</sup>

## SCREENING

There is no worldwide agreement on the best way to screen for GDM. Previously, universal screening at 24–28 weeks of gestation with a 50-g oral glucose challenge test was recommended. Women with a 1-hour glucose level > 140 mg/dl were referred for a diagnostic OGTT.

However, Naylor et al.<sup>22</sup> developed a selective screening approach with data collected from 3,131 pregnant women. They randomly selected data from half of the women and categorized them into three groups (low-, intermediate-, and high-risk) based on a complex scoring system using weighted risk factors: age, BMI before pregnancy, and race. Their strategy did not entail screening women who were low risk. The remainder of women were screened with a 50-g oral glucose challenge test, with the threshold for a positive result based on their risk score. Naylor et al. found that this selective screening approach resulted in a 34.6% reduction in the number of screening tests performed, without a decrease in the detection rate of GDM.<sup>22</sup> The ADA now recommends selective screening for GDM.<sup>1,2</sup>

According to the ADA guidelines, patients should be screened for risk factors for GDM at their initial visit. A woman is considered high risk if she has one or more of the following: marked obesity, personal history of GDM, glucose intolerance or glycosuria, or a strong family history of type 2 diabetes. A woman is considered low risk if she meets all of the following criteria: age < 25 years, normal prepregnancy weight, not a member of an ethnic/racial group with a high prevalence of diabetes (e.g., Hispanic American, Native American, Asian American, African American, or Pacific Islander), no known diabetes in first-degree relatives, no history of abnormal glucose tolerance, and no history of a poor obstetric outcome. A woman is considered intermediate risk if she does not fall into either the high- or low-risk category.

If a woman is high risk, glucose testing should be done as soon as possible. If the initial testing is negative, the woman should be retested between 24 to 28 weeks of gestation. If she is intermediate risk, she should undergo glucose testing at 24 to 28 weeks. If she is low risk, the ADA does not recommend screening for GDM.<sup>1-3</sup> An additional possible risk factor for GDM not men-

tioned in the list above is a history of polycystic ovary syndrome.<sup>23,24</sup> However, other studies have not confirmed this finding.<sup>25,26</sup>

The ADA recommends two approaches to screening for GDM if a woman has one or more risk factors—a one-step or a two-step approach. The more commonly used two-step approach involves initial nonfasting screening with the 50-g oral glucose challenge test, followed by a 1-hour serum glucose concentration. If the glucose level exceeds the glucose threshold value on this test, the patient is further evaluated with the diagnostic OGTT described previously under diagnostic criteria. A 1-hour glucose value > 140 mg/dl identifies ~ 80% of women with GDM. A 1-hour glucose value > 130 mg/dl identifies ~ 90% of women with GDM, but it has a higher false positive rate.<sup>1-3</sup> Either value is accepted by the ADA and the American College of Obstetricians and Gynecologists (ACOG) as abnormal.<sup>1,2,27</sup>

The one-step approach requires a diagnostic OGTT without prior screening with the 50-g 1-hour glucose challenge test. This may be cost-effective in some high-risk patients. Of note, if a patient has a fasting plasma glucose level > 126 mg/dl or a random plasma glucose level > 200 mg/dl, this meets the threshold for diabetes mellitus and should be confirmed on a subsequent day.<sup>1-3</sup>

Screening, whether it is universal or selective, remains a controversial subject. Contradictory to the ADA recommendations described above, the United States Preventive Services Task Force concluded that there was insufficient evidence to recommend for or against screening for GDM. Although they found fair to good evidence that screening and treatment of GDM reduced the rate of fetal macrosomia, they found insufficient evidence that screening significantly reduced important adverse maternal or fetal outcomes, including outcomes related to macrosomia. In addition, they had concerns about the potential harms and costs of screening, especially given the high false-positive

rate (> 80%) of the 50-g glucose challenge test.<sup>4</sup>

## TREATMENT

### Glucose Monitoring

Self-monitoring of blood glucose is recommended for women with GDM. The goal of monitoring is to detect glucose concentrations elevated enough to increase perinatal mortality. The Fourth International Workshop-Conference on Gestational Diabetes Mellitus recommends maintaining the following capillary blood glucose values: preprandial glucose < 95 mg/dl, 1-hour postprandial glucose < 140 mg/dl, and 2-hour postprandial glucose < 120 mg/dl.<sup>3</sup> ACOG guidelines are the same except that the 1-hour postprandial glucose value is considered acceptable at either 130 or 140 mg/dl.<sup>27</sup> Jovanovic-Peterson et al.<sup>28</sup> suggest guidelines that are a little stricter: fasting glucose < 90 mg/dl and 1-hour postprandial glucose < 120 mg/dl.<sup>28</sup>

One prospective study of 668 patients (334 with GDM and 334 control subjects) found that women with GDM who had a mean blood glucose level between 87 and 104 mg/dl had incidence rates of intrauterine growth retardation (IUGR) and large for gestational age (LGA) infants comparable to the control group. However, women who had mean blood glucose values < 87 mg/dl had a higher incidence of infants with IUGR, whereas women who had mean blood glucose values > 104 mg/dl had a higher incidence of LGA infants. This study suggests that although it is important to treat hyperglycemia in GDM, it is also important not to overtreat because this can increase the risk of IUGR.<sup>29</sup>

It is important for women to check postprandial glucose levels because these have been shown to correlate more with macrosomia than do fasting levels. The Diabetes in Early Pregnancy Study found that third-trimester postprandial glucose levels were the strongest predictor of percentile birth weight.<sup>30</sup> In women with GDM who require insulin

therapy, adjustments of their insulin regimens based on postprandial, rather than preprandial, glucose levels decreased the incidence of neonatal hypoglycemia, macrosomia, and cesarean delivery for cephalopelvic disproportion.<sup>31</sup>

### Medical Nutrition Therapy

The goals of MNT are to provide adequate nutrition for the mother and fetus, provide sufficient calories for appropriate maternal weight gain, maintain normoglycemia, and avoid ketosis. In general, there is not an increased energy requirement during the first trimester of pregnancy. However, most normal-weight women require an additional 300 kcal/day in the second and third trimester.<sup>32</sup>

In normal-weight women with GDM, the recommended daily caloric intake is 30 kcal/kg/day based on their present pregnant weight.<sup>33</sup> In women with GDM who are overweight (BMI > 30 kg/m<sup>2</sup>), a 33% calorie restriction of their estimated energy needs is recommended (~ 25 kcal/kg/day based on their present pregnant weight). This level of calorie restriction is not associated with an elevation of free fatty acids or ketonuria.<sup>32,34</sup> Some authors recommend further calorie restriction for women who are morbidly obese.<sup>33</sup> However, caution must be taken to avoid ketosis, which can be seen with more aggressive calorie restriction.<sup>34</sup>

Ketonemia in mothers with diabetes during pregnancy has been associated with lower IQ levels and impaired psychomotor development in their children.<sup>35,36</sup> Monitoring with prebreakfast ketone measurements is recommended for patients who are on a hypocaloric or carbohydrate-restricted diet.<sup>32</sup>

Carbohydrates should be distributed throughout the day.<sup>32</sup> Eating three small-to moderate-sized meals and three snacks per day is recommended. Limiting carbohydrates to 40% of the total daily caloric intake has been shown to decrease postprandial glucose levels.<sup>33</sup> Further limitation of carbohydrates at breakfast to 33% may be required to

meet the desired postprandial glucose goals because insulin resistance is greatest in the morning.<sup>37</sup> In addition, carbohydrate restriction to < 42% in patients with GDM resulted in a decreased incidence of LGA infants, a decrease in cesarean deliveries for macrosomia and cephalopelvic disproportion, and a decreased need for insulin therapy compared to patients on a diet with a higher carbohydrate content (45–50%).<sup>38</sup> Consuming carbohydrates with a low glycemic index also results in lower postprandial glucose levels, especially late in gestation.<sup>39</sup>

### Exercise

The role of exercise in women with GDM has been controversial in the past because maternal exercise on a bicycle ergometer has been associated with fetal bradycardia. Subsequent small studies<sup>40,41</sup> have shown small transient increases in fetal heart rate after maternal exercise. There were no fetal complications in either study.

Durak et al.<sup>42</sup> found that uterine activity, defined as contractions with an external tocometer deflection of > 15 mmHg above baseline for > 30 seconds, varied in response to different types of aerobic exercise, even at comparable levels of exertion. The bicycle ergometer, treadmill, and rowing ergometer led to uterine activity in 50, 40, and 10% of exercise sessions, respectively. The recumbent bicycle and upper body ergometer did not lead to any increase in uterine activity. Therefore, the authors concluded that the recumbent bicycle and upper body ergometer were the safest forms of aerobic exercise for pregnant women. In addition, they recommended teaching women to palpate their uterus during exercise to detect subclinical contractions and to discontinue the exercise if contractions occur.

A potential benefit of exercise in women with GDM is improved glycemic control. One small trial randomized women with GDM to diet and exercise with an arm ergometer versus diet alone for 6 weeks. Researchers

found that the diet-and-exercise group had a significant decrease in glycated hemoglobin levels and in both fasting and 1-hour plasma glucose levels during a glucose challenge test compared to the diet-alone group.<sup>43</sup> Another trial, in which women with GDM were randomized to a partially home-based exercise program, did not find any reduction in blood glucose level, although the women did have an improvement in cardiovascular fitness.<sup>40</sup> Based on the potential benefits of exercise in women with GDM, the ADA recommends starting or continuing a program of moderate exercise in women without medical or obstetrical contraindications.<sup>2</sup>

### Insulin

Insulin therapy is the most commonly used treatment when MNT fails to maintain blood glucose levels at the desired ranges or when there is evidence of excessive fetal growth. Small studies have demonstrated a decrease in macrosomia<sup>44,45</sup> as well as related morbidities including operative deliveries and birth trauma in women with GDM who were treated with insulin.<sup>45</sup>

A large, prospective, population-based study of almost 2,500 women with GDM compared the effect of intensive versus conventional management of GDM. The women randomized to the intensive management group were given memory reflectance meters and instructed to monitor their blood glucose seven times per day (fasting, preprandial, 2-hour postprandial, and bedtime). The women in the conventional management group were instructed to monitor four times per day (fasting and 2-hour postprandial) in addition to weekly fasting and 2-hour postprandial glucose measurements during clinic visits. Both groups were treated with diet and insulin as needed to reach the following goals: overall mean blood glucose 90–100 mg/dl, fasting blood glucose 60–90 mg/dl, and postprandial blood glucose < 120 mg/dl. Overall, 66% of the women in the intensive management group were treated with insulin versus 36% of

women in the conventional management group.

This study demonstrated a decreased rate of macrosomia, cesarean section, fetal metabolic complications, shoulder dystocia, neonatal intensive care unit days, and respiratory complications in the intensive management group. Another important consideration of this study is that GDM was defined as only one or more abnormal OGTT values, rather than the current standard of two or more abnormal glucose levels.<sup>46</sup> Other studies have also shown improvement in rates of macrosomia and other maternal and fetal complications by treating women who do not meet the criteria for GDM but who have evidence of impaired carbohydrate tolerance as determined by an abnormal screening 50-g glucose challenge test and/or one or more abnormal results on OGTT.<sup>47–49</sup>

Because there are no data demonstrating an optimal insulin regimen, the type and dose of insulin must be tailored to meet each patient's requirements.<sup>3,27</sup> Human insulin is currently recommended by the ADA.<sup>2,50</sup> However, one study of 42 women with GDM diagnosed at 14–32 weeks of gestation found that insulin lispro was as effective as regular insulin in controlling glucose levels with fewer episodes of hypoglycemia. Anti-insulin antibody levels were similar in the two groups. Additionally, the results of umbilical cord blood in four patients who received continuous intravenous insulin lispro and dextrose infusions intrapartum to assess placental insulin transfer did not detect any insulin lispro.<sup>51</sup> Although insulin lispro appears to be safe in pregnancy if started after 14 weeks of gestation, it is considered to be in Pregnancy Category B by the Food and Drug Administration (FDA), and the official recommendation of the ADA is to use human insulin until further studies verify the safety of insulin lispro.<sup>2</sup>

The short-term efficacy of insulin aspart was evaluated in a small study of 15 women with GDM during standardized meal tests. Although this study found that insulin aspart was effective in

decreasing postprandial glucose concentration, further studies need to be done to ensure the safety of this medication in pregnant women.<sup>52</sup> Insulin aspart is considered to be in Pregnancy Category C by the FDA.

The use of insulin glargine in humans has only been reported in case reports. There have been no clinical trials evaluating the use of insulin glargine in pregnancy. It is currently considered to be in Pregnancy Category C by the FDA.<sup>53</sup>

### Oral Agents

Currently, oral hypoglycemic agents are not recommended by the ADA or ACOG.<sup>2,27</sup> The older sulfonylureas chlorpropamide and tolbutamide could cross the placenta, stimulate the fetal pancreas, and cause fetal hyperinsulinemia.<sup>22,54</sup> However, the transfer of glyburide, a second-generation sulfonylurea, across the human placenta was insignificant in experimental models.<sup>54,55</sup>

This finding led to a clinical trial of 404 women with GDM randomized to either glyburide or insulin therapy at 11–33 weeks of gestation. There were no significant differences in glycemic control or adverse fetal outcomes. In addition, glyburide was not detected in the cord serum of any infants in the glyburide group.<sup>56</sup>

Smaller studies have also supported the safety of glyburide use in pregnancy.<sup>57–59</sup> In one of these trials, women with GDM who were treated with glyburide had fewer asymptomatic hypoglycemic episodes compared to women with GDM treated with insulin, although the clinical significance of these hypoglycemic episodes is unknown.<sup>59</sup>

Thus, although glyburide appears to be safe in pregnancy based on the above studies, it is important to recognize that these studies in aggregate are small and not adequately powered to detect clinically important, relatively rare outcomes in pregnancy. Furthermore, glyburide is considered to be in Pregnancy Category C by the FDA, and therefore it is not currently recommended by the ADA or ACOG until larger studies confirm its

safety.<sup>2</sup> Another potential concern with the use of glyburide in GDM is possible impairment of myocardial ischemic preconditioning.<sup>60</sup>

Metformin has also been used to treat pregnant women with GDM. A retrospective cohort study found an increased prevalence of preeclampsia and perinatal mortality in women treated with metformin. However, the women in the metformin group were more obese and older, and their treatment was begun later in gestation.<sup>57</sup> Recent studies involving women with polycystic ovary syndrome or women with type 2 diabetes who continue metformin in pregnancy have found no adverse pregnancy outcomes.<sup>61,62</sup>

Although previous studies have been small, there is an ongoing prospective, randomized controlled trial in New Zealand and Australia comparing metformin with insulin in women with GDM. This study will help to answer questions about the safety of metformin during pregnancy.<sup>62</sup> Metformin is listed as Pregnancy Category B by the FDA.

### ANTEPARTUM FETAL ASSESSMENT

ACOG recommends antepartum fetal assessment in women whose blood glucose is poorly controlled, who require insulin therapy, who have a history of an adverse obstetrical event, or who have a history of a hypertensive disorder. Providers can determine which type of antepartum test to use (biophysical profile, nonstress test, or contraction stress test).

The role of antepartum testing in women with well-controlled GDM is less clear.<sup>27</sup> The recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus are to consider nonstress testing starting at 32 weeks of gestation in patients on insulin and at or near term in patients managed by diet alone.<sup>3</sup>

Recent trials have assessed the usefulness of fetal ultrasounds to help guide the management of patients with GDM. One study found that a fetal abdominal

circumference > 70th percentile at 30 weeks of gestation was associated with an increased risk of macrosomia.<sup>63</sup> A subsequent trial randomized 199 women to management based on maternal glycemia alone or glycemia plus ultrasound. The glucose thresholds for the initiation of insulin differed in the two groups. The thresholds in the glycemia-alone group were fasting glucose repeatedly > 90 mg/dl or 2-hour postprandial glucose > 120 mg/dl. The thresholds in the glycemia-plus-ultrasound group were fasting glucose > 120 mg/dl, 2-hour postprandial glucose > 200 mg/dl, or fetal abdominal circumference > 75th percentile. Ultrasound examinations were performed at entry and every 4 weeks starting at 20 weeks of gestation. Researchers found that neonatal outcomes were equivalent and proposed that including fetal growth in the assessment of women with GDM may decrease glucose testing in low-risk pregnancies. Therefore, antepartum fetal assessment with ultrasound may play a role in the future management of patients with GDM.<sup>64</sup>

### PERIPARTUM CONSIDERATIONS

When glycemic control is acceptable and there are no other known complications, routine delivery before 40 weeks of gestation is not recommended.<sup>27</sup> One randomized trial of women with insulin-treated diabetes (93% of whom had GDM) found that although induction of labor at 38 weeks of gestation resulted in a smaller proportion of infants who were large for gestational age, there was no difference in the rates of cesarean delivery or shoulder dystocia.<sup>65</sup> If a delivery is indicated before 39 weeks, pulmonary maturity should be assessed by amniocentesis before induction if possible.<sup>27</sup>

The rate of cesarean deliveries is much higher in women with GDM compared to women without GDM. The increase in rate is higher than would be expected based solely on the associated obstetric complications. Therefore, part of this increase is likely influenced by

physician knowledge of a history of GDM.<sup>13</sup> ACOG recommends counseling women about the possibility of cesarean section without labor when the estimated fetal weight is > 4,500 g. If the estimated fetal weight is 4,000–4,500 g, additional risk factors for shoulder dystocia, such as clinical pelvimetry, progression of labor, and patient's past delivery history, should be considered.<sup>27</sup>

### POSTPARTUM CONSIDERATIONS

Women with GDM have an increased risk of developing diabetes, most commonly type 2 diabetes, after pregnancy. Although follow-up studies on the cohort of patients used to derive the O'Sullivan and Mahan criteria for GDM found diabetes in 50% of women who had previously had GDM,<sup>27</sup> the reported prevalence varies. A recent systematic literature review of 28 studies found that the cumulative incidence of type 2 diabetes ranged from 2.6 to > 70% in studies with postpartum follow-up ranging from 6 weeks to 28 years.<sup>66</sup> A meta-analysis calculated the relative risk for developing diabetes after GDM to be 6.0 (95% CI 4.1–8.8).<sup>67</sup>

Factors associated with an increased risk of progression to diabetes within 5 years of the diagnosis of GDM include gestational age at diagnosis, the level of glycemia at diagnosis and at the first postpartum assessment, impairment of  $\beta$ -cell function, obesity, and further pregnancy.<sup>3</sup> Ethnicity may also be a risk factor for progression to diabetes. However, further studies are needed to clarify this issue.<sup>66</sup>

Maternal glycemic status should be reclassified 6 weeks or more after pregnancy ends and every 3 years thereafter as either diabetes mellitus, impaired fasting glucose, impaired glucose tolerance, or normoglycemia.<sup>1</sup> Normal values for a 2-hour OGTT are fasting < 100 mg/dl and 2-hour post-75-g glucose load < 140 mg/dl. Glucose values that meet the criteria for diabetes mellitus are > 126 mg/dl or 2-hour post-glucose load > 200 mg/dl. Impaired fasting glucose and impaired glucose tolerance

fall between these thresholds. All patients with a history of GDM should be educated about MNT, exercise, maintenance of normal body weight, the need for family planning, and symptoms suggestive of hyperglycemia.

### CONCLUSION

GDM is a common medical problem that results from an increased severity of insulin resistance as well as an impairment of the compensatory increase in insulin secretion. Pregnancy, in essence, serves as a metabolic stress test and uncovers underlying insulin resistance and  $\beta$ -cell dysfunction. GDM is associated with a variety of maternal and fetal complications, most notably macrosomia.

Controversy surrounds the ideal approach for detecting GDM, and the approaches recommended for screening and diagnosis are largely based on expert opinion. Controlling maternal glycemia with MNT, close monitoring of blood glucose levels, and treatment with insulin if blood glucose levels are not at goal has been shown to decrease fetal and maternal morbidities. In addition, certain types of exercise appear to have potential benefits in women without any contraindications.

Other treatment modalities, such as oral agents, need further study to validate their safety and efficacy. Additionally, more research on the use of antepartum fetal assessment to help guide treatment in women with GDM is needed.

Finally, postpartum management of women with GDM is critical because of their markedly increased risk of type 2 diabetes in the future.

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