

# Gestational Diabetes Mellitus

AMERICAN DIABETES ASSOCIATION

## DEFINITION, DETECTION, AND DIAGNOSIS

### Definition

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy (1). The definition applies whether insulin or only diet modification is used for treatment and whether or not the condition persists after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy.

Approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually. The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed.

### Detection and diagnosis

Risk assessment for GDM should be undertaken at the first prenatal visit. Women with clinical characteristics consistent with a high risk of GDM (marked obesity, personal history of GDM, glycosuria, or a strong family history of diabetes) should undergo glucose testing (see below) as soon as feasible. If they are found not to have GDM at that initial screening, they should be retested between 24 and 28 weeks of gestation. Women of average risk should have testing undertaken at 24–28 weeks of gestation. Low-risk status requires no glucose testing, but this category is limited to those women meeting all of the following characteristics:

- Age <25 years
- Weight normal before pregnancy

- Member of an ethnic group with a low prevalence of GDM
- No known diabetes in first-degree relatives
- No history of abnormal glucose tolerance
- No history of poor obstetric outcome

A fasting plasma glucose level >126 mg/dl (7.0 mmol/l) or a casual plasma glucose >200 mg/dl (11.1 mmol/l) meets the threshold for the diagnosis of diabetes, if confirmed on a subsequent day, and precludes the need for any glucose challenge. In the absence of this degree of hyperglycemia, evaluation for GDM in women with average or high-risk characteristics should follow one of two approaches:

**One-step approach:** Perform a diagnostic oral glucose tolerance test (OGTT) without prior plasma or serum glucose screening. The one-step approach may be cost-effective in high-risk patients or populations (e.g., some Native-American groups).

**Two-step approach:** Perform an initial screening by measuring the plasma or serum glucose concentration 1 h after a 50-g oral glucose load (glucose challenge test [GCT]) and perform a diagnostic OGTT on that subset of women exceeding the glucose threshold value on the GCT. When the two-step approach is employed, a glucose threshold value >140 mg/dl (7.8 mmol/l) identifies approximately 80% of women with GDM, and the yield is further increased to 90% by using a cutoff of >130 mg/dl (7.2 mmol/l).

With either approach, the diagnosis of GDM is based on an OGTT. Diagnostic criteria for the 100-g OGTT are derived from the original work of O’Sullivan and

Mahan, modified by Carpenter and Coustan, and are shown in Table 1. Alternatively, the diagnosis can be made using a 75-g glucose load and the glucose threshold values listed for fasting, 1 h, and 2 h (Table 2); however, this test is not as well validated for detection of at-risk infants or mothers as the 100-g OGTT.

## OBSTETRIC AND PERINATAL CONSIDERATIONS

The presence of fasting hyperglycemia (>105 mg/dl or >5.8 mmol/l) may be associated with an increase in the risk of intrauterine fetal death during the last 4–8 weeks of gestation. Although uncomplicated GDM with less severe fasting hyperglycemia has not been associated with increased perinatal mortality, GDM of any severity increases the risk of fetal macrosomia. Neonatal hypoglycemia, jaundice, polycythemia, and hypocalcemia may complicate GDM as well. GDM is associated with an increased frequency of maternal hypertensive disorders and the need for cesarean delivery. The latter complication may result from fetal growth disorders and/or alterations in obstetric management due to the knowledge that the mother has GDM.

### Long-term considerations

Women with GDM are at increased risk for the development of diabetes, usually type 2, after pregnancy. Obesity and other factors that promote insulin resistance appear to enhance the risk of type 2 diabetes after GDM, while markers of islet cell-directed autoimmunity are associated with an increase in the risk of type 1 diabetes. Offspring of women with GDM are at increased risk of obesity, glucose intolerance, and diabetes in late adolescence and young adulthood.

## THERAPEUTIC STRATEGIES DURING PREGNANCY

### Monitoring

- Maternal metabolic surveillance should be directed at detecting hyperglycemia

The recommendations in this paper are based on the evidence reviewed in the following publications: Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 21 (Suppl. 1):S5–S19, 1998; and the Proceedings of the 4th International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 21 (Suppl. 2):B1–B167, 1998.

Originally approved 1986. Most recent review/revision, 2000.

**Abbreviations:** GCT, glucose challenge test; GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; MNT, medical nutrition therapy; OGTT, oral glucose tolerance test; SMBG, self-monitoring of blood glucose.

**Table 1—Diagnosis of GDM with a 100-g oral glucose load**

	mg/dl	mmol/l
Fasting	95	5.3
1-h	180	10.0
2-h	155	8.6
3-h	140	7.8

Two or more of the venous plasma concentrations must be met or exceeded for a positive diagnosis. The test should be done in the morning after an overnight fast of between 8 and 14 h and after at least 3 days of unrestricted diet ( $\geq 150$  g carbohydrate per day) and unlimited physical activity. The subject should remain seated and should not smoke throughout the test.

severe enough to increase risks to the fetus. Daily self-monitoring of blood glucose (SMBG) appears to be superior to intermittent office monitoring of plasma glucose. For women treated with insulin, limited evidence indicates that postprandial monitoring is superior to preprandial monitoring. However, the success of either approach depends on the glycemic targets that are set and achieved.

- Urine glucose monitoring is not useful in GDM. Urine ketone monitoring may be useful in detecting insufficient caloric or carbohydrate intake in women treated with calorie restriction.
- Maternal surveillance should include blood pressure and urine protein monitoring to detect hypertensive disorders.
- Increased surveillance for pregnancies at risk for fetal demise is appropriate, particularly when fasting glucose levels exceed 105 mg/dl (5.8 mmol/l) or pregnancy progresses past term. The initiation, frequency, and specific techniques used to assess fetal well-being will depend on the cumulative risk the fetus bears from GDM and any other medical/obstetric conditions present.
- Assessment for asymmetric fetal growth by ultrasonography, particularly in early third trimester, may aid in identifying fetuses that can benefit from maternal insulin therapy (see below).

**Management**

- All women with GDM should receive nutritional counseling, by a registered dietitian when possible, consistent with the recommendations by the American Diabetes Association. Individualization of medical nutrition therapy (MNT) de-

**Table 2—Diagnosis of GDM with a 75-g oral glucose load**

	mg/dl	mmol/l
Fasting	95	5.3
1-h	180	10.0
2-h	155	8.6

Two or more of the venous plasma concentrations must be met or exceeded for a positive diagnosis. The test should be done in the morning after an overnight fast of between 8 and 14 h and after at least 3 days of unrestricted diet ( $\geq 150$  g carbohydrate per day) and unlimited physical activity. The subject should remain seated and should not smoke throughout the test.

pending on maternal weight and height is recommended. MNT should include the provision of adequate calories and nutrients to meet the needs of pregnancy and should be consistent with the maternal blood glucose goals that have been established. Noncaloric sweeteners may be used in moderation.

- For obese women (BMI  $>30$  kg/m<sup>2</sup>), a 30–33% calorie restriction (to  $\sim 25$  kcal/kg actual weight per day) has been shown to reduce hyperglycemia and plasma triglycerides with no increase in ketonuria (2). Restriction of carbohydrates to 35–40% of calories has been shown to decrease maternal glucose levels and improve maternal and fetal outcomes (3).
- Insulin is the pharmacologic therapy that has most consistently been shown to reduce fetal morbidities when added to MNT. Selection of pregnancies for insulin therapy can be based on measures of maternal glycemia with or without assessment of fetal growth characteristics. When maternal glucose levels are used, insulin therapy is rec-

ommended when MNT fails to maintain self-monitored glucose at the following levels:

- Fasting whole blood glucose  $\leq 95$  mg/dl (5.3 mmol/l)
- Fasting plasma glucose  $\leq 105$  mg/dl (5.8 mmol/l)
- or
- 1-h postprandial whole blood glucose  $\leq 140$  mg/dl (7.8 mmol/l)
- 1-h postprandial plasma glucose  $\leq 155$  mg/dl (8.6 mmol/l)
- or
- 2-h postprandial whole blood glucose  $\leq 120$  mg/dl (6.7 mmol/l)
- 2-h postprandial plasma glucose  $\leq 130$  mg/dl (7.2 mmol/l)

- Measurement of the fetal abdominal circumference early in the third trimester can identify a large subset of infants with no excess risk of macrosomia in the absence of maternal insulin therapy. This approach has been tested primarily in pregnancies with maternal fasting serum glucose levels  $<105$  mg/dl (5.8 mmol/l).
- Human insulin should be used when insulin is prescribed, and SMBG should guide the doses and timing of the insulin regimen. The use of insulin analogs has not been adequately tested in GDM.
- Oral glucose-lowering agents have generally not been recommended during pregnancy. However, one randomized, unblinded clinical trial compared the use of insulin and glyburide in women with GDM who were not able to meet glycemic goals on MNT (4). 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

**Table 3—Criteria for the diagnosis of diabetes mellitus**

Normoglycemia	IFG and IGT	Diabetes mellitus*
FPG $<110$ mg/dl	FPG $\geq 110$ mg/dl and $<126$ mg/dl (IFG)	FPG $\geq 126$ mg/dl
2-h PG <sup>†</sup> $<140$ mg/dl	2-h PG <sup>†</sup> $\geq 140$ mg/dl and $<200$ mg/dl (IGT)	2-h PG <sup>†</sup> $\geq 200$ mg/dl
—	—	Symptoms of DM and casual plasma glucose concentration $\geq 200$ mg/dl

DM, diabetes mellitus; FPG, fasting plasma glucose; 2-h PG, 2-h postload glucose. \*A diagnosis of diabetes must be confirmed on a subsequent day by any one of the three methods included in the chart. In clinical settings, the FPG test is greatly preferred because of ease of administration, convenience, acceptability to patients, and lower cost. Fasting is defined as no calorie intake for at least 8 h. <sup>†</sup>This test requires the use of a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

not FDA approved for the treatment of GDM and further studies are needed in a larger patient population to establish its safety.

- Programs of moderate physical exercise have been shown to lower maternal glucose concentrations in women with GDM. Although the impact of exercise on neonatal complications awaits rigorous clinical trials, the beneficial glucose-lowering effects warrant a recommendation that women without medical or obstetrical contraindications be encouraged to start or continue a program of moderate exercise as a part of treatment for GDM.
- GDM is not of itself an indication for cesarean delivery or for delivery before 38 completed weeks of gestation. Prolongation of gestation past 38 weeks increases the risk of fetal macrosomia without reducing cesarean rates, so that delivery during the 38th week is recommended unless obstetric considerations dictate otherwise.
- Breast-feeding, as always, should be encouraged in women with GDM.

**LONG-TERM THERAPEUTIC CONSIDERATIONS** — Reclassification of maternal glycemic status should be performed at least 6 weeks after delivery

and according to the guidelines of the “Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus” (5). See Table 3 for diagnostic criteria. If glucose levels are normal postpartum, reassessment of glycemia should be undertaken at a minimum of 3-year intervals. Women with IFG or IGT in the postpartum period should be tested for diabetes annually; these patients should receive intensive MNT and should be placed on an individualized exercise program because of their very high risk for development of diabetes. All patients with prior GDM should be educated regarding lifestyle modifications that lessen insulin resistance, including maintenance of normal body weight through MNT and physical activity. Medications that worsen insulin resistance (e.g., glucocorticoids, nicotinic acid) should be avoided if possible. Patients should be advised to seek medical attention if they develop symptoms suggestive of hyperglycemia. Education should also include the need for family planning to ensure optimal glycemic regulation from the start of any subsequent pregnancy. Low-dose estrogen-progestogen oral contraceptives may be used in women with prior histories of GDM, as long as no medical contraindications exist.

Offspring of women with GDM should be followed closely for the development of obesity and/or abnormalities of glucose tolerance.

#### References

1. Metzger BE, Coustan DR (Eds.): Proceedings of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 21 (Suppl. 2):B1–B167, 1998
2. Franz MJ, Horton ES, Bantle JP, Beebe CA, Brunzell JD, Coulston AM, Henry RR, Hoogwerf BJ, Stacpoole PW: Nutrition principles for the management of diabetes and related complications (Technical Review). *Diabetes Care* 17:490–518, 1994
3. Major CA, Henry MJ, De Veciana M, Morgan MA: The effects of carbohydrate restriction in patients with diet-controlled gestational diabetes. *Obstet Gynecol* 91: 600–604, 1998
4. Langer L, Conway DL, Berkus MD, Xenakis EM-J, Gonzales O: A comparison of glyburide and insulin in women with gestational diabetes mellitus. *N Engl J Med* 343: 1134–1138, 2000
5. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 26 (Suppl. 1):S5–S20, 2003