Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. Debate continues to surround both the diagnosis and treatment of GDM despite several recent large-scale studies addressing these issues. The purpose of this document is to 1) provide a brief overview of the understanding of GDM, 2) provide management guidelines that have been validated by appropriately conducted clinical research, and 3) identify gaps in current knowledge toward which future research can be directed.

Background

**Definition and Prevalence**

Gestational diabetes mellitus (GDM) is a condition in women who have carbohydrate intolerance with onset or recognition during pregnancy. The prevalence of GDM varies in direct proportion to the prevalence of type 2 diabetes in a given population or ethnic group. It has been estimated that up to 6–7% of pregnancies are complicated by diabetes mellitus (DM) and that approximately 90% of these cases represent women with GDM (1). An increased prevalence of GDM is found among Hispanic, African American, Native American, Asian, and Pacific Islander women. With the increase in obesity and sedentary lifestyle, the prevalence of DM among reproductive-aged women is increasing globally.

**Maternal and Fetal Complications**

Women with GDM are at higher risk of gestational hypertension, preeclampsia (2), and cesarean delivery and its associated potential morbidities. Most importantly, women with GDM have an increased risk of developing diabetes later in life. It is projected that up to 50% of women with GDM will develop diabetes 22–28 years after pregnancy (3, 4). The progression to type 2 diabetes may be influenced by ethnicity and the incidence of obesity. For example, 60% of Latin-American women with GDM may develop type 2 diabetes by 5 years after the index pregnancy (5).

The offspring of women with GDM are at increased risk of macrosomia, neonatal hypoglycemia, hyperbilirubinemia, operative delivery, shoulder dystocia, and birth trauma. The relationship between maternal hyperglycemia and fetal macrosomia, as well as other adverse outcomes, has been confirmed in the Hyperglycemia and Adverse Pregnancy Outcome study (6). This multicenter international study demonstrated a continuous relationship between maternal glucose levels and cesarean delivery, birth weight greater than the 90th percentile, clinical neonatal hypoglycemia, and fetal hyperinsulinemia. An increase in each of the three values on the 75-g, 2-hour
oral glucose tolerance test (OGTT) used for GDM diagnosis in this study was associated with a graded increase in these outcomes.

**Screening Practices, Diagnostic Thresholds, and Treatment Benefits**

Historically, screening for GDM consisted of obtaining the patient’s medical history, relying primarily on past obstetric outcomes and a family medical history of type 2 diabetes. In 1973, O’Sullivan and Mahan proposed the 50-g, 1-hour oral glucose tolerance test (7). This test has become widely used—an estimated 95% of obstetric groups in the United States report performing universal screening using the 50-g, 1-hour oral glucose tolerance test. However, consistent data that demonstrate an overall benefit to screening all pregnant women for GDM are lacking (8).

The use of traditional historic factors (family or personal history of diabetes, previous adverse pregnancy outcome, glycosuria, and obesity) to identify GDM will miss approximately one half of women with GDM (9). It was recognized at the Fifth International Workshop Conference on Gestational Diabetes Mellitus that certain features place women at low risk of GDM, and it may not be cost-effective to screen this group of women. However, such low-risk women represent only 10% of the population and selecting these individuals who should not be screened may add unnecessary complexity to the screening process (10).

**Clinical Considerations and Recommendations**

- **How is gestational diabetes mellitus diagnosed?**

All pregnant patients should be screened for GDM, whether by the patient’s medical history, clinical risk factors, or laboratory screening test results to determine blood glucose levels. Screening is generally performed at 24–28 weeks of gestation. Early pregnancy screening for undiagnosed type 2 diabetes, also is suggested in women with risk factors, including those with a prior history of GDM (see Box 1) (11). If the result of early testing is negative, repeat screening for high-risk women is recommended at 24–28 weeks of gestation. The two-step approach to testing, commonly used in the United States, is based on first screening with the administration of 50 g of an oral glucose solution followed by a 1-hour venous glucose determination. Those individuals meeting or exceeding the screening threshold undergo a 100-g, 3-hour diagnostic OGTT.

- **Box 1. Early Screening Strategy for Detecting Gestational Diabetes**

- Women with the following risk factors are candidates for early screening:
  - Previous medical history of gestational diabetes mellitus
  - Known impaired glucose metabolism
  - Obesity (body mass index greater than or equal to 30 [calculated as weight in kilograms divided by height in meters squared])
- If gestational diabetes mellitus is not diagnosed, blood glucose testing should be repeated at 24–28 weeks of gestation.

A one-step approach to establishing the diagnosis of GDM using a 75-g, 2-hour OGTT has been used and promoted by other organizations. In 2010, the International Association of Diabetes and Pregnancy Study Group convened a workshop conference to recommend new diagnostic criteria based on the Hyperglycemia and Adverse Pregnancy Outcome study data (12). Based on expert consensus, an odds ratio of 1.75 (compared with the population mean) for various adverse outcomes was used to define blood glucose thresholds for diagnosis of GDM. The International Association of Diabetes and Pregnancy Study Group recommended that a universal 75-g, 2-hour OGTT be performed during pregnancy and that the diagnosis of GDM be established when any single threshold value on the 75-g, 2-hour OGTT was met or exceeded (fasting value, 92 mg/dL; 1-hour value, 180 mg/dL; and 2-hour value, 153 mg/dL) (12). Overall, using the proposed International Association of Diabetes and Pregnancy Study Group criteria would identify approximately 18% of the U.S. population as having GDM, although in some subpopulations, the proportion of women in whom GDM is diagnosed would be even higher. The American Diabetes Association (ADA) endorsed the International Association of Diabetes and Pregnancy Study Group criteria while acknowledging that adopting these cutoffs will significantly increase the prevalence of GDM (11).

There are no data from randomized clinical trials (RCTs) regarding therapeutic interventions for the expanded group of women designated as having GDM based on the International Association of Diabetes and
Pregnancy Study Group criteria. These additional women in whom GDM would be diagnosed may be at a lower risk of adverse outcomes than women in whom GDM was diagnosed by traditional criteria and may not derive similar benefits from interventions (13).

In 2013, a Eunice Kennedy Shriver National Institute of Child Health and Human Development Consensus Development Conference on diagnosing gestational diabetes recommended that health care providers continue to use a two-step approach to screen for and diagnose GDM because no evidence exists that using these 2-hour OGTT criteria to diagnose GDM would lead to clinically significant improvements in maternal or newborn outcomes, but would lead to a significant increase in health care costs (14, 15). The American College of Obstetricians and Gynecologists supports this recommendation and recommends that before the testing approach and diagnostic criteria for GDM are changed, implications of such changes should be studied.

Screening thresholds for the 1-hour glucose challenge have varied from 130 mg/dL to 140 mg/dL, with varying sensitivities and specificities reported. There are no randomized trials to support a clear benefit to one cutoff compared with others. Data also are insufficient with regard to pregnancy outcomes to determine an ideal threshold value, although standardization of a screening threshold has been recently recommended (14). A value of 140 mg/dL has been shown in one cohort study to have lower false-positive rates and improved positive predictive values across various ethnic groups. In this analysis, sensitivities were only marginally improved when using lower thresholds (130 mg/dL and 135 mg/dL) (16). Establishing a higher standardized threshold of 140 mg/dL might identify those women at greater risk of adverse pregnancy outcomes; it may also lower the rate of false-positive screening results and unnecessary administration of 3-h OGTTs, which have been shown to be associated with increased maternal stress and dissatisfaction regarding the process of screening for and diagnosing GDM, in general (17–19). However, in the absence of clear evidence supporting a cutoff of 135 mg/dL versus 140 mg/dL for the 1-hour glucose screening test, it is suggested that health care providers select one of these as a single consistent cutoff for their practice, with factors such as community prevalence rates of GDM considered in that decision.

Table 1 lists the diagnostic thresholds established by both the National Diabetes Data Group and those established by Carpenter and Coustan, with the latter using lower thresholds and subsequently resulting in higher rates of GDM diagnoses. In the absence of clear comparative trials, one set of diagnostic criteria for the 3-h OGTT cannot be clearly recommended above the other. However, given the benefits of standardization, practitioners and institutions should select a single set of diagnostic criteria, either plasma or serum glucose levels designated by the Carpenter and Coustan criteria or the plasma levels established by the National Diabetes Data Group, for consistent use within their patient populations. In one cross-sectional study that compared the two sets of criteria in more than 26,000 women, the diagnosis of GDM increased, on average, by 50% with the use of the Carpenter and Coustan thresholds (20). Considerations for selection of one set of diagnostic criteria over the other could include, but are not limited to, the baseline prevalence of diabetes in their specific communities and the availability of resources to appropriately manage the numbers of women in whom GDM was diagnosed by any given protocol. This approach, while imperfect, avoids establishment of a single set of diagnostic criteria across all populations based on expert opinion alone.

**What is the benefit of treatment of gestational diabetes mellitus?**

The 2005 Australian Carbohydrate Intolerance Study in Pregnant Women trial was the first large-scale (1,000 women) randomized treatment trial for GDM (21). Treatment was associated with a significant reduction in the rate of the primary outcome, a composite of serious complications (perinatal death, shoulder dystocia, and birth trauma, including fracture or nerve palsy). Treatment also reduced the frequency of large for gestational age (LGA)-infants from 22% to 13% and of birth weight greater than 4,000 g from 21% to 10%. Among maternal outcomes, preeclampsia was significantly reduced with treatment (18% versus 12%).

The Australian Carbohydrate Intolerance Study in Pregnant Women was followed by the 2009 report...
of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Network randomized, multicenter treatment trial of 958 women with mild GDM (22). Although there were no differences in the frequency of the primary composite outcome (perinatal death, neonatal hypoglycemia, elevated umbilical cord C-peptide level, or birth trauma), several significant differences in secondary outcomes were observed with treatment, including a lower frequency of LGA-infants, lower frequency of birth weight exceeding 4,000 g, and reduced neonatal fat mass. Moreover, cesarean delivery, shoulder dystocia, and hypertensive disorders were significantly reduced in women who were treated for GDM. Therefore, based on these studies, women in whom GDM is diagnosed should be treated with nutrition therapy and, when necessary, medication for both fetal and maternal benefit.

**What nonpharmacologic treatments are effective in managing gestational diabetes mellitus?**

The goal of nutrition therapy in women with GDM is to achieve normoglycemia, prevent ketosis, provide adequate weight gain, and contribute to fetal well-being. The ADA recommends nutritional counseling for all patients with GDM by a registered dietician, if possible, with a personalized nutrition plan based on the individual’s body mass index. There are some clinical settings in which a dietician may not be readily available. In this circumstance, the clinician should be able to provide recommendations to the patient by remembering three major nutritional components: 1) caloric allotment, 2) carbohydrate intake, and 3) caloric distribution.

A diet composed of 50–60% carbohydrates will often result in excessive weight gain and postprandial hyperglycemia. For this reason, it has been suggested that carbohydrate intake be limited to 33–40% of calories, with the remaining calories divided between protein (20%) and fat (40%) (27). A randomized trial of 99 women with GDM compared a low-glycemic index nutrition plan with a conventional high-fiber diet and found that both produced similar pregnancy outcomes (28). Given these findings, as well as the results of other treatment trials, complex carbohydrates may be preferred to simple carbohydrates because they are less likely to produce significant postprandial hyperglycemia (29). In practice, three meals and two to three snacks are recommended to distribute glucose intake and to reduce postprandial glucose fluctuations.

Although there are multiple RCTs of exercise and lifestyle interventions in adults with diabetes who are not pregnant, there are few published exercise trials in women with GDM, and most have small sample sizes and limited power to show improvement in glucose levels (30–32). In adults with diabetes who are not pregnant, exercise, particularly weight training, increases lean muscle mass and improves tissue sensitivity to insulin. In overweight or obese women with GDM, exercise also may be able to improve glycemic control and facilitate weight loss. Therefore, a moderate exercise program as part of the treatment plan for women with GDM is recommended (11).

**What pharmacologic treatments are effective in managing gestational diabetes mellitus?**

When target glucose levels cannot be consistently achieved through nutrition and exercise therapy, pharmacologic treatment is recommended. However, a systematic review found no conclusive evidence for the threshold value at which clinicians should start medical
therapy (33). When pharmacologic treatment of GDM is indicated, insulin and oral medications are equivalent in efficacy, and either can be an appropriate first-line therapy. Insulin has historically been considered the standard therapy for GDM management in cases refractory to nutrition therapy.

Insulin, which does not cross the placenta, can achieve tight metabolic control and traditionally has been added to nutrition therapy if fasting blood glucose levels are persistently greater than 95 mg/dL, if 1-hour levels are persistently greater than or equal to 140 mg/dL, or if 2-hour levels are persistently greater than or equal to 120 mg/dL. These thresholds have been largely extrapolated from recommendations for managing pregnancy in women with preexisting diabetes. If insulin is used, the typical starting total dosage is 0.7–1.0 units/kg daily, given in divided doses. In cases in which both fasting and postprandial hyperglycemia are present, a regimen of multiple injections using both intermediate-acting insulin and short-acting insulin alone or in combination is administered. Regardless of the starting dosage, subsequent dosage adjustments should be based on the blood glucose levels at particular times of the day. Insulin analogs, including insulin lispro and insulin aspart, have been used in pregnancy and do not cross the placenta. Insulin lispro has a more rapid onset of action than regular insulin and may be useful in improving postprandial glucose levels (Table 2).

Oral antidiabetic medications (eg, glyburide and metformin) are being used increasingly in women with GDM, although they have not been approved by the U.S. Food and Drug Administration for this indication. Glyburide is a sulfonylurea that binds to pancreatic beta-cell adenosine triphosphate calcium channel receptors to increase insulin secretion and insulin sensitivity of peripheral tissues. It should not be used in patients who report a sulfa allergy. Metformin is a biguanide that inhibits hepatic gluconeogenesis and glucose absorption and stimulates glucose uptake in peripheral tissues. Current evidence from randomized trials and several observational studies of oral antidiabetic agents show that maternal glucose levels do not differ substantially between women treated with insulin versus those treated with oral agents, and a meta-analysis suggests that there is no consistent evidence of an increase in any acute or short-term adverse maternal or neonatal outcomes with the use of glyburide or metformin compared with the use of insulin (34). Therefore, both can be considered for glycemic control in women with GDM.

Three trials that compared glyburide with insulin failed to show any significant difference in glycemic control (35–37). Several observational studies also have reported generally good outcomes with the use of glyburide, although 20–40% of women required the addition of insulin to maintain good glycemic control (38–42). The usual dosage of glyburide is 2.5–20 mg daily in divided doses, although pharmacokinetic studies during pregnancy indicate daily doses up to 30 mg may be necessary to achieve adequate control (43). Metformin is primarily used in women with pregestational diabetes and in women with polycystic ovary syndrome and infertility. For treatment of pregestational diabetes, metformin is often continued during pregnancy and insulin is added as appropriate to the therapy regimen. In women with polycystic ovary syndrome, metformin is often continued until the end of the first trimester, with only limited evidence to suggest that such use decreases the risks of adverse pregnancy outcomes, including first-trimester loss (44).

In one large trial, 751 women with GDM were randomly assigned to receive metformin (plus insulin if needed) or insulin therapy. They experienced similar rates of a composite outcome of perinatal morbidity, consisting of neonatal hypoglycemia, respiratory distress, need for phototherapy, birth trauma, prematurity, and low Apgar scores (45). However, one half of the women randomized to receive metformin required insulin supplementation to achieve glycemic control. Another RCT that compared metformin with glyburide for treatment of GDM demonstrated that glyburide may be superior to metformin in achieving satisfactory glycemc control (46). In this study, 35% of women randomized to receive metformin required insulin therapy compared with 16% of those who received glyburide.

Although concerns have been raised about the safety of oral antidiabetic agents during pregnancy, one

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<th>Table 2. Action Profile of Commonly Used Insulin Agents</th>
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<td>Type</td>
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</tr>
<tr>
<td>Insulin lispro</td>
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<tr>
<td>Insulin aspart</td>
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<tr>
<td>Regular insulin</td>
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<td>Isophane insulin suspension</td>
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<td>(NPH insulin)</td>
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<td>Insulin zinc suspension</td>
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<td>Extended insulin zinc suspension</td>
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<td>Insulin glargine</td>
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RCT that used umbilical cord blood analysis revealed no detectable glyburide in exposed pregnancies (35). However, it has been reported that glyburide does cross the placenta (43). Theoretic concerns regarding this issue include whether long-term glucose homeostasis may be affected in exposed offspring. It also is not known whether glyburide can affect the progression to type 2 diabetes later in life in women who were treated during pregnancy. Although current data demonstrate no adverse short-term effects from oral diabetic therapy during pregnancy on maternal or neonatal health, long-term outcomes have yet to be studied. This might suggest a role for counseling when prescribing oral agents to women with GDM.

► Is fetal assessment indicated in pregnancies complicated by gestational diabetes mellitus?

Antepartum fetal testing is recommended for patients with pregestational diabetes. Because the increased risk of fetal demise in patients with pregestational diabetes is related to suboptimal glycemic control, it would be expected that women with GDM who have poor glycemic control also would be at risk. Therefore, for women with GDM with poor glycemic control, fetal surveillance may be beneficial. There is no consensus regarding antepartum testing in women with well-controlled GDM. The specific antepartum test and frequency of testing may be chosen according to local practice.

► What are delivery considerations in pregnancies complicated by gestational diabetes mellitus?

Women with GDM with good glycemic control and no other complications can be managed expectantly. In most cases, women with good glycemic control who are receiving medical therapy do not require delivery before 39 weeks of gestation. In a randomized trial in which women with insulin-treated GDM and fetuses believed to be of appropriate weight for gestational age were randomized at 38 weeks of gestation to induction of labor within 1 week or expectant management, there was no difference in cesarean delivery rates (47). However, the induction group gave birth to a smaller proportion of LGA-infants. In a cohort multiple time series study, a policy of induction of labor at 38–39 weeks of gestation, in whom delivery is recommended after 39 weeks of gestation and by the estimated date of delivery, no evidence-based recommendation can be made regarding timing of delivery in women with GDM that is controlled either with a diet and exercise regimen or with medication (49).

There are insufficient data to determine whether cesarean delivery should be performed in cases of suspected macrosomia to reduce the risk of birth trauma. Macrosomia is distinctly more common in women with GDM, and shoulder dystocia is more likely at a given fetal weight in pregnancies complicated by diabetes than in pregnancies not complicated by diabetes (50, 51). Therefore, in women with GDM, it is reasonable for obstetricians to assess fetal growth either by ultrasoundography or by clinical examination late in the third trimester in an attempt to identify macrosomia before delivery. It has been estimated that up to 588 cesarean deliveries for an estimated fetal weight of 4,500 g and up to 962 cesarean deliveries for an estimated fetal weight of 4,000 g would be needed to prevent a single case of permanent brachial plexus palsy (52). On the basis of available data, it is not completely possible to determine whether the potential benefits of scheduled cesarean delivery at a given estimated fetal weight are similar for women with GDM and those with preexisting diabetes. It appears reasonable, therefore, to recommend that women with GDM be counseled regarding the option of scheduled cesarean delivery when the estimated fetal weight is 4,500 g or more.

► How should women with a history of GDM be screened and counseled postpartum?

Although the carbohydrate intolerance of GDM frequently resolves after delivery, up to one third of affected women will have diabetes or impaired glucose metabolism at postpartum screening, and it has been estimated that 15–50% will develop type 2 diabetes later in life (53–57). Postpartum screening at 6–12 weeks is recommended for all women who had GDM to identify women with DM, impaired fasting glucose levels, or impaired glucose tolerance (IGT) (Fig. 1) (11). Women with a history of GDM have a sevenfold increased risk of developing type 2 diabetes compared with women without a history of GDM (58). Either a fasting plasma glucose test or the 75-g, 2-hour OGGT are appropriate for diagnosing overt diabetes in the postpartum period. Although the fasting plasma glucose test is easier to perform, it
Summary of Recommendations and Conclusions

The following recommendation and conclusion are based on good and consistent scientific evidence (Level A):

- Women in whom GDM is diagnosed should be treated with nutrition therapy and, when necessary, medication for both fetal and maternal benefit.

- When pharmacologic treatment of GDM is indicated, insulin and oral medications are equivalent in efficacy, and either can be an appropriate first-line therapy.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- All pregnant patients should be screened for GDM, whether by the patient’s medical history, clinical
risk factors, or laboratory screening test results to determine blood glucose levels.

- Women with GDM should be counseled regarding the option of scheduled cesarean delivery when the estimated fetal weight is 4,500 g or more.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- In the absence of clear evidence supporting a cutoff of 135 mg/dL versus 140 mg/dL for the 1-h glucose screening test, it is suggested that health care providers select one of these as a single consistent cutoff for their practice, with factors such as community prevalence rates of GDM considered in that decision.

- In the absence of clear comparative trials, one set of diagnostic criteria for the 3-hour OGTT cannot be clearly recommended above the other. However, given the benefits of standardization, practitioners and institutions should select a single set of diagnostic criteria, either plasma or serum glucose levels designated by the Carpenter and Coustan criteria or the plasma levels established by the National Diabetes Data Group, for consistent use within their patient populations.

- Once a woman with GDM begins nutrition therapy, surveillance of blood glucose levels is required to be certain that glycemic control has been established.

- Women with GDM with good glycemic control and no other complications can be managed expectantly. In most cases, women with good glycemic control who are receiving medical therapy do not require delivery before 39 weeks of gestation.

- Postpartum screening at 6–12 weeks is recommended for all women who had GDM to identify women with DM, impaired fasting glucose, or IGT. Women with impaired fasting glucose or IGT or diabetes should be referred for preventive therapy. The ADA recommends repeat testing at least every 3 years for women who had a pregnancy affected by GDM and normal results of postpartum screening.

**Proposed Performance Measure**

Percentage of women in whom GDM is diagnosed who have postpartum screening for type 2 diabetes

**References**


**Resources**

The following resources are for informational purposes only. Referral to these sources and web sites does not imply the endorsement of the American College of Obstetricians and Gynecologists. These resources are not meant to be comprehensive. The exclusion of a source or web site does not reflect the quality of that source or web site. Please note that web sites are subject to change without notice.


25. Ferrara A, Hedden MM, Quesenberry CP, Selby JV. Prevalence of gestational diabetes mellitus detected by the national diabetes data group or the carpenter and coustan plasma glucose thresholds. Diabetes Care 2002;25:1625-30. (Level II-3) [PubMed] [Full Text]

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists’ own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1990–January 2013. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I Evidence obtained from at least one properly designed randomized controlled trial.
II-1 Evidence obtained from well-designed controlled trials without randomization.
II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.
Level B—Recommendations are based on limited or inconsistent scientific evidence.
Level C—Recommendations are based primarily on consensus and expert opinion.

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