



OBSTETRICS

A look at gestational diabetes, noninvasive prenatal testing, and hypertensive disorders in pregnancy



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Dr. Pauli sifts the latest guidance from ACOG on hypertension in pregnancy, at obgmanagement.com

Over the past 20 years, the incidence of preeclampsia in the United States has increased 25%,¹ and the disorder is a leading cause of morbidity and death among both mothers and infants. Although considerable progress has been achieved in elucidating the pathophysiology of preeclampsia, greater understanding has not yet carried over into improved clinical practice.

To address this disconnect between data and practice, the American College of Obstetricians and Gynecologists (ACOG) issued a

99-page document in November 2013 to help establish best practices in the diagnosis and management of hypertensive disorders in pregnancy. We begin this article with a look at its major recommendations.

Other notable developments in obstetrics over the past year have been the rapid evolution of noninvasive prenatal testing and the publication of new guidance on screening, diagnosis, and management of gestational diabetes, all of which are addressed in this article.

ACOG aims to clarify best practices in the management of hypertension in pregnancy

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in Pregnancy. Washington, DC: ACOG; November 2013.

The biggest news of the past year is probably the November 2013 report on hypertension in pregnancy from ACOG, which was developed with three goals in mind:

- to summarize current knowledge

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- to provide best-practice guidelines
- to identify areas in which further research is needed.

The classification, diagnosis, prediction, prevention, and management of gestational hypertension, preeclampsia, and chronic hypertension are addressed in the report. Although space constraints prevent us from summarizing the entire document, we would like to highlight the biggest changes and most relevant additions to clinical practice.

Notable recommendations

Classification. Preeclampsia is no longer characterized as “mild” or “severe” but as “preeclampsia without severe features” and “preeclampsia with severe features.” As justification for these changes, the ACOG Task Force on Hypertension in Pregnancy noted that preeclampsia is progressive by nature, so a characterization of “mild” disease is appropriate only at the time of diagnosis. Therefore, “appropriate management mandates frequent reevaluation for severe features.”

Diagnosis of proteinuria. The options are a 24-hour urine collection demonstrating more than 300 mg of protein or a single-specimen urine protein:creatinine ratio of 0.3 mg/dL or higher. Dipstick values should only be used if these quantitative measures are unavailable.

Signs of severe disease. Fetal growth restriction and proteinuria of more than 5 g/24 hr are no longer considered defining features of severe disease.

Severe features now include any of these:

- systolic blood pressure (BP) of 160 mm Hg or higher, or diastolic BP of 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy is initiated before this time)
- thrombocytopenia (platelets $<100 \times 10^9/L$)
- impaired liver function, as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration) and/or severe, persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses

- progressive renal insufficiency (serum creatinine concentration >1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- pulmonary edema
- new-onset visual or central nervous system disturbances.

Screening for preeclampsia. The use of Doppler studies and serum biomarkers is not recommended, as there is no evidence that early identification translates to improved outcomes.

Prevention of preeclampsia. Low-dose aspirin (60–80 mg/d, starting in the late first trimester) should be offered as primary prevention to:

- women with a history of early-onset preeclampsia and delivery before 34 weeks’ gestation
- women with a history of preeclampsia in multiple pregnancies
- other high-risk patients (chronic hypertension, diabetes).

No other treatments (vitamin C or E, salt restriction, or bed rest) are recommended for the prevention of preeclampsia, although calcium supplementation may be recommended for women with a low baseline dietary intake of calcium.

Use of magnesium sulfate. Universal prophylaxis with magnesium sulfate is not recommended for preeclampsia unless severe features are present or the patient’s clinical condition changes to severe during labor.

Timing of delivery. Recommendations for delivery for patients with hypertensive disorders are:

- gestational hypertension or preeclampsia without severe features: 37 weeks’ gestation
- preeclampsia with severe features: by 34 weeks
- chronic hypertension: not before 38 weeks
- chronic hypertension with superimposed preeclampsia: 34 or 37 weeks, depending on the presence of severe features.

All of these recommendations are contingent upon the clinical status of the patient and her fetus. For example, if the fetus develops severe growth restriction ($<5\%$) or oligohydramnios, delivery may be recommended regardless

FAST TRACK

Fetal growth restriction and proteinuria of more than 5 g/24 hr are no longer considered defining features of severe preeclampsia

of gestational age, based on fetal testing and maternal stability.

Postpartum hypertension. The need for recognition of hypertension in the postpartum period is emphasized, as well as appropriate management, using the following guidelines:

- Be aware that BP decreases initially after delivery and then increases 3 to 6 days postpartum, requiring vigilance on the part of the clinician. For this reason, BP monitoring is recommended 72 hours postpartum (inpatient or outpatient) and again in 7 to 10 days in women diagnosed with a hypertensive disorder of pregnancy.
- Counsel patients who experience a hypertensive disorder and/or preeclampsia during pregnancy about postpartum preeclampsia, providing strict precautions and explicit instructions regarding its signs and symptoms
- If BP remains elevated after the first postpartum day, consider discontinuing nonsteroidal anti-inflammatory drugs (NSAIDs), as they may be related to hypertension
- Treat BP that remains above 150/100 mm Hg with antihypertensive therapy
- If postpartum preeclampsia is suspected, administer magnesium sulfate for 24 hours.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Although we suggest that you read the ACOG report thoroughly, remember that its recommendations are only that—recommendations. Also keep in mind that only six of the approximately 60 “recommendations” provided in this report were accompanied by both high-quality evidence and a strong recommendation. There still is room for clinical judgment and individualization of management to specific patient populations.

A culture shift is needed

At our institution, the most significant potential changes to clinical practice may be the elimination of universal magnesium sulfate prophylaxis and the removal of severe fetal growth restriction from the definition of “severe” preeclampsia.

Also, because the use of NSAIDs is widespread for postpartum pain control, a culture change is needed if we are to follow the postpartum recommendations.



Be aware that blood pressure initially decreases in the postpartum period and then increases 3 to 6 days later, requiring vigilance on the part of the clinician

Noninvasive prenatal screening is expanding rapidly—but don't throw out that CVS kit just yet!

ACOG Committee on Genetics. Committee Opinion #545: Noninvasive prenatal testing for fetal aneuploidy. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2012;120(6):1532–1534.

Mennuti MT, Cherry AM, Morrissette JJD, Dugoff L. Is it time to sound an alarm about false-positive cell-free DNA testing for fetal aneuploidy? Am J Obstet Gynecol. 2013;209(5):415–419.

In last year's Update in Obstetrics, we discussed noninvasive prenatal genetic screening via cell-free fetal DNA, noting that it is a safer (no risk of miscarriage) and faster (starting at 10 weeks' gestation) way to screen for aneuploidy. The sensitivity and specificity of this test for Trisomy 21 and 18 are over 99%, with slightly lower sensitivity for Trisomy 13 and sex chromosome abnormalities and a false-positive rate of 0.5%.

In a committee opinion published in December 2012, ACOG concluded that

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cell-free fetal DNA is an appropriate screening option only for specific groups of patients at risk for aneuploidy:

- women older than age 35
- women with fetal ultrasonography findings that are concerning for aneuploidy
- women with aneuploidy in a prior pregnancy
- women with abnormal first- or second-trimester genetic screening tests
- parents with a balanced translocation and an increased risk of Trisomy 21 or 13.

Noninvasive aneuploidy testing is for screening only

Negative results are not diagnostic, and all positive results should be confirmed with invasive testing (chorionic villus sampling [CVS] or amniocentesis).

ACOG does not recommend routine use of cell-free fetal DNA without a comprehensive history and adequate patient counseling, as well as a designation of “high risk.”

Over the past year, more options have become available for aneuploidy screening via cell-free fetal DNA, including screening in twin gestations (for Trisomy 21, 18, 13, and the presence of a Y chromosome only) and screening for:

- 22q deletion (DiGeorge syndrome)
- 5p- (Cri-du-chat syndrome)
- 15q (Prader-Willi and Angelman syndromes)
- 1p (1p36 deletion syndrome)
- Trisomy 16
- Trisomy 22.

At this rate, the genetic information potentially available via noninvasive testing seems unlimited. It is easy to see how the fact

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Cell-free fetal DNA is a rapidly expanding screening technology, but it is not ready to replace diagnostic testing. Don't throw away those CVS and amniocentesis kits just yet—we are a long way from a completely noninvasive world.

that this is a *screening* test—not a diagnostic test—could get lost in the excitement.

Other limitations: Noninvasive testing is still not validated in low-risk patients, and the false-positive risk may be higher than original estimates.

The problem of false positives

This issue was addressed by Mennuti and colleagues, who presented eight cases of abnormal cell-free fetal DNA results that were not confirmed by invasive testing.

There are few prospective data about the source of false-positive results; potential mechanisms include an inadequate fetal fraction of cell-free DNA, maternal or placental mosaicism, and a vanishing twin.

Mennuti and colleagues propose that a registry of false-positive and false-negative results be established to gather further data. They also note that as low-risk patients and aneuploidies of lower and lower prevalence are incorporated into noninvasive testing, the false-positive rate will rise. Their findings have implications for patient counseling, patient distress, invasive testing, and reimbursement.

FAST TRACK

The false-positive rate for noninvasive prenatal aneuploidy testing may be higher than original estimates

When it comes to gestational diabetes, less may be more

ACOG Committee on Practice Bulletins-Obstetrics. Practice Bulletin #137: Gestational diabetes mellitus. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2013;122(2 Pt 1):406-416.

Gestational diabetes accounts for 90% of diabetic pregnancies, and its incidence has been increasing in the United States along with the obesity epidemic. In recent years, there has been some debate about the



best way to screen for, diagnose, and treat gestational diabetes.

Multiple criteria exist for a positive 1-hour (130–140 mg/dL) or 3-hour glucose tolerance test (Carpenter and Coustan vs National Diabetes Data Group), without comparative trials or consensus as to which version is best. Lower cutoffs increase the rate of gestational diabetes by as much as 50%, whereas higher cutoffs lower the false-positive rate and reduce the need for additional tests.

Some groups have recommended moving away from the traditional two-step process to a one-step approach that utilizes the 2-hour, 75-g glucose tolerance test commonly used outside of pregnancy. They argue that this approach would simplify and standardize the process and could improve outcomes in “borderline” pregnancies that would have been missed by less stringent guidelines.

However, the baseline rate of gestational diabetes using this one-step approach would likely increase from 7% to 18% or higher, depending on the patient population. Such an increase would trigger a huge rise in costs and resources needed to care for these patients, without data on outcomes or appropriate therapy for this expanded group of women with gestational diabetes.

Treatment isn't clear-cut, either

Treatment of gestational diabetes centers on labor-intensive glucose monitoring, nutritional interventions, and insulin therapy.

Until recently, the use of oral hypoglycemic agents was not recommended due to limited data. Multiple studies now have been performed to evaluate the safety and efficacy of glyburide and metformin in pregnancy, demonstrating glucose control similar to that achieved with insulin without short-term adverse effects in the mother or newborn. However, as many as 20% to 40% of women using glyburide and 50% of those using metformin require the addition of insulin for adequate glucose control. The

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Use the two-step screening process to identify gestational diabetes, picking your cutoffs and sticking to them. Oral hypoglycemic agents now are acceptable for treatment, but be prepared to go back to insulin if necessary.

long-term effects of these medications are unknown.

ACOG weighs in

In an attempt to clarify optimal screening, diagnosis, and treatment, ACOG updated its practice bulletin on gestational diabetes in August 2013. Among its recommendations:

- **Avoid the 2-hour glucose tolerance test** because there is no demonstrated benefit for the increased number of mothers (and their fetuses) that would be identified by this approach. Rather, use the two-step approach of a 1-hour 50-g glucose tolerance test followed by a 3-hour 100-g glucose tolerance test.
- **In regard to the 1-hour test**, ACOG finds either 135 or 140 mg/dL acceptable as a cutoff but recommends that each practice choose one value as a standard and use it consistently. **For the 3-hour test**, ACOG recommends that each practice choose the version that best fits its population and prevalence of diabetes. At our institution, for example, we have chosen a 1-hour cutoff of 140 mg/dL and the National Diabetes Data Group criteria for the 3-hour test (105, 190, 165, and 145 mg/dL).
- **Oral glyburide or metformin may be used to treat gestational diabetes**, but glyburide (starting at 2.5 mg/d) may be the better choice for glucose control. ☺

Reference

1. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987–2004. *Am J Hypertens*. 2008;21(5):521–526.

FAST TRACK

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