OBSTETRICS

ACOG and SMFM recently focused on filling in the gaps on necessary surveillance, treatment, and testing for management of twin gestations, hypertension in pregnancy, and cell-free DNA screening. These experts break down the guidance.

›› Jaimey M. Pauli, MD
Dr. Pauli is Assistant Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Penn State University College of Medicine, and Attending Perinatologist at the Milton S. Hershey Medical Center in Hershey, Pennsylvania.

›› John T. Repke, MD
Dr. Repke is University Professor and Chairman of Obstetrics and Gynecology at Penn State University College of Medicine. He is also Obstetrician-Gynecologist-in-Chief at the Milton S. Hershey Medical Center in Hershey, Pennsylvania. Dr. Repke serves on the OBG MANAGEMENT Board of Editors.

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IN THIS ARTICLE

Some areas of obstetric care are not as clearcut as others in this time of rapid medical evolution. In this Update, we discuss 3 of them:

- management of twin gestations
- management of chronic hypertension in pregnancy
- cell-free DNA screening for fetal aneuploidy.

To our benefit, both the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have weighed in on important aspects of these areas of obstetric care.

New guidance on management of twin gestations: Close surveillance often is vital

Society for Maternal-Fetal Medicine, Simpson LL. Twin-twin transfusion syndrome. Am J Obstet Gynecol. 2013;208(1):3–18.

Society for Maternal-Fetal Medicine. Checklists and Safety Bundles. https://www.smfm.org/mfm-practice/checklists-and-safety-bundles. Published March 2015. Accessed December 7, 2015.

American College of Obstetricians and Gynecologists. Practice bulletin No. 144. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. Obstet Gynecol. 2014;123(5):1118–1132.

From the maternal perspective, twin pregnancies are known to have higher risks

than their singleton counterparts for such complications as hypertension, preeclampsia, diabetes, hemorrhage, cesarean delivery, postpartum depression, and anemia. These complications are managed essentially the same way regardless of the number of fetuses.

From the fetal/neonatal perspective, twin gestations may carry increased risks of congenital anomalies, preterm birth, and aneuploidy, which are managed similarly to singleton gestations overall, with certain adjustments as necessary.

Twin pregnancies do have unique risks, however, that are managed differently from the time chorionicity is established until delivery. The level of risk increases as the number of chorions and amnions decreases.

A basic management plan for twin gestations consists of a number of components, elucidated below.

1. Determine chorionicity and amnionicity

This determination is most reliably performed late in the first trimester and must be done using ultrasound. The inter-twin membrane should be identified. At 11 to 14 weeks, the presence of the "lambda sign," a triangular projection of tissue that extends from the chorionic surface, is indicative of a dichorionic pregnancy, while a "T sign" suggests a monochorionic pregnancy (sensitivities 97%–100%; specificities 98%–100%). Alternatively, demonstration of discordant genders or separate placentas may be used later in pregnancy.

2. Monitor growth every 4 weeks in dichorionic twins

Dichorionic twins are, by default, diamniotic. After the anatomic survey, growth surveillance should be conducted approximately every 4 weeks.

Discordant growth usually is defined as a difference of 20% or more in weight between the twins, based on the weight of the larger twin. As an isolated finding with both fetuses of normal weight, this discordance has not been demonstrated to increase adverse outcomes. Routine antenatal surveillance is not necessarily indicated.

Fetal growth restriction of one twin or a coexisting abnormality should prompt antenatal testing and/or earlier delivery. Any maternal comorbidities such as hypertension or diabetes also would be indications for testing. Otherwise, delivery is recommended at 38 weeks' to 38-6/7 weeks' gestation.

After 32 weeks, the mode of delivery may be vaginal if the presenting twin is vertex and the delivery provider can perform breech extraction or internal podalic version, if necessary.

3. Monochorionic/diamniotic twins also warrant regular surveillance

The shared placenta places these pregnancies at increased risk for twin-to-twin transfusion syndrome (TTTS), a fetal-placental imbalance in which one twin "transfuses" the other. Ten percent to 15% of monochorionic pregnancies develop TTTS, which is associated with high rates of morbidity and mortality, even when treated.

Antenatal surveillance of these pregnancies involves ultrasonography assessment every 2 weeks, starting at 16 weeks. At each examination, the deepest vertical pocket (DVP) of fluid and presence of each fetal bladder are documented. This limited assessment alternates with a growth assessment every 2 weeks. SMFM recommends this biweekly assessment until 28 weeks, then every 2 to 3 weeks until delivery.

Stage 1 TTTS is defined by the polyhydramnios/oligohydramnios sequence (DVP of one fetus <2 cm, with DVP of the other >8 cm).

Evaluation for treatment of TTTS with laser coagulation (preferred) or amnioreduction should take place after the diagnosis is made, along with increased fetal surveillance.

SMFM also recommends fetal echocardiography due to the 9-fold increased risk of cardiac anomalies in monochorionic pregnancies.

FAST TRACK

10% to 15% of monochorionic pregnancies develop twin-to-twin transfusion syndrome, which is associated with high rates of morbidity and mortality, even when treated

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Other complications of monochorionic/diamniotic twins include selective fetal growth restriction (due to unequal sharing of the placenta), twin reversed arterial perfusion (TRAP) sequence, and twin anemia-polycythemia sequence (TAPS).

Antenatal surveillance of all monochorionic twins is recommended, given the increased risk of stillbirth; many centers start testing at 32 weeks' gestation. According to ACOG, uncomplicated monochorionic/diamniotic twins should be delivered at 34 weeks' to 37-6/7 weeks' gestation. Fetal growth restriction or other comorbidities may prompt delivery as early as 32 weeks.

4. Know the risks of monoamniotic twin gestations

These twins are at increased risk for intrauterine fetal death due to cord entanglement, as well as TTTS, TAPS, and fetal growth restriction. Routine growth assessment and evaluation for TTTS are similar to those for monochorionic/diamniotic twins (without the option of polyhydramnios/oligohydramnios measurement), but the overall management of these pregnancies is unknown.

Protocols may range from outpatient antenatal testing to hospitalization to 24 to 28 weeks' gestation with daily antenatal testing or attempted continuous monitoring. Delivery by cesarean delivery is recommended at 32 to 34 weeks' gestation.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Monochorionic twins need specific and frequent monitoring due to significantly increased risk for both fetal and placental complications. They justify late preterm or early term delivery.

FAST TRACK

Chronic hypertension complicates up to 5% of pregnancies

Management of chronic hypertension in pregnancy: Reserve therapy for severe hypertension

American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists. Obstet Gynecol. 2013;122(5):1122–1131.

Magee LA, von Dadelszen P, Rey E, et al. Less-tight versus tight control of hypertension in pregnancy. N Engl J Med. 2015;372(5):407–417.

Society for Maternal-Fetal Medicine Statement: benefit of antihypertensive therapy for mild-to-moderate chronic hypertension during pregnancy remains uncertain. Am J Obstet Gynecol. 2015;213(1):3–4.

Chronic hypertension complicates up to 5% of pregnancies and increases the risk of complications such as preeclampsia, fetal growth restriction, cardiovascular disorders, and neonatal and maternal morbidity/mortality. The use of antihypertensive medication during pregnancy is a common practice, as many patients present already on therapy in the first trimester, or are started on medication due to elevated blood pressure (BP) at some point during the pregnancy.

Whether to continue the therapy or start therapy in a pregnant patient is a confusing topic, as the actual diagnosis may not be known (gestational hypertension eventually

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The 2013 ACOG Task Force on Hypertension in Pregnancy recommended medication for chronically hypertensive patients whose systolic blood pressure is persistently 105 mm Hg or whose diastolic blood pressure is persistently 105 mm Hg or higher

becomes chronic hypertension if it persists longer than 12 weeks). Treatment also may mask the potential severe range of BP that may change the diagnosis to superimposed preeclampsia, prompting delivery.

The benefit of antihypertensive use in pregnancy for either the mother or fetus has not been elucidated fully, due to a lack of large randomized controlled trials in this area. Some small studies and meta-analyses have suggested that treatment of mild-moderate hypertension during pregnancy may reduce the risk of severe hypertension (a risk factor for stroke) but does not decrease the rate of preeclampsia and may increase the risk of lower-birth–weight infants.

The 2013 ACOG Task Force on Hypertension in Pregnancy recommended medication for chronically hypertensive patients whose systolic BP is persistently 160 mm Hg or higher or whose diastolic BP is persistently 105 mm Hg or higher. The goal of therapy is a range of 120/80 mm Hg to 160/105 mm Hg. Patients who have BP below 160/105 mm Hg without medication should not be treated unless they have evidence of end-organ damage.

Antihypertensive therapy may, on an individual basis, be discontinued in the first trimester if BP is in the mild to moderate range (and there is no evidence of renal or cardiac disease) and restarted as needed if BP rises later in pregnancy.

The ACOG task force did not specifically address medical therapy for gestational hypertension; if the patient begins to have BPs in the severe range, she is essentially treated and delivered as though she has preeclampsia.

"Less tight" versus "tight" control

A 2015 study by Magee and colleagues explored the effect of "less tight" versus "tight" control of hypertension on a composite outcome of pregnancy loss or need for high-level neonatal care for more than 48 hours. This study looked specifically at women with hypertension in the mild-moderate range—either chronic or gestational, without proteinuria.

There was no difference in primary or secondary outcomes (serious maternal complications). The only significant outcome was an increase in severe hypertension in the less tightly controlled group without other complications.

SMFM released a statement in response to this study, affirming the recommendation from the ACOG task force that mild-moderate hypertension in pregnancy not be treated without end-organ damage. The reasons for not adopting universal treatment were that the study results were not generalizable to the population of pregnant women with mild-moderate hypertension in pregnancy (too few women at less than 20 weeks' gestation and inadequate comparison of women with and without therapy). For now, treatment should be reserved for women with chronic hypertension who have blood pressure persistently in the severe range.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Based on current evidence, patients with mild to moderate hypertension in pregnancy should not be treated with antihypertensive medication.

PHOTO: iSTOCK

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Cell-free DNA screening for fetal aneuploidy: Strengths and limitations

American College of Obstetricians and Gynecologists. Committee Opinion No. 640: cell-free DNA screening for fetal aneuploidy. Obstet Gynecol. 2015;126(3):e31–e37.

Society for Maternal-Fetal Medicine Statement: clarification of recommendations regarding cell-free DNA aneuploidy screening. Am J Obstet Gynecol. 2015;213(6):753–754.

Kaimal AJ, Norton ME, Kuppermann M. Prenatal testing in the genomic age: clinical outcomes, quality of life, and costs. Obstet Gynecol. 2015;126(4):737–746.

FAST TRACK

Cell-free DNA screening has a higher sensitivity, lower false-positive rate, and higher predictive value than standard first-trimester screening for a general obstetric population

Five of the 11 SMFM 2015 publications involved cell-free DNA screening for fetal aneuploidy, reflecting the many changes and updates to this ever-evolving topic.

A catalyst for this was the study by Norton and colleagues, who examined the performance of cell-free DNA screening for Trisomy 21 detection, compared with "standard" first-trimester screening in a large, unselected population (many patients at low risk for aneuploidy). The conclusion of the study was that cell-free DNA screening has a higher sensitivity, lower false-positive rate, and higher predictive value than standard first-trimester screening for a general obstetric population. (For an in-depth look at cell-free DNA screening, see the article entitled, "Cell-free DNA screening for women at low risk for fetal aneuploidy," by Mary E. Norton, MD, on page 34 of this issue.)

The limitations of the study included a lower than expected performance of standard screening, compared with earlier studies, and a high false-positive rate (50% positive predictive value) with stratification of low-risk patients.

Several documents followed from SMFM, including a "rapid response" in April 2015 and a SMFM Consult series in the *American Journal of Obstetrics and Gynecology* in June 2015. By September 2015, a new ACOG committee opinion was released with the following key points:

- **Cell-free DNA is a screening test, and patients need thorough counseling** regarding the difference between screening and diagnostic testing, as well as the limitations of this testing, including false-positive and false-negative results, the limited number of conditions tested, and the option of not pursuing aneuploidy screening or testing.
- **Conventional screening methods are still the preferred first-line choice for the low-risk obstetric population,** but low-risk patients choosing cell-free DNA screening need to be counseled properly. Conventional screening methods include first-trimester nuchal translucency with serum biomarkers and/or second-trimester screening.
- **Patients with cell-free DNA screening results suggesting aneuploidy should be offered diagnostic testing.**
- **Patients with fetal anomalies should be offered diagnostic testing.**
- **Patients with "no-call" results are at increased risk for aneuploidy and should be offered diagnostic testing.** No-call results include "not reported," "indeterminate," or "uninterpretable" findings.
- **Cell-free DNA screening is not currently recommended for multiple gestations.**
- **Routine screening for microdeletions with cell-free DNA is not recommended.**
- **Management decisions, such as pregnancy termination, should not be based on the results of cell-free DNA testing alone.**
- **Negative cell-free DNA results do not guarantee an unaffected pregnancy.**
- **Cell-free DNA screening does not screen for all anomalies or genetic abnormalities.**

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SMFM: Cell-free DNA should not be offered to all women

In October 2015, SMFM released a clarification statement that cell-free DNA should not be offered to all women; nor should it be a requirement that it be covered by insurance for low-risk women. A recent decision analysis by Kaimal and colleagues supports this guidance, demonstrating that cell-free DNA screening is the optimal and most cost-effective test only after age 40. However, women who request it should have it as an option regardless of risk category, with proper counseling.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

For patients at low risk for fetal aneuploidy, conventional first- and second-trimester screening remain the most appropriate strategies. In addition, all women, regardless of age or risk factors, may request diagnostic testing.