

MASTER CLASS

The Complexity of Multiple Gestation



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Multiple gestation is an obstetric condition that confronts every obstetrician at some point. Twin pregnancies, for one, are quite frequent, occurring in 3.2% of all pregnancies. Because of this frequency, it is important that we spend some time reviewing the various presentations of twin pregnancies as well as the potential complications.

Twin pregnancies are not a monolithic condition. As we know, twin pregnancies can present in a two-placenta double-membrane sac (dichorionic diamniotic), in a single-placenta double-membrane sac (monochorionic diamniotic), or in some version thereof.

The clinical presentation of twin pregnancies and the potential complications will vary widely, making it of utmost importance to diagnose chorionicity early on. The simple term “twin pregnancy” is not, as our guest

author says, a term that is precise enough, in and of itself, to ensure optimal management. A distinction between monochorionic and dichorionic twins must be made.

The complications that are of greatest concern in monochorionic pregnancies involve the anastomoses between the twins’ two vasculatures.

In uncomplicated pregnancies, blood is exchanged equally through these anastomoses.

In some pregnancies, however, blood flow becomes unbalanced to the extent that one or both fetuses are compromised.

The management options for complications such as twin-to-twin transfusion syndrome (TTTS) have traditionally been quite limited.

Until recently, management for TTTS involved observation or the removal of excess amniotic fluid.

More recently, however, surgical interventions have been employed with variable success.

Although every obstetrician may not possess the mastery of fetal surgery in these conditions, it is important that all obstetricians nevertheless understand

the options that are available and be able to make accurate diagnoses, offer appropriate counseling, and make referrals if appropriate.

Thus, I believe the focus of this Master Class—monochorionicity, its features, and the facets of good management—will be of significant value to the clinician.

We have invited Dr. Ahmet A. Baschat of the department of obstetrics, gynecology, and reproductive sciences at the University of Maryland, Baltimore, to be our guest professor this month. Dr. Baschat is a recognized national expert in fetal therapy, including various intrauterine surgical procedures. ■

DR. REECE, who specializes in maternal-fetal medicine, is vice president for medical affairs at the University of Maryland, as well as the John Z. and Akiko K. Bowers Distinguished Professor and dean of its school of medicine. He is chair of the Association of American Medical Colleges National Colleges of Deans for 2008-2009. He is a member of the OB.GYN. NEWS Editorial Advisory Board and the medical editor of this column.

Imaging Monochorionic Pregnancies

We now know enough about the development and potential complications associated with monochorionic twin pregnancies that the term “twin pregnancy” is no longer precise enough to be used as a medical term. We must distinguish between monochorionic and dichorionic twins.

Monochorionic twin pregnancies have unique features that substantially increase the risk of fetal death, growth restriction, and other complications. The twins share a single placenta, and their circulations are essentially linked to each other through their placental anastomoses. These linked circulations allow blood to be redirected—sometimes very rapidly—

toward one twin or the other. This is not typically the case in dichorionic pregnancies.

Thus, we must always take both fetuses in a monochorionic twin pregnancy into consideration, because when one fetus is in jeopardy, the other typically is as well. This interdependency is fundamentally different from the less-entwined relationship of dichorionic twins, and makes monitoring more complicated and all the more important.

We must make the distinction between monochorionic and dichorionic twins early on—optimally, in the first trimester. With the opportunity to make this critical distinction—as well as improvements in fetal therapy and advances in ultrasound assessment that allow us to detect potential problems early—we can lay the foundation for the effective, proactive management of these at-risk pregnancies from the first trimester on.

Once the diagnosis of chorionicity is made, medical reports should specify the type of twin pregnancy that is pre-

sent, rather than using what should now be considered the layman’s term “twin pregnancy.”

The Potential Risks

The potential risks of monochorionic pregnancies stem from:

► **Unequal placenta sharing.** In an ideal world, the twins’ single placenta is equally shared. However, it is often the case that one twin will have just 30%-40% of the monochorionic placenta, while the other fetus has the much larger portion. Such unequal placenta sharing leads to an unequal sharing of nutrients, which can lead to growth restriction and severe low birth weight in one of the fetuses.

This type of growth restriction—known as selective intrauterine growth restriction (IUGR)—affects about 10% of all identical twins. It happens quite early in pregnancy and, as we know from singleton growth-restricted fetuses, can lead to a host of troubling complications.

That is why the fetuses in a monochorionic pregnancy can never be treated in isolation. With the early onset of growth restriction in a monochorionic pregnancy, for example, the twin with this complication faces a higher risk of in utero death—an outcome that always negatively impacts the other fetus as well.

In a dichorionic pregnancy, if a co-twin weighs 320 g at 26 weeks and is at high risk of in utero death, we typically would advise the parents to delay delivery. The extremely high likelihood of fetal death of the growth-restricted twin would not justify exposing the otherwise normally grown healthy twin to the risks of prematurity. Accepting the fetal death of the growth-restricted twin and

allowing pregnancy to continue gives the larger fetus a very good chance of being healthy at birth rather than being born premature with a significant risk of prematurity-related complications.

However, in a monochorionic pregnancy, intrauterine demise of the smaller fetus could put the healthy co-twin at a significant risk for acute severe hemorrhage into the placenta and circulation of the growth-restricted twin. This carries the risk of brain, renal, and cardiac damage—or even death—of the co-twin. The option of delaying delivery beyond the point of demise of the smaller twin, therefore, is unacceptable in this setting.

Rather, the fetuses would need intensive monitoring by experts who are alert to all the potential signs of fetal deterioration. Additional options, including fetal therapy, might require even more subspecialty evaluation.

► **Unequal blood volume.** Blood vol-

ume also may be unequally shared. In uncomplicated pregnancies, blood is exchanged equally through the vascular anastomoses that characterize all monochorionic pregnancies. Sometimes, however, the exchange is unbalanced and blood is shunted in one direction without adequate return.

Anastomoses that are between artery and vein act as one-way valves and can lead to significant differences in volume. Artery-to-artery and vein-to-vein connections allow direct exchange in either direction, with the direction of blood flow determined by the difference in blood pressure on either side.

If one fetus develops an unstable circulation or dies, the instability or resultant drop in blood pressure causes the healthy or surviving twin to lose a large amount of blood volume across the connecting vessels and into the sick or dying

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Key Points

- Making an accurate diagnosis of chorionicity early in a twin pregnancy is crucial for the prospective management of potential complications. This is because monochorionic twins have unique features that can lead to unequal placenta sharing and unequal blood volume, increasing the risk of fetal death, growth restriction, and other complications. Early in the first trimester is the optimal time to verify chorionicity.
- Estimating fetal growth by measuring head diameter, abdominal circumference, and femur length is an important aspect of assessing placenta sharing and the availability of nutrients. The abdominal circumference is the single best measurement of fetal nutrient status; a discrepancy

- at 16 weeks increases the risk for subsequent complications.
- Evaluating bladder filling in combination with amniotic fluid volume is an important element of estimating fetal blood volume status.
- Research shows that a combined risk assessment in the first trimester and at 16 weeks can predict selective intrauterine growth restriction and twin-to-twin transfusion syndrome—two of the major complications of monochorionic pregnancies—with greater than 80% accuracy.
- Doppler ultrasound of the umbilical artery is important for assessing placenta sharing and the presence of hemodynamically significant arterio-arterial anastomoses.

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twin. This is why, when one fetus dies, the risk of death for the co-twin can be as high as 60%. It also explains why a surviving co-twin has a significant risk of brain injury.

The intertwin anastomoses account for a range of other pregnancy complications. When placenta sharing is equal but there is a significant mismatch in blood flow and blood volume, twin-to-twin syndrome (TTTS) can develop. In this scenario, the imbalance progresses to the extent that one twin becomes a “donor” of blood volume and the other twin becomes the “recipient.”

A decline in blood volume for the donor twin leads to decreased urine output to the extent that bladder filling virtually ceases and oligohydramnios may progress to anhydramnios. The recipient twin, in the meantime, urinates excessively, leading to polyhydramnios and possibly preterm labor.

TTTS develops in about 10%-15% of monochorionic pregnancies. Overall, however—if you add the approximately 10% that are affected by selective IUGR, and an unknown percentage of pregnancies that may have a bit of both problems or are complicated in other ways to this 10%-15%—I estimate that as many as one-third of monochorionic twins have some kind of significant complication.

For TTTS, endoscopic laser ablation (or laser coagulation) of placental anastomoses has been shown to be an effective treatment and a preferable first-line approach for severe cases diagnosed before 26 weeks. These therapies, however, are available only at specialized centers—a fact that adds to the value of early diagnosis of chorionicity and prospective monitoring for complications.

The Need for Early Diagnosis

We cannot attempt to alleviate complications and improve survival unless a diagnosis of monochorionicity is made early. The diagnosis of chorionicity certainly is more difficult in the second trimester.

However, if a patient has not had a first-trimester scan, a diagnosis should



At left, the presence of chorionic tissue between the layers of amnion from the two sacs produces a “Lambda” sign (circle) that indicates a dichorionic diamniotic pregnancy. At right, the absence of this sign (arrow) indicates monochorionic placentation.



The fetus on the left has a larger abdominal circumference and a higher maximum vertical amniotic fluid pocket, which can point to unequal placenta sharing and/or unequal blood volume and requires follow-up evaluation.

still be attempted.

Monochorionic twin pregnancies remain largely unpredictable. At 12 weeks' gestation, however, if we have diagnosed identical twins, there are several ultrasound parameters we can measure to begin to predict how the pregnancy will proceed and what fetal complications might develop.

Some studies have shown, for instance, that a discrepancy in nuchal translucency between the co-twins of more than 60% means that there is a 60%-70% chance that TTTS will develop.

There also may be some discrepancies in size of other structures that are apparent in the first trimester, such as differences in abdominal circumference, for example, as well as differences in amniotic fluid volume, or bladder size that might be helpful in planning fetal surveillance.

After initial evaluation, we generally recommend that monochorionic twins be evaluated again at 16 weeks, based on research by Dr. Liesbeth Lewi of the University Hospitals in Leuven, Belgium, showing that a combined risk assessment in the first trimester and at 16 weeks can predict selective IUGR or TTTS with greater than 80% accuracy.

In a study of 200 monochorionic diamniotic twin pregnancies, Dr. Lewi found that significant predictors of TTTS, selective IUGR, or intrauterine death in the first trimester were crown-rump length and discordant amniotic fluid volume. At 16 weeks, significant predictors were the differences between the co-twins in abdominal circumference, amniotic fluid volume, and the site of cord insertions. [The site of cord insertion was classified as velamentous, eccentric (more than 2 cm from the placental edge), or marginal (less than 2 cm from the placental edge), and a discordant cord insertion was considered to be the combination of a velamentous cord insertion in one fetus and an eccentric cord insertion in the other fetus.]

The differences between the co-twins in the ultrasound parameters were additive when measured in the first trimester and at 16 weeks. Combined risk assessment detected 58% of the fetal complications by classifying 21% of the 200 pregnancies as high risk, with a false-positive rate of 8%, while the predictive value of one assessment alone was significantly lower (Am. J. Obstet. Gynecol. 2008;199:493.e1-7).

Dr. Lewi's research was among the literature considered recently by a panel of experts assembled by the North Ameri-

can Fetal Therapy Network. The panel has been working on a consensus statement that, when finalized, will make recommendations for early diagnosis of monochorionicity and basic combined risk assessment.

Doppler ultrasound (US) measurements of the umbilical arteries, which depict resistance in the blood vessels and resultant blood flow, also may be helpful. Just as with singleton pregnancies, Doppler US provides information in the monochorionic pregnancy about the vasculature of the placenta and the amount of placenta the fetuses have available for nutrient exchange.

In monochorionic pregnancies, however, Doppler US has the added benefit of being key to diagnosing and evaluating hemodynamically significant arterio-arterial anastomoses that induce variations in diastolic velocity not seen in singleton pregnancies.

The imbalance in blood flow exchange between the co-twins' circulations—again, the primary contributor to the development of TTTS—also can be examined using Doppler assessments of two additional vascular beds: the middle cerebral artery (MCA) and the ductus venosus.

The MCA peak systolic velocity reflects how fast blood is flowing in the brain. Large differences in the MCA can point to TTTS. The ductus venosus, a unique fetal vessel that funnels a proportion of nutrient-rich umbilical venous return directly into the right atrium, similarly can be used to evaluate cardiac status. Doppler screening of the ductus venosus and MCA has its most useful role early in pregnancy.

Again, because most of the amniotic fluid from 16 weeks on is due to fetal urination, and because changes in urine output reflect changes in blood volume status, the assessment of bladder filling and amniotic fluid volume reveals much about blood volume status and possible TTTS.

Whenever we see a monochorionic twin pregnancy, therefore, we face a range of questions: What are the sizes of the fetuses? Is there a discrepancy? What is the ultrasound end-diastolic velocity in each twin? Is it normal? Or, is there variability in the waveform, which is indicative of hemodynamically significant arterio-arterial anastomoses? Is the amniotic fluid volume normal? What do the bladders look like? Does one fetus have a bladder that's barely filling?

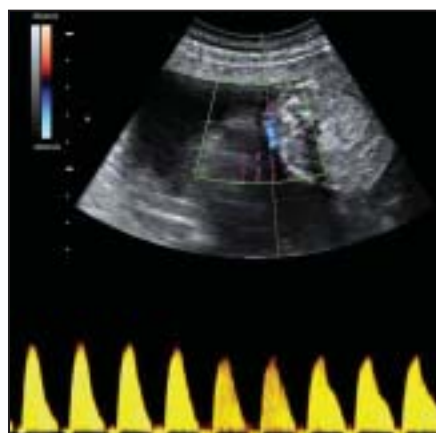
By regularly asking these questions—and using the pregnancy as its own control—we will be alert to the potential problems associated with monochorionicity and more able to proactively plan our monitoring schedules.

A new discrepancy or a change from a previous exam might mean seeing the patient weekly as opposed to every 2 or 3 weeks.

Frequent monitoring is prudent throughout pregnancy as severe TTTS can develop until 22-23 weeks' gestation, even when findings are normal at 18 weeks.

Moreover, milder forms of TTTS, as well as milder forms of selective IUGR, can develop even later. ■

Dr. Baschat reported that he has no disclosures regarding this article.



Umbilical artery Doppler shows significant variation in end-diastolic velocity from positive/absent to markedly reversed, as well as scalloping of the waveform. This indicates the presence of hemodynamically significant arterio-arterial anastomoses.

Finacea Advocated for Treatment Of Acne, Rosacea in Pregnancy

SAN FRANCISCO — For treatment of acne or rosacea in pregnancy, think first, and last, of azelaic acid gel 15% twice daily, Dr. Joseph Bikowski advised.

“It is pregnancy category B. It's the Rice Crispies and Corn Flakes of therapy; you can eat the stuff. It's the one thing you can use for acne and rosacea in pregnancy where you'll never do any harm, and you may do some good,” Dr. Bikowski said in a therapeutic pearls session at the annual meeting of the American Academy of Dermatology.

Other treatments for acne and/or rosacea are rated categories C through X, creating potential medicolegal exposure in the event of a bad pregnancy outcome, he noted. And although other formulations of azelaic acid are also rated category B, azelaic acid gel 15% (Finacea) is less irritating, said Dr. Bikowski, a dermatologist in private practice in Sewickley, Pa.

Dr. Bikowski disclosed that he is a consultant to and on the speakers bureau for Intendis Inc., which markets Finacea.

—Bruce Jancin