ed with small-for-gestational-age infants. Preeclampsia is associated with a fourfold increase in the risk of having a small-for-gestational-age infant.

Maternal autoimmune disorders (lupus and antiphospholipid syndrome, for instance), various medications (including certain anticonvulsants, particular β-blockers, cancer chemotherapy, and steroids), cigarette smoking, and even moderate alcohol use, have also been implicated in causing fetal growth restriction. Treatment of some of these conditions, such as the hypertensive conditions, is necessary for the health of the mother but, unfortunately, will not necessarily improve fetal growth.

Treatment of other conditions, such as those involving maternal lifestyle, will definitely lower the severity of the complication. If the mother is a smoker, for instance, a smoking cessation program is absolutely critical. Her fetus's drop in birth weight will be significantly less if smoking is stopped after the first trimester than if it continues throughout the pregnancy.

Fetal chromosomal abnormalities and congenital malformations are also significantly associated with fetal growth restriction, as is perinatal infection. Malaria may be one of the most significant causes of growth restriction in many countries where this disease is endemic. Even in the United States about 5%-10% of all cases of fetal growth restriction can be attributed to viral or protozoan infections in utero.

Bacterial infections have not traditionally been implicated as causes, but there is emerging evidence that subclinical infection and inflammation, as well as extragenital infection, may be associated with growth restriction.

Experts have long recognized a strong association between fetal growth restriction and prematurity, though it's unclear whether there is a true casual relationship.

Monitoring the Growth-Restricted Baby

When a diagnosis of fetal growth restriction is made, our role then focuses on fetal surveillance and the recognition of fetal stress and compromise.

Ultrasonography, first of all, should be done every 2-4 weeks after the diagnosis is made. Of all the additional modalities that we can use for fetal surveillance, umbilical arterial Doppler, which measures blood-flow impedance in the placenta, is one of the most effective tests we have for detecting a fetus who is getting into trouble. It should be used as our primary test. We now have compelling evidence from more than 20 randomized trials that fetal Doppler surveillance significantly improves outcomes (deaths in utero and other medical outcomes) in well-defined, high-risk pregnancies—most notably those involving fetal growth restriction and preeclampsia.

We can supplement Doppler with traditional tests of fetal heart rate monitoring, namely the nonstress test (NST), and evaluation of amniotic fluid volume. Both nonreactive NST and oligohydramnios have been associated with adverse perinatal outcome.

We also can use the biophysical profile (BPP), which incorporates parameters relating to the heart rate pattern, the fluid levels, umbilical artery Doppler, and examination of growth via ultrasound.

Just as the nonstress test does, the BPP has a low false-negative rate but a high false-positive rate. None of these additional tests is backed by the "level 1" evidence (randomized controlled trials) that Doppler carries, but they have essentially become standards of care. When used once a week, the tests are a valuable part of management, and I have incorporated them into my own evidence-based management guidelines. (See chart below.)

Usually, ominous changes in the fetal heart rate pattern or the BPP will follow nonreassuing Doppler indices—a fact that is indicative not only of the value of umbilical arterial Doppler but the value of these other tests in helping us to assess fetal distress and compromise, and the need for delivery, as completely as possible.

If our umbilical arterial Doppler shows an absence of flow at the end of the cardiac cycle and the other tests are normal, we can—if the pregnancy hasn't reached 34 weeks—step up the frequency of our other tests and attempt to carry the gestation through a bit further. If the end-diastolic flow is reversed, however, we need to intervene promptly. Reversed end-diastolic flow is an ominous sign.

Other ominous signs are a BPP score of 4 or less; an amniotic fluid index of 5 cm or less or a single deepest pocket less than 2 cm; and nonreassuring fetal heart rate patterns such as persistent nonreactive NSTs, continuous deceleration, and poor heart rate variability from one cardiac cycle to another.

The use of venous Doppler sonography is getting more attention today as another back-up test for evaluating fetal well-being when the umbilical arterial Doppler shows absent end-diastolic flow.

Doppler assessment of flow patterns through the inferior vena cava, umbilical vein, and the ductus venosus have all been suggested as supplementary tests—experimentation is underway particularly in Europe—but it is flow through the ductus venosus that may warrant the most attention at this point in time in institutions that have appropriately trained personnel. When flow during atrial contraction is absent or reversed in the ductus venosus, urgent intervention is usually necessary.

Our decisions to deliver, of course, should always be highly individualized, taking into account gestational age, the progression of change, institutional resources and expertise, and other issues. In general, though, once we're at or beyond 34 weeks of gestation, there is no benefit to prolonging the pregnancy if we have any ominous findings.

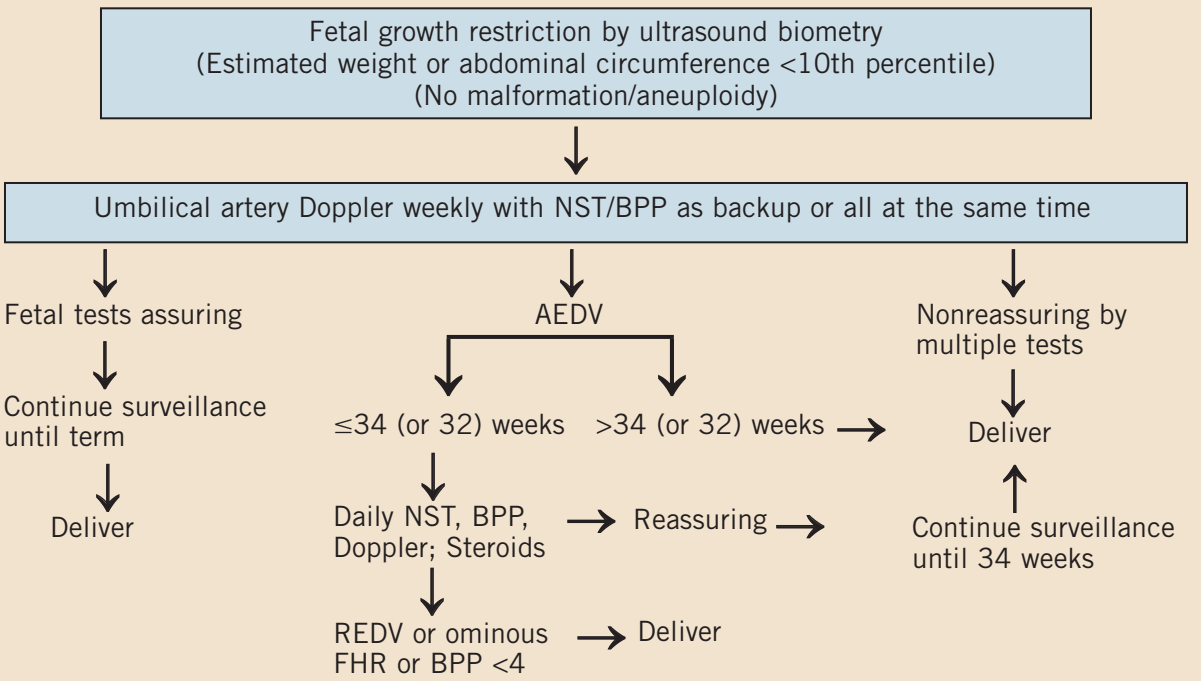
The absence of end-diastolic flow on the umbilical arterial Doppler, for instance, should prompt delivery once we've reached 34 weeks, whereas before 34 weeks we could instead intensify surveillance and watch for additional ominous findings. (Many, however, would use a cutoff of 32 completed weeks based on outcomes in the intensive care nursery of their institution).

We also should not allow pregnancies involving growth restriction to become postdated. There are no clear-cut guidelines addressing the question of whether we should induce babies who have come to term, but if the baby is in jeopardy—if there are multiple signs of compromise or distress—the baby will have a limited ability to tolerate labor, and a cesarean section is best.

Our most difficult decisions come with gestations of less than 28 weeks. Unfortunately, a recent randomized controlled trial of delivering early vs. delaying delivery (the Growth Restriction Invention Trial) brought us no clear answers.

This means that we have to continue utilizing our clinical judgment about the respective risks of a hostile intrauterine environment and the risk of pulmonary immaturity, and have a compassionate, nonpatronizing discussion with the parents. In general, if multiple parameters are abnormal, too much waiting will deprive the fetus of any chance of survival. ■

Fetal Growth Restriction: Fetal Surveillance Guidelines



Note: NST = nonstress test; BPP = biophysical profile; AEDV = absent end-diastolic velocity; REDV = reverse end-diastolic velocity.
Source: Dr. Maulik

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Delaying Umbilical Cord Clamping Precludes Iron Deficiency

BY JOHN R. BELL
Associate Editor

Waiting up to 2 minutes after delivery to cut the umbilical cord led to increased iron status at 6 months, with no adverse associations for mothers or infants, and could be valuable in preventing developmental delays associated with iron deficiencies, according to findings from a large randomized controlled trial.

Dr. Camila M. Chaparro of the University of California, Davis, and colleagues reported results from 358 mother-and-singleton infant pairs delivered at a large obstetric hospital in Mexico City. The primary outcomes were infant blood and iron status at age 6 months—the longest follow-up to date in any trial of delayed cord clamping (Lancet 2006;367:1997-2004).

The investigators randomized mothers to one of two groups: In one group, the umbilical cord was clamped after 10 seconds. In the other group, it was clamped after 2 minutes—coinciding roughly with the usual cessation of cord pulsations—unless the physician determined earlier cord removal was necessary. Ultimately, the mean clamping time for the early-clamping group was roughly 17 seconds, compared with about 94 seconds for the delayed-clamping group—a difference of just over 1 minute.

At 6 months of age, the delayed-clamping infants had significantly higher levels than the early-clamping infants in several measures (adjusted for maternal factors): stored iron (58 mg vs. 31 mg), body iron (343 mg vs. 316 mg), mean corpuscular volume (81.0 fL vs. 79.5 fL), and ferritin (50.7 mcg/L vs. 34.4 mcg/L). Moreover, the incidence of iron deficiency (less than 9 mcg/L) in the early-clamping infants was 7%, compared with 1% in the delayed-clamping group, and unadjusted incidence of iron-deficiency anemia was 4% in early-clamping infants vs. 0% in the delayed-clamping group, the investigators noted. ■