



## OBSTETRICS

### New guidance on timing of elective delivery, screening for thrombophilias, and use of magnesium sulfate for fetal neuroprotection



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From an evolutionary standpoint, not much has changed in pregnancy and childbirth. From a clinical perspective, however, flux is a constant. Three issues, in particular, have seen notable development over the past year:

- optimal timing of elective delivery
- screening for thrombophilias in women who experience recurrent pregnancy loss, fetal growth restriction, preeclampsia, or placental abruption
- use of magnesium sulfate for fetal neuroprotection.

Of course, in the specialties of obstetrics and perinatal medicine, research continues in a variety of other subject areas, as well. Simulation training, diagnosis and manage-

ment of gestational diabetes, and rescue steroid treatment are three examples. Other issues being explored include the use of progesterone to prevent prematurity, the use of ultrasonography to measure cervical length, and the safety of vaginal birth after cesarean delivery. The three areas highlighted here are not the only ones “ready for prime time,” but they are areas of considerable interest and debate.

We have a tradition in obstetrics of not embracing change too quickly. We learned this lesson through our experience with diethylstilbestrol (DES) and thalidomide, and we must continue to use caution whenever new technologies or management approaches are proposed.

## 39 weeks is the rule, provided delivery is truly elective

*Tita ATN, Landon MB, Spong CY, et al. Timing of elective cesarean delivery at term and neonatal outcomes. N Engl J Med. 2009;360(2):111-120.*

When it comes to elective delivery, no one would argue against the wisdom

of continuing pregnancy until at least 39 weeks' gestation in the absence of complications. But what data form the basis of this wisdom, and when might it be prudent to consider earlier delivery?

In a widely publicized study, Tita and colleagues concluded that elective repeat



cesarean delivery before 39 weeks of gestation (i.e., 37 through 38-6/7 weeks) is associated with a higher rate of neonatal respiratory distress and other adverse neonatal outcomes than is delivery at 39 to 40 weeks. Note, however, that the primary outcome of this study was a composite. Therefore, the findings should be interpreted with some caution.

In their report, Tita and coworkers acknowledged that the transient and predominantly minor complications associated with delivery before 39 weeks must be weighed against the risk of fetal death inherent in delaying delivery through 38 full weeks—and an accompanying editorial made the same point.<sup>1</sup> Stillbirth occurs at a rate of 1 case for every 1,000 births in the 37- to 39-week gestational age range—a rate that may be higher than the risks associated with delivery. Even so, the risk of stillbirth at 37 to 39 weeks is very small, and that risk is unlikely to be lowered through routine antenatal fetal testing. We should also remember that the risks of neonatal respiratory distress, transient tachypnea, admission to the neonatal intensive care unit (NICU), and even

cerebral palsy<sup>2</sup> may be increased with delivery at 37 to 38 weeks, or at 42 weeks or later, compared with delivery at 40 weeks.

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

All truly elective deliveries should occur at or after 39 weeks of gestation. However, when indicated, earlier delivery is acceptable—even essential—if we are to minimize maternal and neonatal morbidity and mortality in high-risk circumstances, such as hypertensive disorders of pregnancy, placenta previa, fetal growth restriction, and other conditions.

Investigations are under way to determine whether there is a role for routine betamethasone administration (regardless of indication or gestational age) in the absence of labor before 39 weeks. Until those data come in, we should continue to follow current practice guidelines for antenatal maternal administration of betamethasone—namely, a single course given between 24 and 34 weeks in women who have an elevated risk of preterm delivery.

**FAST TRACK**

All truly elective deliveries should occur at or after 39 weeks

## Population-based screening for thrombophilias is not recommended



Silver RM, Zhao Y, Spong CY, et al, for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (NICHD MFMU) Network. Prothrombin gene G20210A mutation and obstetric complications. *Obstet Gynecol.* 2010;115(1):14-20.

Said JM, Higgins JR, Moses EK, et al. Inherited thrombophilia polymorphisms and pregnancy outcomes in nulliparous women. *Obstet Gynecol.* 2010;115(1):5-13.

Since the mid-1990s, screening for thrombophilias has been recommended in the evaluation of a variety of adverse reproductive

outcomes, including, but not limited to:

- recurrent pregnancy loss
- unexplained stillbirth
- placental abruption
- preeclampsia
- fetal growth restriction.

When a thrombophilia is detected in these settings, the practitioner faces a dilemma—namely, what to do when the mother is otherwise healthy and asymptomatic. All too often the finding of a thrombophilia leads to the initiation of some anticoagulation regimen, ranging from low-dose aspirin all the way to therapeutic anticoagulation with heparin.

Over the past year, several studies and expert opinions have been published that recast the role of thrombophilia screening in obstetric practice.

Writing for the Maternal-Fetal Medicine Units (MFMU) Network, Silver and colleagues concluded that the prothrombin (PT) gene mutation G20210A was not associated with pregnancy loss, preeclampsia, fetal growth restriction, or placental abruption in a low-risk, prospective cohort.

Said and coworkers reached a similar conclusion. In a blinded, prospective cohort study, they screened for the following mutations in 2,034 healthy nulliparous women before 22 weeks' gestation:

- factor V Leiden mutation
- PT gene G20210A mutation
- methylenetetrahydrofolate reductase enzyme (MTHFR) C677T
- MTHFR A1298C
- thrombomodulin polymorphism.

The majority of asymptomatic women who carried an inherited thrombophilia polymorphism had a successful pregnancy outcome. In fact, homozygosity of the MTHFR A1298C mutation was found to be protective.

#### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Population-based screening for thrombophilias is *not* recommended. In fact, some authors have advised against screening for thrombophilias even in the setting of a thrombotic event, suggesting it has limited utility.<sup>3</sup>

The main reason to screen for a thrombophilia at this time is to explore idiopathic thrombosis or a strong family history of the same. There is no need to screen for thrombophilias when the patient has a history of pregnancy loss, placental abruption, preeclampsia, and fetal growth restriction.



**Homozygosity of the MTHFR A1298C mutation was found to be protective in pregnancy**

## If you give magnesium sulfate for fetal neuroprotection, adhere to a protocol

*ACOG Committee Opinion No. 455: Magnesium sulfate before anticipated preterm birth for neuroprotection. Obstet Gynecol. 2010;115(3):669-671.*

**M**agnesium sulfate has a long and glorious history in obstetrics, having been used to prevent eclampsia, to treat preterm

uterine contractions, and now, potentially, to reduce the incidence of central nervous system damage among prematurely delivered infants.

Cerebral palsy (CP) is most commonly associated with prematurity and intrauterine fetal infection. Only in the past two decades has there been a shift away from assigning



the cause of most cases of CP to intrapartum events. Nevertheless, CP remains an important concern among patients and providers, and research continues to find ways to prevent CP or minimize its effects.

Numerous large trials have explored the use of magnesium sulfate to prevent CP in preterm infants. Although their findings have not been as definitive as researchers had hoped, some data do suggest that magnesium sulfate has a protective effect.

The American Congress of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) urge caution in regard to the use of magnesium sulfate for fetal neuroprotection. The SMFM points out that the reported benefits of magnesium sulfate in this setting have been derived largely from secondary analyses. The SMFM recommends that, if magnesium is used at all, it should be administered according to one of the published protocols (three are cited in the ACOG opinion).

The SMFM goes on to warn against choosing magnesium sulfate as a tocolytic solely because of its possible neuroprotective effects.

In a Committee Opinion published last year, ACOG was a bit more definite. "The Committee on Obstetric Practice and the Society for Maternal-Fetal Medicine recognize that none of the individual studies found a benefit with regard to their primary outcome," the opinion states. "However, the available evidence suggests that magnesium sulfate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants. Physicians electing to

use magnesium sulfate for fetal neuroprotection should develop specific guidelines regarding inclusion criteria, treatment regimens, concurrent tocolysis, and monitoring in concordance with one of the larger trials."

Recent editorials have cautioned against using magnesium sulfate for fetal neuroprotection until more data become available,<sup>4</sup> or have left it up to the individual practitioners (or institution) to decide whether it is advisable.<sup>5</sup>

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

The use of magnesium sulfate for fetal neuroprotection when preterm delivery seems likely requires additional research. For now, this practice should be governed strictly by protocol. And it should not be viewed as "standard of care" by our legal colleagues.

When administering magnesium sulfate, avoid giving a cumulative total in excess of 50 g, as this amount may increase the risk of pediatric death.<sup>6</sup>

### FAST TRACK

**If you give magnesium sulfate for fetal neuroprotection, adhere strictly to a protocol**

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