



## INFECTIOUS DISEASE

New guidance this year: We need to be more vigilant for group B strep and influenza in pregnancy and give prophylactic antimicrobials before the incision for cesarean delivery



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Despite continuing advances in obstetric and neonatal care, including the use of antimicrobials, infection remains a major cause of maternal and perinatal morbidity and death. Indeed, infection is among the top five causes of maternal death in the United States, with 10% to 15% of deaths directly linked to it. Maternal and fetal infections are also a common cause of perinatal death. Clearly, interventions to prevent infection or minimize its effect during pregnancy and postpartum are a priority.

This article focuses on three notable

developments of the past year:

- release of revised guidelines on the prevention of perinatal group B streptococcal disease (GBS)
- publication of surveillance data on 2009 influenza A(H1N1) among pregnant women, which reveals the life-threatening nature of the flu in this population
- publication of a Committee Opinion from ACOG on the timing of antimicrobial prophylaxis for cesarean delivery, in which administration within 60 minutes of the start of the procedure is recommended.

## There's room for improvement in GBS screening and prophylaxis, says CDC

*Verani JR, McGee L, Schrag SJ, National Center for Immunization and Respiratory Diseases. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010;59(RR-10):1-36. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm>.*

The latest revision of CDC guidelines on screening and prophylaxis for perinatal group B streptococcal disease were developed by a multidisciplinary working group representing several professional organizations, including ACOG. Information that has

come to light since the most recent guidelines were released in 2002 was incorporated, and areas that have seen suboptimal implementation or interpretation were addressed here as well.

Although the use of prophylactic antibiotics during labor reduces the incidence of invasive GBS during the first week of life, GBS remains a leading cause of neonatal morbidity and death in the United States and elsewhere. Universal screening and intrapartum antibiotic prophylaxis for women who test positive for GBS remain the cornerstone of prevention of early-onset neonatal GBS disease. Penicillin G is still the agent of choice, and ampicillin is an acceptable alternative. When prophylaxis is warranted, intravenous antibiotic administration at least 4 hours before delivery is recommended.

Other recommendations from the CDC include:

- Women who have GBS bacteriuria ( $\geq 10^4$  colony-forming units/mL) any time during pregnancy, and women who had a

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### **WHAT THIS EVIDENCE MEANS FOR PRACTICE**

The implementation of CDC guidelines in 2002 had a salutary impact on the burden of neonatal invasive GBS disease. The 2010 updated guidelines address areas of suboptimal compliance. Health institutions should determine where changes need to be made to better adhere to these guidelines, which are readily available online.<sup>1</sup>

previous infant with invasive GBS disease, should receive intrapartum antibiotic prophylaxis. In these cases, third-trimester screening for GBS is unnecessary.

- All other women should be screened at 35 to 37 weeks' gestation for rectovaginal GBS colonization.
- At the onset of labor or rupture of membranes, antibiotic prophylaxis should be given to all women who tested positive for GBS—with the exception of women who are undergoing cesarean delivery, at any gestational age, with intact membranes.
- If GBS status is unknown, intrapartum prophylaxis should be given for gestational ages below 37 weeks, membrane rupture lasting 18 hours or longer, or temperature of 100.4°F (38.0°C) or above.
- Health-care providers should inform women of their GBS screening results and the recommended interventions.

Some updates to the guidelines clarify areas in which there was some confusion. For example, the guidelines delineate that women who have preterm labor or preterm premature rupture of the membranes (PPROM) should be screened for GBS and started on prophylaxis immediately, unless they have received a negative screen within the preceding 5 weeks. Antibiotics should be discontinued if a woman who has intact membranes is found not to be in true labor or if the GBS culture is negative.

For the woman who has PPROM, antibiotics to prolong latency are sufficient, provided they include adequate GBS coverage; otherwise, GBS prophylaxis is warranted for as long as 48 hours.

### **FAST TRACK**

**Women who have GBS bacteriuria any time during pregnancy, and women who had a previous infant with invasive GBS disease, should receive intrapartum antibiotic prophylaxis**

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In addition:

- Women who are allergic to penicillin and who have no history of anaphylaxis, angioedema, respiratory distress, or urticaria in response to penicillin or a cephalosporin, should be given cefazolin for GBS prophylaxis. Women at risk of anaphylaxis should undergo antimicrobial susceptibility testing. For these women, clindamycin is acceptable if the GBS isolate is susceptible to both clindamycin and erythromycin or resistant to erythromycin with negative inducible clindamycin resistance.
- Otherwise, vancomycin is recommended. Erythromycin is not acceptable because of a high prevalence of resistance.
- The dosage of penicillin is 5 million U initially, followed by 2.5 million to 3 million U every 4 hours.
- If a laboratory providing nucleic acid amplification testing (NAAT) is available, intrapartum testing for women who have unknown GBS status and no intrapartum risk factors (i.e., gestational age <37 weeks, membrane rupture for 18 hours or longer, or temperature  $\geq 100.4^{\circ}\text{F}$ ) is an option.

## Be vigilant for influenza among your pregnant patients—and take necessary action

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

The high incidence of severe morbidity and death among pregnant women who contract H1N1 influenza is consistent with the findings of several studies, suggesting that pregnant women are especially vulnerable to the virus. Although Siston and colleagues focused on pandemic influenza, which may be more severe than seasonal flu, their data and other studies suggest that pregnant women have increased susceptibility to influenza-like illness during regular flu season (October to May).

More than 10% of pregnant women may have confirmed influenza during flu season, making it one of the most common infections during pregnancy. Therefore, during flu season, providers should maintain a high index of suspicion for viral infection. Antiviral treatment—typically oseltamivir (75 mg orally twice daily) or zanamivir (5 mg inhaled twice daily) for 5 days—should be administered promptly, ideally within 2 days of the onset of symptoms.

If a pregnant woman is exposed to influenza, 10 days of prophylactic antiviral therapy (75 mg oral oseltamivir or 10 mg inhaled zanamivir daily) is indicated.

The CDC makes recommendations annually about which antivirals to use. Oseltamivir and zanamivir are preferred because they cover both types of human influenza (A and B), and 99% of circulating influenza viruses are susceptible to them.

ACOG recently emphasized the high-risk nature of influenza during pregnancy and urged universal vaccination of women who will be pregnant or postpartum during the flu season as “an integral element of prenatal care.”<sup>1</sup>

*Siston AM, Rasmussen SA, Honein MA, et al, for the Pandemic H1N1 Influenza in Pregnancy Working Group. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. JAMA. 2010;303(15):1517–1525.*

The recent H1N1 pandemic highlighted the status of influenza as a major public health problem, not only among children and the elderly but especially among pregnant women. This report by Siston and colleagues describes the US experience of the pandemic. To ascertain the severity of infection during pregnancy, the authors analyzed data from 788 pregnant women who developed symptoms of H1N1 infection between April and August 2009. These women were identified through the CDC national surveillance system. Data from an additional 165 women who developed symptoms through December 2011 and who were admitted to an ICU because of influenza were also analyzed.

Siston and colleagues found a high case-fatality rate (5%) among pregnant women who had influenza. Almost one fourth (22.6%) of women who were hospitalized with



influenza were admitted to an ICU because of severe illness.

The timing of antiviral treatment influenced the course of the illness. For example, women who received antiviral treatment within 2 days of the onset of symptoms had a significantly lower risk of death (0.5%), compared with women who received treatment within 3 to 4 days (5%) and with

women who were treated after 4 days (27%). Women who were not treated at all also had an elevated risk of ICU admission and death, although that risk was not as high as it was among women treated 4 days or longer after the onset of symptoms. This finding suggests that severity of illness may play a role in determining who receives antiviral treatment.

## ACOG: Give prophylactic antimicrobials *before* the incision in cesarean delivery

*ACOG committee opinion no. 465: Antimicrobial prophylaxis for cesarean delivery: timing of administration. Obstet Gynecol. 2010;116(3):791-792.*



**Whenever feasible, administer antimicrobials within 60 minutes before the start of cesarean delivery**

The use of antimicrobial prophylaxis for cesarean delivery is associated with a reduction of 50% or more in the rates of post-cesarean infection and severe adverse outcomes, including maternal death. However, there has been some controversy surrounding the question of timing of antimicrobial administration. Should the drugs be administered at the time the cord is clamped or prior to the cesarean skin incision? And, if the latter, just how long before the incision should antimicrobials be given?

ACOG weighed in on this question in September 2010 in a Committee Opinion based on a review of data. It recommended that, whenever feasible, antimicrobials should be administered within 60 minutes before the start of the procedure.

In the past, antimicrobial administration at the time of cord clamping was proposed to reduce fetal exposure and prevent the masking of neonatal infection (falsely negative culture results). However, the data ACOG reviewed from randomized, clinical trials indicate that pre-incision antimicrobials may

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Antimicrobial prophylaxis for surgical-site infection is a well-established practice for both obstetric and gynecologic surgery. Cesarean delivery accounts for one third (more than 1.3 million) of all births in the United States each year and carries a risk of infection at least five times higher than that associated with vaginal delivery. Given the rising incidence of cesarean delivery in the United States and elsewhere, the prevention of postcesarean infection is a priority.

This ACOG Committee Opinion should prompt providers who continue to administer antibiotics after cord clamping to reevaluate the practice.

Even so, given the relative paucity of randomized trials addressing this issue and the mixed results from individual studies, it is essential that we continue to monitor the effectiveness and safety of pre-incision prophylaxis.

Larger follow-up studies to further evaluate resistance profiles and the effects of pre-incision administration on the newborn should be undertaken in concert with implementation of this recommendation.



further reduce the risk of infection (including endometritis and wound infection) without apparent perinatal harm.

First-generation cephalosporins (commonly, 1 g of cefazolin) remain the antibiotic of choice, but the combination of clindamycin and gentamicin was suggested as an acceptable alternative for women who are allergic to penicillin.

ACOG reviewed studies by Thigpen and colleagues and Sullivan and coworkers, as well as a meta-analysis by Costantine and associates.<sup>2-4</sup> The relatively small size of these studies and the mixed results of other studies point to the need for further investigation, a fact acknowledged by ACOG. Nevertheless, the committee concluded that “preoperative

administration significantly reduces endometritis and total maternal infectious morbidity, compared with administration of antimicrobials after umbilical cord clamping.”<sup>2</sup>

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