INFECTIOUS DISEASE

New data elucidate the risk of recurrence for chorioamnionitis, explore the utility of azithromycin as treatment for chorioamnionitis, question the need for universal STI screening at the time of IUD insertion, and highlight the benefits of chlorhexidine in preventing hospital-borne infection

Patrick Duff, MD
Dr. Duff is Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville.

The author reports no financial relationships relevant to this article.

The past year has seen the publication of four studies with immediate relevance for clinicians:

- a retrospective, population-based cohort study that explores whether women who have chorioamnionitis in one pregnancy are at risk for the same type of infection in a subsequent pregnancy
- another retrospective cohort study that assesses the clinical utility of testing for gonorrhea and chlamydia before inserting an intrauterine device (IUD)
- an elegant primate experiment that highlights the value of azithromycin in subjects with chorioamnionitis
- a multicenter, randomized, nonblinded trial in seriously ill patients to determine whether daily bathing with chlorhexidine-impregnated washcloths can reduce the acquisition of multidrug-resistant organisms and the incidence of hospital-acquired bloodstream infection.

Chorioamnionitis in one pregnancy is likely to recur in the next gestation

Cohen-Cline HN, Kahn TR, Hutter CM. A population-based study of the risk of repeat clinical chorioamnionitis in Washington State, 1989–2008. Am J Obstet Gynecol. 2012;207(6):473.e1–e7.

This retrospective, population-based cohort study (Level II evidence) is one of the few to examine the risk of recurrence for chorioamnionitis, and the findings are intriguing. Women who were infected during their first delivery were 3.43 times more likely to become infected in their second delivery than women who did not have chorioamnionitis in their first pregnancy (95% confidence interval [CI], 2.67–4.42; P <.001). This association persisted even after adjustment for potential confounders, such as age, ethnicity, presence of premature rupture of membranes (PROM), and internal fetal monitoring.

Chorioamnionitis is a common affliction

This infection complicates approximately 5% of term deliveries and a significantly higher

IN THIS ARTICLE

WHAT THIS EVIDENCE MEANS FOR PRACTICE

When a patient has a history of chorioamnionitis, we should do everything possible to reduce her risk for recurrent infection. For example, we should screen her for lower genital tract infections that predispose to chorioamnionitis:

- gonorrhea
- chlamydia
- bacterial vaginosis
- GBS.

If the patient has any of the first three infections, treat her immediately with the appropriate antibiotics. If she is colonized with GBS, administer one of the intrapartum antibiotic regimens recommended by the Centers for Disease Control and Prevention (CDC).

If the patient has a history of preterm PROM or spontaneous preterm delivery, initiate prophylaxis with progesterone and assess her cervical length periodically to determine whether cerclage is indicated.

During labor, make every effort to minimize the duration of ruptured membranes, the length of invasive monitoring, and the number of internal vaginal examinations.

At the earliest sign of intra-amniotic infection, treat the patient with broad-spectrum antibiotics, usually ampicillin plus gentamicin.

percentage of preterm deliveries. The principal causative organisms are group B streptococci (GBS), *Escherichia coli* and other aerobic Gram-negative bacilli, both Gram-positive and Gram-negative anaerobes, and genital mycoplasmas.

The main risk factors for chorioamnionitis are:

- prematurity
- prolonged labor
- prolonged rupture of membranes
- multiple internal examinations
- internal fetal monitoring
- low socioeconomic status
- preexisting genital tract infection (eg, bacterial vaginosis, GBS colonization).

Infants delivered to infected mothers are at increased risk for sepsis, pneumonia, and meningitis. Severely infected infants, particularly those who are premature, are also at increased risk for cerebral palsy.

Details of the study

This investigation focused on women in Washington State who had a first pregnancy from 1989 through 2008 and then had at least one additional birth during the study period.

Participants included 6,219 women who had chorioamnionitis in their first pregnancy and 25,294 women who did not. Using logistic regression, Cohen-Cline and colleagues estimated the odds ratio for chorioamnionitis in the second delivery, taking into account the following potential confounders:

- maternal age
- ethnicity
- presence of PROM
- use of internal monitoring
- smoking.

As I stated above, women who had chorioamnionitis in their first pregnancy were 3.43 times as likely to have it again in their second pregnancy.

In low-risk populations, universal screening for sexually transmitted infections is probably unnecessary before IUD insertion

Sufrin CB, Postlethwaite D, Armstrong MA, et al. Neisseria gonorrhea and Chlamydia trachomatis screening at intrauterine device insertion and pelvic inflammatory disease. Obstet Gynecol. 2012;120(6):1314–1321.

This retrospective cohort study (Level II evidence) focused on women who had an IUD inserted in a managed-care practice at Kaiser Permanente of Northern California

CONTINUED ON PAGE 32

CONTINUED FROM PAGE 30

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This study provides reassurance that, at least in a relatively affluent managed-care population, universal testing for STIs is probably not necessary. When testing is indicated, it can be performed on the same day that the IUD is inserted, minimizing the number of office visits.

What is less clear is whether the same protocol can be applied to a population with a significantly higher prevalence of STIs. In such a population, universal screening for gonorrhea and chlamydia may be more prudent. However, screening still can be performed on the same day as IUD insertion.

during a 5-year period. Sufrin and colleagues compared the incidence of pelvic inflammatory disease (PID) within 90 days after insertion among women who were, and were not, screened for gonorrhea and chlamydia.

Among 57,728 IUD insertions, 47% involved women who were unscreened within 1 year of the procedure. Among women who were screened, 19% were tested on the day of IUD insertion.

The overall risk of PID in the study cohort was very low—0.54% (95% CI, 0.48–0.60). Investigators were unable to identify any significant difference in the risk of PID between women who had no screening versus those who were screened. Among women who were screened, same-day screening was equivalent to prescreening.

Investigators concluded that the most reasonable protocol is to screen on the basis of risk factors on the same day as IUD insertion. If the patient has obvious evidence of endocervicitis (ie, mucopurulent discharge), IUD insertion should be delayed. Otherwise, if the patient has risk factors for infection, screening should be followed by IUD insertion.

If the screen is positive, the patient should be treated in accordance with the latest CDC recommendations, and the IUD can be left in place.

Sufrin and colleagues concluded that adherence to this protocol would be associated with a very low, and clinically acceptable, risk of PID.

FAST TRACK

When STI testing is necessary before IUD insertion, it can usually be performed on the same day as insertion

STI screening need not be an obstacle to IUD use

The IUD is an excellent method of contraception, and it is suitable for most patients. It is particularly useful for women who have difficulty remembering to take a pill each day or to use a barrier method of contraception at each episode of coitus.

Obstacles to more widespread use of the IUD include:

- high initial cost
- misconceptions on the part of the patient about the mechanism of action and adverse effects of the device
- cumbersome protocols that require multiple physician visits for counseling and sexually transmitted infection (STI) testing before the device is inserted.

In a primate model of intra-amniotic infection with *Ureaplasma*, maternal azithromycin prolonged gestation

Grigsby PL, Novy MJ, Sadowsky DW, et al. Maternal azithromycin therapy for Ureaplasma intraamniotic infection delays preterm delivery and reduces fetal lung injury in a primate model. Am J Obstet Gynecol. 2012;207(6):475.e1–e14.

Grigsby and colleagues assessed the efficacy of azithromycin—with and without anti-inflammatory agents—in delaying preterm birth and minimizing fetal lung injury in a primate model. They found that azithromycin significantly prolonged gestation.

CONTINUED ON PAGE 34

CONTINUED FROM PAGE 32

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Because IV azithromycin rapidly achieved inhibitory concentrations in amniotic fluid and maintained these concentrations over 10 days of treatment, it significantly reduced the concentration of *Ureaplasma* in the amniotic fluid as well as the risk of histologic injury to the fetal lung.

Accordingly, I recommend that azithromycin remain a key component of the prophylactic regimen for patients with preterm PROM. It also may be advisable to add azithromycin to the usual combination of ampicillin plus gentamicin for empiric treatment of chorioamnionitis.

FAST TRACK

Azithromycin should remain a key component of prophylaxis for patients with preterm PROM

Details of the study

The study involved 16 chronically instrumented rhesus monkeys who received intra-amniotic inoculation with *Ureaplasma parvum* (10^7 colony-forming units/mL) and were then observed. When contractions began, as they invariably did, six monkeys received no treatment, five received intravenous (IV) azithromycin (12.5 mg/kg every 12 hours) for 10 days, and five received azithromycin plus dexamethasone and indomethacin.

Key outcome measures were the intra-amniotic concentration of proinflammatory mediators, the frequency of positive amniotic fluid cultures for *U parvum*, and the extent of histologic fetal lung injury.

In treated animals, the mean (SD) inoculation-to-delivery interval was 20.9 (1.4) days, compared with 13.7 (2.5) days in untreated monkeys ($P < .05$).

In addition, there was a twofold to threefold increase in the percentage of undelivered animals at 18 to 20 days after inoculation in the treatment group, compared with the no-treatment group. Treatment also significantly decreased the *Ureaplasma* colony count in the amniotic fluid, effectively eliminating the organism within 4 days.

In both treatment groups, the amniotic fluid concentration of proinflammatory mediators decreased significantly, compared with the untreated group. Treatment also significantly reduced the magnitude of deleterious histologic changes in the fetal lungs.

Somewhat surprisingly, dexamethasone and indomethacin did not enhance the treatment effect of azithromycin. Moreover, despite prolongation of pregnancy, all animals in the treatment group still delivered prematurely.

Why treatment should target genital mycoplasmas

Chorioamnionitis is an importance cause of preterm labor and preterm delivery. The principal pathogens are part of the normal vaginal flora: aerobic Gram-negative bacilli, aerobic Gram-positive cocci, anaerobes, and genital mycoplasmas.

Most treatment regimens for chorioamnionitis (eg, ampicillin plus gentamicin) do not specifically target the genital mycoplasmas. However, the most commonly recommended prophylactic antibiotic regimens for patients with preterm PROM include agents with specific action against mycoplasmas, namely erythromycin and azithromycin.

In this clinical setting, antibiotic prophylaxis prolongs the latency period and decreases the frequency of both maternal and fetal/neonatal infection.

This elegant basic science investigation sheds new light on the importance of the genital mycoplasmas in the pathogenesis of preterm labor and helps to explain why drugs like erythromycin and azithromycin may be so valuable in prolonging the latent period and reducing the frequency of infection and injury in the baby.

Is there a link between chorioamnionitis and cerebral palsy?

Read the commentary on this possible association by Errol R. Norwitz, MD, PhD, in the December 2010 issue of OBG MANAGEMENT.

It's available in the archive at obgmanagement.com

Daily bathing with chlorhexidine cloths can protect hospitalized patients from serious infection

Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. N Engl J Med. 2013;368(6):533–542.

This multicenter, randomized, nonblinded trial of 7,727 seriously ill patients sought to determine whether daily bathing with chlorhexidine-impregnated washcloths can decrease the acquisition of multidrug-resistant organisms and the incidence of hospital-acquired bloodstream infection.

Each day, patients in eight ICUs and one bone-marrow transplant unit bathed themselves, or were bathed by nursing staff, with 2% chlorhexidine-impregnated cloths or non–antimicrobial washcloths. All body surfaces except the face were cleansed. After 6 months, each unit changed to the other method of bathing.

Investigators focused on two outcomes:

- the prevalence of colonization of the nares with methicillin-resistant *Staphylococcus aureus* (MRSA) or colonization of the perirectal area with vancomycin-resistant enterococci (VRE)
- the frequency of hospital-acquired bloodstream infection (bacterial or fungal) detected more than 48 hours after admission to the unit.

The overall rate of MRSA or VRE acquisition was reduced by 23% when patients were bathed with chlorhexidine (5.10 versus 6.60 cases per 100 patient-days; $P = .03$). The overall rate of hospital-acquired bloodstream infection was reduced by 28% during the intervention period (4.78 vs 6.60 cases per 1,000 patient-days; $P = .006$).

In particular, the rate of central-catheter–associated bloodstream infection was 53% lower during the intervention (1.55 vs 3.30 cases per 1,000 catheter-days; $P = .004$).

The intervention had the greatest impact on infections caused by Gram-positive and fungal organisms.

The protective effect of chlorhexidine bathing was greatest among patients who had the longest length of stay in the unit.

Chlorhexidine did not cause an increased frequency of skin reactions. Moreover, use of the antiseptic washes did not cause the emergence of MRSA or VRA isolates with high-level resistance.

This study is of great interest in light of a recent report that demonstrated that preoperative preparation of the skin with chlorhexidine was more effective than preparation with povidone-iodine in reducing the risk of surgical-site infections after major operative procedures.[1] Not only is chlorhexidine highly active against the usual bacteria that colonize the skin of hospitalized patients, it also has residual antibacterial activity that further decreases the colonization of the patient's skin by microbes.

Reference

1. Darouiche RO, Wall MJ Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. N Engl J Med. 2010;362(1):18–26.

FAST TRACK

Order daily bathing (excluding the face) with chlorhexidine for all seriously ill patients who require prolonged hospitalization

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This study has two clear implications for ObGyns. First, chlorhexidine washes should be used by all patients who are scheduled for surgery, particularly those undergoing procedures that carry a relatively high risk of postoperative wound infection, such as total abdominal hysterectomy, radical hysterectomy, and cesarean delivery. In morbidly obese patients, particular attention should be directed to the skin beneath the abdominal panniculus.

Second, when we have seriously ill obstetric or gynecologic patients, especially those with long-term indwelling catheters who require prolonged hospitalization, we should order daily bathing (excluding the face) with chlorhexidine.