



# INFECTIOUS DISEASE



The focus here is twofold: dealing with H1N1 influenza in vulnerable populations and taking up strategies to prevent post-operative infection in women undergoing cesarean delivery

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Six recent articles stand out in the field of infectious disease:

- an assessment of outcomes of seriously ill patients who were hospitalized early in the course of the H1N1 influenza epidemic. The authors highlight major differences in the epidemiology of this infection, compared with regular seasonal flu
- an examination of outcomes of pregnant women who developed H1N1 influenza
- an exploration of the use of blunt needles during cesarean delivery to prevent glove perforation

- an evaluation of the utility of prophylactic antibiotics in ostensibly low-risk women undergoing scheduled cesarean delivery
- a look at the timing of antibiotic prophylaxis for cesarean delivery
- a comparison of skin preparation techniques in the prevention of surgical-site infection.

The focus on cesarean delivery in most of these studies seems particularly appropriate, now that this operation has become the most frequently performed major surgical procedure in US hospitals.

## H1N1 virus hits hardest during pregnancy and chronic illness

*Jain S, Kamimoto L, Bramley AM, et al, for 2009 Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation Team. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med. 2009;361(20):1935-1944.*

This retrospective survey of patients hospitalized for at least 24 hours for treatment of influenza-like illness included 272 patients who were given a diagnosis of H1N1

influenza, based on real-time, reverse-transcriptase, polymerase chain reaction assay. Sixty-seven (25%) of these patients were admitted to an ICU, and 19 (7%) died. All of the patients who died had been treated in an ICU, and two thirds had an underlying medical condition. Three of the deaths involved pregnant women. None of the patients who died received antiviral therapy within 48 hours of the onset of symptoms. Those who died were also less likely to have been

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**FAST  
TRACK**

**Essentially all strains of H1N1 virus are resistant to amantadine and rimantadine**

vaccinated against seasonal influenza in 2008–2009.

### Details of the trial

The 272 patients included in this study sample represented 25% of the total number of patients hospitalized in the United States for treatment of influenza between April and mid-June 2009. They exhibited the following characteristics:

- **median age:** 21 years
- **race and ethnicity:** 30% were Hispanic, and 27% were non-Hispanic white
- **most common symptoms:** fever and cough, although diarrhea or vomiting was reported in 39% of patients
- **underlying medical illness:** present in 73% (198 patients), including 60% of children and 83% of adults. At least two underlying medical conditions were present in 32% of patients. Asthma was the most common comorbid condition
- **pregnancy:** 18 patients were pregnant. Four of the pregnant patients also had asthma, and two had diabetes
- **obesity:** 29% of adults were obese. Morbid obesity was present in 26%. More than 75% of obese and morbidly obese patients had at least one underlying medical illness
- **bloodwork at admission:** 20% of patients were leukopenic; 37% were anemic; and 14% were thrombocytopenic
- **chest film:** 40% of patients who underwent chest radiography had findings consistent with pneumonia. Findings included bilateral infiltrates in 66 patients, a unilobar infiltrate in 26, and multilobar infiltrates in two
- **antiviral therapy:** 75% ultimately received antiviral drugs, with a median time from onset of illness to initiation of therapy of 3 days (range, 0–29 days). Only 39% received antiviral therapy within 48 hours of the onset of symptoms
- **antibiotic therapy:** 79% of patients received antibiotics for presumed superimposed bacterial infection. The most commonly used antibiotics were ceftri-

axone, azithromycin, vancomycin, and levofloxacin.

### Study offers 4 useful lessons

The study by Jain and colleagues offers clinically applicable lessons:

- it reinforces the point that children and young adults, including pregnant women, are at increased risk of serious morbidity and mortality
- it demonstrates that most seriously affected patients have at least one underlying medical condition, such as asthma
- it highlights the importance of pregnancy and morbid obesity as major conditions that contribute to serious complications from influenza. The 7% prevalence of pregnant patients is significantly higher than the 1% prevalence that would typically be expected with seasonal influenza. Similarly, the 26% prevalence of morbid obesity greatly exceeds the estimated 5% prevalence in the adult US population
- it confirms the importance of treating patients early in the course of their illness with antiviral drugs such as oseltamivir. Notably, none of the patients who died received treatment within 48 hours of the onset of illness, when the drugs are most likely to be effective.

### How to treat H1N1 influenza

The vast majority of strains of the 2009 H1N1 virus are susceptible to oseltamivir and zanamivir, but essentially all strains are resistant to amantadine and rimantadine.<sup>1</sup> Therefore, all individuals who are hospitalized should be treated with one of two regimens:

- oseltamivir, 75 mg orally, twice daily for at least 5 days
- zanamivir, 10 mg by inhalation, twice daily for at least 5 days.

These same regimens should be used for outpatients who are at high risk of complications.

Ideally, antiviral treatment should be administered within 48 hours of the onset of symptoms, but **do not withhold treatment**



**FAST TRACK**

**Vaccinate pregnant women against H1N1 influenza using only the inactivated vaccine, not the live virus**

**even if more than 48 hours have elapsed since the onset of illness.**<sup>2,3</sup>

Both oseltamivir and zanamivir are also effective for *prevention* of infection in susceptible patients who have been exposed to H1N1 influenza. The appropriate dosage of oseltamivir for **prophylaxis** is 75 mg orally once daily for 10 days. The corresponding dosage of zanamivir is 10 mg by inhalation once daily for 10 days.<sup>1</sup>

The most effective method of prophylaxis, of course, is vaccination with the new H1N1 vaccine.<sup>4</sup> There are two forms of the vaccine—a live virus nasal vaccine and an inactivated vaccine for intramuscular administration. Pregnant women should receive only the inactivated vaccine.

The key reservoirs of all influenza A viruses are migrating waterfowl, pigs, and humans. The current H1N1 strain of virus contains eight unique RNA segments that are a mixture of components from avian, pig, and human influenza viruses.<sup>2</sup> The pandemic resulting from this virus is unusual because the continent of origin was North America (Mexico) rather than Asia, the season of

origin was spring rather than fall, and the patients at greatest risk of dying have been children and young adults rather than infants and the elderly.<sup>3</sup>

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

Women who are pregnant or planning to become pregnant should be vaccinated against H1N1 influenza. Use the inactivated virus if a woman is already pregnant.

After exposure to H1N1 influenza, unvaccinated pregnant women and other patients at high risk of developing the virus should be given oseltamivir or zanamivir prophylactically, using the dosage and route of administration described above for **prophylaxis**.

Pregnant women and other high-risk patients who exhibit symptoms of H1N1 influenza should be given oseltamivir or zanamivir, using the dosage and route of administration described above for **treatment**, ideally within 48 hours of the onset of symptoms.

## For pregnant and postpartum patients, base treatment of H1N1 flu on symptoms, not rapid tests

*Louie JK, Acosta M, Jamieson DJ, et al. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. N Engl J Med. 2010;362(1):27-35.*

**L**ouie and coworkers describe the outcome of a statewide surveillance program by the California Department of Public Health. They reviewed the medical records of 94 pregnant women, eight women who were within the first 2 weeks postpartum, and 137 nonpregnant women of reproductive age who were hospitalized with confirmed 2009

H1N1 influenza between April 23 and August 11, 2009.

Eighteen pregnant women and four postpartum patients (22%) required intensive care, and 16 (73%) of these women had to be ventilated mechanically. Of the 18 pregnant women who required treatment in the ICU, 12 delivered in the hospital, and four underwent emergent cesarean delivery in the ICU.

Eight (8%) of the 102 pregnant and postpartum patients died. None of these eight women received antiviral therapy within 48



hours of the onset of symptoms. In fact, for pregnant and postpartum patients, a delay in administration of antiviral therapy beyond 48 hours after the onset of symptoms produced a 4.3 relative risk of death (95% confidence interval [CI], 1.4–13.7), compared with patients who were treated early in the course of their infection.

### Details of the trial

The women in this trial had the following characteristics:

- **gestational age:** five (5%) of the 94 pregnant women were in the first trimester, 35 (37%) were in the second trimester, and 54 (57%) were in the third trimester
- **underlying conditions** were present in 34% of the pregnant and postpartum women and 60% of nonpregnant women. These conditions placed them at increased risk of complications from influenza. The most common underlying condition was asthma
- **antiviral therapy** was administered to approximately 80% of both pregnant and nonpregnant women. However, only 50% of pregnant women and 34% of nonpregnant women received treatment within 48 hours of the onset of symptoms
- **antibiotic therapy** was given to 45% of pregnant women and 58% of nonpregnant women for presumed secondary bacterial infection

- **false-negative test results:** 153 women underwent rapid tests for influenza, 38% of which were falsely negative.

### Treat pregnant patients expediently

This article is an excellent complement to the study by Jain and colleagues described on page 37. It strikingly illustrates the heightened risk of morbidity and mortality that pregnant women face when they develop H1N1 influenza. Louie and coworkers documented an influenza-specific mortality ratio (maternal deaths for every 100,000 live births) of 4.3. They also provide clear evidence of the perils of relying on rapid diagnostic tests and withholding antiviral treatment if the rapid test is negative. In their series, 38% of rapid tests were falsely negative. In pregnant women, when antiviral therapy was delayed more than 48 hours, the relative risk of death was 4.3, compared with patients who were treated within 48 hours of the onset of symptoms.

#### WHAT THIS EVIDENCE MEANS FOR PRACTICE

If there is a clinical suspicion of influenza in a pregnant or postpartum patient, treat her immediately with one of the antiviral regimens outlined on page 38—regardless of the outcome of the rapid test for influenza.



Louie and coworkers documented an H1N1 influenza-specific mortality ratio of 4.3 maternal deaths for every 100,000 live births

## Blunt needles reduce needle sticks during cesarean delivery

Sullivan S, Williamson B, Wilson LK, Korde JE, Soper D. Blunt needles for reduction of needlestick injuries during cesarean delivery. *Obstet Gynecol.* 2009;114 (2 Pt 1):211–216.

Using glove perforation as a proxy for needlestick injuries, Sullivan and col-

leagues compared blunt needles with sharp needles during cesarean delivery. Ninety-seven women had all anatomic layers reapproximated using blunt needles, and 97 had them reapproximated using sharp needles. The overall glove perforation rate was 12.3%. For sharp needles, the perforation rate was 17.5%, and for blunt needles it was 7.2%



**FAST TRACK**

Transmission of hepatitis B via a contaminated surgical needle has been well documented

(relative risk [RR], 0.66; 95% CI, 0.49–0.89). The key protective effect of the blunt needles was confined to the assistant surgeon (RR, 0.54; 95% CI, 0.41–0.71). The RR for glove perforation involving the primary surgeon was 0.8 (95% CI, 0.53–1.2).

**Details of the trial**

Glove type, number of gloves, needle size, and type and gauge of suture material were left to the discretion of the surgeon. Glove perforations were identified by filling the gloves with 1,000 mL of water and applying pressure to the palm and each finger. The secondary endpoint of the study was physician satisfaction with the needle. Primary and assistant surgeons reported comparable levels of dissatisfaction with blunt needles, compared with sharp needles ( $P < .001$ ). However, 92% of primary surgeons and 93% of assistant surgeons rated the blunt needles as at least “acceptable” for use.

**Needle stick has led to hepatitis B transmission**

Earlier studies reported a rate of glove perforation of 20% to 26% during open abdominal procedures. In an investigation at our center, we noted glove perforation in 13% of cesarean deliveries.<sup>5</sup> In this and another investigation, the frequency of perforation did not

vary with the level of training of the surgeon or time of day of the procedure.<sup>5,6</sup> The most common sites of perforation were the thumb, index finger, and middle finger of the non-dominant hand. The most common mechanism of injury was handling the needle with the operator’s gloved hand rather than with an instrument.

Double-gloving significantly reduces the risk of injury to the inner glove and, subsequently, to the surgeon’s skin. (Note: Double-gloving does *not* decrease tactile sensation or increase the risk of mishap.<sup>6</sup>)

The study by Sullivan and colleagues demonstrates that use of blunt needles offers an additional measure of protection against a penetrating injury to the surgeon’s bare skin. Although no surgeon has yet contracted HIV infection from a surgical needle, the transmission of hepatitis B via contaminated surgical needle has been well documented.

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

Prudence dictates that we use all proven measures to prevent intraoperative blood exposure. Use of blunt needles should be added to interventions such as double-gloving and use of a neutral zone in which to pass sharp objects.

# Prophylactic antibiotics reduce postcesarean infection, even in low-risk women

*Dinsmoor MJ, Gilbert S, Landon MB, et al, for Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Perioperative antibiotic prophylaxis for nonlaboring cesarean delivery. Obstet Gynecol. 2009;114(4):752–756.*

**I**nfection is the most common postoperative complication of cesarean delivery, now the most frequently performed major operation in America. The principal infection is endometritis, followed by wound infection and urinary tract infection. The frequency of

wound infection is on the rise because of the steadily increasing prevalence of obesity in the obstetric population.

Dinsmoor and coworkers conducted this secondary analysis using data from an earlier observational study of 9,432 women who underwent cesarean delivery before the onset of labor. Of these women, 6,006 (64%) received antibiotic prophylaxis.

Women treated prophylactically had a significantly lower rate of endometritis (adjusted odds ratio [OR], 0.40; 95% CI, 0.28–0.59) and of wound infection (adjusted OR, 0.49; 95% CI, 0.28–0.86). The frequency of other infection-related complications was not significantly reduced (adjusted OR, 0.39; 95% CI, 0.13–1.12).

Overall, the size of the effect for endometritis was small; endometritis developed in 2.0% of women in the group that received prophylaxis and 2.6% of women in the group that did not. The size of the effect was even smaller for wound infection.

In this uncontrolled series, 113 patients had to be treated to prevent one case of endometritis or wound infection.

## Details of the trial

The original observational study from which this analysis derives was performed by the Maternal-Fetal Medicine Units Network at 13 centers in 1999–2000. The choice of antibiotics and the timing of administration were left to the discretion of the attending physician.

Principal endpoints were the occurrence of postoperative endometritis and wound infection. Secondary endpoints were less common infection-related complications such as maternal sepsis, fascial dehiscence or evisceration, necrotizing fasciitis, pelvic abscess, and septic pelvic vein thrombophlebitis.

Of the women who were given prophylactic antibiotics, 88% received only a cephalosporin, 7% received only a broad-spectrum penicillin, and 6% received other regimens.

Approximately 1% of patients received more than one antibiotic for prophylaxis.

## Averting infection pays dividends

More than 90% of patients who have endometritis respond promptly to broad-spectrum antibiotic therapy. However, some women with postcesarean endometritis develop serious complications such as septic shock, septic pelvic vein thrombophlebitis, and pelvic abscess.

Treatment of wound infection is not so straightforward as treatment of endometritis. Wound infections may well require surgical intervention to drain an incisional abscess. They also necessitate a change in antibiotic therapy, and they are one of the two most important risk factors for fascial dehiscence and intestinal evisceration.

Multiple studies have confirmed that antibiotic prophylaxis significantly reduces the risk of endometritis and wound infection in women who undergo cesarean after the start of labor, with or without ruptured membranes.<sup>7,8</sup> Recent publications have also demonstrated that prophylaxis before the start of surgery offers a greater protective effect than administration after the infant's umbilical cord is clamped.<sup>9,10</sup> Other investigations have demonstrated that broader-spectrum prophylaxis further improves outcomes in women undergoing cesarean delivery.<sup>11,12</sup>

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Antibiotic prophylaxis reduces the frequency of postcesarean endometritis and wound infection, even in very low-risk patients. I strongly support the use of prophylactic antibiotics in all women undergoing cesarean delivery. I believe that the best available evidence supports the use of cefazolin (1 g) plus azithromycin (500 mg), administered intravenously before the start of surgery.<sup>9–12</sup>



**Antibiotic prophylaxis is recommended for all women undergoing cesarean delivery**

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**FAST TRACK**

**Virtually every investigation has confirmed that prophylactic antibiotics reduce the frequency of postcesarean endometritis and, usually, wound infection as well**

# Administer antibiotics *before* making the incision for greatest effectiveness

Owens SM, Brozanski BS, Meyn LA, Wisenfeld HC. Antimicrobial prophylaxis for cesarean delivery before skin incision. *Obstet Gynecol.* 2009;114(3):573-579.

**I**n this retrospective investigation, Owens and colleagues compared antibiotic prophylaxis in two groups of women undergoing cesarean delivery:

- 4,229 women who received antibiotics *after* the infant's umbilical cord was clamped, from July 2002 to November 2004 (Group 1)
- 4,781 women who received antibiotics *before* the skin was incised, from June 2005 to August 2007 (Group 2).

Both scheduled and unscheduled cesarean deliveries were included, as were women who received antibiotics intrapartum for group B *streptococcus* prophylaxis and treatment of chorioamnionitis. The most commonly used antibiotic was intravenous cefazolin (1 g).

After excluding women who received group B *streptococcus* prophylaxis or intrapartum treatment of chorioamnionitis, the authors demonstrated a nearly 50% reduction in the rate of endometritis among women who received antibiotics before surgery (OR, 0.54; 95% CI, 0.38-0.75). They also documented a 30% reduction in the rate of wound infection in these patients (OR, 0.72; 95% CI, 0.55-0.46).

## Details of the trial

Principal outcome measures were the rates of maternal endometritis and wound infection and rates of proven and presumed neonatal infection. The mean age and racial distribution were similar in the two groups, but the percentage of patients treated on a resident teaching service was lower in Group 2 (14.9% vs. 18.9%;  $P < .001$ ). The two groups did not differ in mean body mass index or in the percentage of patients who were in labor before surgery. Colonization with group B

*streptococcus* was more common in Group 2 (24.4% vs. 22.2%;  $P = .5$ ). However, chorioamnionitis was less prevalent in Group 2 (5.6% vs. 10.3%;  $P < .001$ ).

The rates of culture-proven neonatal infection within the first 3 days of life (early-onset infection) were similar between groups (1.3% in Group 1 vs. 0.7% in Group 2). Culture-proven late-onset neonatal infection was less common in Group 2 (1.8% vs. 5.7%;  $P < .001$ ). The groups did not differ in the proportion of newborns treated for presumed infection (24.1% in Group 1 vs. 22.2% in Group 2).

## Plentiful data confirm the superiority of preoperative administration

Endometritis is the most common postoperative complication associated with cesarean delivery. Wound infection is less common but more likely to lead to prolonged postoperative morbidity and extended hospitalization. Reducing both of these complications is a critical clinical objective.

Virtually without exception, every investigation has confirmed that prophylactic antibiotics reduce the frequency of postcesarean endometritis and, usually, wound infection as well. One dose of a given antibiotic is clearly as effective as multiple doses.


Classic animal investigations by Burke demonstrated that prophylaxis was most effective when antibiotics were present in tissue prior to the surgical incision.<sup>13</sup> Nevertheless, early investigators in obstetrics argued that preoperative exposure to antibiotics increased the likelihood that the neonate would require an evaluation for sepsis and that delaying antibiotics until after cord clamping did not compromise the effectiveness of prophylaxis.<sup>14,15</sup>

Sullivan and colleagues were the first authors to successfully challenge this dictum.<sup>9</sup> In a well-designed investigation, they



demonstrated that preoperative administration of antibiotics significantly reduces the frequency of endometritis (RR, 0.22) but not wound infection, and does not increase the need for neonatal sepsis evaluation. Kaimel and coworkers later confirmed these findings,<sup>16</sup> and this study by Owen and associates offers additional proof of the effectiveness and safety of preoperative antibiotic administration.

I offer only one addendum to the conclusions presented by Owen and colleagues. Two recent investigations from the University of Alabama conclusively demonstrate that, by extending the spectrum of antibiotic coverage by combining azithromycin and cefazolin, we can further reduce postcesarean endometritis and wound infection.<sup>11,17</sup> Accordingly, at

our center, we now administer both intravenous (IV) azithromycin (500 mg over 1 hour) and IV cefazolin (1 g) approximately 30 to 60 minutes before the start of surgery. 

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Antibiotic prophylaxis reduces the rates of postcesarean endometritis and wound infection, and preoperative administration is superior to administration after cord clamping. Preoperative administration is also safe for the neonate.

Administer IV azithromycin (500 mg over 1 hour) and IV cefazolin (1 g) approximately 30 to 60 minutes before the start of surgery.

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**Preoperative administration of prophylactic antibiotics for women undergoing cesarean delivery is safe for the newborn**

## READ MORE ONLINE



In the Web version of this Update on Infectious Disease, Dr. Duff explains why chlorhexidine solutions are superior to povidone-iodine for surgical site antisepsis.

You can find the full article at [obgmanagement.com](http://obgmanagement.com)