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## Perioperative Antibiotic Prophylaxis for Non-Laboring Cesarean Delivery

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### Abstract

**Objective**—To estimate the efficacy of antibiotic prophylaxis at time of non-laboring cesarean delivery in reducing postpartum infection-related complications.

**Methods**—We performed a secondary analysis of an observational study of cesarean deliveries performed at 13 centers from 1999–2000. Patients were included if they had a cesarean delivery prior to labor, did not have an antepartum or intrapartum infection, and were not given antibiotics at delivery for reasons other than prophylaxis. The occurrence of postpartum endometritis, wound infection, and other less common infection-related complications was compared between those who did and did not receive antibiotic prophylaxis. Results were adjusted for smoking, payor status, gestational age and body mass index (BMI) at delivery, race, diabetes, antepartum infections, presence of anemia, operative time, type of cesarean delivery (primary or repeat), and center.

**Results**—Of the 9,432 women who met study criteria, the 6,006 (64%) who received antibiotic prophylaxis were younger, heavier at delivery, and were more likely to be African American, receive public insurance, and have diabetes. Patients who received antibiotic prophylaxis were less likely to develop postpartum endometritis [121 (2.0%) vs 88 (2.6%); adjusted odds ratio [OR] 0.40; 95% confidence interval [CI] 0.28–0.59] or wound infection [31 (0.52%) vs 33 (0.96%); adjusted OR 0.49; 95% CI 0.28–0.86].

**Conclusion**—Antibiotic prophylaxis at the time of non-laboring cesarean delivery significantly reduces the risks of postpartum endometritis and wound infection.

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\*For a list of other members of the NICHD MFMU, see the Appendix online at <http://links.lww.com/xxx>.

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## Introduction

Mothers delivering by cesarean are at a 5 to 30-fold increased risk for postpartum infection-related complications, compared to those delivering vaginally. (1,2) Mothers undergoing a cesarean delivery prior to labor or membrane rupture are at much lower risk for infection-related complications than those having a cesarean delivery during labor, in which the risk of postpartum infections (without antibiotic prophylaxis) is as high as 45-85% in some populations (3,4). The efficacy of perioperative antibiotics in reducing infection-related complications following cesarean deliveries performed in laboring women has been documented in a number of studies. In these patients, the use of perioperative antibiotics reduces the risk of postpartum endometritis by 75%, the risk of wound infection by 65%, and may also decrease the risk of urinary tract infection.(5) The efficacy of perioperative antibiotics at the time of “elective” (non-laboring) cesarean delivery is not as well-studied, and antibiotic prophylaxis practices vary widely. The American College of Obstetricians and Gynecologists has recently recommended that antibiotic prophylaxis be administered to all women undergoing cesarean delivery. (6) In this study, we sought to estimate the efficacy of antibiotic prophylaxis at time of non-laboring cesarean delivery in reducing postpartum infection-related complications.

## Materials and Methods

This study is a secondary analysis of a prospectively collected database of all cesarean deliveries performed between January 1, 1999 and December 31, 2000, in 13 academic centers of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. The original study was approved by the participating institutions' IRBs. Data were collected on demographic characteristics, medical and obstetric history, course of labor and delivery, short term neonatal outcomes and intraoperative and postoperative maternal complications. The use and type of antibiotics and the indication for the antibiotics was recorded. All interventions, including administration, timing, and type of antibiotics given, were at the discretion of the delivering physician.

Only those women who had a cesarean delivery prior to the onset of labor were included. Women delivering preterm (< 37 weeks' gestation) were excluded, as were women who had an active infection during the pregnancy or at delivery (for example, pyelonephritis, pneumonia, cervicovaginal infection, and clinical chorioamnionitis). Women who received perioperative antibiotics for indications other than surgical antibiotic prophylaxis (for example, subacute bacterial endocarditis prophylaxis and group B streptococcus prophylaxis) were not included. Women who were colonized with GBS but not given GBS prophylaxis prior to delivery were not excluded. Additional analyses that excluded those women with spontaneous rupture of the membranes (i.e. rupture of the membranes prior to performing the cesarean section) were also performed.

The occurrence of postpartum endometritis, wound infection, and other less common infection-related complications was compared between those who did and did not receive antibiotic prophylaxis. For the purposes of this study, postpartum endometritis (PPE) was defined as a postpartum temperature of 38 degrees C (100.5F) or higher with receipt of postpartum antibiotics, and the clinical diagnosis of PPE. The clinical diagnosis of PPE was based on the presence of abnormal uterine tenderness in the absence of other clinical or laboratory findings suggestive of another source of infection. The diagnosis of a wound infection was based on chart review of clinical criteria, specifically erythema of the incision accompanied by purulent drainage that required wound care. Other infections that were recorded included maternal sepsis, fascial dehiscence or evisceration, necrotizing fasciitis, pelvic abscess and septic pelvic thrombophlebitis.

Statistical analysis included the Wilcoxon rank sum test for continuous variables and the chi-square for categorical variables. Multivariable logistic regression analyses were performed on three outcomes, adjusting for variables that were significantly different on the univariable analysis and were felt to be clinically relevant differences, or were suspected risk factors for infection-related outcomes. For the regression analysis, dichotomization of the center of enrollment was based on whether the center predominately administered intrapartum antibiotics prophylactically. The confidence interval for number needed to treat was calculated using the Wilson score method. (7) Nominal two-tailed P values were reported with statistical significance considered as a P value of  $<.05$ . No adjustment was made for multiple comparisons. SAS software (SAS Institute, Cary, NC) was used for analysis.

## Results

Of the 9432 women delivered by primary or repeat cesarean delivery prior to labor and meeting our inclusion criteria, 6006 (64%) received perioperative surgical antibiotic prophylaxis. Use of prophylactic antibiotics for women undergoing a cesarean delivery prior to labor varied widely between centers, ranging from 13 to 98%. Five thousand two hundred and fifty-seven (87.5%) received only a cephalosporin, 401 (6.7%) women received only a broad-spectrum penicillin, 7 (0.1%) received both, and the remaining women (N=341, 5.7%) received another type of primary antibiotic for surgical prophylaxis. Eighty-five women (1.4%) received more than one antibiotic for surgical prophylaxis.

Demographic characteristics are shown in Table 1. Women who received antibiotic prophylaxis were younger and heavier at delivery, and were more likely to be African American, and to receive public insurance. Antepartum complications, including diabetes, anemia (most recent hemoglobin prior to delivery of  $< 10\text{gm/dl}$ ), and antepartum infection (remote from delivery) were also more common in the prophylaxis group. (Table 2) The indications for cesarean delivery are listed in Tables 3 and 4. Although some obstetric outcomes were statistically significantly different between the two populations, including gestational age at delivery, birth weight and operative time, these differences are likely not clinically significant. (Tables 1 and 5).

After adjusting for smoking, payor status, gestational age and BMI at delivery, race, diabetes, antepartum infections, anemia, operative time, primary or repeat cesarean delivery, and study center, multivariate analyses revealed that use of prophylactic antibiotics resulted in a significant reduction in the rates of postpartum endometritis (adjusted OR 0.40; 95% CI 0.28-0.59) and wound infection (adjusted OR 0.49; 95% CI 0.28-0.86). Other infection-related morbidity was not significantly reduced (adjusted OR 0.39; 95% CI 0.13-1.12). (Table 6) However, the effect size for endometritis was small, as the rate was only 2.0% in the prophylaxis group and 2.6% in the no prophylaxis group. Wound infections and other infection-related morbidity were even less common. Results were similar when patients with spontaneous rupture of the membranes (N=653) or with an unknown type of rupture (N=13) were excluded (Table 7). The analysis was also repeated limiting the patient population to the lowest risk group of patients (N=5148). As such, patients with diabetes, heart disease, renal disease, connective tissue disease, and smoking were excluded, as well as those who may have had an emergency cesarean section, including a cesarean for non-reassuring fetal heart tracing, bleeding previa, or abruption. In addition, patients with complications such as intraoperative transfusion or severe postpartum anemia (hemoglobin  $< 8\text{gm/dl}$ ), uterine or hypogastric artery ligation, bowel perforation, cystotomy, ureteral injury, broad ligament hematoma, uterine rupture or cesarean hysterectomy were excluded. After adjusting for all the variables as listed in Table 6, with the exception of diabetes and smoking, the rate of endometritis was still significantly lower in the prophylaxis group (adjusted OR 0.29; 95% CI 0.17 – 0.51). However,

the decreased rate of wound infection was no longer statistically significant (adjusted OR 0.81; 95% CI 0.34 – 1.97).

Based on this analysis, for every serious infection prevented, 113 women (95% CI 60 - 575) must receive antibiotic prophylaxis at the time of their non-laboring cesarean delivery. This may be an overestimation for populations that are at higher risk for postpartum infection related complications than those delivering in Maternal Fetal Medicine Unit hospitals, where the rates of postpartum endometritis and wound infection were low (2.2% and 0.7%, respectively).

## Discussion

We found that the use of perioperative antibiotics at the time of non-laboring cesarean delivery significantly reduced the risks of postpartum endometritis and wound infection. It is well established that both the presence and duration of labor and rupture of the membranes are associated with an increased risk of postpartum infection in women undergoing cesarean delivery. (5) The current study appears to be the largest single study to evaluate the efficacy of perioperative antibiotics in the prevention of postpartum infection-related complications in women undergoing a cesarean delivery prior to the onset of labor. (8-10; Medline search 1902-December 2008, key words cesarean section, endometritis, antibiotic prophylaxis; all languages) Because this was not a randomized trial, the antibiotic-treated group might be expected to be at a higher risk for infection-related complications, given that based on their risk profiles, their obstetric providers elected to administer prophylactic antibiotics. As a result, one would anticipate that any potential bias would lead to a higher rate of infection-related complications in the treated group, leading to a decrease in the treatment effect.

In a prospective observational study of 1863 women in four community centers, Ehrenkrantz and colleagues reported that endometritis and/or wound infection occurred in 3.7% of women undergoing a non-laboring cesarean delivery who did not receive antibiotic prophylaxis, compared to 0.9% of those who did receive antibiotic prophylaxis ( $P < .01$ ). (8) However, in a randomized, double-blind, placebo controlled trial, Bagratee and colleagues found no difference in rates of wound infection, endometritis, urinary tract infection, pneumonia, or febrile morbidity following antibiotic prophylaxis in 480 patients undergoing an elective cesarean delivery. (9) A meta-analysis of four studies by Chelmow and colleagues concluded that the risk of postpartum infection-related complications was significantly reduced by the use of perioperative antibiotics in patients undergoing cesarean delivery prior to labor and membrane rupture. (10) The use of prophylactic antibiotics reduced the rates of postoperative fever (RR 0.25; 95% CI 0.14-0.44), and the risk of endometritis (RR 0.05; 95% CI 0.01-0.38). Only two studies reported rates of wound infection, and the meta-analysis showed only a trend towards a reduction in wound infection (0.59; 95% CI 0.24-1.45). Our study revealed a much more modest reduction in the risk of endometritis (adjusted OR 0.40; 95% CI 0.28-0.59), with a similar reduction in the rate of wound infection (adjusted OR 0.49; 95% CI 0.28-0.86). Our results are similar to those reported in the Cochrane Database of Systematic Reviews (OR 0.38; 95% CI 0.22-0.64 for endometritis and OR 0.7; 95% CI 0.53-0.99 for wound infections) following “elective” cesarean deliveries. (5)

Ehrenkrantz and colleagues estimated that the use of antibiotic prophylaxis in low risk women undergoing pre-labor cesarean delivery could result in an annual national savings of approximately \$9 million dollars. (8) Using their own data, a cost-benefit analysis was also performed by Chelmow and colleagues. They used a relative risk of endometritis of 0.18 (95% CI 0.07-0.45) following antibiotic prophylaxis, and of fever 0.47 (95% CI 0.32-0.66) in their calculations. (11) Overall, administration of prophylactic antibiotics for “elective” cesarean delivery reduced costs by \$30.66 per case (2% of the total cost). The authors concluded that “prophylactic antibiotic administration results in cost savings for elective cesarean delivery”.

Given the small effect size and the number of women that might be exposed to antibiotics to prevent a single case of endometritis, when choosing to administer prophylactic antibiotics in this clinical scenario, the practitioner must also consider the potential risks of antibiotic allergy, selection of resistant organisms, and the relative ease with which most postoperative infections are treated.

Due to the limitations of our database, we are unable to address the important issue of whether prophylactic antibiotic administration should be administered prior to skin incision or following cord clamping. We are also unable to address the efficacy of the different types of antibiotics used. Our study does confirm, however, that the use of perioperative antibiotics at the time of cesarean delivery prior to labor, regardless of the presence of membrane rupture, significantly decreases the risks of endometritis and wound infection. Although there was also a reduction in other infection-related complications, this analysis did not reach statistical significance. However, the effect size is small, and a large number of women would need to be treated with antibiotics to prevent a single infection.

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## Appendix

In addition to the authors, other members of the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network are as follows:

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**Table 1**

## Patient Demographics

	<b>Prophylaxis (N=6006)</b>	<b>No Prophylaxis (N=3426)</b>	<b>P-value</b>
Maternal age (yrs)	28.9 ± 5.8	30.4 ± 5.7	<0.001
Maternal BMI at delivery (kg/m <sup>2</sup> )	33.9 ± 7.3	32.8 ± 6.8	<0.001
Gestational age at delivery (wks)	39.1 ± 1.1	39.0 ± 1.0	<0.001
African American	1498 (24.9)	641 (18.7)	<0.001
Married	3696 (61.5)	2485 (72.5)	<0.001
Public Insurance	3636 (60.6)	1339 (39.1)	<0.001

Data presented as n (%) or mean ± standard deviation

**Table 2**

## Antepartum Complications

	<b>Prophylaxis (N=6006)</b>	<b>No Prophylaxis (N=3426)</b>	<b>P-value</b>
Smoker	735 (12.3)	386 (11.3)	0.16
Antepartum infection	1587 (26.4)	709 (20.7)	<0.001
Diabetes	630 (10.5)	312 (9.1)	0.03
Antepartum anemia (Hb < 10gm/dl)	428 (8.2)	190 (5.8)	<0.001

Data presented as n (%)



**Table 3**

## Indications for Primary Cesarean Delivery

	<b>Prophylaxis (N=1227)</b>	<b>No Prophylaxis (N=776)</b>	<b>P-Value</b>
Abnormal Presentation	866 (70.6)	553 (71.3)	0.43
Multiple Gestation	33 (2.7)	26 (3.4)	
Suspected Macrosomia	139 (11.3)	79 (10.2)	
Placenta Previa	53 (4.3)	40 (5.2)	
Prior Myomectomy	60 (4.9)	43 (5.5)	
Genital Herpes	76 (6.2)	35 (4.5)	

**Table 4**

## Indications for Repeat Cesarean Delivery

	<b>Prophylaxis (N=4779)</b>	<b>No Prophylaxis (N=2650)</b>	<b>P-Value</b>
Abnormal Presentation	149 (3.1)	116 (4.4)	< 0.001
Multiple Gestation	12 (0.3)	13 (0.5)	
Suspected Macrosomia	56 (1.2)	38 (1.4)	
Placenta Previa	14 (0.3)	15 (0.6)	
Prior Myomectomy	34 (0.7)	14 (0.5)	
Genital Herpes	18 (0.4)	9 (0.3)	
Prior Classical/Vertical Incision	176 (3.7)	33 (1.2)	
Unknown Incision	422 (8.8)	24 (0.9)	
Elective Repeat	3898 (81.6)	2388 (90.1)	

Data presented as n (%)

**Table 5**

## Obstetric Outcomes

	<b>Prophylaxis (N=6006)</b>	<b>No Prophylaxis (N=3426)</b>	<b>P-Value</b>
Birth Weight (g)	3463 ± 523	3491 ± 511	0.001
Operative time (min)	57.4 ± 23.2	50.4 ± 20.1	< 0.001
Rupture to delivery (hrs)	0.9 ± 10.0	0.5 ± 8.7	<0.001
Primary Cesarean	1227(20.4)	776 (22.7)	0.011
Uterine incision			0.007
Transverse	5795 (96.5)	3352 (97.8)	
Classical	112 (1.9)	42 (1.2)	
Low vertical	64 (1.1)	21 (0.6)	
“T” or “J”	25 (0.4)	9 (0.3)	
Unknown	10 (0.2)	2 (0.1)	

Data presented as n (%) or mean ± standard deviation

**Table 6**

## Maternal Infection-related Outcomes

	<b>Prophylaxis (N=6006)</b>	<b>No Prophylaxis (N=3426)</b>	<b>OR (95% CI)</b>	<b>Adjusted OR <sup>†</sup> (95% CI)</b>
Postpartum Endometritis	121 (2.0)	88 (2.6)	0.78 (0.59-1.03)	0.40 (0.28-0.59)
Wound infection	31 (0.52)	33 (0.96)	0.53 (0.33-0.87)	0.49 (0.28-0.86)
Other infection-related complications *	9 (0.15)	11 (0.32)	0.47 (0.19-1.13)	0.39 (0.13-1.12)

Data presented as N (%); CI Confidence Interval; OR Odds Ratio

<sup>†</sup> Adjusted for smoking, payor status, gestational age and BMI at delivery, race, diabetes, antepartum infections, anemia, operative time, primary or repeat cesarean delivery and study center. Eighty-five percent of observations available for analysis.

\* maternal sepsis, wound dehiscence or evisceration, necrotizing fasciitis, pelvic abscess and septic pelvic thrombophlebitis

**Table 7****Maternal Infection-related Outcomes in Patients without Spontaneous Rupture of Membranes**

	<b>Prophylaxis (N=5475)</b>	<b>No Prophylaxis (N=3291)</b>	<b>OR (95% CI)</b>	<b>Adjusted OR <sup>†</sup> (95% CI)</b>
Postpartum Endometritis	101 (1.8)	81 (2.5)	0.75 (0.55 – 1.00)	0.40 (0.27 – 0.60)
Wound infection	28 (0.51)	31 (0.94)	0.54 (0.32 – 0.90)	0.50 (0.28 – 0.91)
Other infection-related complications	8 (0.15)	11 (0.33)	0.44 (0.18 – 1.09)	0.35 (0.12 – 1.05)

Data presented as N (%); CI Confidence Interval; OR Odds Ratio

<sup>†</sup> Adjusted for smoking, payor status, gestational age and BMI at delivery, race, diabetes, antepartum infections, anemia, operative time, primary or repeat cesarean delivery and study center. Eighty-six percent of observations available for analysis.

\* maternal sepsis, wound dehiscence or evisceration, necrotizing fasciitis, pelvic abscess and septic pelvic thrombophlebitis