

Antibiotic Prophylaxis in Obstetric Procedures

This Clinical Practice Guideline has been prepared by the Infectious Diseases Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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2009 were incorporated in the guideline. Current guidelines published by the American College of Obstetrics and Gynecology were also incorporated. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The evidence obtained was reviewed and evaluated by the Infectious Diseases Committee of the Society of Obstetricians and Gynaecologists of Canada under the leadership of the principal authors, and recommendations were made according to guidelines developed by the Canadian Task Force on Preventive Health Care (Table 1).

Benefits, Harms, and Costs: Implementation of this guideline should reduce the cost and harm resulting from the administration of antibiotics when they are not required and the harm resulting from failure to administer antibiotics when they would be beneficial.

Summary Statements

1. Available evidence does not support the use of prophylactic antibiotics to reduce infectious morbidity following operative vaginal delivery. (II-1)
2. There is insufficient evidence to argue for or against the use of prophylactic antibiotics to reduce infectious morbidity for manual removal of the placenta. (III)
3. There is insufficient evidence to argue for or against the use of prophylactic antibiotics at the time of postpartum dilatation and curettage for retained products of conception. (III)
4. Available evidence does not support the use of prophylactic antibiotics to reduce infectious morbidity following elective or emergency cerclage. (II-3)

Recommendations

1. All women undergoing elective or emergency Caesarean section should receive antibiotic prophylaxis. (I-A)
2. The choice of antibiotic for Caesarean section should be a single dose of a first-generation cephalosporin. If the patient has a penicillin allergy, clindamycin or erythromycin can be used. (I-A)
3. The timing of prophylactic antibiotics for Caesarean section should be 15 to 60 minutes prior to skin incision. No additional doses are recommended. (I-A)
4. If an open abdominal procedure is lengthy (> 3 hours) or estimated blood loss is greater than 1500 mL, an additional dose of the prophylactic antibiotic may be given 3 to 4 hours after the initial dose. (III-L)
5. Prophylactic antibiotics may be considered for the reduction of infectious morbidity associated with repair of third and fourth degree perineal injury. (I-B)

Abstract

Objective: To review the evidence and provide recommendations on antibiotic prophylaxis for obstetrical procedures.

Outcomes: Outcomes evaluated include need and effectiveness of antibiotics to prevent infections in obstetrical procedures.

Evidence: Published literature was retrieved through searches of Medline and The Cochrane Library on the topic of antibiotic prophylaxis in obstetrical procedures. Results were restricted to systematic reviews, randomized controlled trials/controlled clinical trials, and observational studies. Searches were updated on a regular basis and articles published from January 1978 to June

Key Words: Antibiotic prophylaxis, surgical prophylaxis, obstetrical procedures, surgical site infection, SSI, endometritis, endocarditis

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Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.⁴⁰

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the The Canadian Task Force on Preventive Health Care.⁴⁰

- 6. In patients with morbid obesity (BMI > 35), doubling the antibiotic dose may be considered. (III-B)
- 7. Antibiotics should not be administered solely to prevent endocarditis for patients who undergo an obstetrical procedure of any kind. (III-E)

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INTRODUCTION

Infectious complications following obstetric surgical procedures are a significant source of morbidity and potential mortality. They include urinary tract infection, endometritis, wound infection, perineal infection, and sepsis, which lead to prolonged hospital stays and increased health care costs. Much work has been done to study the effect of prophylactic antibiotics in reducing infectious morbidity. A plethora of antibiotic types, dosing schedules, and routes of administration have been investigated. There is evidence to support the use of prophylactic antibiotics for a number of procedures in obstetrics. Unfortunately, few comparative trials have been conducted, leaving the clinician with uncertainty as to which regimen is superior.

The presence of antibiotic resistant organisms is a reality in Canadian health care facilities.¹ These organisms include

methicillin resistant *Staphylococcus aureus*, vancomycin resistant *Enterococcus*, and extended-spectrum beta-lactamase-producing organisms.

Both morbidity and mortality are increased in infections caused by these organisms, as they may be more virulent and are more difficult to treat because therapeutic options are limited. Antibiotic resistance development results mainly from the inappropriate use of antibiotics. Incomplete courses of antibiotic therapies and the unnecessary use of broader spectrum regimens play a role.² Adherence to both treatment and prophylaxis guidelines likely assists in reducing infection and antibiotic resistance. Physician adherence to antibiotic prophylaxis guidelines is variable and usually at odds with published guidelines.^{3,4}

In addition to antibiotic prophylaxis, it is essential to review all factors that affect infectious risk reduction in obstetrical care.⁵ Adherence to appropriate skin preparation procedure, including hair clipping as opposed to shaving, and effective antisepsis of both patient and staff are required.⁶ Sterile surgical fields must be ensured, and ongoing quality assessment of sterilization technique, air ventilation, and postoperative wound care is needed. Consistent infection control surveillance and reporting of infectious complications track ability to minimize these morbidities and possibly to identify clusters of infection and the emergence of antibiotic resistant organisms. This will dictate changes to operative routines to respond to evolving microbial diversity that seems inevitable.

ABBREVIATIONS

- CDC Centers for Disease Control and Prevention
- IE infective endocarditis
- SSI surgical site infection

PRINCIPLES OF ANTIBIOTIC PROPHYLAXIS

The purpose of antibiotic prophylaxis in surgical procedures is not to sterilize tissues but to reduce the colonization pressure of microorganisms introduced at the time of operation to a level that the patient's immune system is able to overcome.⁷ Prophylaxis does not prevent infection caused by postoperative contamination. Prophylactic antibiotic use differs from treatment with antibiotics⁵ in that the former is intended to prevent infection, whereas the latter is intended to resolve an established infection, typically requiring a longer course of therapy. Prophylaxis is intended for elective procedures when the incision will be closed in the operating room.

Before an agent can be considered for use as a prophylactic antibiotic, there must be evidence that it reduces postoperative infection. It must also be safe and inexpensive, and it must be effective against organisms likely to be encountered in the surgical procedure.

The agent must be administered in a way that ensures that serum and tissue levels are adequate before an incision is made and that therapeutic levels of the agent can be maintained in serum and tissue during surgery and for a few hours (at most) after the incision is closed.⁷

Wound infections—surgical site infections—in the form of cellulitis, abscess, or dehiscence can occur following laparotomy. Pelvic infections, such as an abscess or infected hematoma, are a risk with any surgical procedure that enters the abdominal cavity. Cuff cellulitis is a specific risk for hysterectomy. Endometritis can result from Caesarean section or surgical abortion. Urinary tract infections can occur as a result of any procedure that involves catheterization of the bladder.

A 1999 guideline published by the US Centers for Disease Control and Prevention lists the specific and stringent criteria that must be met for diagnosis of a surgical site infection.⁷ Accurate surveillance for SSI monitoring requires follow-up for 30 days postoperatively, and the trend towards early discharge from hospital makes surveillance a challenge. It is estimated that up to 84% of surgical site infections occur following discharge from hospital.⁷

If prophylactic antibiotics are to be given, they should be administered shortly prior to or at bacterial inoculation.^{8,9} The majority of studies suggest that a single dose is effective, but for lengthy procedures (> 3 hours) the dose should be repeated at intervals 1 or 2 times the half-life of the drug. It has also been suggested that with large blood loss (> 1500 mL), a second dose should be given.¹⁰

USE OF ANTIBIOTIC PROPHYLAXIS IN OBSTETRICS

Procedures reviewed in this section include Caesarean section, operative vaginal delivery, manual removal of placenta,

repair of third or fourth degree perineal laceration, cervical cerclage, and postpartum dilatation and curettage. Recent changes to endocarditis prophylaxis guidelines are also reviewed.

Caesarean Section

The single most important risk factor for postpartum maternal infection is Caesarean section.¹¹ Women having Caesarean section have a 5- to 20-fold greater risk of infection than women having vaginal delivery. Rates of wound infection and serious infectious complications can be as high as 25%.¹² There is no consistent application of definitions for SSI, and the practice of post-discharge surveillance varies widely.¹³ A recent prospective study with proper application of CDC definitions for surgical site infection with follow-up to 30 days post-Caesarean section identified a wound infection rate of 8.9%.¹⁴ It is likely that post-Caesarean wound infection rates are inaccurate, because up to 84% of infections occur after discharge,⁷ when surveillance may be lacking.

Endomyometritis, urinary tract infection, wound infection, and sepsis may occur following Caesarean section. Numerous studies have investigated the use of prophylactic antibiotics to reduce these complications, the rates of which are all higher in the case of emergency Caesarean section, with or without the presence of maternal fever and/or chorioamnionitis.

A Cochrane review published in 2002 included 81 randomized trials assessing antibiotic prophylaxis versus placebo or no treatment for both elective and emergency Caesarean sections. The review included just over 2000 women in each arm. When antibiotics were given rather than placebo or no treatment, the relative risk of endometritis in both elective and emergency Caesarean sections was reduced (RR 0.38; 95% CI 0.22 to 0.64 and RR 0.39; 95% CI 0.34 to 0.46), as was the risk of wound infection (RR 0.36; 95% CI 0.26 to 0.51 and RR 0.73; 95% CI 0.53 to 0.99).¹⁵

There has been debate about the benefit of prophylactic antibiotics for a woman who has an elective Caesarean section with intact membranes and without labour. A meta-analysis of 4 studies found that antibiotic prophylaxis resulted in a decrease in postoperative fever (RR 0.25; 95% CI 0.14 to 0.44) and endometritis (RR 0.05; 95% CI 0.01 to 0.38).¹⁶ Taken together, these data support the recommendation to use prophylactic antibiotics for all women undergoing Caesarean section.

Controversy also exists about whether prophylactic antibiotics in Caesarean section should be given prior to skin incision or at the time of the umbilical cord clamping. Traditionally, prophylaxis has been delayed in an effort to avoid masking a neonatal infection and to prevent an unnecessary septic work-up. However, recent evidence may change this practice. A randomized trial compared maternal infectious and

neonatal outcomes in women randomized to receive cefazolin 15 to 60 minutes before incision versus at cord clamp. Three hundred fifty-seven women were enrolled. Overall maternal infectious morbidity was reduced in the pre-treatment group (RR 0.4; 95% CI 0.18 to 0.87); in particular, endometritis was reduced (RR 0.2; 95% CI 0.15 to 0.94). No increase in neonatal sepsis, investigation, or length of stay was observed.¹⁷ A recent meta-analysis supports the use of prophylactic antibiotics prior to Caesarean incision to prevent total infectious morbidity (RR 50; 95% CI 0.33 to 0.78, $P = 0.002$). Neonatal outcomes were not affected.¹⁸ The most widely studied antibiotics for surgical prophylaxis are cephalosporins. Cefazolin is a first-generation cephalosporin and is a Pregnancy Category B drug. When given intravenously, its half-life is 1.8 hours. It provides good coverage for gram positive organisms and has modest gram negative coverage. In a 1999 guideline, the US Centers for Disease Control and Prevention recommended its use at Caesarean section.⁷ It is recommended that 1 to 2 grams should be administered intravenously not more than 30 minutes before the skin is cut. An additional dose can be considered if blood loss exceeds 1500 mL or at 4 hours if the procedure lasts more than 4 hours (i.e., up to 2 half-lives of the drug).¹⁹ Trials have shown that broader spectrum antibiotics for Caesarean section do reduce infectious morbidity. Superiority trials with cefazolin have not been conducted. Given the potential for antibiotic resistance in both mother and neonate, recommendations for the use of broader spectrum antibiotics require further study.²⁰

Operative Vaginal Delivery

A 2004 Cochrane review investigated the use of prophylactic antibiotics for operative vaginal delivery, with either forceps or vacuum assisted deliveries, to determine if prophylaxis reduces the incidence of postpartum infections.²¹ The review identified only one trial of 393 women, and only 2 of 9 outcomes deemed appropriate by the reviewers were assessed in this study: endometritis and length of hospital stay. These did not differ between those who received prophylaxis and those who received no treatment. The review concluded there were insufficient data on which to base recommendations for practice and that further research is needed. No additional studies addressing this issue have been published to date.

Manual Removal of Placenta

There is limited information regarding the use of prophylactic antibiotics to reduce the development of postpartum endometritis following manual removal of the placenta. A Cochrane review, updated in April 2009, did not identify any randomized controlled trials.²² The World Health Organization suggests that prophylaxis should be offered but recognizes that there is no direct evidence of the value

of antibiotic prophylaxis after manual removal of the placenta and bases the recommendation on studies involving Caesarean section and abortion and on observational studies of other intrauterine manipulations.²³

The effect of operator glove change before manual removal of the placenta at Caesarean section was studied in a group of 228 women, with operators changing gloves in one half of the cases. No difference in post-Caesarean endometritis was noted between the 2 groups.²⁴ However, the incidence of endometritis was decreased when the placenta delivered spontaneously rather than being manually removed at Caesarean section in a study of 333 women, all of whom received prophylactic antibiotics (15% vs. 26%, RR 0.6; $P = 0.01$).²⁵

Third or Fourth Degree Perineal Laceration

A 2005 Cochrane review²⁶ on this subject found there were no randomized trials comparing prophylactic antibiotics with placebo or no treatment in fourth degree perineal tears during vaginal birth. A well-designed randomized trial was recommended. This was undertaken by Duggal et al.²⁷ and published in 2008. This prospective trial followed 107 women post third or fourth degree laceration repair for 2 weeks; the women had been randomly assigned to receive a single intravenous dose of cefotetan, cefoxitin, or placebo. Four of 49 (8%) who received antibiotics and 14 of 58 (24%) who received placebo developed perineal wound complication ($P = 0.037$). This suggests a benefit to using prophylactic antibiotics to reduce morbidity following significant perineal laceration.²⁷

Elective and Emergency Cerclage, With or Without Exposed Membranes

There is insufficient evidence to support the use of prophylactic antibiotics with the placement of cervical cerclage in any clinical setting. One study²⁸ investigated the use of continuous low-dose antibiotics in women with a history of second trimester pregnancy loss with the placement of cerclage at 14 to 24 weeks' gestation on the basis of transvaginal sonographic findings of cervical funnelling. Each of the 10 patients had a live birth, and pregnancy was prolonged by a mean of 13.4 ± 4.2 weeks beyond the previous pregnancy. There was no control group.²⁸ In a second retrospective study of 116 mid-trimester cerclage placements, antibiotic use was not associated with a decreased risk of delivery before 28 weeks' gestation.²⁹ Randomized clinical trials are needed to confirm the role of antibiotics in these high-risk pregnancies.

Postpartum Dilatation and Curettage

No studies were identified that investigated the use of prophylactic antibiotics for postpartum dilatation and curettage.

Table 2. Cardiac conditions associated with the highest risk of adverse outcome from endocarditis

Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
Previous infective endocarditis
Congenital heart disease (CHD)
Unrepaired cyanotic CHD (including palliative shunts and conduits)
Completely repaired CHD with prosthetic material < 6 months after procedure
Repaired CHD with residual defects at/near site of prosthetic material
Cardiac transplant recipient with cardiac valvulopathy

Adapted from Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al.³⁸

Table 3. Prophylactic antibiotic recommendations for obstetrical procedures

Procedure	Antibiotic	Dosage	Level of evidence
Emergency or elective caesarean section (no labour, no rupture of membranes)	Cefazolin IV 15–60 mins prior to skin incision	1–2 g IV	I-A
If penicillin allergic	Clindamycin OR erythromycin	600 mg IV 500 mg IV	
Operative vaginal delivery	None recommended	N/A	II-1C
Manual removal placenta	None recommended	N/A	III-L
Repair third or fourth degree laceration	Cefotetan Cefoxitin	1 g IV 1 g IV	I-B I-B
Postpartum dilatation and curettage	None recommended	N/A	No evidence
Cerclage	None recommended	N/A	II-3C

Dosage of Antibiotic Prophylaxis in Obesity

Increased BMI is associated with higher rates of both obstetric and infectious complications.³⁰ Controlled trials assessing the required dosage for antibiotic prophylaxis based on patient BMI have not been assessed in our specialty. Expert opinion recommends twice the normal dose of prophylaxis for morbidly obese patients, who have a BMI > 35.¹⁹ Future research in this area is needed.

RECOMMENDATIONS FOR PENICILLIN / CEPHALOSPORIN ALLERGY

Penicillin allergy is self-reported by up to 10 % of patients, yet only 10 % of those are actually allergic when skin testing is performed.^{31–33} True anaphylactic response to penicillin is rare, occurring in 1 to 4 of 10 000 administrations.³⁴ An allergic reaction to cephalosporins in those with a penicillin allergy occurs at rates of 0.17% to 8.4%.^{35–37} An alternative to cephalosporins should be given only to individuals with a history of penicillin anaphylaxis (shortness of breath or evidence of airway edema rather than just rash or other allergic reaction) or cephalosporin allergy. Alternative prophylactic antibiotics include clindamycin 600 mg IV or erythromycin 500 mg IV.

PREVENTION OF INFECTIVE ENDOCARDITIS

An American Heart Association guideline³⁸ published in 2007 found no evidence that genitourinary procedures cause IE or that administration of antibiotics prevents IE following such procedures. The American Heart Association therefore does not recommend prophylactic antibiotics for patients undergoing genitourinary procedures; this is a change from their 1997 guideline. They identified 4 conditions that are at highest risk of adverse outcome (Table 2). For patients with the conditions listed in Table 2 who have an established gastrointestinal or genitourinary tract infection or for those who receive antibiotic therapy for another reason (e.g., to prevent wound infection), they suggest it may be reasonable that the choice of antibiotic also be active against enterococci (i.e., ampicillin, piperacillin, or vancomycin). They also suggest that it may be reasonable for patients at high risk of IE who have a known enterococcal urinary tract infection or colonization to receive antibiotic treatment prior to any urinary tract manipulation. A review on this recommendation change has been recently published.³⁹

SUMMARY

For a number of procedures in obstetrics and gynaecology, the use of prophylactic antibiotics has been shown to reduce infectious morbidity in a safe and cost-effective manner (Table 3).

There remain a number of procedures where the utility of prophylactic antibiotics is either unclear or not well studied. Appropriate antibiotics used at the correct dose and time and with the appropriate frequency will reduce infectious postoperative complications and minimize the development of antibiotic resistant organisms.

Summary Statements

1. Available evidence does not support the use of prophylactic antibiotics to reduce infectious morbidity following operative vaginal delivery. (II-1)
2. There is insufficient evidence to argue for or against the use of prophylactic antibiotics to reduce infectious morbidity for manual removal of the placenta. (III)
3. There is insufficient evidence to argue for or against the use of prophylactic antibiotics at the time of postpartum dilatation and curettage for retained products of conception. (III)
4. Available evidence does not support the use of prophylactic antibiotics to reduce infectious morbidity following elective or emergency cerclage. (II-3)

Recommendations

1. All women undergoing elective or emergency Caesarean section should receive antibiotic prophylaxis. (I-A)
2. The choice of antibiotic for Caesarean section should be a single dose of a first-generation cephalosporin. If the patient has a penicillin allergy, clindamycin or erythromycin can be used. (I-A)
3. The timing of prophylactic antibiotics for Caesarean section should be 15 to 60 minutes prior to skin incision. No additional doses are recommended. (I-A)
4. If an open abdominal procedure is lengthy (> 3 hours) or estimated blood loss is greater than 1500 mL, an additional dose of the prophylactic antibiotic may be given 3 to 4 hours after the initial dose. (III-L)
5. Prophylactic antibiotics may be considered for the reduction of infectious morbidity associated with repair of third and fourth degree perineal injury. (I-B)
6. In patients with morbid obesity (BMI > 35), doubling the antibiotic dose may be considered. (III-B)
7. Antibiotics should not be administered solely to prevent endocarditis for patients who undergo an obstetrical procedure of any kind. (III-E)

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