

# Infectious Morbidity After Cesarean Delivery: 10 Strategies to Reduce Risk

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Puerperal infection remains a major cause of maternal morbidity and mortality. The primary risk factor is cesarean delivery, which increases the risk 5- to 20-fold. This article reviews in detail the risk of puerperal infection following cesarean delivery, both endometritis and surgical site infection, in both high- and low-risk populations. Strategies to prevent such infections are also discussed using a systematic evidence-based approach.

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## KEY WORDS

Cesarean delivery • Endometritis • Surgical site infection • Pregnancy-related mortality • Puerperal infection

**P**uerperal infection remains a significant cause of maternal morbidity and mortality both in the United States and in developing countries. The United States has a pregnancy-related mortality ratio of 14.5 pregnancy-related deaths per 100,000 live births, with approximately 10% resulting from puerperal infection.<sup>1</sup> Although the data are limited, these risks are undoubtedly higher in developing countries where less attention is paid to sterile techniques and

where access to antibiotics may be more restricted. With an estimated 5- to 20-fold increase in incidence,<sup>2</sup> cesarean delivery is the single most important risk factor for puerperal infection.<sup>3</sup> Although a number of sources exist for postoperative infectious morbidity following cesarean delivery (such as urinary tract infection/pyelonephritis, pneumonia, mastitis, septic pelvic thrombophlebitis, and drug fever), in this review we focus on the two main types of infection:

(1) endometritis, an infection of the lining of the uterus, which typically results from ascension of vaginal flora through the cervix and into the uterus; and (2) surgical site infection (SSI), which refers to infection of the skin and subcutaneous tissue at the surgical incision site and is typically caused by skin flora such as *Streptococcus* species, *Staphylococcus* species, or mixed aerobic/anaerobic bacteria.<sup>4</sup> Given that cesarean deliveries continue to represent a significant proportion of all births in the United States (an estimated 34.0% according to a recent report<sup>5</sup>), the overall health and socioeconomic burden of these infections is substantial.

### Assessing Risk for Postcesarean Infection

Although all women are at risk for infection in the postpartum

infection have been identified (Table 1). This explains, at least in part, why the reported incidence of postcesarean infectious morbidity varies so widely in the literature. In an effort to report the incidence of postoperative infection by risk category, the Centers for Disease Control and Prevention (CDC) in the United States use the National Healthcare Safety Network (NHSN) to collect data about all healthcare-associated infections, including those following cesarean delivery.<sup>6</sup> Within this framework, surgical patients are categorized using three surgical risk stratification criteria, each of which is assigned a score of 0 or 1 (Table 2). These include: length of surgery, which for cesarean delivery is  $\geq 56$  minutes; the extent of surgical wound contamination (Table 3), and the

score (Table 4).<sup>6</sup> Based on the total number of points accrued from the risk index, patients are categorized into one of three groups for each operative procedure: category 0 (lowest risk), 1, or 2/3 (highest risk). Although the NHSN surgical risk stratification criteria may be suitable for the general surgery patient population, its focus on length of surgery, wound class, and ASA score may not adequately distinguish among patients undergoing cesarean delivery.

### Establishing National Benchmarks for Infectious Morbidity

Individual healthcare facilities may find it challenging to identify an appropriate national benchmark for comparison, given the range of published rates between the 2009 NHSN report and the available literature. We identified publications in which rates of postcesarean SSI and/or endometritis were reported in the English language between January 1998 and December 2010. A summary of these data are shown

*Although all women are at risk for infection in the postpartum period, not all are at equal risk.*

period, not all are at equal risk. A number of antepartum and intrapartum risk factors for puerperal

patient's preoperative medical status as defined by the American Society of Anesthesiologists (ASA)

**TABLE 1**

**Risk Factors for Postcesarean Infectious Morbidity**

Variable	Reported Odds Ratio (95% CI)	Study
Cesarean versus vaginal delivery	4.71 (4.08-5.43)	Leth RA et al <sup>2</sup>
Emergency versus elective cesarean delivery	1.39 (1.11-1.75)	Leth RA et al <sup>2</sup>
Presence of labor	2.16 (1.36-3.44)	Guimarães EE et al <sup>31</sup>
Presence of ruptured membranes	1.3 (1.1-1.5)	Killian CA et al <sup>32</sup>
Rupture of membranes > 18 h	3.13 (1.34-7.38)	Chang and Newton <sup>33</sup>
Obesity (BMI > 30 kg/m <sup>2</sup> )	1.60 (1.31-1.95)	Robinson HE et al <sup>19</sup>
Number of vaginal examinations in labor (eg, > 7)	1.9 (1.2-3.1)	Olsen MA et al <sup>34</sup>
Absence of antibiotic prophylaxis	2.63 (1.50-4.6)	Killian CA et al <sup>32</sup>
Length of surgery (> 60 min vs $\leq 60$ min)	1.01 (1.00-1.02)	Killian CA et al <sup>32</sup>
ASA score (> III)	1.3 (0.77-2.0)	Killian CA et al <sup>32</sup>
Diabetes	1.4 (1.1-1.5)	Schneid-Kofman N et al <sup>9</sup>

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval.

**TABLE 2**

**National Healthcare Safety Network Surgical Site Infection Basic Risk Index**

Risk Points Assigned	Category	Reason for Assigning Points
1 point	Duration of surgery	If the operation lasts longer than the duration cutpoint, where the duration cutpoint is the 75th percentile of the duration of surgery in minutes for any particular operative procedure (defined as $\geq 56$ min for cesarean delivery)
1 point	Class of wound	If the wound is categorized as contaminated (class 3) or dirty/infected (class 4)
1 point	Physical status of the patient	If the American Society of Anesthesiologists Classification of Physical Status (the patient's preoperative medical status) is defined as class III, IV, or V

Data from Edwards JR et al.<sup>7</sup>

**TABLE 3**

**Surgical Wound Classes**

Classification	Definition
Clean (class I)	An uninfected operative wound in which no inflammation is encountered on entry and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered
Clean-Contaminated (class II)	Operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination (this is the case for most cesarean deliveries)
Contaminated (class III)	Open, fresh, accidental wounds or operations with major breaks in sterile technique, gross spillage from the gastrointestinal tract, or incisions with acute, nonpurulent inflammation
Dirty/Infected (class IV)	Old traumatic wounds with retained devitalized tissue or those involving existing clinical infection

**TABLE 4**

**American Society of Anesthesiologists Classification of Physical Status**

Class*	Definition
I	A normally healthy patient
II	A patient with mild systemic disease
III	A patient with severe systemic disease that is not incapacitating
IV	A patient with an incapacitating systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive for 24 h with or without the operation

\*If the surgery is an emergency, then the physical status classification is followed by the letter E.

in Table 5. We identified seven articles that reported the rate of endometritis following cesarean delivery. There were 1298 cases of endometritis among 41,569 deliveries, for an overall rate of endometritis rate following cesarean delivery of 3.1% (Table 5). Similarly, we identified 18 articles reporting the rate of SSI after cesarean delivery. There were 68,424 cases of SSI among 1,440,104 deliveries, for an overall rate of SSI after cesarean of 4.8% (Table 5). However, these crude infection rates do not take into account the a priori surgical risk of the patient.

To address this limitation, the 2009 NHSN report published pooled mean rates of SSI after cesarean delivery of 1.46%, 2.43%, and 3.82% for risk index category 0, 1, and 2/3, respectively.<sup>7</sup> Although comparison to a national benchmark is helpful for individual institutions to gauge their clinical performance, there are a number of limitations to the utilization of 2009 NHSN risk categorization benchmarks. First, the 2009 NHSN report only describes the rate of SSI following cesarean delivery without considering the rate of endometritis. Second, rates of SSI are based on voluntary reporting data from only 59, 61, and 52 hospitals for risk index categories 0, 1, and 2/3, respectively.<sup>7</sup> Given the lack of mandatory reporting and the limited number of hospitals, this may not qualify as an accurate national representation. Finally, the data do not distinguish between low-risk community and high-risk academic institutions, which limits the ability to make an accurate comparison to national benchmarks for high-risk patients. With known risk factors for wound infection such as body mass index (BMI),<sup>8</sup> diabetes, and severe hypertension,<sup>9</sup> an institution that delivers patients with many of these pre-existing

conditions is likely to have a higher rate of postcesarean infectious morbidity. Furthermore, for some procedures, the focus on length of surgery, wound classification, and ASA score within the NHSN criteria may not be useful. In some surgical specialties, these three variables have not been associated with an increased risk of infection,

*Using a combination of pre-existing maternal risk factors and intraoperative risk factors, a new risk categorization may provide a better estimation of the true risk for infection following cesarean delivery.*

may not be particularly important in the risk they confer, and should likely be replaced by other more important risk factors. For example, a recent study demonstrated that inclusion of BMI and the presence of labor resulted in significant improvement in predictive performance for a postcesarean infection when compared with procedure duration, wound class, and ASA score alone.<sup>10</sup>

For the obstetric population, there is little variation in the ASA score between patients (most with an ASA score of I or II [Table 4]) and in the duration of operating time (usually less than the established cutpoint of 56 minutes). The 2009 NHSN scoring system does not allow such stratification of high-risk patients and does not consider risk factors that may develop during the intrapartum period. Although an increased duration of surgery has been associated with higher rates of infection,<sup>11</sup> this is heavily dependent on maternal predisposing factors, such as obesity or prior surgeries resulting in dense adhesions. In addition, almost all cesarean wounds are categorized as clean contaminated (Table 3); as such, obstetric patients are not likely to be assigned a third point within the risk categorization schema (Table 2), thereby greatly limiting the value

of including wound class for these patients.

Given these limitations, we propose the use of a more robust risk stratification schema, one that is specific for cesarean delivery and includes risk factors more commonly encountered in pregnancy (Table 6). Using a combination of pre-existing maternal risk factors

and intraoperative risk factors, a new risk categorization may provide a better estimation of the true risk for infection following cesarean delivery. The identification of potential risk factors for infection is vital to the categorization of obstetric patients, as well as to the development of targeted interventions.

### **Risk Factors for Infectious Morbidity and Preventative Strategies**

#### *Preoperative Considerations*

According to the CDC Guidelines for Prevention of Surgical Site Infection,<sup>6</sup> there are multiple preoperative considerations that have been studied in an attempt to reduce the incidence of postoperative infection, including antiseptic showering, hair removal, and patient skin preparation.

Preoperative antiseptic showering on the morning of surgery has been shown to decrease skin microbial colony counts, but has not definitively been shown to reduce rates of postoperative infection. One study of more than 700 patients showed that chlorhexidine reduced bacterial colony counts 9-fold compared with only 1.3-fold for povidone-iodine.<sup>12</sup> However, a recent Cochrane review of six randomized, controlled trials did not show a statistically

**TABLE 5**

**Rates of Infection Following Cesarean Delivery**

Study	Type		Surgical Site Infection Rate (%)	Endometritis Rate (%)
Couto RC et al <sup>35</sup>	Prospective observational	In-hospital surveillance	32/951 (3.4)	—
		Postdischarge surveillance	196/951 (20.6)	—
Hebert PR et al <sup>36</sup>	Retrospective cohort		588/7441 (7.9)	—
Mah MW et al <sup>37</sup>	Prospective surveillance		20/735 (2.7)	15/735 (2.0)
Allen VM et al <sup>38</sup>	Retrospective cohort	Absence of labor	11/721 (1.5)	—
		Presence of labor	32/1480 (2.2)	—
Robinson HE et al <sup>19</sup>	Retrospective population-based cohort	Nonobese	633/14,666 (4.3)	341/14,666 (2.3)
		Moderately obese	129/2858 (4.5)	44/2858 (1.5)
		Severely obese	30/311 (9.6)	5/311 (1.6)
Olsen MA et al <sup>34</sup>	Retrospective case control		81/1695 (4.8)	—
Asch DA et al <sup>39</sup>	Retrospective		65,103/1385,180 (4.7)	—
Dumas AM et al <sup>40</sup>	Prospective surveillance	Joel-Cohen	34/2909 (1.2)	9/2909 (0.3)
		Pfannenstiel	29/2214 (1.3)	18/2214 (0.8)
CAESAR <sup>26</sup>	Randomized control trial	Single-layer uterine closure	188/1483 (12.7)	63/1483 (4.2)
		Double-layer uterine closure	188/1496 (12.6)	62/1496 (4.1)
		Closure of pelvic peritoneum	182/1496 (12.2)	59/1496 (3.9)
		Nonclosure of pelvic peritoneum	200/1499 (13.3)	66/1499 (4.4)
		Liberal use of drain	186/1398 (13.3)	65/1398 (4.6)
		Restricted use of drain	178/1398 (12.7)	53/1398 (3.8)
Cardoso Del Monte and Pinto Neto <sup>41</sup>	Prospective observational cohort		44/187 (23.5)	—
Rauk PN <sup>42</sup>	Prospective surveillance		20/441 (4.5)	13/441 (2.9)
Riley MM et al <sup>43</sup>	Prospective observational		26/1286 (2.0)	26/1286 (2.0)
Smaill and Gyte <sup>44</sup>	Cochrane review	Before cord clamp	129/2706 (4.8)	103/2367 (4.3)
		After cord clamp	107/3751 (2.8)	302/4139 (7.3)
		Timing not specified	2/193 (1.0)	16/215 (7.4)
Thurman AR et al <sup>45</sup>	Retrospective chart review		56/658 (8.5)	36/658 (5.4)
<b>Total</b>			<b>68,424/1,440,104 (4.8)</b>	<b>1298/41,569 (3.1)</b>

CAESAR, Caesarean Section Surgical Techniques: A Randomised Factorial Trial.

**TABLE 6**

**Proposed New Risk Stratification Schema: Infectious Risk Following Cesarean Delivery**

Risk Category	Factors
Low	Elective cesarean delivery (in the absence of labor or rupture of membranes) Absence of diabetes BMI < 25 kg/m <sup>2</sup>
Moderate	Low-risk surgical case (NHSN category 0) Nonelective cesarean (after labor and/or rupture of membranes) Well-controlled pregestational or gestational diabetes BMI 25-35 kg/m <sup>2</sup>
High	Moderate risk surgical case (NHSN category 1) Manual extraction of placenta <i>or</i> closure of skin using staples Emergency cesarean (often performed without adequate skin preparation or antibiotic prophylaxis) Chorioamnionitis Poorly controlled pregestational or gestational diabetes BMI > 35 kg/m <sup>2</sup> High-risk surgical case (NHSN category 2 or 3) Manual extraction of placenta <i>and</i> closure of skin using staples

BMI, body mass index; NHSN, National Healthcare Safety Network.

significant difference in the rate of SSI for patients who showered with 4% chlorhexidine gluconate compared with placebo or bar soap (relative risk [RR] 0.91; 95% confidence interval [CI], 0.80-1.04). However, when compared with no washing, one large clinical trial did demonstrate a statistically significant difference in favor of bathing with chlorhexidine (RR 0.36; 95% CI, 0.17-0.79).<sup>13</sup>

Although hair removal may be necessary to perform the Pfannenstiel skin incision, several studies have compared the

to clipped (RR 2.09; 95% CI, 1.15-3.80).<sup>14</sup> The increased risk of post-operative infection with shaving has been attributed to microscopic skin abrasions that serve as foci for bacterial growth. For this reason, if hair removal is deemed necessary immediately prior to surgery, the use of clippers is preferred over shaving.

Several antiseptic agents are available for immediate preoperative preparation of the incision site, including povidone-iodine, alcohol-containing products, and chlorhexidine gluconate. The use

of chlorhexidine-alcohol skin preparation resulted in a lower rate of SSI (RR 0.59; 95% CI, 0.41-0.85), but no significant difference in the incidence of organ-space infection.<sup>15</sup> The superior clinical protection of chlorhexidine preparations such as ChlorPrep® (CareFusion, San Diego, CA; 2% chlorhexidine gluconate, 70% isopropyl alcohol) is thought to be due to its more rapid action, persistent activity despite exposure to body fluids, and residual effect for up to 6 hours.<sup>16</sup>

**Antibiotic Prophylaxis**

The American Congress of Obstetricians and Gynecologists (ACOG) recommends the use of a single dose of a narrow spectrum first-generation cephalosporin (cefazolin), or a single-dose combination of clindamycin with an aminoglycoside for those with a significant penicillin allergy, as prophylaxis for cesarean delivery.<sup>17</sup> However, several studies have suggested that

*Several antiseptic agents are available for immediate preoperative preparation of the incision site, including povidone-iodine, alcohol-containing products, and chlorhexidine gluconate.*

risk of SSI when pubic hair is left intact, shaved, or clipped. In a 2011 Cochrane review of preoperative hair removal, three trials showed an increased risk of SSI when hair was shaved as opposed

of chlorhexidine-alcohol skin preparation has been shown to result in a reduction in postcesarean infection rates when compared with povidone-iodine. In a randomized multicenter trial of 849 patients,



extended spectrum antibiotic prophylaxis may further reduce the risk of postcesarean infection. In particular, narrow-spectrum antibiotics do not provide adequate coverage for *Ureaplasma* infection, which has been disproportionately isolated in patients with postcesarean endometritis. In a recent cohort study of more than 10,000 patients, the use of azithromycin-based extended spectrum prophylaxis showed a significant decrease in the rate of endometritis (RR 0.41; 95% CI, 0.31-0.54) compared with narrow-spectrum antibiotic prophylaxis.<sup>18</sup>

ACOG guidelines currently recommend that antibiotic prophylaxis be administered within 60 minutes of the start of the cesarean delivery.<sup>17</sup> With prior concerns about the sequelae of fetal antibiotic exposure, the former standard practice was administration of narrow-spectrum antibiotic prophylaxis after clamping of the umbilical cord. However, a recent systematic review concluded that antibiotic prophylaxis administered prior to the incision decreased the overall incidence of postcesarean infection and, even more importantly, did not increase the likelihood of neonatal infection, frequency of evaluations for neonatal sepsis, or the duration of neonatal hospitalization.<sup>3</sup> The authors concluded that administration of antibiotics within 30 to 60 minutes of surgery appears to be optimal in order to maximize tissue and blood concentrations at the surgical site.<sup>3</sup>

Given the known increased risk of postcesarean infection for obese patients, it is important to consider the appropriate antibiotic prophylaxis for cesarean delivery in these patients. Although a single dose of a first-generation cephalosporin may maintain a therapeutic level for approximately 3 to 4 hours in

most patients, this may not apply to obese women. A recent study demonstrated that moderately obese women with a prepregnancy weight of 90 to 100 kg were 1.6 times more likely to have a wound infection (95% CI, 1.31-1.95), whereas severely obese women (> 120 kg) were 4.45 times more likely to have a wound infection (95% CI, 3.00-6.61).<sup>19</sup> Given the increased amount of poorly perfused adipose tissue and the corresponding increased volume of distribution in obese patients, pharmacokinetic studies suggest that a higher dose of antibiotic prophylaxis be administered in these patients.<sup>20</sup>

ACOG guidelines recommend that antibiotic prophylaxis at the time of cesarean delivery be accomplished with the use of a narrow-spectrum first-generation cephalosporin (cefazolin), 2 g intravenously, or clindamycin, 900 mg intravenously, if there is a significant penicillin allergy, to be given within 60 minutes prior to incision. Extended-spectrum antibiotic prophylaxis, with an agent such as azithromycin, may be beneficial in patients at higher risk of

to result in a lower rate of postpartum endometritis in both a prospective, randomized trial (RR 0.6; 95% CI, 0.4-0.9)<sup>21</sup> and a subsequent Cochrane review.<sup>22</sup>

Compared with subcuticular sutures, the use of staples for skin closure at cesarean delivery has been associated with an increased risk of wound complications in a recent meta-analysis of six studies (13.4% vs 6.6%, pooled odds ratio 2.06; 95% CI, 1.43-2.98).<sup>23</sup> However, both closure techniques have been shown to be equivalent with regard to postoperative pain, cosmetic outcome, and patient satisfaction.<sup>24</sup>

### Postoperative Considerations

Strict glycemic control in diabetic women in the immediate postoperative period will help limit infectious complications. Similarly, early removal of bladder catheters has been shown to decrease the risk of infection.<sup>25</sup>

### Other Interventions

Although several interventions have been shown to be beneficial in reducing the rate of postcesar-

*Extended spectrum antibiotic prophylaxis, with an agent such as azithromycin, may be beneficial in patients at higher risk of postcesarean infectious morbidity, such as those who are obese or diabetic.*

postcesarean infectious morbidity, such as those who are obese or diabetic.<sup>17</sup>

### Intraoperative Considerations

With respect to intraoperative interventions, both manual removal of the placenta and method of skin closure have been studied with respect to their effects on postcesarean infection. As compared with manual removal of the placenta, delivery of the placenta by fundal massage and traction on the umbilical cord has been shown

ean infection (Table 7), there are others that have not been shown to do so. For example, studies have demonstrated no statistically significant difference in the rates of postcesarean infectious morbidity with closure of the pelvic peritoneum,<sup>26</sup> single- versus double-layer uterine closure,<sup>26</sup> exteriorization of the uterus for repair,<sup>27</sup> preoperative vaginal cleansing with povidone iodine,<sup>28</sup> administration of a high concentration of perioperative oxygen,<sup>29</sup> and saline wound irrigation.<sup>30</sup>

**TABLE 7**

**10 Strategies to Prevent Postcesarean Infectious Morbidity**

1. Shower with 4% chlorhexidine gluconate the night before elective surgery
2. If necessary, clip rather than shave pubic hair
3. Avoid unnecessary vaginal examinations in labor
4. Avoid unnecessary instrumentation in labor (including fetal scalp electrodes and intrauterine pressure catheters)
5. Prep the skin with an antiseptic agent (chlorhexidine-alcohol skin preparation) immediately prior to surgery
6. Administer appropriate intravenous antibiotic prophylaxis within 60 min prior to incision
7. Avoid manual removal of the placenta and fetal membranes
8. Avoid closure of the skin with staples
9. Maintain strict glycemic control in women with diabetes
10. Consider early removal of bladder catheters postoperatively

**Infection Surveillance**

Given the short duration of hospitalization following cesarean delivery, many infections may not be detected until after discharge from hospital and treatment may occur solely in the outpatient setting. Indeed, published postdischarge infection rates suggest that anywhere from 27% to 95% of all postcesarean infectious morbidity occurs after discharge from hospital.<sup>11</sup> This may explain, at least in part, the wide variation in reported SSI rates in studies using prospective compared with retrospective surveillance methods. Moreover, institutions with a more strict infection surveillance program are likely to have higher rates of postcesarean infection, thereby placing them at a disadvantage when comparing rates against other less meticulous institutions or national benchmarks. Appropriate surveillance methods

mail or telephone, pharmacy records for antibiotic prescriptions, and surgeon surveys by mail or telephone.

**Conclusions**

A significant proportion of all deliveries in the United States are achieved by cesarean delivery, which remains the single most important risk factor for postpartum infection, resulting in major financial and health implications for affected patients and for society in general. In order to provide better care for obstetric patients, it is vital that hospitals track their rates of postcesarean infection, identify appropriate national benchmarks with which to compare these rates, and develop and implement strategies to minimize infectious morbidity. Although the 2009 NHSN report defines SSI benchmarks in various risk stratification catego-

which provides data on infectious morbidity that is specific for cesarean delivery and includes risk factors commonly encountered in pregnancy. ■

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*Appropriate surveillance methods should include daily monitoring of outpatient microbiology reports and regular review of outpatient medical records.*

should include daily monitoring of outpatient microbiology reports and regular review of outpatient medical records with analysis of ambulatory encounters for relevant diagnosis codes, patient surveys by

ries,<sup>7</sup> it is focused only on surgical risk and is not specific for obstetric surgery, in addition to not addressing the risk of postpartum endometritis. We propose that a new risk categorization schema be used,



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## MAIN POINTS

- Puerperal infection remains a significant cause of maternal morbidity and mortality both in the United States and in developing countries. With an estimated 5- to 20-fold increase in incidence, cesarean delivery is the single most important risk factor for puerperal infection.
- There are numerous ways in which to reduce the risk of infection. These include preoperative antiseptic showering on the morning of surgery, the use of clippers for hair removal rather than shaving, the use of chlorhexidine-alcohol skin preparation, and extended-spectrum antibiotic prophylaxis.
- Given the known increased risk of postcesarean infection for obese patients, it is important to consider the appropriate antibiotic prophylaxis for cesarean delivery in these patients.
- Given the short duration of hospitalization following cesarean delivery, many infections may not be detected until after discharge from hospital and treatment may occur solely in the outpatient setting.