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CME REVIEW ARTICLE 5

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Prevention of Cesarean Delivery Surgical Site Infections

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Importance: Surgical site infection (SSI) is a common complication of cesarean delivery. Seen in up to 12% of cesarean deliveries, it is a major cause of prolonged hospital stay and a burden to the healthcare system. Interventions and techniques must be identified to decrease the risk of cesarean delivery SSIs.

Objective: We review the categories of SSI, current studies that have focused on various interventions to decrease SSI, and preoperative, intraoperative, and postoperative recommendations for cesarean delivery SSI prevention.

Evidence Acquisition: A thorough search of PubMed for all current literature was performed. Various surgical interventions and techniques were reviewed. We included studies that looked at preoperative, intraoperative, and postoperative interventions for SSI prevention.

Results: We have summarized several surgical interventions and techniques as well as current consensus statements to aid the practitioner in preventing SSIs after cesarean delivery.

Conclusions and Relevance: Upon analysis of current data and consensus statements pertaining to cesarean deliveries, there are certain preoperative, intraoperative, and postoperative interventions and techniques that can be recommended to decrease the risk of cesarean delivery SSI.

Target Audience: Obstetricians and gynecologists; family physicians

Learning Objectives: After completing this CME activity, physicians should be better able to evaluate preoperative considerations when preparing for a cesarean delivery; distinguish the recommended antiseptic choices for preoperative cleansing/prepping before cesarean delivery; propose the appropriate use of prophylactic antibiotics for prevention of cesarean delivery SSI; and select the surgical techniques that have been shown to decrease the risk of cesarean delivery SSI.

Cesarean delivery is the most common surgical procedure performed in the United States, with approximately 1.3 million being performed every year.[1] One of the most common complications of a cesarean delivery is a surgical site infection (SSI), which is seen in 5% to 12% of cesarean deliveries and is a major cause of prolonged hospital stay and a burden to the healthcare system.[2] There are established recommendations for the prevention of SSI after gynecologic procedures.[3] The purpose of this review is to recommend preoperative, intraoperative, and postoperative interventions to prevent SSIs after cesarean deliveries.

Surgical site infection can be subcategorized into incisional and organ/space infections. Incisional infections can be further divided into superficial (involving skin and subcutaneous tissue) versus deep (involving deeper soft tissue of the incision, such as muscle or fascia; Fig. 1),[3,4] The most common SSIs seen after cesarean deliveries are incisional infections (2%–7%) and endometritis (2%–16%).[5] In obese individuals, these rates are even higher, approaching 30%.[6,7]

All authors, faculty, and staff in a position to control the content of this CME activity and their spouses/life partners (if any) have disclosed that they have no financial relationships with, or financial interests in, any commercial organizations relevant to this educational activity.

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Defining Surgical Site Infections	
Superficial Incisional	• Occurs within 30 days postoperatively AND • Involves only skin and/or subcutaneous tissue AND • Has at least one of the following: ▪ Purulent drainage from the incision ▪ Organisms isolated from culture of fluid or tissue from the incision ▪ At least one of the following signs or symptoms of infection: o Pain or tenderness o Localized swelling, redness, or heat o Superficial incision opened by surgeon and is culture-positive or not cultured
Deep Incisional	• Occurs within 30 days postoperatively AND • Involves deep soft tissues (fascial or muscle layers) AND • Has at least one of the following: ▪ Purulent drainage from the deep incision but not from organ/space component of surgical site ▪ Deep incision spontaneously dehisces or deliberately opened by surgeon and is culture-positive or not cultured ▪ At least one of the following signs or symptoms of infection: o Fever (greater than 38°C) o Localized pain or tenderness o An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination
Organ/Space	• Occurs within 30 days postoperatively AND • Involves any part of the body, excluding skin incision, fascia, or muscle layers, that is open or manipulated during the operation AND • Has at least one of the following: ▪ Purulent drainage from a drain that is placed into the organ/space ▪ Organisms isolated from culture of fluid or tissue in the organ/space ▪ An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination

FIG. 1. Defining SSIs.[3]

Risk factors for SSI include (1) those that estimate the intrinsic degree of microbial contamination of the surgical site (Fig. 2),[3] (2) the type and duration of surgery, and (3) those that serve as markers for host susceptibility, which include but are not limited to perioperative hyperglycemia, smoking, obesity, nutritional status, depth of subcutaneous tissue greater than 3 cm, coexistent infection at a remote body site, vagina colonization with pathogenic microorganisms, ASA physical status, immunodeficiency, and MRSA status.[8] Risk factors for SSI after cesarean delivery are the same as those for SSI after gynecologic procedures as the intraoperative exposure to the abdominal and vaginal microbiome is similar.

Surgical Wound Classification	
Class I/Clean	Uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered
Class II/Clean-contaminated	Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions without unusual contamination
Class III/Contaminated	Open, accidental wounds and operations with breaks in sterile technique, gross spillage from gastrointestinal tract, or acute, non-purulent inflammation
Class IV/Dirty or Infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection

FIG. 2. Surgical wound classification.[3]

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PREOPERATIVE INTERVENTIONS

Diabetes and Glycemic Control

Diabetes and poor glycemic control are well-known risk factors for SSI.[9,10] In 1973, Cruse and Foord[11] did a retrospective study, which demonstrated that patients with diabetes had 5 times the risk of developing a SSI when compared with patients without diabetes. The CDC current guidelines recommend blood glucose target levels of less than 200 mg/dL in both patients with diabetes and patients without diabetes as levels above this have been associated with an increased risk of SSIs in multiple randomized controlled trials (RCTs) pertaining to cardiac surgery.[12–14] Other guidelines use a slightly lower target goal of less than 180 mg/dL[15,16] based on an RCT done by Lazar et al in 2004.[17] However, in this study, the control group was treated with insulin for a glucose level of greater than 250 and not greater than 200. There is currently insufficient evidence to recommend a target goal of less than 180 over less than 200. Although some studies have looked at stricter glycemic control (target goal of 80–110), a Cochrane review from 2009 suggested there was insufficient evidence to recommend strict control over conventional control.[18] Antenatal glucose control is routine for women with diabetes complicating pregnancy. In addition, parenteral insulin infusion before delivery with a target serum glucose goal between 70 and 110 mg/dL for prevention of neonatal hyperglycemia and subsequent neonatal hypoglycemia is commonly used. The decision to continue the insulin infusion postoperatively depends largely on glycemic control. In 2015, Al-Niaimi et al[19] demonstrated improvement in SSI rates of gynecologic oncology patients when an insulin infusion protocol was administered in comparison to the traditional sliding scale. Whether using an insulin infusion or sliding scale regimen, the recommended serum glucose target goal is less than 200 and should contribute to a decreasing SSI rate.

Routine Screening for Bacterial Vaginosis

Bacterial vaginosis (BV) is a complex alteration of vaginal flora resulting in an increased concentration of potentially pathogenic anaerobic bacteria.[3] It is associated with a variety of different organisms, most commonly *Gardnerella vaginalis*, *Bacteroides*, and *Peptostreptococcus*.[20] In gynecologic surgeries where the vagina is entered, before the routine use of antibiotic prophylaxis, BV was associated with an increased risk of vaginal cuff cellulitis.[21,22] Furthermore, Larsson et al performed an RCT in 2002 looking at the effect of preoperative and postoperative treatment of BV with metronidazole in women undergoing abdominal hysterectomy; this study demonstrated a significant reduction in vaginal cuff infections but not wound infections in those who underwent treatment.[23] Based on these studies, ACOG's recent practice bulletin on "Prevention of Infection after Gynecologic Procedures" states that testing for BV before surgery and treatment if present can be considered to decrease the risk of SSI in that population.[3] As the pathophysiology (ascending infection) and responsible pathogens for vaginal cuff cellulitis after hysterectomy and endometritis after cesarean delivery are similar, it seems reasonable to make a similar recommendation for women undergoing cesarean delivery.

Screening for and treatment for BV in the pregnant patient to prevent preterm labor and birth has been studied and found to be not beneficial.[24] However, screening for and treatment for BV in the pregnant patient to prevent SSI, specifically endometritis, is an idea that has not received much attention to date. Studies have shown BV to be a risk factor for the development of chorioamnionitis,[25,26] which is a well-known risk factor for endometritis.[27] Furthermore, an association between BV and postpartum endometritis has been demonstrated. In 1989, Watts et al[20] conducted a study looking at the role of BV in early postpartum endometritis and isolated microorganisms associated with BV (*Gardnerella vaginalis*, *Bacteroides*, and *Peptostreptococcus*) from 60% of endometrial cultures obtained from women diagnosed with postpartum endometritis. They followed up this investigation with an RCT that demonstrated that women with BV diagnosed antenatally by Gram stain criteria were approximately 6 times more likely to develop postpartum endometritis after cesarean delivery when compared with women with a normal Gram stain. This link between BV and postpartum endometritis was strengthened by the fact that women diagnosed with antepartum BV were significantly more likely to have *Gardnerella vaginalis*, *Bacteroides*, and *Peptostreptococcus* isolated from their endometrial cultures when compared with normal flora by Gram stain criteria.[28] In addition, a small retrospective cohort study in 2002 demonstrated that the risk of postpartum endometritis was tripled among women with BV in early pregnancy.[29]

Although future RCTs regarding this topic are necessary, given the biologic plausibility and the association of BV with upper genital tract infection during labor and after delivery, we recommend screening for BV at 35 to 37 weeks' gestation, coinciding with GBS testing, followed by treatment if BV is discovered.

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Preoperative Cleansing

Preoperative showering is a low-risk intervention recommended by the CDC,[12] as well as other professional organizations[30] for prevention of SSIs. There is general agreement that preoperative cleansing with chlorhexidine reduces bacterial colonization of the skin; however, whether or not it reduces SSI risk is unclear.[12] A Cochrane review performed in 2015 found no difference in SSI risk between preoperative cleansing using antiseptic agents and soap or placebo.[31] Similarly, a meta-analysis in 2013, which consisted of 17,000 patients, found no significant benefit of preoperative bathing with soap compared with placebo or no bathing.[32] In contrast, a meta-analysis performed by Wang et al[33] in 2017 found a significant decrease in total knee arthroplasty SSIs with preoperative cleansing with chlorhexadine when compared with control washes in moderate-risk and high-risk individuals. Similarly, another meta-analysis done by Cai et al[34] in 2017 found a decrease SSIs with the preoperative cleansing with chlorhexidine when compared with iodine/alcohol with no incidence of adverse effects. Although studies are contrasting with regards to preoperative showering and none focus on cesarean deliveries in particular, the intervention is considered low-risk with evidence of possible effect on decreasing SSI risk, and thus, it is recommended. A study done by Cruse and Foord[11] in 1980 demonstrated a lower SSI rate in those who showered with hexachlorophene before surgery compared with those who did not shower or those who showered with unmedicated soap. Although further high-quality RCTs are needed to further research the superiority of chlorhexidine for preoperative cleansing, we consider it a low-risk intervention and recommend a chlorhexidine shower both the night before and the morning of a scheduled cesarean delivery.

Antiseptic Choice for Skin Preparation and Vaginal Preparation

Current clinical guidelines for prevention of SSIs recommend using an alcohol-containing preoperative skin antiseptic agent.[12] Randomized trials have been undertaken to determine the most effective disinfectant to pair with alcohol. Those that have been published have mostly involved patients undergoing general surgical procedures and have suggested superiority of chlorhexidine-based agents over iodine-based agents.[35,36] Given that SSIs during cesarean delivery result from both skin pathogens as well as vaginal pathogens, it is unclear whether or not the results of these trials can be generalized to cesarean deliveries. There have been a few small trials in which antiseptic agents were compared for preoperative abdominal skin preparation in cesarean deliveries. In 2015, Ngai et al[37] compared chlorhexidine with alcohol, povidone-iodine with alcohol, and a sequential combination of both and found no difference in SSI rates. Similar findings were demonstrated in other small clinical trials.[38,39] However, in 2016, a single-center, randomized, controlled trial was performed to evaluate whether the use of chlorhexidine-alcohol for preoperative skin antisepsis was superior to the use of iodine-alcohol for the prevention of SSI after cesarean delivery.[40] This study demonstrated roughly a 50% decrease in SSIs in the chlorhexidine group, which is consistent with the previously mentioned studies not particular to cesarean deliveries. Given the current CDC guidelines of using an alcohol-containing skin agent and multiple studies demonstrating superiority of chlorhexidine-based over iodine-based preparations, we recommend a chlorhexidine-alcohol preparation before cesarean, unless it is otherwise contraindicated.

Cleansing of the vagina before cesarean delivery can contribute to the prevention of SSI. An RCT done by Ahmed et al[41] assessed vaginal preparation with chlorhexidine compared with no vaginal preparation and found a lower rate of endometritis in those who underwent prep. A recent Cochrane review including 11 RCTs in which vaginal preparation was done (using povidone-iodine, chlorhexidine, or benzalkonium chloride) and compared with no vaginal prep demonstrated decreased rates of endometritis in the groups who underwent prep (3.8% vs 8.7%, respectively).[42] The reduction in risk was most strong in those individuals whose membranes had already ruptured. We recommend vaginal preparation with a 4% chlorhexidine solution before cesarean delivery for prevention of endometritis. Currently, only povidone-iodine preparations are approved by the US Food and Drug Administration for vaginal surgical site antisepsis, yet the American College of Obstetrics and Gynecology states that chlorhexidine with low levels of alcohol (4%) may be used off-label as a substitution for povidone-iodine in cases of allergy or when preferred by surgeon.[3]

Hair Removal

Studies of hair removal before surgery to prevent SSI are rather limited and have mostly occurred in surgical fields other than obstetrics and gynecology, thus, recommendations are extrapolated to cesarean deliveries. A Cochrane review done by Tanner et al in 2012 suggested that hair removal at the time of surgery is not associated with decreased SSIs and should only be done if needed for better visualization. If removal is required for visualization or per patient preference, clipping is preferred to shaving as studies have shown that shaving

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is associated with more SSIs.[43] Given this association, patients and physicians should be encouraged to refrain from shaving the suprapubic area before a cesarean delivery.

Preoperative Antibiotic Regimen

Antibiotics that are effective against Gram-positive bacteria, Gram-negative bacteria, and some anaerobic bacteria, are recommended for prophylaxis before cesarean delivery.[44] Although a variety of antibiotics have been shown to be equally efficacious for prophylaxis, cefazolin and ampicillin have been shown to be the most cost-effective when compared with second- and third-generation cephalosporins.[45,46] Given the shorter half-life of ampicillin when compared with cefazolin, administration of single-dose cefazolin has been the mainstay agent for prevention of SSIs after cesarean delivery. The use of first-generation cephalosporins compared with no antibiotics has been shown to decrease the risks for development of wound infections and endometritis by 60% to 70%.[47] The administration of the cephalosporin is most beneficial if given before the skin incision as opposed to at the time of cord clamping.[48]

A major current focus regarding antibiotic prophylaxis during cesarean delivery is the addition of broad-spectrum antibiotics to complement cefazolin. Historically, the rationale with regards to these broad-spectrum agents is to ensure coverage of the organisms most commonly involved in cesarean surgical site contamination and infection. As stated before, intraoperative contamination and infection is usually polymicrobial, consisting of aerobes, anaerobes, and, frequently, ureaplasma or mycoplasma.[49] The mycoplasmas and some anaerobes may be resistant to cephalosporins resulting in a gap in coverage for some of the most common and infection-producing pathogens associated with cesarean SSI.[29,50,51] Given this concern, extending the antibiotic coverage by adding either metronidazole or azithromycin to cefazolin to improve anaerobic and/or ureaplasma coverage is being considered.[52] A Cochrane review from 2009 done by Tita et al found that extended-spectrum antibiotics (cefazolin plus metronidazole, azithromycin, or gentamicin) was effective in decreasing the risk of maternal infection (by 30%–60%) and shortening hospital stays and costs when compared with single-agent regimens.[49] Tita et al[53] strengthened this review with an RCT done in 2016, which revealed that adding azithromycin 500 mg intravenous to the standard preoperative antibiotic prophylaxis lead to a significant 50% reduction in endometritis (3.8% vs 6.1%) and wound infection (2.4% vs 6.6%) with no change in neonatal outcomes. The majority of these individuals were obese with a BMI greater than 30 kg/m^2 and 25% were morbidly obese with a BMI greater than 40 kg/m^2. We recommend the use of extended-spectrum antibiotic prophylaxis before cesarean delivery, ideally within 60 minutes before skin incision.

Weight-Based Dosing of Preoperative Antibiotics

In 2013, the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America released a joint statement recommending 2 g of cefazolin for less than 120 kg and 3 g of cefazolin for greater than 120 kg for surgical antimicrobial prophylaxis for common procedures.[12] ACOG's Committee Opinion titled "Gynecologic Surgery on the Obese Woman" (2015, reaffirmed 2017)[54] and ACOG's new "Practice Bulletin #195: Prevention of Infection after Gynecologic Procedures" agree with this recommendation. This has prompted discussion of whether the morbidly obese gravid patient would benefit from 3 g of cefazolin for prevention of SSI at the time of cesarean delivery. As the GFR increases in pregnancy, drug clearance increases and half-life decreases, suggesting that adjustment of single-dose preoperative antibiotics in pregnant patients, specifically in the morbidly obese, is reasonable.

A retrospective cohort study by Ahmadzia et al[55] in 2015 did not demonstrate a difference in SSIs in morbidly obese patients when comparing 2 g of cefazolin versus 3 g of cefazolin. On the other hand, a retrospective cohort study done in 2016 showed a lower risk of wound complications after cesarean with 3 g of cefazolin dosing in the morbidly obese (BMI > 40 kg/m^2).[56] Although ACOG typically recommends 2 g of cefazolin for BMI less than 120 kg/m^2 and 3 g of cefazolin for BMI greater than 120 kg/m^2 in gynecologic procedures, they do not specifically address cesarean deliveries. Although more RCTs are needed to further support or refute weight-based antibiotics for cesarean deliveries, given the similarities between cesarean deliveries and gynecologic surgeries, we recommend weight-based dosing with cefazolin at 2 g (<120 kg) versus 3 g (>120 kg).

INTRAOPERATIVE INTERVENTIONS

Redosing of Antibiotics

In 2013, the joint guidelines of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America also put forth the following recommendation in regards

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to surgical procedures: "for all patients, intraoperative redosing is needed to ensure adequate serum and tissue concentrations of the antimicrobial if the duration of the procedure exceeds 2 half-lives of the drug or if there is excessive blood loss during the procedure."[12] Administration of additional antibiotics intraoperatively is an established practice based on the current guidelines for surgery in general and this is supported by multiple studies. From a pharmacokinetic standpoint, in 1996, Swodoba et al[57] revealed that cefazolin concentration in patient serum and tissue was inversely proportional to patient blood loss. Both Ohge et al[58] and Koopman et al[59] showed that cefazolin levels were below MIC for common pathogens in patients' tissue after 3 hours. From a clinical standpoint, Morita et al[60] assessed redosing of antibiotics 4 hours after open colorectal surgery cases and found a significant decrease in rates of SSI in those patients who received an additional dose (8.5%) compared with those patients who did not (26.5%). Given these findings and recommendations, the American College of Obstetrics and Gynecology endorses the principles of intraoperative redosing of antibiotics for prevention of infection in gynecologic procedures; however, such firm recommendations do not exist in the obstetrical field.[3] In April 2018, Fay and Yee discussed the idea of applying these current surgical antimicrobial standards to cesarean deliveries based on the fact that cesarean deliveries, although not well studied compared with other gynecologic procedures, have much in common with major surgical procedures and, thus, should have similar recommendations. The article even suggests that redosing in this population may be particularly important given the increased renal clearance associated with the pregnancy state.[61]

In Practice Bulletin #120: Use of Prophylactic Antibiotics in Labor and Delivery, The American College of Obstetrics and Gynecology does state "as for surgical prophylaxis in general, patients with lengthy surgical procedures or those who experience excessive blood loss should receive an additional intraoperative dose of the antibiotic used for preincision prophylaxis"; however, they do not firmly state this in relation to cesarean deliveries.[44] The joint guidelines mentioned previously similarly vaguely state that "additional intraoperative doses may be warranted for patients with excessive blood loss or for whom the duration of the procedure is extended" in reference to cesarean deliveries. Although many cesarean deliveries will not exceed an operation time of 3 to 4 hours, postpartum hemorrhage in cesarean deliveries has been on the rise, meaning that blood loss of 1500 mL is common. Although both ACOG and the joint guidelines do not explicitly recommend redosing in cesarean deliveries, some institutions in the United States have made it part of their practice based on previous evidence from similar surgical procedures. Randomized controlled trials on this particular topic should be performed to reinforce the argument; however, the evidence from similar surgeries is already strong enough for us to recommend redosing of antibiotics during cesarean delivery complicated by long operating time (>3–4 hours) or excessive blood loss (>1500 mL).

Type of Skin Incision

Low transverse skin incisions have been the primary incisions used to perform cesarean deliveries in the past, as they are associated with fewer SSIs and wound complications when compared with vertical midline incisions.[62] Although this is the typical choice for gravidas of normal weight, there has been discussion and research in more recent years focusing on best skin incision for the obese gravid patient. Previously, it had been written that transverse abdominal incisions made under the pannicular fold existed in "a warm, moist, anaerobic environment associated with impaired bacteriostasis that promotes the proliferation of numerous microorganisms, producing a cesspool"[63]; however, this statement has not been supported by research. Even now, the appropriate choice in the obese patient continues to be debated and has yet to be extensively studied.[64] In the limited studies that have been performed, however, evidence tends to support the use of a low transverse skin incision in the obese population if it is possible with body habitus and if the patient's respiratory status can tolerate cephalad retraction of the pannus due to the increased risk of wound complications with a midline vertical incision.[65] Wall et al[66] found a significantly higher rate of cesarean wound complications in severely obese individuals receiving vertical midline incisions (35%) compared with transverse incisions (9%). This study, however, is limited by small sample size. Alanis et al[6] revealed similar findings when looking at a population of gravid patients of BMI greater than 50 kg/m^2, with a 38% wound complication rate in the vertical incision group versus 21% wound complication rate in the transverse group.

More recently, Marrs et al[67] performed an RCT that suggests that there are no major differences in wound outcomes based on Pfannensteil versus midline vertical skin incisions in gravid patients with class III obesity. This finding is contrary to previous findings and additional, larger RCTs should be done in the future to further determine whether there is an increased risk of wound infection with vertical midline incisions, as these incisions can often provide better exposure and a smaller distance to the uterus in the extremely obese population.

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Current evidence supports and we recommend the use of a low transverse skin incision whenever possible, even in obese individuals. However, the decision regarding what type of cesarean skin incision to perform on an individual patient certainly depends on a number of factors, including but not limited to body habitus, respiratory status, and prior abdominal surgeries. That being said, the provider must take into account all aspects of the patient's presentation when choosing the ideal skin incision.

Manual Extraction of Placenta

Delivery of the placenta at time of cesarean delivery can be done via umbilical cord traction and fundal massage or manual extraction. A meta-analysis done by Atkinson et al[68] in 1996 demonstrated that manual extraction of the placenta was associated with significantly higher levels of endometritis when compared with umbilical cord traction and fundal massage (31% vs 22%, respectively). A Cochrane review from 2010 reinforced these findings.[69] We recommend umbilical cord traction with fundal massage to decrease endometritis risks during cesarean delivery.

Intra-abdominal Irrigation

Intra-abdominal irrigation is a current practice used during cesarean delivery by some providers to assist in clearance of blood clots; its use for prevention of SSI has also been studied. Two RCTs from 2003 and 2012 revealed that intra-abdominal irrigation with normal saline did not demonstrate decreased risks of wound infections or endometritis[70,71]; furthermore, a systematic review in 2016 showed association between intra-abdominal irrigation and increased risks of intraoperative and postoperative nausea without a significant reduction in infectious morbidity.[72] At this time, intra-abdominal irrigation is not recommended for prevention of SSI after cesarean delivery.

Management of Subcutaneous Tissue

Management of the subcutaneous space during cesarean deliveries has been a popular area of research, especially in the overweight and obese population.[73] A Cochrane review in 2004 demonstrated that in women with subcutaneous thickness greater than 2 cm, closure of the space decreased the risk of hematoma, seroma, wound infection, and separation compared with nonclosure.[74] Chelmow et al[75] performed a meta-analysis in 2004 that investigated the benefits of subcutaneous closure and demonstrated a 34% decrease in risk of wound disruption in women with a subcutaneous tissue thickness greater than 2 cm. A recent meta-analysis performed in 2017 reinforced this finding.[76]

Currently, the recommendation is for subcutaneous closure in any patient with a subcutaneous tissue depth of greater than 2 cm.[77] However, an area of possible future research is to focus on morbidly obese gravid patients with a subcutaneous tissue depth much greater than 2 cm to see if a multilayer closure of the subcutaneous tissue further reduces the risk of SSI in that population.

There have been some studies that have focused on subcutaneous drain placement to help prevent SSI in cesarean deliveries. Earlier studies support possible drain placement in individuals with subcutaneous tissue depth greater than 2 cm.[77] In 1988, Loong et al[78] performed an RCT that assessed subcutaneous drain placement after cesarean delivery and actually saw an increase in wound infection rates in those individuals who underwent drain placement. In later studies by Allaire et al[79] and Magann et al,[80] drainage was compared with no drainage or to no closure and was found to be associated with a decrease in wound complications. In more recent studies, the use of a subcutaneous drain, regardless of tissue thickness, did not demonstrate decreased wound complications, including wound infection.[81,82] Given these more recent findings, subcutaneous drain placement at time of cesarean delivery is not recommended.

Skin Closure Technique

The 2 most common skin closure techniques studied in cesarean delivery are suture and staples; current evidence for skin closure supports the use of subcuticular suture.[73] An RCT by Mackeen et al[83] in 2014 demonstrated a 57% decrease in incidence of wound complications, including wound infection, with suture closure when compared with staples at time of cesarean delivery. In a meta-analysis by Tuuli et al[84] in 2011, subcuticular suture closure was found to have a lower wound separation and complication rate when compared with staples. Similar meta-analyses have been done and have produced similar outcomes.[85,86] In regards to the superobese population, the data regarding skin closure is limited. There has been 1 RCT that has shown an increased risk of infection with staple closure; however, in a subgroup analysis with obese individuals (BMI > 30 kg/m^2), there was no difference between staples and sutures.[87] A recent RCT done by Zaki et al[88] demonstrated no difference between wound complications in class III obesity patients when comparing staples versus suture closure. Given these studies, we recommend a subcuticular suture closure;

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however, more larger RCTs should be performed to further investigate the best skin closure in the more obese population.

Negative-Pressure Wound Therapy

Negative-pressure wound therapy (NPWT) has been well-recognized for the management of open wounds. The device ensures negative pressure to the wound bed and removes fluids, which leads to the creation of characteristic pattern of blood flow around the wound, a reduction in tissue edema, and stimulation of granulation tissue formation. More recently, NPWT use has been extended to treat closed surgical incisions, specifically in those at high risk of SSI (ie, obese individuals or those with diabetes). With closed incisions, NPWT reduces lateral tension, improves lymphatic clearance, and reduces hematoma and seroma formation.[89] A systematic review and meta-analysis in 2016 compared NPWTs to standard postoperative dressings on closed SSIs and found that NPWTs significantly reduced the rate of wound infection and seroma when applied to closed surgical wounds.[89] A subsequent meta-analysis focused on RCTs showed a clear and significant benefit in favor of prophylactic NPWT to reduce SSIs (12.5%–5.2%, a reduction of approximately 58%) and wound dehiscence (17.4%–12.8%) when the device was applied to a closed surgical incision.[90] Although the 2 previously mentioned studies included many types of closed surgical incisions, Yu et al performed a systematic review that focused on the impact of NPWT and prevention of SSIs specifically with regards to cesarean deliveries. This systematic review consisted of 6 RCTs and 3 cohort studies and included heterogeneity in patient population (though mostly obese) and in type of NPWT applied. Although heterogeneous, the study did suggest a reduction in SSI and overall wound complications.[91]

As stated in the Strugala study, NPWT devices are expensive and there needs to be stronger evidence and proof of cost-benefit before NPWT will be recommended for prevention of SSIs going forward. Echebiri et al designed a decision-analytic model from a third party payers perspective to assess the cost-benefit of prophylactic application of NPWT after cesarean delivery; this model provides economic evidence suggesting that NPWT should not be used on closed laparotomy incisions of patients who are at low risk of post-cesarean delivery SSIs; however, among patients with a high risk of SSIs (>14% risk), prophylactic NPWT is potentially cost-beneficial.[92] We recommend considering the use of NPWT for women undergoing cesarean delivery with a high risk (ie, BMI > 30 kg/m^2, patients with diabetes, immunosuppressed individuals) for SSI.

POSTOPERATIVE INTERVENTIONS

Timing of Dressing Removal

The Centers for Disease Control and Prevention recommend dressing removal between 24 and 48 hours after surgery.[5] In 2015, a Cochrane review focused on early (<48 hours) versus delayed dressing removal (>48 hours) and found no difference in SSI rate.[93] In 2016, Peleg et al[26] performed an RCT comparing dressing removal 6 hours postoperatively versus 24 hours postoperatively and demonstrated no difference in wound complication rates and higher maternal satisfaction with earlier dressing removal.[94] This study, however, focused on a low-risk population (BMI < 35) and excluded individuals with diabetes, preeclampsia, prolonged labor, and premature rupture of membranes, among others. In 2017, Nesrallah et al[95] performed an RCT comparing removal of post-cesarean dressing at 12 to 30 hours versus removal at 30 to 48 hours and found no difference in SSI rates (7% vs 9%, respectively).

Although studies are limited with regards to optimal timing for removal of dressing, there does not appear to be any increased risk of infection with earlier removal. Further RCTs should be performed to assess whether this holds true for the higher-risk population. Nonetheless, earlier removal has been shown to increase patient satisfaction, as well as decrease hospital stay length. We recommend removal within the first 24 hours after surgery.

Postoperative Antibiotics

Despite clear cut evidence that multiple dose antibiotic prophylaxis is not superior to single-dose administration,[96] there has been renewed discussion regarding the continuation of an antibiotic regimen into the postoperative period for prevention of SSIs post-cesarean delivery. In 2003, Andrews et al performed an RCT that compared post-cesarean SSI rates between individuals who received intraoperative (after cord clamp) cefotetan alone versus individuals who received intraoperative cefotetan and doxycycline (after cord clamp) plus azithromycin 6 to 12 hours post-cesarean delivery. They found that the addition of postoperative antibiotics significantly reduced the frequency of SSIs (19% in the group that received postoperative azithromycin vs 28% in the group that did not receive azithromycin).[97] The joint guidelines previously did not include postoperative antibiotics as part of their guidelines as previous studies had not supported this. However, in 2017,

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Valent et al performed an RCT that compared postcesarean SSIs rates between obese individuals who received preoperative cephalosporin antibiotics only versus obese individuals who received preoperative cephalosporin antibiotics and a 48-hour postoperative course of oral cephalexin and metronidazole. Their results demonstrated a greater than 50% reduction in SSIs in the postoperative antibiotics group (6.4%) versus the placebo group (15.4%).[98] This finding was significantly different than previous studies mentioned in the joint guidelines, possibly due to its focus on a higher-risk population.

The idea of oral postoperative antibiotics after cesarean delivery to prevent SSIs is a rather new one; previous studies and Valent's study suggests that while it may not be necessary in a low-risk population, it is a practice worth considering in select high-risk individuals, including those with obesity (BMI > 30), diabetes, immunosuppression, or other risk factors that put them at a higher risk of SSI.[99] We have significant concern that this practice will lead to emerging antibiotic resistance to the multidose antibiotic regimens used. We have not observed microbial resistance with single-dose regimens, so caution needs to be exercised before adopting this practice. We do not recommend the continuation of postoperative antibiotic prophylaxis or exceeding single-dose administration unless indicated for excessive blood loss or extended surgical duration.

Postoperative Care

Although the above interventions can result in a lower rate of SSI associated with cesarean delivery, we cannot forget that the patient remains at risk after discharge from the hospital. Most incisional infections are diagnosed 2

TABLE 1
Recommendations for SSI Prevention After Cesarean Delivery

Recommendations for Prevention of Cesarean Delivery SSIs	
Preoperative	
Glycemic control	Obtain ideal serum glucose range from 140–200 once infant delivered via insulin infusion or sliding scale regimen (Category IA).
Routine screening for bacterial vaginosis	Screen for bacterial vaginosis at 35 to 37 weeks' gestation, coinciding with GBS testing, followed by treatment if bacterial vaginosis is discovered (Category II).
Preoperative cleansing	Cleanse skin with a chlorhexidine shower both the night before and the morning of a scheduled cesarean delivery (Category IB).
Antiseptic choice for abdominal/vaginal preparation	Use of chlorhexidine-alcohol for abdominal preparation before cesarean delivery, unless it is otherwise contraindicated. Use of 4% chlorhexidine solution for vaginal preparation before cesarean delivery (Category IA).
Hair removal	Only remove hair if needed for better visualization. If removal is required, clipping is preferred to shaving. Encourage patients to refrain from shaving in the suprapubic region before cesarean delivery (Category IA).
Antibiotic regimen	Use extended-spectrum antibiotics (cefazolin with metronidazole, azithromycin, or gentamicin) before cesarean delivery (Category IB).
Weight-based dosing of preoperative antibiotics	Administer weight-based dosing of preoperative antibiotics with cefazolin 2 g (<120 kg) versus 3 g (>120 kg) (Category II).
Intraoperative	
Redosing of antibiotics	Redose antibiotics during cesarean delivery complicated by long operating time (>3–4 hours) or excessive blood loss (>1500 mL) (Category II).
Type of skin incision	Perform a low transverse skin incision whenever possible; however, be sure to take into account all aspects of patient's presentation (ie, body habitus, respiratory status, prior abdominal surgeries) to aid in decision making (Category II).
Manual extraction of placenta	Remove placenta via umbilical cord traction and fundal massage (Category IA).
Intra-abdominal irrigation	Do not perform intra-abdominal irrigation during cesarean delivery (Category IA).
Management of subcutaneous tissue	Close the subcutaneous space in any patient with a subcutaneous tissue depth of >2 cm. Subcutaneous drain placement is not recommended (Category IB).
Skin closure technique	Close the skin using subcuticular suture (Category IB).
Negative-pressure wound therapy	Consider use of NPWT for women undergoing cesarean delivery with a high risk for SSI (Category II).
Postoperative	
Timing of dressing removal	Remove incisional dressing within the first 24 hours after surgery (Category IB).
Postoperative antibiotics	Do not continue postoperative antibiotic prophylaxis or exceed single-dose administration unless indicated for excessive blood loss or extended surgical duration (Category IA).
Postoperative care	Have patient to return to clinic within 2 weeks of surgery for a postoperative appointment (Category II).

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TABLE 2
Strength of Recommendation Categories for Prevention of Cesarean Delivery SSIs

Recommendation Categories
• Category IA: A strong recommendation supported by high- to moderate-quality evidence suggesting net clinical benefits or harms.
• Category IB: A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms or an accepted practice supported by low to very low-quality evidence.
• Category IC: A strong recommendation required by state or federal regulation.
• Category II: A weak recommendation supported by any quality evidence suggesting a trade-off between clinical benefits and harms.

Adapted from Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. Healthcare Infection Control Practices Advisory Committee. *JAMA Surg* 2017;152:784–791.[12]

weeks postoperatively.[100] Patients need to be instructed in postoperative wound care to keep the incision clean by using soap and water on a regular basis. In addition, diabetes control needs to continue to be emphasized until incisions are healed. We need to ensure that patients with diabetes have their medications at discharge and the resources to maintain their serum glucose levels at recommended levels (<200 mg/dL). An early return appointment within 2 weeks of surgery is recommended.

CONCLUSIONS

Surgical site infection is one of the most common complications after cesarean delivery, impacting approximately 10% of cases. It is a major cause of prolonged hospital stays and a burden to healthcare costs. Much research has been done in regards to the prevention of SSIs after surgery; however, this is the first review article that specifically addresses recommendations for prevention of SSI after cesarean delivery (Tables 1 and 2). Although some of the above recommendations are based on well-established data (ie, glycemic control, antiseptic choice for abdominal/vaginal preparation, appropriate antibiotic regimen), other recommendations are based on less-established data, presenting ample research opportunities moving forward. In regards to screening for BV with treatment if diagnosed, much of the evidence behind this is in relation to hysterectomies; future RCTs focusing on diagnosis and treatment of BV and incidence of postpartum endometritis should be undertaken. Although weight-based dosing of antibiotics is recommended by ACOG, further RCTs should be done to further support this intervention for the prevention of SSI in cesarean deliveries in particular. Although NPWT thus far has not been shown to reduce SSIs, there is some suggestion of possibly being effective in a higher-risk population; there is ample opportunity to perform RCTs addressing this. Certainly, some of the above recommendations are still novel ideas and require further research to strengthen support of their use; however, most of the above interventions show likely benefit with minimal associated risks. Thus, they are recommended for prevention of SSI after cesarean delivery.

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