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# **Surgical Site Infections (SSI) – Prophylaxis and Management**

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# **Background**

Surgical site infections (SSIs) are a common and potentially disastrous complication in the perioperative setting, resulting in increased morbidity, prolonged hospitalizations, and death. SSIs are one of the more common hospital-acquired infections (HAIs) in low- and middle-income countries, with an incidence of 11.8 per 100 surgical procedures [\[1](#page-8-0)]. In the United States, it is estimated that SSIs account for approximately 1% of all surgical hospitalizations and can be upward to 4–5% in other higher-income countries [\[2](#page-8-1)]. The variability noted in these rates depends on many factors, including patient population and the nature of the procedure performed (e.g., extra-abdominal surgery vs intra-abdominal surgery) [[3\]](#page-8-2).

SSIs are also the most costly type of hospital acquired infection, with an estimated cost of \$3.3 billion per year [[4\]](#page-8-3). In addition to patient morbidity, prolonged hospitalizations, subsequent complications, and even mortality during the acute phase of the infection, other long-term costs can include the pain and anxiety experienced by the patient in the long-term [[5](#page-8-4)]. It is now required for institutions to report processes, outcomes, and measures regarding SSIs. Reimbursements for the treatment of SSIs often depend on the utilization of various evidencebased strategies [\[4\]](#page-8-3).

SSIs can be categorized as superficial incisional, deep incisional, and organ or space SSIs (see Table [7.1](#page-1-0)). Direct colonization of the wound by microorganisms in addition to compromised patient immunity is the primary pathophysiologic characteristic of all types of SSI.

Risk factors can be categorized as those related to the patient condition as well as that of potential pathogens (see Table [7.2](#page-1-1)). Factors may be categorized as either patient-related (endogenous), pathologic microorganism characteristics (microbial), or related to the surgical procedure (exogenous). Current data has predominantly been obtained within the adult population and have identifed patient risk factors including malnutrition, hyperglycemia, prior infections, and number of comorbidities. Data specifc to the pediatric population is less robust and often inferred. Nevertheless, there are a number of

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<span id="page-1-0"></span>**Table 7.1** Types of surgical site infections

Refs. [[2,](#page-8-1) [6](#page-8-8)].

<span id="page-1-1"></span>**Table 7.2** Risk factors for surgical site infections

Endogenous	Microbial	Exogenous
Poor nutritional status Poor glycemic control Poor perioperative thermoregulation American Society of Anesthesiologists (ASA) physical status score $\geq$ 3 High body mass index Co-existing infections and known infected wound status Immunocompromised conditions Preoperative hospital stay $\geq$ 2 days Known pre-existing colonization	Polysaccharide capsule formation Enzyme production Biofilm formation	Intra-abdominal surgery Overall discipline of surgery (cardiac, general, neurosurgery, orthopedic) Inadequately prepared equipment Lack of appropriate surgical hygiene
[3, 4, 7]		

factors studied specifcally within the pediatric and neonatal populations; the nature of the surgery (e.g., cardiovascular, general surgery, neurosurgery, and orthopedic) and increased operative time were all associated with an increased risk of developing an SSI [[7\]](#page-8-5).

*Staphylococcus aureus* is the pathogen most commonly identifed as causing an SSI, isolated in 20–30% of infections [[8](#page-8-6), [9\]](#page-8-7). *Escherichia coli* is the second most commonly identifed pathogen, isolated in 11–14% of SSIs (see Table [7.3\)](#page-1-2). The pathogens responsible for organ <span id="page-1-2"></span>**Table 7.3** Frequency of pathogens causing SSIs reported to the National Healthcare Safety Network, 2011–2014



Adapted from [\[9\]](#page-8-7)

space infections vary by site of infection; for example, Gram-negative enteric pathogens are more commonly associated with organ space SSIs from clean-contaminated procedures involving the alimentary tract. Local epidemiology and microbiologic susceptibility patterns must be taken into consideration to account for antimicrobial resistance patterns that vary geographically. For example, rates of methicillinresistant *Staphylococcus aureus* (MRSA) can vary widely within the United States, ranging from 7% to 60% [[10\]](#page-8-9).

# **Management and Prevention of Surgical Site Infections**

### **Preoperative Concerns**

A thorough history and physical examination will help the anesthesiologist identify significant patient risk factors that may predispose a patient for surgical site infection. Other concerns should be taken into account in efforts to reduce complications of SSIs.

### **Active Infections**

If the patient is arriving in the operating room with an active infection, it should be treated aggressively prior to surgery whenever possible. Ideally, the active infection will have resolved, either through treatment or spontaneously, prior to elective procedures [\[3](#page-8-2)].

# **Decolonization in** *Staphylococcus aureus* **Carriers for Cardiothoracic and Orthopedic Procedures**

Nasal carriage of *S. aureus*, which is prevalent in one-third of the US population, is a known risk factor for developing a *S. aureus* infection [\[11,](#page-8-10) [12\]](#page-8-11). In patients known to be colonized with *S. aureus*, patients who were treated with intranasal mupirocin 2% ointment with or without chlorhexidine soap body wash perioperatively have a signifcantly lower rate of developing SSI compared to patients without treated or treated with placebo [[1\]](#page-8-0). Most of these studies pertained to patients undergoing cardiothoracic or orthopedic surgical procedures; however, subsequent *S. aureus* infection rate did not differ between different surgical procedures. Based on these compelling data, the World Health Organization (WHO) Global Guidelines for the Prevention of Surgical Site Infections make a strong recommendation for perioperative intranasal application of mupirocin 2% ointment with or without chlorhexidine body wash in patients with known *S. aureus* colonization undergoing cardiothoracic or orthopedic surgery [[1](#page-8-0)]. For patients with known *S. aureus* colonization undergoing other types of surgery, the WHO guideline suggests considering treatment with intranasal mupirocin with or without chlorhexidine body washes [\[1](#page-8-0)].

### **Surgical Site Considerations**

While certain measures to prevent SSIs are driven primarily by the surgeon, it is important for the anesthesiologist to be aware of their impact. It has been widely recognized that certain practices when preparing the surgical site may predispose the patient to an SSI. Metaanalyses show that no hair removal or hair removal via the use of clippers has a signifcantly lower risk of SSI when compared with hair removal via shaving, preoperatively or just prior to incision [\[1](#page-8-0), [13,](#page-9-0) [14\]](#page-9-1).

Additional elements of surgical site preparation include the agent used for skin antisepsis. Recent studies have shown that of the two most common antiseptic agents used, chlorhexidine gluconate vs iodophor, chlorhexidine resulted in lower amount of bacterial skin colonization [[15\]](#page-9-2).

Surgical hand preparation also plays an important factor in reducing the risk of SSIs, and proper technique prior to donning sterile gloves has been shown to reduce the incidence of SSIs [\[1\]](#page-8-0).

### **Patient Optimization Prior to Procedure**

*Nutrition* Ideally the patient's nutritional status should be addressed preoperatively. Studies in the adult population have shown that wellmanaged nutritional support may decrease the incidence of SSIs when compared to patients that were signifcantly malnourished [\[16\]](#page-9-3). *Immunosuppressive medications* Other patients may be on immunosuppressive agents prior to the operating room, and many organizations do not recommend discontinuation prior to surgery in efforts to reduce the risk of SSI. Studies observing the discontinuation of methotrexate or other anti-tumor necrosis factor agents did not have a signifcant improvement on the risk of SSIs when compared with cohorts where the agents were maintained intraoperatively [[17](#page-9-4), [18\]](#page-9-5).

# **Intraoperative Concerns**

Most vital to the concern of the anesthesiologist in preventing SSIs is the decision to administer antibiotic therapy if the patient is not receiving any prior to arrival to the operating room. It is often based on a number of different factors, including nature of the procedure, institutional guidelines, known local antibiograms, and a comprehensive discussion with the surgeon. An understanding of the antimicrobial agent's pharmacokinetics is also important in order to determine proper timing of administration to maximize its effectiveness in preventing SSIs.

### **Choice of Antibiotic Agent**

Prophylactic antibiotics are indicated when the risk of morbidity associated with infection is greater than the risk of morbidity associated with prophylaxis. In general, antibiotic prophylaxis is indicated for surgical procedures associated with a relatively high rate of infection, including clean-contaminated and contaminated operative wounds (see Table [7.4](#page-3-0)), as well as certain clean procedures where there are severe consequences of infection, such as prosthetic implants and cardiac surgery.

Cefazolin, a frst-line antibiotic for methicillinsusceptible *Staphylococcus aureus* (MSSA) infections, is the most widely studied antibiotic for surgical antibiotic prophylaxis [[23\]](#page-9-6). The choice of antibiotic should be made at the institution-level tailored to the type of procedure performed and taking into consideration local antimicrobial resistance patterns, as well as accounting for patient factors including antibiotic allergies and history of MRSA infection and/or colonization. A multidisciplinary team including practitioners from surgical specialties, anesthesiology, infectious diseases, and pharmacy should be involved in developing an institution-specifc protocol to guide the choice of antibiotic agent by specific procedure (Table [7.5\)](#page-4-0).

# **Penicillin Allergies and Cephalosporin Administration**

In a retrospective cohort study of 8385 adult patients who underwent procedures, patients with reported penicillin allergy had a 50%

Surgical wound class	Definition	Example	SSI rate
I. Clean	Uninfected, no inflammation Respiratory, alimentary, genital, or uninfected urinary tracts are not entered	Thyroidectomy	$1.3 - 2.9\%$
II. Clean- contaminated	Respiratory, alimentary, genital, or urinary tracts entered under controlled conditions	Appendectomy without perforation	$2.4 - 7.7\%$
III. Contaminated	Open, fresh accidental wounds Major breaks in sterile technique Acute, nonpurulent inflammation	Hemorrhoidectomy	$6.4 - 15.2\%$
	IV. Dirty or infected Old traumatic wounds with retained devitalized tissue Existing clinical infection or perforated viscera	Chronic wound debridement	$7 - 40\%$

<span id="page-3-0"></span>**Table 7.4** Surgical wound classification [[19](#page-9-7)[–22\]](#page-9-8)

Surgical woundstate

increased odds of SSI, attributable to receipt of second-line perioperative antibiotics [[24\]](#page-9-9). This highlights the importance of thoughtful consideration when dealing with reported penicillin and/ or cephalosporin allergies.

Penicillin allergy is reported by parents of about 10% of children. However, the true frequency of immediate-type drug hypersensitivity is <0.1% [[25](#page-9-10)]. Cross-reactivity between penicillins and cephalosporins is dependent on the side chain of the beta-lactam drug and therefore differs based on the drugs. While previously overestimated, the proportion of patients with allergy to penicillin who will also react to a frst-generation cephalosporin such as cefazolin is  $<3\%$  [[26\]](#page-9-11).

<span id="page-4-0"></span>

#### **Surgical Antibiotic Prophylaxis Protocol (Appendix A)**

Please contact pharmacy (x4080) with dosing questions. For patients with a history of drug-resistant organisms please contact<br>infections Disease to determine need for broader antibiotic coverage. Duration of prophylaxis is nfections Dise<br>stated. **Neonate = Post-natal age < 45 weeks; Pediatric = Post-menstrual age > 45 weeks – 18 years; Adult =** ≥ **18 years Usual Dose Antibiotic** | Ampicilin | Cefazolin | Metronidazole | Cefoxitin | Ciprofloxacin | Clindamycin | Gentamicin | Vancomycin\*\* Adult 3gm 30mg/kg Radult, Pediatric 15mg/kg *Max 500 mg* Appendictis: 30 mg/kg *Max 1000 mg 30mg/kg max 2g; or 3g if body weight >120kg 40mg/kg Max 2g 10mg/kg Max 400mg 10mg/kg Max 600mg* 15mg/kg *Max 1000mg* Adult: 5mg/kg Pediatric: 2.5mg/kg Pediatric/ neonate 50mg/kg Neonate (<1200 g) 7.5mg/kg IV over 15 minutes IV push IV over 30 minutes IV push IV over 60 minutes IV over 15- 30 minutes IV over 15-30 minutes IV over 60 minutes **Administration CrCl > 60 CrCl 30-60 CrCl 10-29 CrCl<10, dialysis** Adult: 4 Adult: 12 Pediatric: 1 Neonate: 6 Neonate: N/A Adult: 2 Pediatric: 2 Neonate: 3 6 12 None 4 8 12 Adult: 12 Pediatric Neonate 8 12 None Adult: 6 Pediatric Neonate 8 6 6 Adult: 6 Pediatric Neonate None None None Adult: 8 Pediatric: 8 Neonate: 12 8 12 None 3 6 \*cardiac cases 4 8<br>\*cardiac cases 6 **None** \*cardiac cases 6 6 6 \*\* If an agent is infused over 1-2 hours, such as vancomycin, the administration should begin 120 minutes prior to surgical mcision\*\*<br>Patients on antimicrobials prior, follow the already scheduled regimen prior to the surg \*\* The only exception to this is vancomycin:<br>• If already on vancomycin AND using for surgical prophylaxis, utilize docmented trough or obtain random level prior to going to OR: If documented trough or random level is therapeutic (≥ 10 mcg/mL), vancomycin should be given on the same interval as patient is already on.<br>If documented trough or random level is sub-therapeutic (≥ 10 mcg/mL), give a do If said antimicrobial is the same as prophylaxis agent, another dose should be given within 1-59 minute time window prior to surgical incision. **Full antibiotic Dose must be administered 1-59 minutes before inc Recommended Re-dosing interval (hours) In addition to re-dosing by time interval, also re-dose all antibiotics after 30% blood volume loss, or > 1500mL if >50kg and normal renal function.** recommendations





#### **Table 7.5** (continued)

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In addition to providing inferior bactericidal activity against methicillin-susceptible *S. aureus*, non-beta-lactam antibiotics are also associated with more adverse drug events and greater cost [[24\]](#page-9-9).

Recommended practice for the anesthetist would be to fully explore the patient's history preoperatively regarding to the reported penicillin allergy and to determine the true nature of the reaction. Reported reactions that are low-risk include intolerance (GI upset, chills, headache, or fatigue), an unknown or remote (>10 years ago) reaction, family history of penicillin allergy, pruritis without rash, or patient denial of allergy (but presence in medical record). Low-risk patients could be managed with a direct oral amoxicillin challenge. Testing is not necessary if a penicillin class antibiotic has been tolerated since the index reaction. If history reveals a reaction suggestive of potential IgE-mediated pathophysiology (urticarial, laryngeal edema, bronchospasm, or anaphylaxis), a penicillin skin test may be recommended if feasible. In the case of high-risk reactions to penicillins such as Stevens-Johnson syndrome, organ injury, serum sickness, or hemolytic anemia, though rare, expert consultation regarding appropriate therapy is recommended, and cephalosporins should be avoided [[26,](#page-9-11) [27](#page-9-12)].

### **Timing of Antibiotic Administration**

The optimal time for administering surgical antibiotic prophylaxis is within 1–2 hours prior to incision. Clinical practice guidelines for antimicrobial prophylaxis in surgery published by the American Society of Health-System Pharmacists recommend that antibiotics be given within 1 hour of incision [[23\]](#page-9-6). Based on these recommendations, administration of antibiotics within 1 hour has been used as a quality metric by several best practices hospital surveys and regulatory agencies [\[28](#page-9-13)]. The WHO Global Guidelines for the Prevention of Surgical Site Infections recommend that antibiotics be given within 2 hours of incision and, for drugs with shorter half-lives, indicate a preference toward administering antibiotics within 1 hour of incision [[1\]](#page-8-0). These recommendations were made based on both pharmacokinetic and epidemiologic data.

From a pharmacokinetics standpoint, antibiotics should be given at a time such that the peak drug concentration occurs at the time of incision. Thus the ideal timing of antibiotic administration depends on the pharmacokinetic properties of the antibiotic being used (Table [7.6\)](#page-6-0). Cefazolin, the most commonly used and studied antibiotic for surgical antibiotic prophylaxis [\[23](#page-9-6)], achieves a peak serum concentration

	Time to peak,	Time to peak,		
Antibiotic	serum	tissue	Distribution	Half-life
Cefazolin	$10-20$ minutes	Up to $1$ hour	Widely into most body tissues and fluids	1.8 hours
Cefuroxime 20 minutes		35 minutes	Lower in bone and body tissue compared to serum	1.3 hours
Vancomycin 1 hour		Up to $3.5$ hours	Lower in fat, sternum and bone compared to tissue and serum	4–6 hours $(5-13$ hours)

<span id="page-6-0"></span>**Table 7.6** Common antibiotic prophylactic agent pharmacokinetics [[29](#page-9-17)]

10–20 minutes after administration and a peak tissue concentration close to 1 hour after administration [[23](#page-9-6)]. Whereas, vancomycin, which is often used when there is a known history of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization, reaches its peak serum concentration in 1 hour and peak concentration in the tissues in 3.5 hours.

Clinically, the frst landmark clinical study demonstrating association between timing of antibiotic and SSI risk categorized the timing of antibiotics administered into "early" (2–24 hours pre-incision), "preoperative" (0–2 hours pre-incision), "perioperative" (within 3 hours post-incision), and "postoperative" (>3 hours post-incision) [[30](#page-9-14)]. Controlling for multiple potential confounding factors, the investigators found a signifcantly lower rate of infections among the group that received antibiotics 0–2 hours pre-incision. However, one more recent study evaluating >32,000 patients from the Veterans Administration undergoing orthopedic, colorectal, vascular, and gynecologic procedures found in an unadjusted analysis signifcantly decreased SSI risk when antibiotics were given in the 60 minute window prior to incision. However, after adjusting for drug, procedure, and patient characteristics, timing of antibiotic was not independently associated with SSI risk, but drug and patient factors were [[31](#page-9-15)].

# **Dosing and Pharmacokinetic Considerations, Redosing During Prolonged Procedures**

### **Duration of Antibiotics**

A single dose of preoperative antibiotics should be administered, and for long procedures, repeat doses should be administered throughout the procedure. Additional antibiotics beyond the operative period have not been shown to be benefcial in further reducing the risk of surgical site infection [[1](#page-8-0)].

The recommended duration of antibiotics has gotten shorter over the years, as studies have shown that prolonged surgical antibiotic prophylaxis beyond the postoperative period has no additional beneft in reducing SSI after surgery when compared to a single dose or maintaining doses throughout the operative procedure [[32](#page-9-16)]. Data from 44 randomized controlled trials show that prolonging surgical antibiotic prophylaxis beyond the postoperative period has no additional beneft in reducing SSI after surgery when compared to providing a single preoperative dose and for long procedures, maintaining doses throughout the operative procedure  $[1]$  $[1]$ . Based on a systematic review and meta-analysis of these data, the WHO Global Guidelines for the Prevention of SSIs recommends against prolongation of surgical antibiotic prophylaxis after completion of operation for the purpose of preventing SSI. In their systematic review, this question was addressed by analyzing all pooled eligible randomized controlled trials for surgical procedures, as well as stratifying by type of surgical procedure. The WHO Global Guidelines recognize that there are some low-quality evidence (low to very low quality) [[1](#page-8-0)] that a prolonged operative postoperative antibiotics may be beneficial in cardiac, vascular, and orthognathic surgery when compared to single-dose prophylaxis, which is what had led previously published guidelines [[23](#page-9-6)] to extend the recommended duration to 24 hours or to 48 hours post-op for cardiac procedures [[32](#page-9-16)].

### **Other Anesthetic Considerations**

There are other important intraoperative elements that play a signifcant role in reducing the risk of morbidity from SSIs. However, while these factors have been studied in the adult population, they may have additional consideration when administering anesthesia for our pediatric patients.

It has been well-known that maintaining euglycemia is important and hyperglycemia increases the risk of SSIs within the adult population [[33\]](#page-9-18). Many studies have observed adverse events, including SSIs, at different blood glucose targets, but several meta-analyses show that an increased risk of morbidity is due to compromised immune function [[34\]](#page-9-19). Glycemic control may often be difficult, especially within our neonatal population, whose immature endocrinologic development may make it more diffcult to achieve true euglycemia.

Normothermia is also a primary concern with relation to SSI risk, as alterations in thermoregulation may directly impair neutrophil function or trigger vasoconstriction and can lead to tissue hypoxia [\[6](#page-8-8)]. It is therefore recommended to maintain normothermia as much as possible. Within our neonatal population, the normal thermoregulatory processes are hindered even more so under general anesthesia, and additional care should be taken.

Adequate oxygenation and avoidance of hypoxic states is well-documented in the prevention of SSIs, but this does provide a paradox with relation to our neonatal population. Maintaining a patient with a fraction of inspired oxygen above 80% (which has been recommended in the adult population) can prove to be a challenge within our neonatal population, as prolonged exposures of high concentrations of oxygen may predispose to additional complications such as retinopathy of prematurity. These factors must be taken into consideration when implementing an anesthetic for our pediatric and neonatal patients.

Ensuring adequate analgesia, both intraoperative and postoperative, has also been shown to have a signifcant impact on the risk of SSIs. The stress response that is mounted in response to pain has, in some studies, thought to have con-

tributed to impaired immunity. While no direct correlation has been seen to a reduction in the incidence of SSIs, multimodal analgesia, including the use of regional anesthesia, may be explored as an option in order to reduce the morbidity that may be encountered with relation to SSI risk [[6\]](#page-8-8).

Additional elements of infection control with regard to the anesthetist's workstation have also been studied, but current data show that the relation to SSIs remains inconclusive. Several tenets are still agreed upon: appropriate and frequent hand hygiene (including maintaining aseptic technique between procedures) can help reduce cross contamination to other work surfaces [\[35\]](#page-9-20).

#### **Surgical Considerations**

Other measures specifc to surgical technique may play a factor when considering the risk of SSIs. The use of antibiotic-coated sutures appears to be effective in reducing the incidence of infection regardless of type of suture, procedure, or wound classifcation. When triclosan-coated sutures have been compared to non-coated sutures, the incidence of SSIs has been shown to be significantly lower  $[36]$  $[36]$ . The use of wound protectors, particularly within gastrointestinal and biliary tract surgery, has been shown to reduce the incidence of SSIs within cleancontaminated, contaminated, and dirty procedures  $[6]$  $[6]$ .

New data are now showing that multiple procedures performed under a single anesthetic may also pose an increased risk for SSIs, citing that timing of appropriate prophylactic antibiotics and lack of standardized sequencing of cases may expose the patient to potentially increased morbidity [\[37](#page-9-22)].

### **Future Opportunities for Research and Quality Improvement**

Prevention of SSIs is a measure that is often targeted for quality improvement projects, as it is well-studied and often seen as preventable. There are a number of different opportunities in which many institutions are seeking to further study and reduce the incidence of SSIs, particularly within pediatric populations.

With many institutions implementing selfdriven protocols for surgical antibiotic prophylaxis based on local microbiology patterns, there can often be a variety of provider practices as seen throughout various regions. This may lead to overprescribing of antibiotics when they may not be indicated, ultimately contributing to antibiotic resistance. Further studies may help clarify true indications and standardize which procedures truly require surgical antibiotic prophylaxis.

As is very typical of most operating room environments, many now perform checklistdriven reminders to ensure that all staff within the operating room are aware of key details regarding the procedure, including safety concerns and equipment availability. With regard to preventing surgical site infections, an element of the checklist most commonly identifed is a prompt to discuss the use of antibiotics prior to incision, to ensure that the surgeon and anesthesiologist are both aware if an antibiotic would be required and to choose the most appropriate agent(s) if necessary [[38\]](#page-9-23).

Electronic health records offer a variety of ways to ensure antibiotics are optimally administered for maximal effectiveness. Implementing real-time alerts to administer antibiotics within a timely fashion signifcantly improves compliance when compared to prior interventions when paper records were the primary method of intraoperative documentation [[39\]](#page-9-24).

# **Conclusion**

SSIs can be a disastrous complication from any procedure. Perioperative measures can be undertaken to optimize the patient in order to reduce the risk of acquiring an SSI and prevent the number of different complications that can arise. While the majority of current data relates primarily to the adult patient population, further studies specific to pediatric patients are ongoing.

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