Antimicrobial prophylaxis for prevention of surgical site infection

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Surgical site infections (SSIs) are a common cause of health care-associated infection. That define surgical site infection as infection related to an operative procedure that occurs at or near the surgical incision within 30 or 90 days of the procedure.

Clinical criteria for defining SSI include one or more of the following :

- A purulent exudate draining from a surgical site
- A positive fluid culture obtained from a surgical site that was closed primarily
- A surgical site that is reopened in the setting of at least one clinical sign of infection (pain, swelling, erythema, warmth) and is culture positive or not cultured
- The surgeon makes the diagnosis of infection

Antimicrobial prophylaxis is justified for most clean-contaminated procedures. The use of antimicrobial agents for dirty procedures or established infection is not classified as prophylaxis; rather, it represents treatment for presumed infection

MICROBIOLOGY — The predominant organisms causing surgical site infections (SSIs) after clean procedures are skin flora, including streptococcal species, *Staphylococcus aureus*, and coagulase-negative staphylococci. In clean-contaminated procedures, the predominant organisms include gram-negative rods and enterococci in addition to skin flora. When the surgical procedure involves a viscus, the pathogens reflect the endogenous flora of the viscus or nearby mucosal surface; such infections are typically polymicrobial.

The causative pathogens associated with SSIs in the United States have changed over time. Between 1986 and 2003, the percentage of SSIs caused by gram-negative bacilli decreased from 56 to 33 percent. *S. aureus* was the most common pathogen, causing 22 percent of SSIs during this time period. Between 2006 and 2007, the proportion of SSIs caused by *S. aureus* increased to 30 percent, with methicillin-resistant *S. aureus* (MRSA) comprising nearly half of these isolates.

Exogenous sources of infection include contamination of the surgical site by organisms from the operating room environment or personnel. Anal, vaginal, or nasopharyngeal carriage of group A streptococci by operating room personnel has been implicated as a cause of several SSI outbreaks.

Carriage of gram-negative organisms on the hands has been shown to be greater among surgical personnel with artificial nails . Rarely, outbreaks or clusters of surgical site infections caused by unusual pathogens have been traced to contaminated dressings, bandages, irrigants, or disinfection solutions.

ANTIMICROBIAL PROPHYLAXIS

The goal of antimicrobial prophylaxis is to prevent surgical site infection (SSI) by reducing the burden of microorganisms at the surgical site during the operative procedure.

The efficacy of antibiotic prophylaxis for reducing SSI has been clearly established. Preoperative antibiotics are warranted if there is high risk of infection or if there is high risk of deleterious outcomes should infection develop at the surgical site (such as in the setting of immune compromise, cardiac surgery, and/or implantation of a foreign device)

Patients who receive prophylactic antibiotics within one to two hours before the initial incision have lower rates of SSI than patients who receive antibiotics sooner or later than this window.

Patients receiving antimicrobial prophylaxis are at relatively low risk for adverse drug events such as development of *Clostridioides difficile* and postoperative infection due to drug-resistant organisms

Patient risk factors — These risk factors include extremes of age, poor nutritional status, obesity, diabetes mellitus, tobacco use, coexistent infections, immune suppression, corticosteroid therapy, recent surgical procedure, length of preoperative hospitalization, and known colonization with resistant bacteria

Spinal procedures Hip fracture Internal fixation Total joint replacement Removal of orthopedic hardware used for treatment of lower extremity fractures[§]	*Staphylococcus aureus*, *Staphylococcus epidermidis*	Cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		OR vancomycin[Δ◊]	15 mg/kg IV (max 2 g)	N/A
		OR clindamycin	900 mg IV	6 hours

Cefazolin is a drug of choice for many procedures; it is the most widely studied antimicrobial agent with proven efficacy for antimicrobial prophylaxis. Cefazolin has a desirable duration of action, spectrum of activity against organisms commonly encountered in surgery and it has an excellent safety profile and low cost. It is active against streptococci, methicillin-susceptible staphylococci, and many gram-negative organisms.

Patients with history of penicillin intolerance manifesting as an uncomplicated skin rash may be treated with a cephalosporin; allergic cross-reactions between penicillin and cephalosporins are infrequent except in patients with severe IgE-mediated reactions to penicillin. Cephalosporins should be avoided in patients with a history of IgE-mediated reaction to penicillin.

Alternatives to cephalosporins include intravenous vancomycin (15 to 20 mg/kg) or clindamycin (600 to 900 mg); in some cases, an agent with activity against gram-negative bacteria must be added

Use of vancomycin may be acceptable in the following circumstances:

- A cluster of SSIs due to MRSA or methicillin-resistant coagulase-negative staphylococci has been detected at an institution.
- A patient is known to be colonized with MRSA.
- A patient is at high risk for MRSA colonization in the absence of surveillance data (eg, patients with recent hospitalization, nursing home residents, patients on hemodialysis, patients on immunosuppressive medications).

In such cases, a beta-lactam antibiotic (first- or second-generation cephalosporin) should be added for activity against gram-negative organisms; alternatives for patients allergic to cephalosporins include gentamicin, ciprofloxacin, levofloxacin, or aztreonam. Vancomycin appears to be less effective than cefazolin for preventing SSIs caused by MSSA.

Choice of dose:

Administration of 1 or 2 g of cefazolin may not be sufficient to produce serum and tissue concentrations exceeding the minimum inhibitory concentration (MIC) for most common pathogens.Therefore, we are in agreement with the 2013 guidelines developed by the American Society of Health-System Pharmacists that recommend administration of a minimum 2 g dose and administration of 3 g for patients ≥120 kg.

Timing

Antimicrobial therapy should be initiated within the 60 minutes prior to surgical incision to optimize adequate drug tissue levels at the time of initial incision. The half-life of the antibiotic should be considered; administration of vancomycin or a fluoroquinolone should begin 120 minutes before surgical incision because of the prolonged infusion times required for these drugs.

There was no difference in the risk of infection between patients who received antimicrobial prophylaxis within 30 minutes prior to incision and patients who received antimicrobial prophylaxis 31 to 60 minutes prior to incision.

Repeat dosing

To ensure adequate antimicrobial serum and tissue concentrations, repeat intraoperative dosing is warranted for procedures that exceed two half-lives of the drug and for procedures in which there is excessive blood loss (>1500 mL)

Duration

In general, repeat antimicrobial dosing following wound closure is not necessary and may cause patient harm due to an increase in the risk for development of antimicrobial resistance and *C. difficile* infection (CDI). In a systematic review of randomized trials, there was no difference in the rate of SSI with single dose compared with multiple-dose regimens given for less than or more than 24 hours

If prophylaxis is continued beyond the time of surgery, the duration should not exceed 24 hours . In one study including more than 11,000 surgical admissions, the risk of CDI was significantly higher among patients whose antibiotic prophylaxis was continued >24 hours postoperatively . In addition to increased CDI risk, prolonged postoperative antibiotics may increase the risk for acute kidney injury (AKI)

Spinal procedures

Antimicrobial prophylaxis is warranted for orthopedic spinal procedures with and without instrumentation, including fusion, laminectomy, and minimally invasive disk procedures . Cefazolin is the agent of
choice. Clindamycin and vancomycin are acceptable alternatives for patients with beta-lactam hypersensitivity; in the setting of risk for SSI due to gram-negative pathogens, an additional agent may be warranted (such as an aminoglycoside, aztreonam, or a fluoroquinolone).

SSIs after spinal procedures are associated with high morbidity; invasion of the epidural space is uncommon but serious when it occurs. Risk factors for SSI include extended duration of procedure (longer than two to five hours), excessive blood loss (>1 liter), multilevel fusions, foreign body placement, and combined anterior and posterior fusion

The SSI rate in patients receiving antimicrobial prophylaxis ranges from 2.8 to 9.7 percent. Lower rates of SSI have been observed with procedures at the cervical spine level or with an anterior surgical approach