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Antimicrobial prophylaxis for prevention of surgical site infection in adults

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INTRODUCTION — Surgical site infections (SSIs) are a common cause of healthcare-associated infection [1-3]. The United States Centers for Disease Control and Prevention (CDC) has developed criteria 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, depending on the type of procedure performed [2]. SSIs are often localized to the incision site but can also extend into deeper adjacent structures. (See 'Definitions' below.)

SSIs are the most common and the costliest healthcare-associated infections [4,5]. Among surgical patients, SSIs account for 38 percent of nosocomial infections. It is estimated that SSIs develop in 2 to 5 percent of the more than 30 million patients undergoing surgical procedures each year (ie, 1 in 24 patients who undergo inpatient surgery in the United States has a postoperative SSI) [6,7].

Antimicrobial prophylaxis for prevention of SSI will be reviewed here. Issues related to epidemiology and adjunctive measures for prevention of SSI are discussed separately. (See "Overview of control measures for prevention of surgical site infection in adults" and "Risk factors for impaired wound healing and wound complications", section on 'Infection'.)

DEFINITIONS — The United States Centers for Disease Control and Prevention (CDC) has developed criteria that define surgical site infection (SSI) as infection related to an operative procedure that occurs at or near the surgical incision (incisional or organ/space) within 30 days of the procedure or within 90 days if prosthetic material is implanted at surgery [8]. These criteria have become the national standard and are widely used by surveillance and surgical personnel [9-11].

Clinical criteria for defining SSI include one or more of the following [12,13]:

- 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

SSIs are classified as incisional or organ/space. Incisional SSIs are further divided into superficial (ie, those involving only the skin or subcutaneous tissue) or deep (ie, those involving deep soft tissues of an incision). An organ/space SSI may involve any part of the anatomy (other than the incision) that was opened or manipulated during the operative procedure (eg, meningitis following an elective neurologic procedure or mediastinitis following coronary artery bypass surgery). Organ/space SSIs account for one-third of all SSIs but are associated with more than 90 percent of deaths related to SSIs [14].

- **Clean wounds** are uninfected operative wounds in which no inflammation is encountered and the wound is closed primarily. By definition, a viscus (respiratory, alimentary, genital, or urinary tract) is not entered during a clean procedure.
- **Clean-contaminated wounds** are operative wounds in which a viscus is entered under controlled conditions and without unusual contamination.
- **Contaminated wounds** are open, fresh accidental wounds, operations with major breaks in sterile technique, or gross spillage from a viscus. Wounds in which acute, nonpurulent inflammation was encountered also were included in this category.
- **Dirty wounds** are old traumatic wounds with retained devitalized tissue, foreign bodies, or fecal contamination or wounds that involve existing clinical infection or perforated viscus.

Several studies have found a moderate correlation between the wound classification and the SSI rate. SSI rates according to wound class were [16-19]:

- Clean – 1.3 to 2.9
- Clean-contaminated – 2.4 to 7.7
- Contaminated – 6.4 to 15.2
- Dirty – 7.1 to 40.0

While widely used, this classification scheme may be a poor predictor of overall risk of SSI. Other factors, such as the operative technique, length of surgery, and health of the surgical patient, may be as important as wound classification in predicting infectious risks for SSI.

Available data suggest that the relative risk reduction of SSI from the use of antimicrobial prophylaxis is the same in clean and in higher-risk procedures [20]. Antimicrobial prophylaxis is justified for most clean-contaminated procedures. The use of antimicrobial agents for dirty procedures or established infection is classified as treatment of presumed infection, not prophylaxis [12].

MICROBIOLOGY — The predominant organisms causing surgical site infections (SSIs) after clean procedures are skin flora, including streptococcal species, *Staphylococcus aureus*, and coagulase-negative staphylococci [21]. 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 [22]. *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 [21]. Another study noted that, between 2003 and 2007, the proportion of infections caused by MRSA increased from 16 to 20 percent, and MRSA infections were associated were higher mortality rates, longer hospital stays, and higher costs [23].

The percentage of SSIs caused by antibiotic-resistant pathogens has increased (eg, MRSA, methicillin-resistant *Staphylococcus epidermidis* [MRSE], vancomycin-resistant enterococci [VRE]) [24]. (See

trend toward resistant organisms and *Candida* species probably is due to the widespread use of prophylactic and empiric antibiotics, increased severity of illness, and greater numbers of immunocompromised patients undergoing surgical procedures.

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 [26,27]. Carriage of gram-negative organisms on the hands has been shown to be greater among surgical personnel with artificial nails [28]. 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 [29]. Other interventions for prevention of SSI are discussed separately. (See "Overview of control measures for prevention of surgical site infection in adults".)

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). Antimicrobial therapy administered in the setting of contaminated wounds is not considered prophylactic; in such cases, a therapeutic course of antimicrobial therapy is warranted. 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 (table 1) [30,31]. (See 'Timing' below.)

Patients receiving antimicrobial prophylaxis are at relatively low risk for adverse drug events such as development of *C. difficile* and postoperative infection due to drug-resistant organisms [32].

Errors in selection or dose of prophylactic antimicrobials are common. Among 34,133 patients undergoing surgery in centers around the United States, an antimicrobial was administered within one hour before incision to only 56 percent of patients, and antimicrobials were discontinued within 24 hours of surgery in only 41 percent of patients [33]. Initiatives such as the Surgical Care Improvement Project have improved the rates of compliance since these earlier studies were performed [29,34].

Indications and goals — The relative risk reduction of SSI from the use of antimicrobial prophylaxis is the same in clean and in higher-risk procedures [20]. Antimicrobial prophylaxis is justified for most clean-contaminated procedures. The use of antimicrobial agents for dirty procedures or established infection is classified as treatment of presumed infection, not prophylaxis [12]. (See 'Wound classification' above.)

Ideally, antimicrobial prophylaxis should prevent SSI, prevent related morbidity and mortality, reduce duration and cost of healthcare, cause minimal adverse drug effects, and have minimal adverse effects for the microbial flora of the patient or the hospital [35]. To achieve these goals, an antimicrobial agent should be active against the pathogens most likely to contaminate the surgical site, be administered in an appropriate dose and at an appropriate time to ensure adequate serum and tissue concentrations during the period of potential contamination, and be administered for the shortest effective period to minimize adverse effects, emergence of resistance, and cost [12].

Antibiotic selection

General approach — In general, antimicrobial selection for SSI prophylaxis is based on cost, safety, pharmacokinetic profile, and antimicrobial activity. Comparative studies of antibiotics for surgical prophylaxis

- Cardiac surgery (table 2)
- Gastrointestinal surgery (table 3)
- Genitourinary surgery (table 4)
- Gynecologic and obstetric surgery (table 5)
- Head and neck surgery (table 6)
- Neurosurgery (table 7)
- Orthopedic surgery (table 8)
- Thoracic surgery (table 9)
- Vascular surgery (table 10)
- Percutaneous procedures (table 11)
- Breast surgery (table 12)

Cefazolin is a drug of choice for many procedures; it is the most widely studied antimicrobial agent with proven efficacy for antimicrobial prophylaxis [12,36]. It has a desirable duration of action, spectrum of activity against organisms commonly encountered in surgery, reasonable safety, and low cost. It is active against streptococci, methicillin-susceptible staphylococci, and some gram-negative organisms.

Second-generation cephalosporins (such as cefuroxime) have broader coverage against gram-negative organisms than cefazolin. Cefoxitin and cefotetan also have some anaerobic activity.

Patients with reported antibiotic allergy have been observed to have increased risk for SSI [37]. Clarification of such allergies as part of routine preoperative care may decrease SSI risk. (See "Antimicrobial stewardship in hospital settings".)

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. (See "Choice of antibiotics in penicillin-allergic hospitalized patients".)

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 as outlined in the discussions of individual types of surgery below. (See 'Types of surgery' below.)

S. aureus — There is no consensus regarding the benefit of routine preoperative screening for *S. aureus* colonization. Issues related to use of vancomycin and decolonization in the setting of methicillin-resistant *S. aureus* (MRSA) are discussed in the following sections.

Role of vancomycin — There is no role for routine use of vancomycin prophylaxis for any procedure [12,38]. A study of preoperative testing for nasal colonization with methicillin-resistant or methicillin-susceptible *S. aureus* (MSSA) concluded that preoperative prophylaxis with vancomycin was associated with an **increased** risk (relative risk 4.34; 95% CI 2.19-8.57) of postoperative SSI in patients who had negative nasal testing for MRSA but not in those who had positive nasal tests for MRSA [39].

- 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 [36].

Vancomycin appears to be less effective than cefazolin for preventing SSIs caused by MSSA [41,42]. For this reason, we favor use of vancomycin in combination with cefazolin for prevention of SSI due to MRSA and coagulase-negative staphylococci in the above scenarios.

When vancomycin is used, a single dose is almost always acceptable given its long half-life.

Role of decolonization — Issues related to decolonization are discussed separately. (See "Overview of control measures for prevention of surgical site infection in adults", section on 'S. aureus decolonization'.)

Resistant organisms — The approach to selecting antimicrobial surgical prophylaxis for patients known to be colonized or recently infected with drug-resistant pathogens must be individualized. Whether prophylaxis should include coverage for such pathogens depends on many factors including the pathogen, its antimicrobial susceptibility profile, the host, the planned procedure, and the proximity of the likely reservoir of the pathogen to the incision and operative sites [12]. Specific prophylaxis for a resistant gram-negative pathogen in a patient with past infection or colonization may not be necessary for a cutaneous procedure.

Antibiotic administration

Initial dosing

Choice of dose — Antibiotic prophylaxis should be administered in doses sufficient to achieve adequate serum and tissue drug levels for the interval during which the surgical site is open. For most adults, it is acceptable to dose antimicrobials based on standardized doses for safety, efficacy, and convenience. However, the serum and tissue concentrations of some drugs administered to obese patients may differ from those in nonobese patients for a number of reasons, including pharmacokinetic variability related to the lipophilicity of the administered drug [43].

There are limited data for determining the optimal approach to antimicrobial dosing for obese patients [44,45]. Two small pharmacokinetic studies noted that 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 [46,47]. Doubling the normal dose of cephalosporins may produce similar concentrations in obese patients to those achieved with standard doses in nonobese patients, with relatively low cost and favorable safety profile [45]. 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 [12].

Administration of gentamicin as a single 5 mg/kg dose has been observed to be more effective for SSI prevention than multiple doses of gentamicin given in a dose of 1.5 mg/kg every eight hours [48]. In obese patients who weigh 20 percent above their ideal body weight, the gentamicin dose should be calculated using the ideal body weight plus 40 percent of the difference between the actual and ideal weights [49].

Some studies suggest lower infection risk with initiation of antimicrobial administration within 30 minutes before surgical incision, although thus far data are insufficient to support this approach as a routine practice [31,50-52]. In one study including more than 4000 patients undergoing cardiac surgery, hysterectomy, or hip or knee arthroplasty, 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 (1.6 and 2.4 percent, respectively) [51]. In another study including more than 5500 patients undergoing general surgery, there was no difference in the rate of SSI between patients who received "early" antimicrobial prophylaxis (median 42 minutes prior to incision) or "late" (median 16 minutes prior to incision); the overall SSI rate was 5 percent [53].

There are retrospective data noting absence of significant correlation between SSI and timing of antimicrobial prophylaxis [54-59], although they are burdened by methodologic flaws including combined analysis of heterogenous patients groups, heterogeneous antibiotic regimens, and incomplete information regarding antibiotic redosing [60]. Therefore, we are in agreement with major society groups representing surgery, pharmacology, and infectious disease expertise regarding the timing guidelines described above.

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) [12]. Redosing may also be warranted in the setting of factors that shorten antimicrobial half-life, such as extensive burns. The dosing interval should be measured from the time of the preoperative dose (not from the beginning of the procedure). Redosing may not be warranted for patients in whom the antimicrobial half-life is prolonged, such as renal insufficiency. Intervals for redosing are summarized in the tables.

For clean and clean-contaminated procedures, readministration of antimicrobial prophylaxis following closure of the surgical incision is not warranted, even in the presence of a drain [1].

Duration — In general, repeat antimicrobial dosing following wound closure is not necessary and may increase the risk for development of antimicrobial resistance and *C. difficile* infection (CDI) [36,61-66]. 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 (combined odds ratio 1.04, 95% CI 0.86-1.25) [62].

For cases in which prophylaxis beyond the time of surgery is warranted, in general, the duration should be less than 24 hours [12,38]. 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 (odds ratio 3.74) [66]. Issues related to duration of antimicrobial prophylaxis following cardiothoracic procedures are discussed below. (See 'Cardiac surgery' below.)

TYPES OF SURGERY

Cardiac surgery — Cardiac procedures include coronary artery bypass graft (CABG), valve procedures, and device placement (table 2). Forms of surgical site infection (SSI) include mediastinitis and sternal wound infection. In patients undergoing CABG, the mean frequency of SSI ranges from 0.35 to 8.49 per 100 operations (including donor site SSI); for patients with chest incision, only the mean frequency ranges from 0.23 to 5.67 per 100 operations [67]. Most of these infections are superficial. Antimicrobial prophylaxis in cardiac procedures reduces the occurrence of SSI up to fivefold [68].

Risk factors for SSI after cardiac procedures include peripheral vascular disease, chronic obstructive pulmonary disease, heart failure, involvement of internal mammary artery, increased number of grafts, and *S.*

organisms are less commonly isolated; they are most frequently observed in the setting of saphenous vein harvesting and include Enterobacteriaceae, *Pseudomonas*, and *Acinetobacter* [73,74]. Data from the early years of cardiac surgery suggest that gram-negative pathogens were relatively common causes of postoperative SSI prior to the widespread use of first- and second-generation cephalosporins as preoperative surgical prophylaxis [75].

Cephalosporins (first and second generation) are the best studied antimicrobials for SSI prevention in cardiac procedures [68,76,77]. There is no evidence to support routine use of vancomycin for antimicrobial prophylaxis, even in institutions where the prevalence of methicillin-resistant *S. aureus* (MRSA) is high [12,78]. Prophylaxis with vancomycin is warranted for patients known to be colonized with MRSA [12]. For patients with beta-lactam allergy, vancomycin or clindamycin are acceptable alternatives for gram-positive coverage. An additional agent may be needed for gram-negative pathogens (such as an aminoglycoside, aztreonam, or a fluoroquinolone) in the setting of risk for SSI due these organisms.

Some favor decolonization of patients known to be colonized with *S. aureus* who undergo cardiac surgery [79]. The benefit of this practice has not been clearly established; the approach should be tailored to individual patient circumstances. (See "Overview of control measures for prevention of surgical site infection in adults", section on 'S. aureus decolonization'.)

The optimal duration of antimicrobial prophylaxis following cardiothoracic procedures is controversial; appropriate prophylaxis consists of the duration of the procedure and less than 24 hours thereafter [12]. Durations of up to 48 hours have been administered because the available data are insufficient to establish the optimal approach. Several reports have noted that prophylaxis for duration of one to four days failed to show any reduction in SSIs compared with single-dose prophylaxis or prophylaxis only during the operation [76,80,81]. There is no benefit to extending the duration of antimicrobial prophylaxis pending removal of indwelling lines, drains, and catheters [82].

The use of an investigational *S. aureus* vaccine (V710) among patients undergoing cardiothoracic surgery with median sternotomy did not reduce the rate of serious postoperative *S. aureus* infections in a large trial and was associated with increased mortality among patients who developed *S. aureus* infection [83].

Device placement — Routine antimicrobial prophylaxis is warranted for device implantation or generator replacement for permanent pacemakers, implantable cardioverter defibrillators, and cardiac resynchronization devices [12,84,85]. A large randomized trial noted a significantly lower rate of SSI among patients who received a single dose of cefazolin prior to device implantation (0.6 versus 3.3 percent) [86]. The rate of SSI after pacemaker placement is 0.44 per 100 procedures [67]. Risk factors for device-related infection include fever within 24 hours before implantation, temporary pacing before implantation, early intervention for hematoma or lead replacement, corticosteroid use for more than one month during the preceding year, presence of more than two leads, and development of pocket hematoma [86-88].

The optimal approach to antimicrobial prophylaxis in the setting of ventricular assist devices (VADs) is uncertain. Data are limited on infection rates and there are no published studies demonstrating the effectiveness of preoperative antimicrobial therapy. Most infections are bacterial (87 percent); fungal infections have also been observed (9 percent) [89]. Antimicrobial prophylaxis is appropriate in the setting of VAD replacement due to infection and should include coverage directed at the offending organism(s) [12].

Antimicrobial prophylaxis for placement of a new pacemaker or replacement of a pulse generator is discussed separately. (See "Infections involving cardiac implantable electronic devices: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

Thoracic surgery procedures include lobectomy, pneumonectomy, thoracoscopy, lung resection, and thoracotomy (table 9). Infections associated with thoracic surgery include SSI, pneumonia, and empyema. The rate of infection associated with thoracic surgery is 0.7 to 2.0 percent [67]. The rate of infection in the setting of video-assisted thoracoscopic surgery (VATS) is lower than the rate associated with open surgical procedures [91].

Organisms reported from SSIs among patients undergoing thoracic procedures include *S. aureus* and *S. epidermidis*. Organisms isolated in patients with postoperative pneumonia include gram-positive (*Streptococcus* and *Staphylococcus* species), gram-negative (*Haemophilus influenzae*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Acinetobacter* species, *Pseudomonas aeruginosa*, and *Moraxella catarrhalis*), and fungal (*Candida* species) pathogens [92].

The optimal antimicrobial agent is uncertain; reasonable agents include cefazolin and ampicillin-sulbactam [12,93,94]. Prophylaxis with vancomycin is warranted for patients known to be colonized with MRSA [12]. For patients with beta-lactam allergy, vancomycin or clindamycin are acceptable alternatives for gram-positive coverage. For circumstances in which there is risk for gram-negative infection based on local surveillance or surgical site contamination, an additional agent should be added to vancomycin or clindamycin (such as cefazolin or a fluoroquinolone).

Issues related to antimicrobial prophylaxis for tube thoracostomy are discussed separately. (See "Placement and management of thoracostomy tubes".)

Vascular surgery — Issues related to vascular surgery are summarized in the tables (table 10 and table 11) and discussed separately. (See "Carotid endarterectomy", section on 'Prophylactic antibiotics' and "Endovascular repair of abdominal aortic aneurysm", section on 'Antibiotic prophylaxis' and "Lower extremity amputation", section on 'Antibiotics'.)

Gastrointestinal surgery — Issues related to gastrointestinal surgery are summarized in the table (table 3) and discussed separately. (See "Control measures to prevent surgical site infection following gastrointestinal procedures in adults".)

Genitourinary surgery — Issues related to urologic procedures are summarized in the table (table 4) and discussed separately. (See "Prostate biopsy", section on 'Prophylactic antibiotics' and "Placement and management of indwelling ureteral stents", section on 'Antibiotics' and "Surgical treatment of erectile dysfunction", section on 'Antimicrobial prophylaxis'.)

Gynecologic and obstetric surgery — Issues related to gynecologic and obstetric surgery are summarized in the table (table 5) and discussed separately. (See "Overview of preoperative evaluation and preparation for gynecologic surgery" and "Cesarean delivery: Preoperative planning and patient preparation", section on 'Antibiotic prophylaxis'.)

Neurosurgery — A classification system for neurosurgery divides procedures into five categories: clean, clean with foreign body, clean-contaminated, contaminated, and dirty (table 7) [95]. Risk factors for postoperative infections following neurologic procedures include diabetes, procedure duration longer than two to four hours, placement of a foreign body, repeat surgery, emergency surgery, cerebrospinal fluid (CSF) leak, postoperative intracranial pressure monitoring or presence of a ventricular drain for more than five days postoperatively, and concurrent or prior infection of an incision or shunt [96-101].

Antimicrobial prophylaxis is warranted for patients undergoing clean craniotomy, CSF shunt procedures, or intrathecal pump placement [12,102-104]. In one series including more than 4500 patients, the infection rate

among patients who required repeat surgery or whose operative time exceeded four hours.

Neurosurgical SSIs are usually due to *S. aureus* or coagulase-negative staphylococci. Other organisms include *C. acnes* and gram-negative bacteria [99]. A single dose of cefazolin is appropriate for patients undergoing clean craniotomy and spinal procedures, CSF shunt procedures, or intrathecal pump placement. Reasonable alternatives for patients with beta-lactam allergy include clindamycin or vancomycin [12].

Orthopedic surgery — Antimicrobial prophylaxis is warranted for spinal procedures, repair of hip and other closed fractures, implantation of internal fixation device (screws, nails, plates, and pins), and total joint replacement (table 8). If the potential for implantation of foreign materials is unknown, the procedure should be treated as with implantation [12]. Antimicrobial prophylaxis is not warranted for clean orthopedic procedures; these include arthroscopy and other procedures involving the hand, knee, or foot with no implantation of foreign materials [12,105,106].

The role of antimicrobial prophylaxis prior to removal of orthopedic hardware used for treatment of lower extremity factures is controversial. We favor administration of preoperative antimicrobial prophylaxis in such cases, because relatively high SSI rates have been described for this procedure [107,108], even though it is considered a "clean" surgical procedure according to United States Centers for Disease Control and Prevention definitions (for which preoperative antibiotic prophylaxis is not routinely recommended) [1]. This remains our approach in spite of results from a randomized trial including more than 470 patients who underwent removal of orthopedic implants treated with preoperative cefazolin (single dose of 1 g intravenously) or placebo, in which no difference in the overall SSI rate was observed between the groups (13 versus 15 percent); there was a nonsignificant difference in the rate of deep infection (2.9 versus 0.4 percent), but the sample size was underpowered to detect a difference [109].

The risk of SSI per 100 procedures has been reported as follows: 0.7 to 4.1 for spinal fusion, 0.7 to 2.3 for laminectomy, 0.7 to 2.4 for hip prosthesis, and 0.6 to 1.6 for knee prosthesis [67].

The most common pathogens are *S. aureus*, gram-negative bacilli, coagulase-negative staphylococci, and beta-hemolytic streptococci [110]. Bacterial biofilm formation on inert surfaces of orthopedic devices is a contributing factor for SSI, particularly in the setting of infection due to *S. aureus* and *S. epidermidis*. Biofilm makes antimicrobial penetration difficult and confers antimicrobial resistance [111].

Some favor decolonization of patients known to be colonized with *S. aureus* who undergo orthopedic surgery [79]. The benefit of this practice has not been clearly established; the approach should be tailored to individual patient circumstances. (See "Overview of control measures for prevention of surgical site infection in adults", section on 'S. aureus decolonization'.)

Issues related to spinal procedures and hip fracture repair are discussed below; issues related to open fractures and joint replacement are discussed separately. (See "Treatment and prevention of osteomyelitis following trauma in adults" and "Prevention of prosthetic joint and other types of orthopedic hardware infection", section on 'During hardware replacement'.)

Spinal procedures — Antimicrobial prophylaxis is warranted for orthopedic spinal procedures with and without instrumentation, including fusion, laminectomy, and minimally invasive disk procedures (table 8) [12]. 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 of particular concern. Risk factors for SSI include extended duration of procedure (longer than two to five hours),

Hip fracture repair — Antimicrobial prophylaxis is warranted for hip fracture repair and other orthopedic procedures involving internal fixation (table 8) [12]. 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).

The efficacy of antimicrobial prophylaxis in hip fracture has been illustrated in two meta-analyses [114,115]. One meta-analysis of 15 hip fracture procedure trials (most procedures involved closed, proximal femoral, or trochanteric fractures with internal fixation) demonstrated that any dose and duration of prophylaxis are superior to no prophylaxis with respect to preventing SSIs [114]. The rate of SSI in the control and treatment group was 10.4 and 5.4 percent, respectively.

Head and neck surgery — Elective procedures of the head and neck are predominantly clean or clean-contaminated (table 6) [116]. Clean procedures include thyroidectomy and lymph node excisions; the frequency of SSIs for clean procedures without antimicrobial prophylaxis is less than 1 percent. Clean-contaminated procedures include all procedures that involve an incision through the oral pharyngeal mucosa; these range from parotidectomy, submandibular gland excision, tonsillectomy, adenoidectomy, and rhinoplasty to complex tumor debulking and mandibular fracture repair requiring reconstruction [12]. The infection rates among patients undergoing complex head and neck surgery in the absence of antimicrobial prophylaxis are high (24 to 78 percent); rates are markedly lower with prophylaxis (5 to 38 percent) [117,118].

Risk factors for SSI include age, nutritional status, diabetes, anemia, peripheral vascular disease, preoperative radiation and/or chemotherapy, and use of tobacco, alcohol, or other illicit drugs (particularly in the setting of mandibular fracture) [118-121]. Procedures associated with increased risk for infection include radical or bilateral neck dissection and reconstruction with myocutaneous flaps or microvascular free flaps [118,120].

Most infections following clean-contaminated head and neck procedures are caused by the normal flora of the mouth and the oropharynx; these include aerobic and anaerobic bacteria, and therefore postoperative SSIs are usually polymicrobial [122-124]. The predominant oropharyngeal organisms include various streptococci (aerobic and anaerobic species), other oral anaerobes including *Bacteroides* species (but not *B. fragilis*), *Peptostreptococcus* species, *Prevotella* species, *Fusobacterium* species, *Veillonella* species, Enterobacteriaceae, and staphylococci. Nasal species include *Staphylococcus* and *Streptococcus* species.

Antimicrobial prophylaxis is not warranted for patients undergoing clean procedures of the head and neck [12,117]. A preoperative dose of cefazolin or cefuroxime (or clindamycin in the setting of beta-lactam allergy) is reasonable in the setting of prosthetic material placement, although data on the efficacy of this practice are limited.

Antimicrobial prophylaxis is warranted for most clean-contaminated procedures [118,125], although randomized trials have shown no benefit for routine prophylaxis in the setting of adenoidectomy, tonsillectomy, or septoplasty [126,127]. Reasonable regimens for patients undergoing other clean-contaminated procedures include a cephalosporin (cefazolin or cefuroxime) plus metronidazole, or ampicillin-sulbactam [122]. Clindamycin is a reasonable alternative for patients with beta-lactam allergy; the addition of an aminoglycoside may be appropriate when there is risk of site contamination with gram-negative organisms.

Breast surgery — Antimicrobial prophylaxis is not warranted for clean breast procedures in the absence of additional risk factors for infection. In such cases, prophylaxis does not significantly reduce the risk of

patients with other risk factors for infection [131]. 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).

The most common organisms are *S. aureus*, other staphylococci, and streptococci. A higher rate of infection due to gram-negative organisms occurs in the setting of procedures involving macerated, moist environments (such as under the axilla of an obese individual), and among patients with diabetes.

One review of seven randomized trials including nearly 2000 patients undergoing breast cancer procedures without reconstruction noted that prophylactic antibiotics significantly reduced the incidence of SSI (relative risk 0.66; 95% CI 0.48-0.89) [132].

Issues related to prophylactic antibiotics for patients undergoing breast reconstruction with placement of prosthetic material are discussed separately. (See "Breast implant infections".)

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Prevention of surgical site infections in adults".)

SUMMARY AND RECOMMENDATIONS

- Surgical site infection (SSI) is an infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure (or within 90 days if an implant is left in place). SSIs are often localized to the incision site but can also extend into deeper adjacent structures. Incisional SSIs may be superficial (ie, those involving only the skin or subcutaneous tissue) or deep (ie, those involving deep soft tissues of an incision). Organ/space SSIs may involve any part of the anatomy (other than the incision) that was opened or manipulated during the operative procedure. (See 'Definitions' above.)

- Wounds may be classified as clean, clean-contaminated, contaminated, or dirty. Clean wounds are uninfected operative wounds in which no viscus is entered, no purulence is encountered, and the wound is closed primarily. Clean-contaminated wounds are operative wounds in which a viscus is entered under controlled conditions and without unusual contamination. Contaminated wounds include open accidental wounds, wounds in which purulence was encountered during the procedure, wounds from operations with major breaks in sterile technique, or wounds from operations with gross viscus spillage. Dirty wounds are old traumatic wounds with retained devitalized tissue, foreign bodies, or fecal contamination or wounds that involve existing clinical infection or perforated viscus. (See 'Wound classification' above.)

- The predominant organisms causing SSIs after clean procedures are skin flora, including streptococcal species, *S. 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. (See 'Microbiology' above.)

- The goal of antimicrobial prophylaxis is to prevent SSI by reducing the burden of microorganisms at the surgical site during the operative procedure. 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. (See 'Antimicrobial prophylaxis' above.)

- In general, antimicrobial selection for SSI prophylaxis is based on cost, safety, pharmacokinetic profile, and antimicrobial activity. There is little evidence to suggest that broad-spectrum antimicrobial agents result in lower rates of postoperative SSI compared with narrower spectrum antimicrobial agents. The clinical approach is summarized in the tables:

- Genitourinary surgery (table 4)
- Gynecologic and obstetric surgery (table 5)
- Head and neck surgery (table 6)
- Neurosurgery (table 7)
- Orthopedic surgery (table 8)
- Thoracic surgery (table 9)
- Vascular surgery (table 10)
- Percutaneous procedures (table 11)
- Breast surgery (table 12)

- Cefazolin is a drug of choice for many procedures; it has a desirable duration of action, spectrum of activity against organisms commonly encountered in surgery, reasonable safety, and low cost. Some pharmacokinetic studies have noted that 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. In addition, doubling the normal dose of cephalosporins may produce similar concentrations in obese patients to those achieved with standard doses in nonobese patients, with relatively low cost and favorable safety profile. Therefore, we favor administration of cefazolin 2 g for patients <120 kg and cefazolin 3 g for patients ≥120 kg (**Grade 2B**). (See 'Choice of dose' above.)

- Antimicrobial therapy should be administered within 60 minutes before surgical incision to ensure adequate drug tissue levels at the time of initial incision. If the preferred agent is vancomycin or a fluoroquinolone, administration should begin 120 minutes before surgical incision because of the prolonged infusion times required for these drugs. (See 'Timing' above.)

- To ensure adequate antimicrobial serum and tissue concentrations, repeat intraoperative dosing is warranted for procedures that exceed two half-lives of the drug or for procedures in which there is excessive blood loss (>1500 mL). Redosing may also be warranted in the setting of factors that shorten antimicrobial half-life, such as extensive burns. The dosing interval should be measured from the time of the preoperative dose (not from the beginning of the procedure). Redosing may not be warranted for patients in whom the antimicrobial half-life is prolonged, such as renal insufficiency. (See 'Repeat dosing' above.)

- In general, repeat antimicrobial dosing following wound closure is not necessary and may increase antimicrobial resistance. For cases in which prophylaxis beyond the period of surgery is warranted, in general, the duration should be less than 24 hours. (See 'Duration' above.)

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Topic 4043 Version 67.0

Time of administration*	Percent with SSI	Odds ratio¶	95 percent CI
Early	3.8	4.3	1.8-10.4
Preoperative	0.6	1	-
Perioperative	1.4	2.1	0.6-7.4
Postoperative	3.3	5.8	2.4-13.8

SSI: surgical site infection.
* "Early" denotes 2 to 24 hours before incision, "preoperative" 0 to 2 hours before incision, "perioperative" within 3 hours after incision, and "postoperative" more than 3 hours after incision.
¶ Odds ratio determined by logistic-regression analysis.

Adapted from: Classen DC, Evans RS, Pestotnik SL, et al, N Engl J Med 1992; 326:281.

Graphic 79097 Version 7.0

operation	pathogens	antimicrobials	dose	interval
Cardiac procedures: coronary artery bypass, cardiac device insertion procedures (eg, pacemaker implantation), placement of ventricular assist devices	*Staphylococcus aureus*, *S. epidermidis*	Cefazolin	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		OR cefuroxime	1.5 g IV	4 hours[Δ]
		OR vancomycin[◇]	15 mg/kg IV (max 2 g)	N/A
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ Some experts recommend an additional dose when patients are removed from bypass during open-heart surgery.

◇ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with MRSA or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (gentamicin 5 mg/kg IV), aztreonam (2 g IV), or a fluoroquinolone (ciprofloxacin 400 mg IV or levofloxacin 500 mg IV).

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 76499 Version 14.0

Operation	Likely pathogens	Antimicrobials	Dose	Interval
Gastroduodenal surgery				
Procedures involving entry into lumen of gastrointestinal tract	Enteric gram-negative bacilli, gram-positive cocci	Cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
Procedures not involving entry into lumen of gastrointestinal tract (selective vagotomy, antireflux)	Enteric gram-negative bacilli, gram-positive cocci	High risk[◇] only: cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
Biliary tract surgery (including pancreatic procedures)				
Open procedure or laparoscopic procedure (high risk)[§]	Enteric gram-negative bacilli, enterococci, clostridia	Cefazolin[Δ¥]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
		OR cefotetan	2 g IV	Six hours
		OR cefoxitin	2 g IV	Two hours
		OR ampicillin-sulbactam	3 g IV	Two hours
Laparoscopic procedure (low risk)	N/A	None	None	None
Appendectomy[‡]				
	Enteric gram-negative bacilli, anaerobes, enterococci	Cefoxitin[Δ]	2 g IV	Two hours
		OR cefotetan[Δ]	2 g IV	Six hours
		OR cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
		PLUS metronidazole	500 mg IV	N/A
Small intestine surgery				
Nonobstructed	Enteric gram-negative bacilli, gram-positive cocci	Cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
Obstructed	Enteric gram-negative bacilli, anaerobes, enterococci	Cefoxitin[Δ]	2 g IV	Two hours
		OR cefotetan[Δ]	2 g IV	Six hours
		OR cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
		PLUS metronidazole	500 mg IV	N/A
Hernia repair				
	Aerobic gram-	Cefazolin[Δ]	<120 kg: 2 g IV	Four hours

	negative bacilli, anaerobes, enterococci	Cefoxitin[Δ]	2 g IV	Two hours
		OR cefotetan[Δ]	2 g IV	Six hours
		OR cefazolin[Δ]	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
		PLUS metronidazole	500 mg IV	N/A
		OR ampicillin-sulbactam[Δ,**]	3 g IV (based on combination)	Two hours
		Oral (used in conjunction with mechanical bowel preparation):		
		Neomycin PLUS erythromycin base or metronidazole	¶¶	¶¶

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin or a fluoroquinolone is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug.

Δ For patients allergic to penicillins and cephalosporins, clindamycin (900 mg) or vancomycin (15 mg/kg IV; not to exceed 2 g) with either gentamicin (5 mg/kg IV), ciprofloxacin (400 mg IV), levofloxacin (500 mg IV), or aztreonam (2 g IV) is a reasonable alternative. Metronidazole (500 mg IV) plus an aminoglycoside or fluoroquinolone are also acceptable alternative regimens, although metronidazole plus aztreonam should not be used, since this regimen does not have aerobic gram-positive activity.

◇ Morbid obesity, gastrointestinal (GI) obstruction, decreased gastric acidity or GI motility, gastric bleeding, malignancy or perforation, or immunosuppression.

§ Factors that indicate high risk may include age >70 years, pregnancy, acute cholecystitis, nonfunctioning gall bladder, obstructive jaundice, common bile duct stones, immunosuppression.

¥ Cefotetan, cefoxitin, and ampicillin-sulbactam are reasonable alternatives.

‡ For a ruptured viscus, therapy is often continued for approximately five days.

† Use of ertapenem or other carbapenems not recommended due to concerns of resistance.

** Due to increasing resistance of *Escherichia coli* to fluoroquinolones and ampicillin-sulbactam, local sensitivity profiles should be reviewed prior to use.

¶¶ In addition to mechanical bowel preparation, the following oral antibiotic regimen is administered. 1 g of neomycin plus 1 g of erythromycin base at 1 PM, 2 PM, and 11 PM, or 2 g of neomycin plus 2 g of metronidazole at 7 PM and 11 PM the day before an 8 AM operation. Issues related to mechanical bowel preparation are discussed further separately. Refer to UpToDate topic on overview of colon resection.

Data from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infec (Larchmt) 2013; 14:73.*

Graphic 65369 Version 31.0

operation	pathogens	antimicrobials	dose	interval
Cystoscopy alone	Enteric gram-negative bacilli, enterococci	High-risk[Δ] only: ciprofloxacin[◇]	500 mg orally or 400 mg IV	N/A
		OR trimethoprim-sulfamethoxazole	One 160/800 mg (double strength, DS) tablet orally	N/A
Cystoscopy with manipulation or upper tract instrumentation[§]	Enteric gram-negative bacilli, enterococci	Ciprofloxacin[◇]	500 mg orally or 400 mg IV	N/A
		OR trimethoprim-sulfamethoxazole	One 160/800 mg (double strength, DS) tablet orally	N/A
Open or laparoscopic surgery[¥]	Enteric gram-negative bacilli, enterococci	Cefazolin[‡]	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If a fluoroquinolone is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ Urine culture positive or unavailable, preoperative catheter, transrectal prostatic biopsy, or placement of prosthetic material.

◇ Due to increasing resistance of *Escherichia coli* to fluoroquinolones and ampicillin-sulbactam, local sensitivity profiles should be reviewed prior to use.

§ Shock wave lithotripsy, ureteroscopy.

¥ Including percutaneous renal surgery, procedures with entry into the urinary tract, and those involving implantation of a prosthesis. If manipulation of bowel is involved, prophylaxis is given according to colorectal guidelines.

‡ For patients allergic to penicillins and cephalosporins, clindamycin (900 mg IV) or vancomycin (15 mg/kg IV not to exceed 2 g) with either gentamicin (5 mg/kg IV), ciprofloxacin (400 mg IV), levofloxacin (500 mg IV), or aztreonam (2 g IV) is a reasonable alternative.

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87199 Version 12.0

	regimen		**regimens**	
Hysterectomy (abdominal, vaginal, laparoscopic, or robotic) Urogynecology procedures including those involving mesh	Cefazolin, cefoxitin or cefotetan	Cefazolin: <120 kg: 2 g IV ≥120 kg: 3 g IV Cefoxitin or cefotetan: 2 g IV	**Regimen:**	
			Ampicillin-sulbactam	3 g IV
			Regimen:	
			Clindamycin **OR**	900 mg IV ◇
			Vancomycin ¶	15 mg/kg IV (not to exceed 2 g per dose)
			PLUS one of the following:	
			Gentamicin **OR**	5 mg/kg IV (if overweight or obese, based on dosing weight) §
			Aztreonam **OR**	2 g IV
			Fluoroquinolone ¶ ¥	
			Regimen:	
			Metronidazole	500 mg IV
			PLUS one of the following:	
			Gentamicin **OR**	5 mg/kg IV (if overweight or obese, based on dosing weight) §
			Fluoroquinolone ¶ ¥	
Cesarean section	Cefazolin	<120 kg: 2 g IV ≥120 kg: 3 g IV	**Regimen:**	
			Ampicillin-sulbactam	3 g IV
			Regimen:	
			Clindamycin **OR**	900 mg IV ◇
			Vancomycin ¶	15 mg/kg IV (not to exceed 2 g per dose)
			PLUS one of the following:	
			Gentamicin **OR**	5 mg/kg IV (if overweight or obese, based on dosing weight) §
			Aztreonam	2 g IV
			Regimen:	
			Metronidazole **PLUS**	500 mg IV
			Gentamicin	5 mg/kg IV (if overweight or

		procedure and 200 mg orally after procedure		five days
			Azithromycin	1 g orally one hour before procedure
Hysterosalpingogram or chromotubation	Doxycycline‡	100 mg orally twice daily for five days		
Laparoscopy (diagnostic, tubal sterilization, operative except for hysterectomy) Other transcervical procedures: Hysteroscopy (diagnostic or operative, including hysteroscopic sterilization) Intrauterine device insertion Endometrial biopsy	None			

IV: intravenous; IDSA: Infectious Diseases Society of America; ASHP: American Society of Health-System Pharmacists; ACOG: American College of Obstetricians and Gynecologists.

* Common pathogens: Enteric gram-negative bacilli, anaerobes, group B *Streptococcus*, enterococci.

¶ Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin or a fluoroquinolone is used, the infusion should be given over 60 to 90 minutes and started within 60 to 120 minutes before the initial incision.

Δ An alternative regimen should be used in women with history of immediate hypersensitivity to beta-lactam agents. Due to increasing resistance of *Escherichia coli* to ampicillin-sulbactam and fluoroquinolones, local sensitivity profiles should be reviewed prior to use.

◇ When clindamycin prophylaxis is warranted, UpToDate authors prefer a single dose of 900 mg based upon pharmacokinetic considerations according to 2013 IDSA/ASHP surgical antibiotic prophylaxis guidelines.[1] However, a 600 mg dose consistent with ACOG guidance may be sufficient.[2,3]

§ Gentamicin use for surgical antibiotic prophylaxis should be limited to a single dose given preoperatively. Based on evidence from colorectal procedures, a single dose of approximately 5 mg/kg gentamicin appears more effective for the prevention of surgical site infection than multiple doses of gentamicin 1.5 mg/kg every eight hours.[4] However, a lower dose of 1.5 mg/kg, consistent with ACOG guidance, may be adequate.[2,3] For overweight and obese patients (ie, actual weight is >125% of ideal body weight), a dosing weight should be used. A calculator to determine ideal body weight and dosing weight is available in UpToDate.

¥ Ciprofloxacin 400 mg IV **OR** levofloxacin 500 mg IV **OR** moxifloxacin 400 mg IV. Fluoroquinolones are contraindicated in pregnancy and in women who are breastfeeding.

‡ Prophylaxis is warranted for patients with history of pelvic inflammatory disease or if the procedure demonstrates dilated fallopian tubes. No prophylaxis is indicated for patients without dilated tubes.

References:

1. *Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013; 70:195.*

4. Zelenitsky SA, Silverman RE, Duckworth H, Harding GK. A prospective, randomized, double-blind study of single high dose versus multiple standard dose gentamicin both in combination with metronidazole for colorectal surgical prophylaxis. J Hosp Infect 2000; 46:135.

Adapted from: Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.

Graphic 87200 Version 29.0

operation	pathogens	antimicrobials	dose	interval
Clean	–	None	–	–
Clean with placement of prosthesis (excludes tympanostomy tube placement)	*Staphylococcus aureus*, *S. epidermidis*, streptococci	Cefazolin*	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		OR cefuroxime	1.5 g IV	4 hours
		OR vancomycin[Δ]	15 mg/kg (max 2 g)	N/A
		OR clindamycin	600 to 900 mg IV	N/A
Clean-contaminated	Anaerobes, enteric gram-negative bacilli, *S. aureus*	Cefazolin	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		PLUS metronidazole	500 mg IV	N/A
		OR cefuroxime	1.5 g IV	4 hours
		PLUS metronidazole	500 mg IV	N/A
		OR ampicillin-sulbactam[◇]	3 g IV	2 hours
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) or *S. epidermidis* are frequent causes of postoperative wound infection, in patients previously colonized with MRSA, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (such as gentamicin 5 mg/kg IV), aztreonam (2 g IV), or a fluoroquinolone (such as levofloxacin 500 mg IV or ciprofloxacin 400 mg IV).

◇ Some experts recommend an additional dose when patients are removed from bypass during open-heart surgery.

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87201 Version 11.0

operation	pathogens	antimicrobials	dose	interval
Elective craniotomy Cerebrospinal fluid shunting procedures Implantation of intrathecal pumps	*Staphylococcus aureus*, *S. epidermidis*	Cefazolin	<120 kg: 2 g ≥120 kg: 3 g	4 hours
		OR vancomycin[Δ]	15 mg/kg IV (max 2 g)	12 hours
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.
* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.
¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug (cefazolin every four hours, clindamycin every six hours, vancomycin every 12 hours) for the duration of the procedure in patients with normal renal function.
Δ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with MRSA, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (such as gentamicin 5 mg/kg IV), aztreonam (2 g IV), or a fluoroquinolone (such as ciprofloxacin 400 mg IV or levofloxacin 500 mg IV).

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87202 Version 10.0

operation	pathogens	antimicrobials	dose	interval
Clean operation involving hand, knee, or foot with no implantation of foreign material	–	None	–	–
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$^{\Delta}$	<120 kg: 2 g IV ≥120 kg: 3 g IV	Four hours
		OR vancomycin$^{\Delta\diamond}$	15 mg/kg IV (max 2 g)	N/A
		OR clindamycin	900 mg IV	Six hours

IV: intravenous; N/A: not applicable; MRSA: methicillin-resistant *Staphylococcus aureus*.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ If a tourniquet is to be used in the procedure, the entire dose of antibiotic must be infused prior to its inflation.

◇ Use of vancomycin is appropriate in hospitals in which MRSA and *Staphylococcus epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with MRSA, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. Some experts would give 15 mg/kg of vancomycin to patients weighing more than 75 kg, up to a maximum of 1.5 g, with a slower infusion rate (90 minutes for 1.5 g).

§ The role of antimicrobial prophylaxis prior to removal of orthopedic hardware used for treatment of lower extremity factures is controversial. According to the guidelines issued by the United States Centers for Disease Control and Prevention, this is considered a "clean" surgical procedure (ie, without skin contamination or local infection), for which preoperative antibiotic prophylaxis is not routinely recommended. However, relatively high rates of surgical site infection have been reported for this procedure; therefore, we favor administration of preoperative antimicrobial prophylaxis. Refer to the text for further discussion.

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87204 Version 18.0

operation	pathogens	antimicrobials	dose	interval
Thoracic (noncardiac) procedures: lobecotomy, pneumonectomy, lung resection, thoractomy	*Staphylococcus aureus*, *S. epidermidis*, streptococci, enteric gram-negative bacilli	Cefazolin	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		OR ampicillin-sulbactam Δ	3 g IV	2 hours
		OR vancomycin ◇	15 mg/kg IV (max 2 g)	N/A
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ Due to increasing resistance of *Escherichia coli* to fluoroquinolones and ampicillin-sulbactam, local sensitivity profiles should be reviewed prior to use.

◇ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with MRSA, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (gentamicin 5 mg/kg IV), aztreonam (2 g IV), or a fluoroquinolone (ciprofloxacin 400 mg IV or levofloxacin 500 mg IV).

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87205 Version 11.0

operation	pathogens	antimicrobials	dose	interval
Arterial surgery involving a prosthesis, the abdominal aorta, or a groin incision	*Staphylococcus aureus*, *S. epidermidis*, enteric gram-negative bacilli	Cefazolin	<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
Lower extremity amputation for ischemia	*S. aureus*, *S. epidermidis*, enteric gram-negative bacilli, clostridia	Cefazolin	<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

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug for the duration of the procedure in patients with normal renal function.

Δ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with methicillin-resistant *S. aureus*, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (such as gentamicin 5 mg/kg IV), aztreonam (2 g), or a fluoroquinolone (such as ciprofloxacin 400 mg IV or levofloxacin 500 mg IV).

Adapted from:

1. *Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.*
2. *Bratzler DW, et al. Clinical guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.*

Graphic 87206 Version 10.0

Procedure	Organisms encountered	prophylaxis recommended	choice antibiotic	antibiotic choices	Comments
Angiography, angioplasty, thrombolysis, arterial closure device placement, stent placement	*Staphylococcus aureus*, *S. epidermidis*	No	None	Cefazolin (2 g IV if <120 kg, 3 g IV if ≥120 kg IV) (if high-risk stent infection). If penicillin-allergic, can use vancomycin (15 mg/kg IV; max 2 g) or clindamycin (900 mg IV).	Procedure classification: clean
Endograft placement	*S. aureus*, *S. epidermidis*	Yes	Cefazolin (2 g IV if <120 kg, 3 g IV if ≥120 kg IV)	If penicillin-allergic, can use vancomycin or clindamycin	Procedure classification: clean
Superficial venous insufficiency treatment	*S. aureus*, *S. epidermidis*	No	None	None	Procedure classification: clean
IVC filter placement	*S. aureus*, *S. epidermidis*	No	None	None	Procedure classification: clean
Tunneled central venous access	*S. aureus*, *S. epidermidis*	No consensus	None	Cefazolin (2 g IV if <120 kg, 3 g IV if ≥120 kg IV) (eg, immunocompromised patients before chemotherapy; history of catheter infection). If penicillin-allergic, can use vancomycin (15 mg/kg IV; max 2 g) or clindamycin (900 mg IV).	Procedure classification: clean (nontunneled catheter: no prophylaxis)

IV: intravenous; IVC: inferior vena cava.

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Graphic 63103 Version 9.0

operation	pathogens	antimicrobials	dose	interval
Reduction mammoplasty Mammoplasty Lumpectomy Mastectomy Axillary node dissection	–	None	–	–
Breast cancer procedures	*Staphylococcus aureus*, *S. epidermidis*, streptococci*	Cefazolin	<120 kg: 2 g IV ≥120 kg: 3 g IV	4 hours
		OR vancomycin	15 mg/kg (max 2 g)	N/A
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.

* A higher rate of infection due to gram-negative organisms occurs in the setting of procedures involving macerated, moist environments (such as under the axilla of an obese individual) and among patients with diabetes. In the setting of risk for surgical site infections due to gram-negative pathogens, an additional agent may be warranted (such as an gentamicin 5 mg/kg IV, aztreonam 2 g IV, ciprofloxacin 400 mg IV, or levofloxacin 500 mg IV).

Source: Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.

Graphic 89540 Version 6.0

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