Chapter 132. Antimicrobial Prophylaxis in Surgery XING JIN

Key Concepts:

Prophylactic antibiotic therapy differs from presumptive and therapeutic antibiotic therapy in that the latter two involve treatment regimens for documented or presumed infections, whereas the goal of prophylactic therapy is to prevent infections in high-risk patients or procedures.

The risk of a surgical site infection (SSI) is determined from both the type of surgery and the patient-specific risk factors; however, most commonly used classification systems account for only procedure-related risk factors.

The timing of antimicrobial prophylaxis is of paramount importance. ***Antibiotics should be administered within 1 hour before surgery*** to ensure adequate drug levels at the surgical site prior to the initial incision.

Antimicrobial agents with short half-lives (e.g., cefazolin) may require intraoperative redosing during long (>3 hours) procedures.

The type of surgery, intrinsic patient risk factors, most commonly identified pathogenic organisms, institutional antimicrobial resistance patterns, and cost must be considered when choosing an antimicrobial agent for prophylaxis.

Single-dose prophylaxis is appropriate for many types of surgery. ***First-generation cephalosporins (e.g., cefazolin) are the mainstay*** for prophylaxis in most surgical procedures because of their spectrum of activity, safety, and cost.

Vancomycin as a prophylactic agent should be limited to patients with ***a documented history of life-threatening -lactam hypersensitivity*** or those in whom the incidence of ***infections with organisms resistant to cefazolin*** (e.g., methicillin-resistant Staphylococcus aureus) is high enough to justify use.

Introduction:

By definition, ***SSIs must occur within 30 days of surgery. If a prosthetic implant is involved, a deep incisional or organ/space SSI can be reported up to 1 year from the date of surgery.***

Although microbiologic testing of surgical drainage material or sites may help to guide care, ***the specificity of a negative culture is poor and generally does not rule out an SSI.***

Table 132-1 National Research Council Wound Classification, Risk of Surgical Site Infection, and Indication for Antibiotics

	SSI Rate (%)			
Classification	**Preoperative Antibiotics**	**No Preoperative Antibiotics**	**Criteria**	**Antibiotics**
Clean	5.1	0.8	No acute inflammation or transection of GI, oropharyngeal, genitourinary, biliary, or respiratory tracts; elective case, no technique break	***Not indicated unless high-risk procedure***[a]
Clean–contaminated	10.1	1.3	Controlled opening of aforementioned tracts with minimal spillage/minor technique break; clean procedures performed emergently or with major technique breaks	***Prophylactic antibiotics indicated***
Contaminated	21.9	10.2	Acute, nonpurulent inflammation present; major spillage/technique break during clean–contaminated procedure	***Prophylactic antibiotics indicated***
Dirty	N/A	N/A	Obvious preexisting infection present (abscess, pus, or necrotic tissue present)	***Therapeutic antibiotics required***

Table 132-2 Patient and Operation Characteristics That May Influence the Risk of Surgical Site Infection

Patient	**Operation**
Age	Duration of surgical scrub
Nutritional status	Preoperative skin preparation
Diabetes	Preoperative shaving
Smoking	Duration of operation
Obesity	Antimicrobial prophylaxis
Coexisting infections at distal body sites	Operating room ventilation
Colonization with resistant microorganisms	Sterilization of instruments

Altered immune response	Implantation of prosthetic materials
Length of preoperative stay	Surgical drains Surgical technique

Colonization of the nares with Staphylococcus aureus is a well-described SSI risk factor.3 Although ***intranasal application of mupirocin (Bactroban®) ointment*** reduces the rate of nasal carriage of S. aureus, one large, randomized, double-blind study of 4,030 surgical patients found that prophylactic intranasal mupirocin did ***not reduce the rate of S. aureus SSI***, although it ***did reduce the rate of nosocomial S. aureus infections*** among patients who were S. aureus carriers.

Table 132-5 Major Pathogens in Surgical Wound Infections	
Pathogen	**Percent of Infections[a]**
Staphylococcus aureus	***20***
Coagulase-negative staphylococci ***S. epidermis and S. saphrophyticus***	***14***
Enterococci - E. faecalis and E. faecium (VRE)	***12***
Escherichia coli	8
Pseudomonas aeruginosa	8
***Enterobacter* species**	7
Proteus mirabilis	3
Klebsiella pneumoniae	3
Other *Streptococcus species*	3
Candida albicans	3
Group D streptococci	2
Other gram-positive aerobes	2
Bacteroides fragilis	2

Postoperative factors associated with MRSA include discharge to a long-term care facility and duration of postoperative antibiotic treatment for more than 1 day.

Although presurgical *Candida* colonization is associated with a higher risk of fungal SSIs, **routine preoperative use of prophylactic antifungal agents is not being advocated at this time.**

Antibiotics should be administered with anesthesia just prior to the initial incision.
Administration of antibiotics too early may result in concentrations below the MIC toward the

end of the operation, and administration too late leaves the patient unprotected at the time of initial incision.

prophylactic antibiotics should not be prescribed to be given "on call to the operating room (OR)," which can occur 2 or more hours prior to the initial incision, **nor should concurrent therapeutic antibiotics be relied on to provide adequate protection.**

immediately prior to the incision may not allow enough time for the drug to distribute throughout the tissues involved in the surgery.

In a large prospective observational study of 3,836 visceral, trauma, and vascular surgeries where antimicrobial prophylaxis with cefuroxime and metronidazole was employed, the incidence of SSIs was analyzed according to the timing of antimicrobial administration. When antimicrobial prophylaxis was administered within 30 minutes or between 1 and 2 hours before the initial incision, the risk of SSI was greater when compared to antimicrobial prophylaxis administered 30 to 59 minutes prior to the initial incision. **The authors conclude that the optimal window for antimicrobial (cefuroxime and metronidazole) is between 30 and 59 minutes prior to the initial incision**.

One study of patients undergoing clean-contaminated operations **suggests that procedures longer than 3 hours require a second intraoperative dose of cefazolin or substitution of cefazolin with a longer-acting antimicrobial agent**.4 A second study of patients undergoing elective colorectal surgery suggests that low serum antimicrobial concentrations at the time of surgical closure is the strongest predictor of postoperative SSI.

patients with **thermal burn and spinal cord injuries eliminate certain classes of antibiotics, primarily the aminoglycosides and beta-lactams**

Individuals undergoing cardiac bypass may have altered antibiotic disposition related to increased volume of distribution and reduced total body clearance and thus require special dosing consideration.

Although most SSIs involve the patient's **normal flora**, antimicrobial selection also must take into account the susceptibility patterns of **nosocomial pathogens** within each institution. Typically, **gram-positive coverage should be included** in the choice of surgical prophylaxis because organisms such as **S. aureus and S. epidermidis** are encountered commonly as skin flora. The decision to broaden antibiotic prophylaxis to agents with **gram-negative and anaerobic spectra of activity depends on both the surgical site** (e.g., **upper respiratory, gastrointestinal (GI), or genitourinary tract**) and whether the operation will transect a hollow viscous or mucous membrane that may contain resident flora.

Although antimicrobial prophylaxis can be administered through a variety of routes (e.g., oral, topical, or intramuscular), the **parenteral route is favored** because of the reliability by which adequate tissue concentrations may be acheived.41 Cephalosporins are the most commonly

prescribed agents for surgical prophylaxis because of their broad antimicrobial spectrum, favorable pharmacokinetic profile, low incidence of adverse side effects, and low cost. First-generation cephalosporins, such as **cefazolin**, are the preferred choice for surgical prophylaxis, particularly for clean surgical procedures.3,4,7 In cases where **broader gram-negative and anaerobic coverage** is desired, **antianaerobic cephalosporins, such as cefoxitin and cefotetan, are appropriate choice**s. Although third-generation cephalosporins (e.g., ceftriaxone) have been advocated for prophylaxis because of their increased gram-negative coverage and prolonged half-lives, their inferior gram-positive and anaerobic activity and high cost have discouraged the widespread use of these agents.

Allergic reactions are the most common side effects associated with cephalosporin use.

Vancomycin can be considered for **prophylactic therapy** in surgical procedures **involving implantation of a prosthetic device** in which the **rate of MRSA is high**. ***If the risk of MRSA is low, and a beta-lactam hypersensitivity exists, clindamycin can be used*** for many procedures instead of cefazolin to limit vancomycin use. Infusion-related side effects, such as thrombophlebitis and hypotension, particularly with vancomycin, usually can be controlled by adequate dilution and slower administration rates.

Pseudomembranous colitis secondary to cephalosporins is uncommon and generally easily **treated with a short course of oral metronidazole**. Although infrequent, **bleeding abnormalities** related to cephalosporin use have been reported.45 The primary hematologic effect appears to be **inhibition of vitamin K–dependent clotting factors** that results in prolongation of the prothrombin time. The mechanism for this effect, most commonly seen with **cefotetan**, is related to the **methylthiotetrazole side chain** of the -lactam molecule. Patients at greatest risk for this hypoprothrombinemic effect have received a prolonged course of these agents and have underlying risk factors for vitamin K deficiency, such as malnutrition.

Potential sources of **inappropriate antibiotic prophylaxis include the use of broad-spectrum antimicrobials when a narrow-spectrum agent is warranted, extending prophylaxis for durations beyond that recommended in published guidelines, and using expensive antibiotics when equivalent, less expensive agents are available**.

Table 132-6 Most Likely Pathogens and Specific Recommendations for Surgical Prophylaxis				
Type of Operation	**Likely Pathogens**	**Recommended Prophylaxis Regimen[a]**	**Comments**	**Grade of Recommendation[b]**
GI surgery				
GI surgery can be categorized according to surgical site and infectious risk. **Gastroduodenal surgery and hepatobiliary surgery generally are considered to be clean or clean-contaminated surgeries**, with SSI rates generally less than 5%. **Colorectal surgery, including appendectomies, is considered contaminated** because of the large quantities and polymicrobial nature of bacterial flora within the colon. SSI rates for these types of surgeries generally range from 15% to 30%. **Emergent abdominal surgery involving bowel perforation or peritonitis is considered a dirty surgical procedure**, associated with a greater than 30% risk of SSI, and **should be treated with therapeutic rather than prophylactic antibiotics**.				
Gastroduodenal: lactam allergy, po ciprofloxacin is as efficacious as parenteral cefuroxime as prophylactic therapy	Enteric gram-negative bacilli, gram-positive cocci, oral anaerobes	Cefazolin 1 g x 1 (see text for recommendations for percutaneous endoscopic gastrostomy)	High-risk patients only (obstruction, hemorrhage, malignancy, acid suppression therapy, morbid obesity)	IA
Cholecystectomy: Ciprofloxacin and levofloxacin are effective alternatives for lactam-allergic patients undergoing open cholecystectomy.	Enteric gram-negative bacilli, anaerobes	Cefazolin 1 g x 1 for high-risk patients Laparoscopic: none	High-risk patients only (acute cholecystitis, common duct stones, previous biliary surgery, jaundice, age >60 years, obesity, diabetes mellitus)	IA
Transjugular intrahepatic portosystemic shunt (TIPS)	Enteric gram-negative bacilli, anaerobes	Ceftriaxone 1 g x 1	Longer-acting cephalosporins preferred	IA
Appendectomy	Enteric gram-negative bacilli, anaerobes	Cefoxitin or cefotetan 1 g x 1	Second intraoperative dose of cefoxitin may be required if procedure lasts longer than 3 hours	IA
Colorectal: Reducing	Enteric gram-negative bacilli,	IV: cefoxitin or	Benefits of oral plus IV is	IA

bacterial load with a thorough bowel preparation regimen (PEG) is controversial; however, 99% of surgeons in a survey routinely use mechanical preparation.	anaerobes	cefotetan 1 g x 1 Orally: neomycin 1 g + erythromycin base 1 at 1 PM, 2 PM, and 11 PM 1 day preoperatively plus mechanical bowel preparation	controversial except for colostomy reversal and rectal resection	
GI endoscopy: Single-dose preprocedural regimens similar to those for endocarditis prophylaxis are most common	Variable, depending on procedure, but typically enteric gram-negative bacilli, gram-positive cocci, oral anaerobes	Orally: amoxicillin 2 g x 1 IV: ampicillin 2 g x 1 or cefazolin 1 g x 1	Recommended only for high-risk patients undergoing high-risk procedures (see text)	IA
Urologic surgery				
Prostate resection, shock-wave lithotripsy, ureteroscopy	*Escherichia coli*	Ciprofloxacin 500 mg orally or trimethoprim-sulfamethoxazole 1 DS tablet	All patients with positive pre-operative urine cultures should receive a course of antibiotic treatment	IA–IB
removal of external urinary catheters, cystography, urodynamic studies, simple cystourethroscopy	*E. coli*	Ciprofloxacin 500 mg orally or trimethoprim-sulfamethoxazole 1 DS tablet	Should be considered only in patients with risk factors (see text)	IB
Gynecological surgery				
Cesarean section	Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci	Cefazolin **2** g x 1	Can be given before initial incision or after cord is clamped	IA
Hysterectomy	Enteric gram-negative bacilli, anaerobes, group B streptococci,	Vaginal: cefazolin 1 g x 1 Abdominal:	Metronidazole 1 g IV x 1 is recommended alternative for	IA

	enterococci	cefotetan 1 g x 1 or cefazolin 1 g x 1	penicillin allergy	
Head and neck surgery				
Maxillofacial surgery	*Staphylococcus aureus*, streptococci oral anaerobes	Cefazolin **2** g or clindamycin 600 mg	Repeat intraoperative dose for operations longer than 4 hours	IA
Head and neck cancer resection	*S. aureus*, streptococci oral anaerobes	Clindamycin 600 mg at induction and every 8 hours x 2 more doses	Add gentamicin for clean–contaminated procedures	IA
Cardiothoracic surgery				
Cardiac surgery	*S. aureus*, *Staphylococcus epidermidis*, *Corynebacterium*	Cefazolin 1 g every 8 hours x 48 h	Patients >80 kg (176 lb) should receive 2 g of cefazolin instead; in areas with high prevalence of *S. aureus* resistance, vancomycin should be considered	IA
Thoracic surgery: pathogenic organisms likely migrate from the oral cavity or pharynx.	*S. aureus*, *S. epidermidis*, *Corynebacterium* , enteric gram-negative bacilli	Cefuroxime 750 mg IV every 8 hours x 48 hours	First-generation cephalosporins are deemed inadequate, and shorter durations of prophylaxis have not been adequately studied	IA
Vascular surgery: lactam allergy, 24 hr PO ciprofloxacin has been shown to be effective.				
Abdominal aorta and lower extremity vascular surgery	*S. aureus*, *S. epidermidis*, enteric gram-negative bacilli	Cefazolin 1 g at induction and every 8 hours x 2 more doses	Although complications from infections may be infrequent, graft infections are associated with significant morbidity	IB

Orthopedic surgery: prophylactic antibiotics generally are indicated only when prosthetic materials are implanted.				
Joint replacement	*S. aureus, S. epidermidis*	Cefazolin 1 g x 1 preoperatively, then every 8 hours x 2 more doses	Vancomycin reserved for penicillin-allergic patients or where institutional prevalence of methicillin-resistant *S. aureus* warrants use	IA
Hip fracture repair	*S. aureus, S. epidermidis*	Cefazolin 1 g x 1 preoperatively, then every 8 hours for 48 hours	Compound fractures are treated as if infection is presumed	IA
Open/compound fractures	*S. aureus, S. epidermidis*, gram-negative bacilli, polymicrobial	Cefazolin 1 g x 1 preoperatively, then every 8 hours for a course of presumed infection	Gram-negative coverage (i.e., gentamicin) often indicated for severe open fractures	IA
Neurosurgery				
CSF shunt procedures	*S. aureus, S. epidermidis*	Cefazolin 1 g every 8 h x 3 doses or ceftriaxone 2 g x 1	No agents have been shown to be better than cefazolin in randomized comparative trials.	IA
Spinal surgery	*S. aureus, S. epidermidis*	Cefazolin 1 g x 1	Limited number of clinical trials comparing different treatment regimens	IB
CSF shunt procedures	*S. aureus, S. epidermidis*	Cefazolin 1 g every 8 h x 3 doses or ceftriaxone 2 g x 1	No agents have been shown to be better than cefazolin in randomized comparative trials.	IA

Craniotomy	*S. aureus, S. epidermidis*	Cefazolin 1 g x 1 or cefotaxime 1 g x 1	IV x 1 can be substituted for patients with penicillin allergy Trimethoprim-sulfamethoxazole (160/800 mg)	IA

Minimally Invasive and Laparoscopic Surgery: need to know site and risk factors

Nonpharmacologic Interventions: Strategies other than antimicrobial and aseptic technique for reducing postoperative infections have been investigated in different types of surgeries. The most commonly cited and practiced interventions include **intraoperative maintenance of normothermia**, provision of **supplemental oxygen in the perioperative period**, and **aggressive perioperative glucose control.**

Evaluation: Many SSIs will not be evident during acute hospitalization. In fact, SSIs may not become evident until up to 30 days later or, in the case of prosthesis implantation, up to 1 year later.