**Antimicrobial Prophylaxis in Surgery**

Pharmacotherapy: A Pathophysiologic Approach, 8e – Section 16. Infectious Diseases

Chapter 132. Antimicrobial Prophylaxis in Surgery – Salmaan Kanji

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15. **Key Concepts**

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| |  | | --- | | 1. 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](javascript:PopupGlossaryTerm(2752670);). 2. The risk of a surgical site infection (SSI) is determined from both the type of surgery and the patient-specific [risk factors](javascript:PopupGlossaryTerm(2752404);); however, most commonly used classification systems account for only procedure-related risk factors. 3. 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. 4. Antimicrobial agents with short half-lives (e.g., [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');)) may require intraoperative redosing during long (>3 hours) procedures. 5. 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. 6. 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. 7. [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) as a prophylactic agent should be limited to patients with a documented history of life-threatening beta-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. | |

Summary:

1. Prophylactic therapy is to prevent infections in high-risk patients or [procedures](javascript:PopupGlossaryTerm(2752670);)
2. The risk of a surgical site infection (SSI) is determined from both the type of surgery and the patient-specific [risk factors](javascript:PopupGlossaryTerm(2752404);)
3. The timing of antimicrobial prophylaxis prior to initial incision for anti-infection preventive action during procedures
4. Administration of short half-life vs long half-life antibiotics
5. Type of surgery, patient risk factors, pathogenic organisms, antimicrobial resistance patterns and cost must be considered when choosing antimicrobial agent for prophylaxis
6. Single-dose prophylaxis is appropriate for many types of procedures considering acceptable spectrum, safety and cost
7. Vancomycin as a prophylactic agent should be limited to life-threatening hypersensitivity to beta-lactam and resistant to cefazolin, e.g., MRSA
8. **Learning Objectives**
9. Differentiate among prophylactic, presumptive, and therapeutic antibiotics in the perioperative patient.
10. Identify patient-specific [risk factors](javascript:PopupGlossaryTerm(2752404);) for surgical site infections.
11. Identify procedure-specific risk factors for surgical site infections (SSIs).
12. List common [pathogens](javascript:PopupGlossaryTerm(2752355);) responsible for surgical site infections.
13. Explain the importance of timing of antimicrobial prophylaxis for surgery.
14. Apply pharmacokinetic principles for antimicrobial prophylactic regimens for surgeries of different durations.
15. Choose an evidence-based prophylactic antimicrobial regimen for specific types of surgeries.
16. Individualize prophylactic antimicrobial regimens by considering the type of surgery, intrinsic patient risk factors, and knowledge of common pathogenic organisms.
17. Recommend an alternative prophylactic antimicrobial regimen for patients with life-threatening allergies to first-line therapies.
18. Identify [clinical scenarios](javascript:PopupGlossaryTerm(2752205);) where multiple dose regimens of prophylactic antimicrobials are appropriate as compared with single-dose regimens.
19. Discuss the role of preoperative mechanical bowel preparations in the setting of elective colorectal surgery.
20. Differentiate between traditional and minimally invasive surgeries and the [relative risk](javascript:PopupGlossaryTerm(2752405);) of SSIs.
21. Debate the consequences of overzealous use of broad-spectrum antibiotics in the context of antimicrobial resistance and the changing epidemiology of pathogens responsible for SSIs.
22. List nonpharmacologic interventions effective at reducing the risk of postoperative SSIs.
23. Formulate an appropriate monitoring plan for surgical patients at risk for SSIs.

**Glossary**

Risk factor

An attribute or agent suspected to be related to the occurrence of a particular disease

Pathogen

An agent responsible for the development of a particular disease

Clinical scenario

One of two or more alternative paths of management available in a decision analysis

Relative risk or risk ratio

The likelihood of the occurrence of a particular disease among persons exposed to a given risk factor divided by the corresponding likelihood among unexposed persons

1. **Antimicrobial Prophylaxis in Surgery: Introduction**

Statistics:

~ 46 million surgical procedures / year in the US with majority in outpatient setting

Surgical site infections (SSIs) occur in 3-6% of patients & prolong hospitalization (~7 days) … cost $5 – 10 billion/ year

Among hospitalized patients:

* SSIs (14-16%) are the third most frequent cause of nosocomial infections
* SSIs (40%) are the primary cause of nosocomial infection in surgical patients

Prevention of hospital-acquired infections is a major goal of antibiotic prophylaxis

Both SSIs and infections not directly related to the surgical site (e.g., urinary tract infections and pneumonia) are termed *nosocomial*

Preexisting, unrelated to surgery infections are not part of prophylactic regimen

Presumptive antibiotic therapy is administered when an infection is suspected but not yet proven

With unexpected findings (perforation/ wounds in operative organs) …. Therapeutic antibiotic regimen required

No sign of unexpected findings during surgery …. Prophylactic antibiotic regimen suggested

According to the Centers for Disease Control and Prevention's (CDC) National [Nosocomial Infections](javascript:PopupGlossaryTerm(2753538);) Surveillance System (NNIS),[3](http://www.accesspharmacy.com.libproxy.temple.edu/content.aspx?aID=8006535" \l "8006535" \t "_parent) SSIs can be categorized as either incisional (e.g., [cellulitis](javascript:PopupGlossaryTerm(2753074);) of the incision site) or organ/space (e.g., [meningitis](javascript:PopupGlossaryTerm(2753470);); [Fig. 132–1](javascript:windowReference('Reference',%20'popup.aspx?aID=8006393');)).

Incisional SSIs are subcategorized into superficial (involving only the skin or subcutaneous tissue) and deep (fascial and muscle layers) infections

Organ/space SSIs can involve any anatomic area other than the incision site

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

1. **Risk Factors for Surgical Site Infections**

SSI incidence depends on both procedure- and patient-related factors. Traditionally, the risk for SSIs has been stratified by surgical procedure in a classification system developed by the National Research Council based on:

Microbiology of the surgical site

Presence of a preexisting infection

Likelihood of contaminating previously sterile tissue during surgery

Events during and after surgery

Because a patient's NRC wound classification is influenced by surgical findings (e.g., gangrenous gallbladder) and perioperative events (e.g., major technique breaks), categorization generally occurs intraoperatively

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  if SSI = 5.1% then give preoperative antiboitics | 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](javascript:PopupGlossaryTerm(2752670);) 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 | |

The NRC classification system does not account for the influence of underlying patient [risk factors](javascript:PopupGlossaryTerm(2752404);) for SSI development, instead categorizing the risks for SSIs simply based on a specific surgical procedure – Ex: Diabetic, HIV, malnutrition

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 |

Two large epidemiologic studies have objectively quantified SSI risk based on specific patient- and procedure-related factors

The Study on the [Efficacy](javascript:PopupGlossaryTerm(2751024);) of [Nosocomial Infection](javascript:PopupGlossaryTerm(2753538);) Control (SENIC)

National Nosocomial Infections Surveillance **(**NNIS**)**

**SENIC study** - Abdominal operations, operations lasting longer than 2 hours, contaminated or "dirty" [procedures](javascript:PopupGlossaryTerm(2752670);) (as per NRC classification), and more than three underlying medical diagnoses each was associated with an increased incidence of SSI. When NRC classification was stratified by number of SENIC risk factors present, SSI incidence varied by as much as a factor of 15 within the same NRC operative category ([Table 132–3](javascript:windowReference('Reference',%20'popup.aspx?aID=8006406');))

Table 132-3 Surgical Site Infection Incidence (%) Stratified by NRC Wound Classification and SENIC Risk Factors

| **No. of SENIC Risk Factors** | **Clean** | **Clean–Contaminated** | **Contaminated** | **Dirty** |
| --- | --- | --- | --- | --- |
| 0 | 1.1 | 0.6 | N/A | N/A |
| 1 | 3.9 | 2.8 | 4.5 | 6.7 |
| 2 | 8.4 | 8.4 | 8.3 | 10.9 |
| 3 | 15.8 | 17.7 | 11.0 | 18.8 |
| 4 | N/A | N/A | 23.9 | 27.4 |

**NNIS study** - Quantification of intrinsic patient risk using the American Society of Anesthesiologists' (ASA) preoperative assessment score ([Table 132–4](javascript:windowReference('Reference',%20'popup.aspx?aID=8006408');)). The NNIS basic SSI risk index is composed of the following criteria: ASA score = 3, 4, or 5; wound class; and duration of surgery - An ASA score ≥ 3 was a strong predictor for the development of an SSI

Table 132-4 American Society of Anesthesiologists’ Physical Status Classification

| **Class** | **Description** |
| --- | --- |
| 1 | Normal healthy patient |
| 2 | Mild systemic disease |
| 3 | Severe systemic disease that is not incapacitating |
| 4 | Incapacitating systemic disease that is a constant threat to life |
| 5 | Not expected to survive 24 hours with or without operation |

Overall, for 34 of the 44 NNIS procedure categories, SSI rates increased proportionally with the number of risk factors present. The SSI rate was generally lower when the procedure was done laparoscopically.

Laparoscopic surgery includes operations within the abdominal or pelvic cavities, whereas keyhole surgery performed on the thoracic or chest cavity is called thoracoscopic surgery. Laparoscopic and thoracoscopic surgery belong to the broader field of [endoscopy](http://en.wikipedia.org/wiki/Endoscopy).

1. **Bacteriology**

The most important consideration when choosing antibiotic prophylaxis is the bacteriology of the surgical site. Organisms involved in an SSI are acquired by one of two ways:

* Endogenously (from the patient's own normal flora)
* Exogenously (from contamination during the surgical procedure)

With the widespread use of broad-spectrum antibiotics, however, *Candida* species and methicillin-resistant *S. aureus* (MRSA) are becoming more prevalent

Factors affecting the ability of an organism to induce an SSI depend on:

Organism count

Organism virulence

Host immunocompetency

Table 132-5 Major Pathogens in Surgical Wound Infections

| **Pathogen** | **Percent of Infections*a*** |
| --- | --- |
| *Staphylococcus aureus* | 20 |
| Coagulase-negative staphylococci | 14 |
| Enterococci | 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 |

Organisms in the commensal flora generally are not pathogenic. Opportunistic organisms usually are kept in check by normal flora and rarely are problematic unless they are present in large numbers. The loss of normal flora through the use of broad-spectrum antibiotics can destabilize homeostasis, allowing pathogenic bacteria to proliferate and infection to occur.

Secondary infections:

Normal flora translocated to a normally sterile tissue site or fluid during a surgical procedure can become pathogenic. For example, S. aureus or Staphylococcus epidermidis may be translocated from the surface of the skin to deeper tissues or E. coli from the colon to the peritoneal cavity, bloodstream, or urinary tract.

Impaired host defense reduces the number of bacteria required to establish an infection

1. **Antimicrobial Resistance**

Colonization of the host with antibiotic-resistant hospital flora prior to or during surgery may lead to an SSI that is unresponsive to routine antibiotic therapy.

* With cephalosporins established as first-line agents for prophylaxis over the past decade, organisms resistant to cephalosporins represent the majority of [pathogens](javascript:PopupGlossaryTerm(2752355);) causing SSIs.
* The CDC has reported an alarming increase in the incidence of [vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');)-resistant enterococci (VRE) infections, particularly those with *Enterococcus.*
* [Risk factors](javascript:PopupGlossaryTerm(2752404);) for VRE colonization include severe concomitant diseases, immunosuppression, admission to the intensive care unit (ICU), previous intraabdominal or cardiothoracic surgery, placement of indwelling catheters, and prolonged courses of antimicrobials, particularly vancomycin.
* The guidelines by CDC suggest vancomycin substitution for [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) as SSI prophylaxis only in cases with a high suspicion of MRSA or in patients with a documented history of a life-threatening allergy to penicillins or cephalosporins.
* Cefazolin remains the drug of choice for SSI prophylaxis in cardiovascular surgery

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

1. **Scheduling Antibiotic Administration**

The following principles must be considered when providing antimicrobial surgical prophylaxis:

(a) The agents (antibiotic + anesthesia) should be delivered to the surgical site prior to the initial incision

(b) Bactericidal antibiotic concentrations should be maintained at the surgical site throughout the surgical procedure

**Study 1** - Risk of SSI rate in the landmark study by Classen et al

* Early Preoperative (2–24 hours before surgery) 3.8% Highest
* Preoperative prophylaxis (0–2 hours prior to surgery) 0.6% Lowest
* Perioperative prophylaxis (up to 3 hours after first incision) 1.4% Moderate
* Postoperative prophylaxis (>3 hours after first incision) 3.3% High

For these reasons, 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.

**Study 2** - Risk of SSI rate in an [Observational study](javascript:PopupGlossaryTerm(2752346);) of visceral, trauma, and vascular surgeries where antimicrobial prophylaxis with [cefuroxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5849');) and [metronidazole](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6573');)

* Within 30 minutes before the initial incision Greater
* Between 30 and 59 minutes before the initial incision Optimum
* Between 1 and 2 hours before the initial incision Greater

This effect may be a function of the [pharmacodynamics](javascript:PopupGlossaryTerm(2753618);) and pharmacokinetics of the antimicrobial chosen for the prophylactic regimen

**Study 3** – Risk of SSI rate in a study with patients undergoing cardiac, orthopedic, and gynecologic surgery with a variety of antimicrobial prophylactic regimens

There was a statistically nonsignificant trend toward fewer SSIs in patients who received their prophylactic regimen within the 30 minutes prior to incision as compared with those who received the regimen 31 to 60 minutes prior to incision

Potential barrier on administration timing

Few patients receive antibiotics at the optimal time in relation to surgery

One study assessed the timing of prophylactic antibiotics in 100 patients and found that only 26% of patients received an antibiotic dose within 2 hours of the initial surgical incision

Single vs Multiple dose

Although most studies comparing single versus multiple doses of prophylactic antibiotics have failed to show a benefit of multidose regimens, the duration of operations in these studies may not be as long as that frequently observed in clinical practice

* One study of patients undergoing clean-contaminated operations suggests that [procedures](javascript:PopupGlossaryTerm(2752670);) longer than 3 hours require a second intraoperative dose of [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) or substitution of cefazolin with a longer-acting antimicrobial agent
* 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
* Studies of patients undergoing cardiac surgery also have demonstrated a higher infection rate among patients with undetectable antibiotic serum concentrations at the conclusion of the procedure

Strategies to ensure appropriate redosing of prophylactic antibiotics during long operations

* Use of a visual or auditory reminder system
* Continuous infusions of [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');)

Underlying disease states that may affect antibiotic metabolism and/or elimination should be considered

* Ex: Patients with thermal burn and spinal cord injuries eliminate certain classes of antibiotics, primarily the aminoglycosides and beta-lactams, at unusually high rates compared with controls
* Individuals undergoing cardiac bypass may have altered antibiotic disposition related to increased [volume of distribution](javascript:PopupGlossaryTerm(2753908);) and reduced [total body clearance](javascript:PopupGlossaryTerm(2752814);)

1. **Antimicrobial Choice**

The choice of prophylactic antibiotic depends on

* The type of surgical procedure
* The most frequent [pathogens](javascript:PopupGlossaryTerm(2752355);) seen with this procedure
* Safety and [efficacy](javascript:PopupGlossaryTerm(2751024);) profiles of the antimicrobial agent
* Current literature evidence supporting its use
* Cost

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.

Antibiotic prophylaxis can be broadened 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.

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 ([cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');)) are the preferred choice for surgical prophylaxis, particularly for clean surgical [procedures](javascript:PopupGlossaryTerm(2752670);)
* Second-generation cephalosporins (cefoxitin, cefotetan) are appropriate choices in cases where broader gram-negative and anaerobic coverage is desired
* Third-generation cephalosporins (ceftriaxone) – Although they 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

The true incidence of cross-reactivity with penicillin likely is less than 1%

In summary, the administration of cephalosporins is both safe and cost-effective for many patients who are labeled "penicillin allergic," and they can be used by patients who have not experienced an immediate or type I penicillin allergy.

[Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) can be considered for prophylactic therapy in surgical [procedures](javascript:PopupGlossaryTerm(2752670);) 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](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5917');) can be used for many procedures instead of [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 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](javascript:PopupGlossaryTerm(2753691);) secondary to cephalosporins is uncommon and generally easily treated with a short course of oral [metronidazole](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6573');).

Pseudomembranous colitis: Inflammation of the colon caused by the toxin of *Clostridium difficile* and resulting in bloody diarrhea

1. **Recommendations for Specific Types of Surgery**

The choice of antimicrobial prophylaxis is always best evaluated using the results of properly conducted [clinical trials](javascript:PopupGlossaryTerm(2752206);). In the absence of studies specific to the procedure in question, extrapolation from data on regimens for different procedures in the same anatomic site in question usually can be made. Subsequent modifications to each prophylactic regimen should be based on intraoperative findings or events.

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** |  |  |  |  |
| Gastroduodenal | Enteric gram-negative bacilli, gram-positive cocci, oral anaerobes | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 (see text for recommendations for percutaneous endoscopic gastrostomy) | High-risk patients only (obstruction, hemorrhage, [malignancy](javascript:PopupGlossaryTerm(2752317);), acid suppression therapy, morbid obesity) | IA |
| Cholecystectomy | Enteric gram-negative bacilli, anaerobes | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 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](javascript:PopupGlossaryTerm(2752236);)) | IA |
| Transjugular intrahepatic portosystemic shunt (TIPS) | Enteric gram-negative bacilli, anaerobes | [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) 1 g x 1 | Longer-acting cephalosporins preferred | IA |
| Appendectomy | Enteric gram-negative bacilli, anaerobes | [Cefoxitin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5842');) or [cefotetan](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5841');) 1 g x 1 | Second intraoperative dose of [cefoxitin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5842');) may be required if procedure lasts longer than 3 hours | IA |
| Colorectal | Enteric gram-negative bacilli, anaerobes | Orally: [neomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6637');) 1 g + [erythromycin base](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6128');) 1 at 1 PM, 2 PM, and 11 PM 1 day preoperatively plus mechanical bowel preparation  IV: [cefoxitin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5842');) or [cefotetan](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5841');) 1 g x 1 | Benefits of oral plus IV is controversial except for colostomy reversal and rectal resection | IA |
| GI endoscopy | Variable, depending on procedure, but typically enteric gram-negative bacilli, gram-positive cocci, oral anaerobes | Orally: [amoxicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5631');) 2 g x 1  IV: [ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) 2 g x 1 or [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 | Recommended only for high-risk patients undergoing high-risk [procedures](javascript:PopupGlossaryTerm(2752670);) (see text) | IA |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Urologic surgery** | | | | |
| Prostate resection, shock-wave lithotripsy, ureteroscopy | *Escherichia coli* | [Ciprofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');) 500 mg orally  or  [trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');)-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](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');)  500 mg orally or [trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');)-sulfamethoxazole 1 DS tablet | Should be considered only in patients with [risk factors](javascript:PopupGlossaryTerm(2752404);) (see text) | IB |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Gynecological surgery** | | | | |
| Cesarean section | Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 2 g x 1 | Can be given before initial incision or after cord is clamped | IA |
| [Hysterectomy](javascript:PopupGlossaryTerm(2753370);) | Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci | Vaginal: [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1  Abdominal: [cefotetan](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5841');) 1 g x 1 or [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 | [Metronidazole](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6573');) 1 g IV x 1 is recommended alternative for penicillin allergy | IA |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Head and neck surgery** | | | | |
| Maxillofacial surgery | *Staphylococcus aureus*, streptococci oral anaerobes | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 2 g or [clindamycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5917');) 600 mg | Repeat intraoperative dose for operations longer than 4 hours | IA |
| Head and neck cancer resection | *S. aureus,* streptococci oral anaerobes | [Clindamycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5917');) 600 mg at induction and every 8 hours x 2 more doses | Add [gentamicin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6261');) for clean–contaminated procedures | IA |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Cardiothoracic surgery** | | | | |
| Cardiac surgery | *S. aureus, Staphylococcus epidermidis, Corynebacterium* | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g every 8 hours x 48 h | Patients >80 kg (176 lb) should receive 2 g of [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) instead; in areas with high [prevalence](javascript:PopupGlossaryTerm(2752381);) of *S. aureus* resistance, [vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) should be considered | IA |
| Thoracic surgery | *S. aureus, S. epidermidis, Corynebacterium,* enteric gram-negative bacilli | [Cefuroxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5849');) 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 |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Vascular surgery** | | | | |
| Abdominal aorta and lower extremity vascular surgery | *S. aureus, S. epidermidis,* enteric gram-negative bacilli | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 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 |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Orthopedic surgery** | | | | |
| Joint replacement | *S. aureus, S. epidermidis* | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 preoperatively, then every 8 hours x 2 more doses | [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) 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](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 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](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 preoperatively, then every 8 hours for a course of presumed infection | Gram-negative coverage (i.e., [gentamicin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6261');)) often indicated for severe open fractures | IA |

| **Type of Operation** | **Likely Pathogens** | **Recommended Prophylaxis Regimena** | **Comments** | **Grade of Recommendationb** |
| --- | --- | --- | --- | --- |
| **Neurosurgery** | | | | |
| CSF shunt procedures | *S. aureus, S. epidermidis* | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g every 8 h x 3 doses or [ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) 2 g x 1 | No agents have been shown to be better than [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) in randomized comparative trials. | IA |
| Spinal surgery | *S. aureus, S. epidermidis* | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 | Limited number of [clinical trials](javascript:PopupGlossaryTerm(2752206);) comparing different treatment regimens | IB |
| Craniotomy | *S. aureus, S. epidermidis* | [Cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) 1 g x 1 or [cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) 1 g x 1 | IV x 1 can be substituted for patients with penicillin allergy  [Trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');)-sulfamethoxazole (160/800 mg) | IA |

GI Surgery

***Gastroduodenal Surgery*** clean or clean-contaminated surgeries - SSI rates < 5%

Insignificant numbers of bacteria usually are found in the stomach and duodenum because of their acidity

The risk for an SSI in this population increases ONLY with any condition that can lead to bacterial overgrowth, such as obstruction, hemorrhage, or [malignancy](javascript:PopupGlossaryTerm(2752317);), or increasing the pH of gastroduodenal secretions with concomitant acid suppression therapy

In most cases, a single dose of intravenous (IV) [**cefazolin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) will provide adequate prophylaxis

If allergic with beta-lactam …… then oral [ciprofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');) is as efficacious as parenteral [cefuroxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5849');)

Antimicrobial prophylaxis is indicated in esophageal surgery only in the presence of obstruction

Postoperative therapeutic antibiotics may be indicated if perforation is detected during surgery

Use of antibiotic prophylaxis for percutaneous endoscopic gastrostomy placement is controversial

***Hepatobiliary Surgery*** clean or clean-contaminated surgeries - SSI rates < 5%

Bile contamination (bactobilia) can increase the frequency of SSIs and is present in many patients (e.g., those with acute cholecystitis or biliary obstruction and those of advanced age).

Trials comparing first-, second-, and third-generation cephalosporins have not demonstrated benefit over **single-dose** [**cefazolin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) prophylaxis even in high-risk patients (e.g., age >60 years, previous biliary surgery, acute cholecystitis, jaundice, obesity, diabetes, and common bile duct stones).

Beta lactam allergic patients …. Ciprofloxacin & levofloxacin are effective alternatives

The risk for SSIs in cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt surgery may be reduced with a single prophylactic dose of [ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) but not with single doses of shorter-acting cephalosporins

Cefoxitin or Cefotetan with additional anti-anaerobic activity is needed for:

Presumptive antibiotic therapy for patients with acute cholecystitis or cholangitis

Postoperative therapeutic if detection of an active infection during surgery (e.g., gangrenous gallbladder and suppurative cholangitis)

***Appendectomy*** contaminated surgeries - SSI rates 15 - 30%

Recommended first-line therapy with anti-anaerobic activity:

**Cefoxitin** or

**Cefotetan** may be superior because of its longer duration of action

Beta lactam allergic patients …. Metronidazole + Gentamycin

Broad-spectrum antibiotics covering nosocomial pathogens (e.g., *Pseudomonas*) do not further reduce SSI risk and instead may increase the cost of therapy and promote bacterial resistance.

Although single-dose therapy with cefotetan is adequate, prophylaxis with cefoxitin may require intraoperative dosing if the procedure extends beyond 3 hours.

***Colorectal Surgery*** contaminated surgeries - SSI rates 15 - 30%

Anaerobes and gram-negative aerobes predominate, but gram-positive aerobes also may play an important role.

[Risk factors](javascript:PopupGlossaryTerm(2752404);) for SSIs include

* Age over 60 years
* Hypoalbuminemia
* Poor preoperative bowel preparation
* Corticosteroid therapy
* [Malignancy](javascript:PopupGlossaryTerm(2752317);)
* Operations lasting longer than 3.5 hours.

The combination of

* **1 g** [**neomycin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6637');) **and 1 g** [**erythromycin base**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6128');)
* Orally 19, 18, and 9 hours preoperatively is the regimen most commonly used in the United States

Neomycin kills most of gram-negative aerobes

Erythromycin suppresses common anaerobes

Patients who cannot take oral medications should receive parenteral antibiotics. [Cefoxitin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5842');) or [cefotetan](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5841');) is used most commonly, but other second- and some third-generation cephalosporins also are effective

Optimally, the bowel preparation regimen should be completed prior to starting the oral antibiotic regimen

Beta lactam allergic patients …. Gentamicin & Metronidazole have been used

*Sidebar: Clinical controversy*

SSIs are not reduced by preoperative mechanical bowel preparation. However, mechanical bowel preparations continue to be a standard of practice prior to elective bowel surgery

Gastrointestinal Endoscopy

Although postprocedural bacteremia can occur in as many as 22% of patients, the bacteremia usually is transient (<30 minutes) and rarely results in clinically significant infection.

Therefore, antimicrobial prophylaxis is routinely recommended only for high-risk patients (e.g., patients with prosthetic heart valves, a history of [endocarditis](javascript:PopupGlossaryTerm(2753226);), systemic-pulmonary shunt, synthetic vascular graft <1 year old, complex cyanotic congenital heart disease, obstructed bile duct, or liver cirrhosis, as well as immunocompromised patients) undergoing high-risk procedures (e.g., stricture dilation, variceal sclerotherapy, and endoscopic retrograde cholangiopancreatography).

Single-dose preprocedural regimens similar to those for endocarditis prophylaxis are most common:

* **Amoxicillin** for patients who can tolerate oral premedication OR
* Either IV [**ampicillin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) or [**cefazolin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');)

Consensus guidelines have adopted this recommendation and suggest a single dose of cefazolin within 30 minutes prior to the procedure

Urologic Surgery

Patients with sterile urine preoperatively are at low risk for developing an SSI, and the benefit of prophylactic antibiotics in this setting is controversial

Antibiotic prophylaxis is recommended for all patients undergoing

* transurethral resection of the prostate or bladders tumors
* shock-wave lithotripsy
* percutaneous renal surgery, or ureteroscopy

Patients with risk factors should receive antimicrobial prophylaxis

* Patients of advanced age
* those with anatomic anomalies
* poor nutritional history
* externalized catheters
* colonized endogenous/exogenous material
* distant coexistent infection
* smokers
* immunocompromised patients
* those who are hospitalized for a prolonged stay

*E. coli* is the most frequently encountered organism

Routine use of broad-spectrum antibiotics, such as third-generation cephalosporins and fluoroquinolones, does not decrease SSI rates more than [cefazolin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');), but the ability to administer fluoroquinolones orally rather than intravenously makes antimicrobial prophylaxis with [**ciprofloxacin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');) easier and less expensive

First- or second-generation cephalosporins are considered the antimicrobial agents of choice for patients undergoing

* open or [laparoscopic](javascript:PopupGlossaryTerm(2753430);) [procedures](javascript:PopupGlossaryTerm(2752670);) involving entry into the urinary tract
* any urologic surgical procedures involving the intestine, rectum, vagina, or implanted prosthesis

Obstetric and Gynecologic Surgeries

***Cesarean Section***

Prophylactic antibiotics are given to prevent endometritis, the most commonly occurring SSI

[**Cefazolin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) remains the drug of choice despite the wide spectrum of potential [pathogens](javascript:PopupGlossaryTerm(2752355);), and a single 2 g dose appears to be superior to single or multiple 1 g doses

Beta-lactam allergy ….. preop **Metronidazole** is an acceptable alternative

*Sidebar: clinical controversy Antibiotic administration Before vs After initial incision*

Traditionally, antimicrobials were administered after the initial incision and when the umbilical cord was clamped in an attempt to minimize infant drug exposure, which theoretically could mask the signs of [neonatal](javascript:PopupGlossaryTerm(2753972);) sepsis and select resistant organisms in infants who develop infections. Recent studies and [systematic reviews](javascript:PopupGlossaryTerm(2752432);), however, suggest that preincision antibiotics are more effective at preventing postoperative endometritis and other SSIs but are underpowered to evaluate the impact on [neonatal](javascript:PopupGlossaryTerm(2753972);) infectious complications

***Hysterectomy*** *incision of the uterus*

Vaginal …….. **Cefazolin** is the drug of choice

The American College of Obstetricians and Gynecologists (ACOG) recommends a single dose of either cefazolin or [cefoxitin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5842');)

Beta-lactam allergy ….. preop **Metronidazole or Doxycycline** is an acceptable alternative

Abdominal …….. Single-dose **cefotetan** is superior to single-dose cefazolin

The ACOG guidelines suggest that first-, second-, or third-generation cephalosporins can be used for prophylaxis

Beta-lactam allergy ….. preop **Metronidazole** is an acceptable alternative

Antibiotic prophylaxis may not be required in [laparoscopic](javascript:PopupGlossaryTerm(2753430);) gynecologic surgery or tubal microsurgery

Head and Neck Surgery

Clean procedure per National Research Council (NRC) with a low incidence of SSI

The normal flora of the mouth is polymicrobial; both anaerobes and gram-positive aerobes predominate

Although typical doses of [**cefazolin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5835');) usually are ineffective for anaerobic infections, a 2 g dose produces concentrations high enough to inhibit these organisms

For most head and neck cancer resection surgeries, including free-flap reconstruction, 24 hours of clindamycin is appropriate, and no additional benefit of extending therapy beyond 24 hours is seen.

A combination of **clindamycin** and [**gentamicin**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6261');) to cover aerobic, anaerobic, and gram-negative bacteria in clean-contaminated oncologic surgery is recommended.

Cardiothoracic Surgery

Although cardiac surgery generally is considered a clean procedure, antibiotic prophylaxis lowers SSI incidence (Coronary artery bypass graft surgery with 22% mortality rate at one year vs 0.6% without SSI)

Risk factors:

* obesity
* renal insufficiency
* connective tissue disease
* reexploration for bleeding
* poorly timed administration of antibiotics

**Cefazolin** is the drug of choice

Patients weighing >80 kg (176 lb) should receive 2 g cefazolin rather than 1 g.

Doses should be administered no earlier than 60 minutes before the first incision and no later than the beginning of induction

Extending therapy beyond 48 hours does not further reduce SSI rates

Single-dose cefazolin therapy may be sufficient but is not recommended by the Society of Thoracic Surgeons at this time pending further study

First-generation cephalosporins are inadequate; 48 hours of [**cefuroxime**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5849');) (2nd generation) is preferred

Vascular Surgery

Clean procedure by NRC definition

Prophylactic antibiotics are of benefit, particularly for [procedures](javascript:PopupGlossaryTerm(2752670);) involving the abdominal aorta and the lower extremities

**Cefazolin** is the drug of choice

Beta-lactam allergy ….. preop 24 hrs of **Ciprofloxacin PO** is an acceptable alternative

Orthopedic Surgery

Most orthopedic surgery is clean by definition

Staphylococci are the most frequently encountered [pathogens](javascript:PopupGlossaryTerm(2752355);); gram-negative aerobes are infrequent

**Cefazolin** is the drug of choice

Although effective, Vancomycin is not recommended for routine use unless a patient has a documented history of a serious allergy to *beta*-lactams, or the propensity for MRSA infections at a particular institution necessitates its use

Neurosurgery

Although the rates of SSI after these generally clean operations are low, the morbidity and mortality of SSI, should they occur, are high.

Definitive recommendations on the role of antibiotic prophylaxis in neurosurgery cannot be made at this time

Minimally Invasive and Laparoscopic Surgery

Laparoscopic surgeries are being performed more frequently for a variety of different operations, including gynecologic, orthopedic, and biliary surgeries. This minimally invasive technique is associated with smaller wounds, fewer infectious complications, smaller inflammatory response, and therefore a better-preserved immune response to infection compared with the open surgical approach

The role of antimicrobial prophylaxis depends on preexisting patient risk factors & types of surgery performed.

Patients undergoing endoscopic retrograde cholangiopancreatography do not need antimicrobial prophylaxis unless biliary obstruction is evident.

Single 1 g dose of **Cefazolin** will suffice.

For transurethral resection of the prostate is better established. A third-generation cephalosporin such as [**ceftriaxone**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (or cotrimoxazole for severely *beta*-lactam-allergic patients) can be recommended as single-dose prophylaxis, especially for patients with nonsterile urine preoperatively or indwelling catheters

Insertion of [peritoneal dialysis](javascript:PopupGlossaryTerm(2753611);) catheters by laparoscopic technique is associated with significantly lower rates of postoperative infection. If the decision to provide antimicrobial prophylaxis is made, a single dose of **cefazolin** will suffice.

1. **Nonpharmacologic Interventions**

The most commonly cited and practiced interventions include

* Intraoperative maintenance of normothermia
* Provision of supplemental [oxygen](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6705');) in the perioperative period
* Aggressive perioperative [glucose](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6009');) control.

Core body temperature can fall by 1°C to 1.5°C (33.8–34.7°F) intraoperatively in patients under general anesthesia. Intraoperative hypothermia has been associated with impaired immune function, decreased blood flow to the surgical site, decreased tissue [oxygen](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6705');) tension, and an increased risk of SSI.

Low [oxygen](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6705');) tension in the tissues that make up the surgical site increases the risk of bacterial colonization and subsequent SSI by decreasing the efficiency of [neutrophil](javascript:PopupGlossaryTerm(2752340);) activity.

Diabetes and poor [glucose](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6009');) control are well-known [risk factors](javascript:PopupGlossaryTerm(2752404);) for SSI

However, they cannot be generalized to all types of surgeries

<http://en.wikipedia.org/wiki/Perioperative>

Perioperative period

The duration of a patient's [surgical procedure](http://en.wikipedia.org/wiki/Surgical_procedure); this commonly includes ward admission, [anesthesia](http://en.wikipedia.org/wiki/Anesthesia), surgery, and recovery

Although many clinicians are exploring the role of supplements such as [glutamine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6270');), [arginine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5665');), omega fatty acids, and nucleotides, no study to date has shown a significant reduction in postoperative infection rates using these formulations.