Chapter 146: Antimicrobial Prophylaxis in Surgery

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 49, Surgical Prophylaxis.

KEY CONCEPTS

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

2. 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.

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 (eg, cefazolin) may require intraoperative redosing during procedures that last more than 3 hours or 2.5 half-lives of the antimicrobial used.

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 (eg, cefazolin) are the mainstay for prophylaxis in most surgical procedures because of their spectrum of activity, safety, and cost.

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

BEYOND THE BOOK

BEYOND THE BOOK

Watch the video entitled "WHO: Prevention of surgical site infections (WHO Global Guidelines 2016)" at https://tinyurl.com/yyocdygz. In 2017, the World Health Organization (WHO) published global recommendations for the prevention of surgical site infections and produced this promotional video. After viewing the video, read the official press release at https://tinyurl.com/zttj3s9. These two media releases highlight the global impact of surgical site infections and the need for a world-wide approach to prevention.

INTRODUCTION

According to the National Center for Health Statistics and the National Hospital Discharge Survey, nearly 57 million outpatient and 51 million inpatient surgical procedures are performed annually in the United States.[1,2] Infection is the most common complication of surgery.[3] Surgical site infections (SSIs) occur in approximately 3% to 6% of patients and prolong hospitalization by an average of 7 days at a direct annual cost of $5 billion to $10 billion.[4,5] SSIs that involve a prosthetic joint or antimicrobial-resistant organism can cost in excess of $90,000.[6] SSIs are now the most common cause of nosocomial infections among hospitalized patients (20% of all hospital-acquired infections).[7] Incidence rates are likely under-reported, as approximately 50% of SSIs occur after hospital discharge and the Centers for Disease Control and Prevention (CDC) defines SSI as an infection affecting the surgical incision or deep tissue at the operation site that occurs up to 30 days after surgery or even up to a year after surgery for patients receiving implants.[8] Prophylactic administration of antibiotics decreases the risk of infection after many surgical procedures and represents an important component of care for this population.

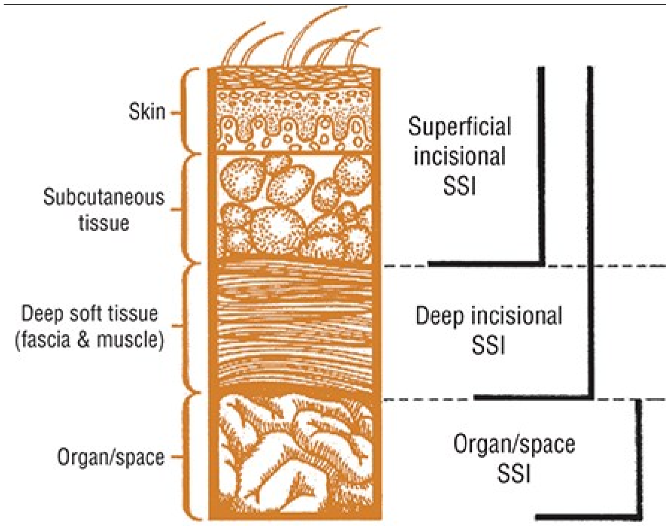
Antibiotics administered prior to the contamination of previously sterile tissues or fluids are called prophylactic antibiotics. The goal of prophylaxis is to prevent an infection from developing. Although eradication of distal (preexisting, unrelated to surgery) infections lowers the risk for subsequent postoperative infections, it does not per se constitute a prophylactic regimen. In fact, surgical prophylaxis should be prescribed concurrently under these circumstances because of important antimicrobial spectrum- and timing-related concerns. Both SSIs and hospital-acquired infections not directly related to the surgical site (eg, urinary tract infections and pneumonia) are termed *nosocomial.* Prevention of hospital-acquired infections is a major goal of antibiotic prophylaxis.

1 Presumptive antibiotic therapy is administered when an infection is suspected but not yet proven. Clinical scenarios where presumptive therapy is used commonly include acute cholecystitis, open compound fractures, and acute appendicitis of less than 24-hour duration. In these situations, if signs of perforation, contamination, or infection are absent during surgery, then routine prophylactic treatment rather than presumptive therapy is warranted. An operative finding of a gangrenous gallbladder or a perforated appendix, however, is suggestive of an established infectious process, and a therapeutic antibiotic regimen is required.[4]

According to the CDC's National Nosocomial Infections Surveillance System (NNIS),[4,7] SSIs can be categorized as either incisional (eg, cellulitis of the incision site) or organ/space (eg, meningitis; Fig. 146-1). 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. For example, a patient who develops bacterial peritonitis after bowel surgery has an organ/space SSI. 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.[4,7] Clinical signs or symptoms of SSI may include localized heat, erythema, swelling, fever, and purulent drainage from the wound.

FIGURE 146-1

Cross-section of abdominal wall depicting Centers for Disease Control and Prevention classifications of surgical site infections (SSI). (*Reprinted, with permission, from Alexander JW, Solomkin JS, Edwards MJ. Updated recommendations for control of surgical site infections. Ann Surg. 2011;253:1082–1093.*)



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

RISK FACTORS FOR SURGICAL SITE INFECTIONS

2 SSI incidence depends on both procedure- and patient-related factors. The risk for SSIs has been stratified by surgical procedure in a classification system developed by the National Research Council (NRC; Table 146-1). The NRC classification system proposes that the risk of an SSI depends on the microbiology of the surgical site, the presence of a preexisting infection, the likelihood of contaminating previously sterile tissue during surgery, and the events during and after surgery.[8,9] A patient's NRC procedure classification is the primary determinant of whether antibiotic prophylaxis is warranted. However, because a patient's NRC wound classification is influenced by surgical findings (eg, gangrenous gallbladder) and perioperative events (eg, major technique breaks), categorization generally occurs intraoperatively.[10] Colon surgery has the highest rates of SSI followed by gall bladder, cardiac, gynecologic, orthopedic, and spinal surgery. Minimally invasive approaches to surgery, when available, tend to be associated with lower rates of SSI when compared to traditional approaches to the same surgery.[8]

TABLE 146-1

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	0.8	5.1	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	1.3	10.1	Controlled opening of aforementioned tracts with minimal spillage/minor technique break; clean procedures performed emergently or with major technique breaks	Prophylactic antibiotics indicated
Contaminated	10.2	21.9	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

N/A, not applicable; SSI, surgical site infection.

[a]High-risk procedures include implantation of prosthetic materials and other procedures where SSI is associated with high morbidity (see the text).

Data from References 5 and 8.

Inherent Patient Risk

The NRC classification system does not account for the influence of underlying patient risk factors for SSI development, instead categorizing the risks for SSIs simply based on a specific surgical procedure. Certain disease states and conditions (listed in Table 146-2) are known to increase SSI risk by either increasing the length or complexity of the surgery (eg, obesity) or reducing the immune response (eg, diabetes). Preexisting distal infections increase SSI rates and should be resolved prior to surgery whenever possible. Diabetic patients have an increased risk for SSIs, especially those with uncontrolled perioperative blood sugars where risk is doubled.[11] Preoperative smoking is an independent risk factor for SSI because of the deleterious effects of nicotine on wound healing. Preoperative immunosuppression, including corticosteroid use, may also increase infection risk. Patients coinfected with human immunodeficiency virus (HIV) and hepatitis C are at approximately double the risk of SSI as the general population.[12] Malnutrition is a well-described risk factor for postoperative complications, including SSI, impaired wound and colonic anastomosis healing, and prolonged hospital stay. Although enteral feeding during the perioperative period can reduce bacterial translocation by maintaining the integrity of the intestinal mucosa, nutritional supplementation does not decrease the incidence of infection.[13] Some patient-related risk factors are potentially modifiable (glycemic control, alcohol and smoking status, preoperative albumin, and obesity). These represent opportunities for optimization prior to elective surgical procedures.[7]

TABLE 146-2

Patient and Operation Characteristics That May Influence the Risk of Surgical Site Infection

Patient	Operation
Age	Duration of surgical scrub
Nutritional status (preoperative albumin <3.5 g/dL [35 g/L])	Preoperative skin preparation
Diabetes and preoperative glycemic control	Preoperative shaving
Smoking and alcohol use	Duration of operation
Obesity	Antimicrobial prophylaxis
Coexisting infections at distal body sites	Operating room ventilation
Colonization with resistant microorganisms Altered immune response Length of preoperative stay	Sterilization of instruments Implantation of prosthetic materials Surgical drains Surgical technique

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Colonization of the nares with *S. aureus* is a well-described SSI risk factor.[4] A large multicenter study involving more than 38,000 patients undergoing more than 42,000 cardiac and orthopedic procedures showed that preoperative screening for carriers of *S. aureus* followed by intranasal mupirocin administration and chlorhexidine bathing for 5 days before surgery significantly reduced *S. aureus* SSI from 0.36% to 0.2%.[11] Although the absolute risk difference is small, this represents a 44% relative risk reduction.[8] The potential impact on patient outcomes and health resource utilization is large, given the number of surgeries performed annually. However, the logistics and cost of prescreening and treatment of colonized patients represent a challenge. Other factors shown to increase the risk of SSI are age, length of preoperative hospital stay, and obesity.[4]

Identifying SSI Risk

Two large epidemiologic studies have objectively quantified SSI risk based on specific patient- and procedure-related factors. The Study on the Efficacy of Nosocomial Infection Control (SENIC) analyzed more than 100,000 surgery cases to identify and validate risk factors for SSI.[14] Abdominal operations, operations lasting longer than 2 hours, contaminated or “dirty” procedures (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 the number of SENIC risk factors present, SSI incidence varied by as much as a factor of 15 within the same NRC operative category (Table 146-3).[15]

TABLE 146-3

Surgical Site Infection Incidence (%) Stratified by NRC Wound Classification and SENIC Risk Factors[a]

Number 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

[a]Study on the Efficacy of Nosocomial Infection Control (SENIC) risk factors include abdominal operation, operations lasting >2 hours, contaminated or dirty procedures by National Research Council (NRC) classification, and more than three underlying medical diagnoses.

N/A, not applicable; NRC, National Research Council; SENIC, Study on the Efficacy of Nosocomial Infection Control.

Data from Reference 15.

In a subsequent analysis of more than 84,000 surgical cases, the NNIS attempted to simplify and refine the SENIC system by quantifying intrinsic patient risk using the American Society of Anesthesiologists' (ASA) preoperative assessment score (Table 146-4).[16,17] An ASA score greater than or equal to 3 was a strong predictor for the development of an SSI. Other factors associated with increased SSI incidence are contaminated or "dirty" operations (NRC criteria) and surgical procedures lasting longer than average. As in the SENIC study, the SSI rate was linked to the number of risk factors present and varied considerably within NRC class. The NNIS basic SSI risk index is composed of the following criteria: ASA score = 3, 4, or 5; wound class; and duration of surgery. Overall, for 34 of the 44 NNIS procedure categories, SSI rates increased proportionally with the number of risk factors present.[8] The SSI rate was generally lower when the procedure was done laparoscopically.

TABLE 146-4

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

Data from Reference 17.

While these tools are able to broadly predict SSI risk, a more individualized approach to quantifying a patient's risk of developing an SSI is possible using the Surgical Site Infection Risk Score (SSIRS) which is a validated scoring system that incorporates both patient- and procedure-related risk factors.[18] Although evidence-based recommendations for antimicrobial prophylaxis during surgery are best established using the results of randomized clinical trials, many studies have small sample sizes and do not stratify patients according to overall SSI risk. Future studies, particularly those involving clean procedures, should be stratified by SSI risk so that the subset of high-risk patients who might benefit the most from prophylaxis is clearly established.

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) or exogenously (from contamination during the surgical procedure). Based on the type and anatomic location of the procedure and the NRC classification (see Table 146-1), resident flora can be predicted and appropriate antibiotic choices made. According to NNIS data, *S. aureus,* coagulase-negative staphylococci, enterococci, *Escherichia coli*, and *Pseudomonas aeruginosa* are the pathogens most commonly isolated (Table 146-5).[16] With the widespread use of broad-spectrum antibiotics, however, *Candida* species and methicillin-resistant *Staphylococcus aureus* (MRSA) are becoming more prevalent.[16]

TABLE 146-5

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

[a]Data reported by the National Nosocomial Infections Surveillance System from January 1992 through June 2004.

Data from Reference 5.

Factors affecting the ability of an organism to induce an SSI depend on organism count, organism virulence, and host immunocompetency. Organisms in the commensal flora generally are not pathogenic. These organisms often serve the host as a form of protection against invasive organisms that otherwise would colonize the surgical site. 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.[5]

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. Studies in animals and healthy volunteers have shown bacterial virulence to be an important determinant in the development of secondary infections.[19,20] Whereas more than one million *S. aureus* per square centimeter or gram of tissue are required to produce infection in animals, less than 100,000 *Streptococcus pyogenes* per square centimeter or gram of tissue are required at the same site.[20,21]

Impaired host defense reduces the number of bacteria required to establish an infection. A breach of normal host defenses through surgical intervention (eg, insertion of a prosthetic device) may enable organisms to cause infection. In addition, the loss of specific immune factors, such as complement activation, tissue-derived inhibitors (eg, proinflammatory cytokines), cell-mediated response (eg, T-cell function), and granulocytic or phagocytic function (eg, neutrophils or macrophages), can greatly increase the risk for SSI development.[22] Vascular occlusive states related to the surgical procedure or those occurring from hypovolemic shock can greatly affect blood flow to the surgical site, thus diminishing host defense mechanisms against microbial invasion. Traumatized tissue, hematomas, and the presence of foreign material also lead to more infections. When a foreign body is introduced during a surgical procedure, fewer than 100 bacterial colony-forming units are required to cause an SSI.[23] Studies examining *S. aureus*-contaminated wound infections on the skin of healthy volunteers demonstrate a 10,000-fold reduction in the number of organisms required to establish a wound infection if sutures are not present.[19]

ANTIMICROBIAL RESISTANCE AND STEWARDSHIP

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. The most common cause of nosocomially acquired multiresistant organisms is transmission from hospital personnel.[24] Patients treated with broad-spectrum antibiotic therapy are at increased risk for colonization with hospital flora.

With cephalosporins established as first-line agents for prophylaxis, organisms resistant to cephalosporins represent the majority of pathogens causing SSIs. MRSA and coagulase-negative staphylococci have emerged as the most common pathogens in patients who develop SSIs despite prophylaxis with cephalosporins particularly in cardiothoracic, vascular, orthopedic, and neurologic surgery. Methicillin resistance not only limits the treatment/-prophylaxis options available, but it also is associated with increased mortality, longer hospital lengths of stay, and increased costs. Although the use of vancomycin for prophylaxis may be appropriate for some operations performed in hospitals with a high rate of infection due to MRSA, there is little guidance on what constitutes a “high rate” of MRSA infection and whether providing prophylaxis with vancomycin alone will result in fewer SSIs.[25] A more effective strategy would be to screen elective surgical candidates for MRSA colonization preoperatively. MRSA colonization is predictive of MRSA SSI and thus effective prophylaxis with vancomycin is then reserved for carriers only. Some single center studies evaluating the decolonization of MRSA carriers preoperatively (ie, with intranasal mupirocin, chlorhexidine showers) have yielded mixed results and may not be cost-effective.[25]

The increase in frequency of fungal infections in surgical patients has drawn concern. In hospitalized patients, the incidence of nosocomial *Candida* infections nearly doubled from 1992 to 2004.[16,26] Overzealous use of broad-spectrum antibiotics is the most likely cause for this increase. A study of patients undergoing cardiovascular surgery identified female sex, length of stay in the ICU, and duration of central venous catheterization as risk factors for postoperative *Candida* infections. 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.[26]

Antimicrobial stewardship programs are typically run by multidisciplinary teams in hospitals to promote responsible antimicrobial use and optimize antimicrobial therapy through multimodal educational and clinical interventions with an aim to reduce antimicrobial resistance and infection-related morbidity and mortality. Systematic reviews suggest that these programs are effective in reducing the development of antimicrobial resistance and hospital-acquired infections.[27] Typically antimicrobial stewardship programs target areas of the hospital where there is high use of antimicrobials but surgical units and operating rooms are often overlooked. Given that approximately 15% of all antimicrobials prescribed in hospital are for surgical prophylaxis and the opportunity to improve the outcomes of surgical patients with respect to SSIs, surgical units would benefit from antimicrobial stewardship programs and surgeons should be part of the multidisciplinary team.[28] Table 146-7

SCHEDULING ANTIBIOTIC ADMINISTRATION

3 4 The following principles must be considered when providing antimicrobial surgical prophylaxis: (a) the agents should be delivered to the surgical site prior to the initial incision, and (b) bactericidal antibiotic concentrations should be maintained at the surgical site throughout the surgical procedure. Although animal and human models have demonstrated the efficacy of a single dose of an antibiotic administered just prior to bacterial contamination, long operations often require intraoperative doses of antibiotics to maintain adequate concentrations at the surgical site for the duration of surgery.[29] Antibiotic administration should be completed within 60 minutes prior to the initial incision, preferably at the time of anesthetic induction. Since the administration duration varies between antimicrobials, this needs to be considered when determining when to start the infusion. Administration of antibiotics too early may result in concentrations below the minimum inhibitory concentration (MIC) toward the end of the operation, and administration too late leaves the patient unprotected at the time of initial incision. In a study examining the timing of antibiotic administration to 2,847 patients receiving prophylaxis, Classen et al.[29] evaluated patients who received prophylaxis early (2-24 hours before surgery), preoperative prophylaxis (0-2 hours prior to surgery), perioperative prophylaxis (up to 3 hours after first incision), and postoperative prophylaxis (greater than 3 hours after the first incision). The risk of infection was lowest (0.6%) for patients who received preoperative prophylaxis, moderate (1.4%) for those who received perioperative antibiotics, and greatest for those who received postoperative antibiotics (3.3%) or preoperative antibiotics too early (3.8%). The risk for an SSI increases dramatically with each hour from the time of initial incision to the time when antibiotics are eventually administered. For these reasons, prophylactic antibiotics should not be prescribed to be given “on call to the operating room (OR),” which can occur two or more hours prior to the initial incision, nor should concurrent therapeutic antibiotics be relied on to provide adequate protection. In both situations, the chance for improperly timed doses is high. Although the landmark study by Classen et al.[29] confirmed that antimicrobial prophylaxis should be administered within 2 hours prior to the initial incision, administration 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 randomized controlled trial in Switzerland, hospitalized surgical patients were randomized to early (in the anesthesia room) or late (in the operating room) prophylactic antimicrobials.[30] A total of 2,589 patients in the early group received their antimicrobials a median of 42 minutes prior to the incision while 2,586 patients in the late group received their antimicrobials a median of 16 minutes prior to the incision. All patients received cefuroxime (plus metronidazole for colorectal surgery) as a single dose except for long operations where the cefuroxime (and metronidazole for colorectal surgery) was readministered every 4 hours during the operation. SSIs were 5% in both groups suggesting that the current recommendation to administer surgical prophylaxis within 60 minutes prior to the incision is adequate.

Despite the importance of appropriately timed prophylactic antibiotic therapy, many patients receive antibiotics outside of the optimal time window in relation to surgery. Potential barriers include antibiotics ordered after the patient has arrived in the OR, delayed antibiotic preparation or delivery, and use of antibiotics that require long infusion times. One retrospective study assessed the timing of prophylactic antibiotics in more than 32,000 patients and found that 91.9% of patients received an antibiotic dose within 60 minutes of the initial surgical incision.[31]

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. Proponents of administering a second antibiotic dose during lengthy operations suggest that the risk for SSI is just as great at the end of surgery (during wound closing) as it is during 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.[5] 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.[32] 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.[33] Ideally antibiotic prophylaxis should be repeated when surgeries last longer than two half-lives of chosen antibiotic (ie, 4 hours for cefazolin) or if intraoperative blood loss exceeds 1.5 L.[7]

One strategy to ensure appropriate redosing of prophylactic antibiotics during long operations is use of a visual or auditory reminder system. One hospital reported its experience with such a system, finding that an automated reminder improved compliance and reduced SSIs. However, even with the reminder system, intraoperative redosing was done in only 68% of eligible patients.[34] Although optimizing the efficacy of antimicrobial prophylaxis is often the main focus of guideline documents, equal emphasis should be placed on avoidance of harms associated with unnecessary or prolonged courses of prophylactic antibiotics. A recent cohort study of more than 79,000 patients suggests that prolonged courses of prophylactic antibiotics (eg, more than 24-hour post–skin closure) was associated with higher risks of acute kidney injury and *C. difficile* infection without further reducing the rates of SSIs.[35]

ANTIMICROBIAL CHOICE

5 The choice of prophylactic antibiotic depends on the type of surgical procedure, the most frequent pathogens seen with this procedure, safety and efficacy profiles of the antimicrobial agent, current literature evidence supporting its use, and cost. 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 (eg, upper respiratory, GI, or genitourinary tract) and whether the operation will transect a hollow viscous or mucous membrane that may contain resident flora.[4]

Although antimicrobial prophylaxis can be administered through a variety of routes (eg, oral, topical, or intramuscular), the parenteral route is favored because of the reliability by which adequate tissue concentrations may be acheived.[36] 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.[4,5,10] In cases where broader gram-negative and anaerobic coverage is desired, antianaerobic cephalosporins, such as cefoxitin and cefotetan, are appropriate choices. Although third-generation cephalosporins (eg, 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.[4,5,10]

Allergic reactions are the most common side effects associated with cephalosporin use. Reactions can range from minor skin manifestations at the site of infusion to rash, pruritus, and rarely anaphylaxis (less than 0.02%). The structural similarity between penicillins and cephalosporins (each contains a β-lactam ring) has led to considerable confusion about the cross-allergenicity between these two classes of drugs. Twenty percent of the general population is labeled "penicillin allergic," yet of these patients, only 10% to 20% have positive results of a penicillin skin test.[37] The rate of cross-reactivity with cephalosporins is approximately 2%, but as only 20% of all "penicillin-allergic" patients truly are penicillin allergic, the true incidence of cross-reactivity likely is less than 1%. Routine penicillin skin testing is not cost-effective.[37] 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 can be considered for prophylactic therapy in surgical procedures involving implantation of a prosthetic device in which the rate of MRSA is high.[38] If the risk of MRSA is low, and a β-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.[39] 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 β-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.

Because inappropriate prophylactic antibiotic use not only can induce antibiotic resistance but also can negatively affect an institution's antibiotic budget, initiatives to curtail inappropriate antibiotic use have become the focus of many drug use evaluation efforts. 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. Individualized institutional guidelines that take into account the best literature evidence, institution-based antibiotic susceptibility data, and surgeon preference are important tools for rationalizing antibiotic prophylaxis use.[40] This also highlights a potential role for antimicrobial stewardship.

RECOMMENDATIONS FOR SPECIFIC TYPES OF SURGERY

Guidelines for surgical prophylaxis usually are structured according to the tissues affected during an operation. Although many different surgical procedures may be performed at any one anatomic site, this method of categorization still is optimal because the factors related to the success of a prophylactic regimen, such as the endogenous flora that are expected and the pharmacokinetics, pharmacodynamics, and spectrum of selected antimicrobials, generally, are constant for a particular surgical site (see the discussion above). The choice of antimicrobial prophylaxis is always best evaluated using the results of properly conducted clinical trials. 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.

6 A comprehensive review of the surgical prophylaxis literature is beyond the scope of this chapter, but important factors are reviewed here for common types/sites of surgery. Specific recommendations are summarized in Table 146-6. The reader is referred to published guidelines and review articles.[3-5,10,36,41]

TABLE 146-6

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 1 g × 1	High-risk patients only (obstruction, hemorrhage, malignancy, acid suppression therapy, morbid obesity)	IA
Bariatric surgery	Enteric gram-negative bacilli, gram-positive cocci, oral anaerobes	Cefazolin 2 g x 1	Intraoperative redosing required for procedures longer than 4 hours	IB
Cholecystectomy	Enteric gram-negative bacilli, anaerobes	Cefazolin 1 g × 1 for high-risk patients; Laparoscopic: controversial	High-risk patients only (open biliary tract procedures, 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 × 1	Longer-acting cephalosporins preferred	IA
Appendectomy	Enteric gram-negative bacilli, anaerobes	Cefoxitin or cefotetan 1 g × 1 or cefazolin 1 g plus metronidazole 1 g × 1	Second intraoperative dose of cefoxitin may be required if procedure lasts longer than 3 hours	IA

Colorectal	Enteric gram-negative bacilli, anaerobes	Orally: neomycin 1 g + erythromycin base 1 g at 1, 2, and 11 PM 1 day preoperatively plus mechanical bowel preparation IV: cefoxitin or cefotetan 1 g × 1	Role of mechanical bowel preparation is controversial. It is widely used despite evidence suggesting it may have no effect on SSI or other clinical outcomes	IA
GI endoscopy	Variable, depending on procedure, but typically enteric gram-negative bacilli, gram-positive cocci, oral anaerobes	Orally: amoxicillin 2 g × 1 IV: ampicillin 2 g × 1 or cefazolin 1 g × 1	Recommended only for high-risk patients undergoing high-risk procedures (see the text)	IA
Urologic Surgery				
Prostate resection, shock-wave lithotripsy, ureteroscopy	*E. coli*	Ciprofloxacin 500 mg orally or Trimethoprim–sulfamethoxazole 1 DS tablet	All patients with positive preoperative 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 the text)	IB
Gynecological Surgery				
Cesarean section	Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci	Cefazolin 1 g × 1 (<80 kg), Cefazolin 2 g x 1 (>80 kg). Add azithromycin 500 mg IV × 1 if non-elective procedure	Antimicrobial administration should be prior to the initial incision as opposed to after umbilical cord clamping	IA
Hysterectomy	Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci	Vaginal: cefazolin 2 g × 1 (3 g if >120 kg) Abdominal: cefotetan 1 g × 1 or cefazolin 2 g × 1	Metronidazole 1 g IV × 1 is recommended alternative for penicillin allergy	IA
Head-and-Neck Surgery				
Maxillofacial surgery	*Staphylococcus aureus*, streptococci spp., 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 spp., oral anaerobes	Clindamycin 600 mg at induction and every 8 hours × 2 more doses	Ampicillin/sulbactam 3 g for clean–contaminated procedures	IA
Cardiothoracic Surgery				
Cardiac surgery	*S. aureus*, *S. epidermidis*, *Corynebacterium*	Cefazolin 1 g every 8 hours × 48 hours	Patients >80 kg (176 lb) should receive 2 g of cefazolin instead; in areas with	IA

		Intranasal mupirocin twice daily for 5 days preoperatively for patients colonized with *S. aureus*	high prevalence of *S. aureus* resistance, vancomycin should be considered	
Thoracic surgery	*S. aureus*, *S. epidermidis*, *Corynebacterium*, enteric gram-negative bacilli	Cefuroxime 750 mg IV every 8 hours × 48 hours	First-generation cephalosporins are deemed inadequate, and shorter durations of prophylaxis have not been adequately studied	IA
Vascular Surgery				
Abdominal aorta and lower extremity vascular surgery	*S. aureus*, *S. epidermidis*, enteric gram-negative bacilli	Cefazolin 1 g at induction and every 8 hours × 2 more doses	Although complications from infections may be infrequent, graft infections are associated with significant morbidity	IB
Orthopedic Surgery				
Joint replacement	*S. aureus*, *S. epidermidis*	Cefazolin 1 g × 1 preoperatively, then every 8 hours × 2 more doses. Intranasal mupirocin twice daily for 5 days preoperatively for patients colonized with *S. aureus*	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 × 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-negativebacilli, polymicrobial	Cefazolin 1 g × 1 preoperatively, then every 8 hours for a course of presumed infection	Gram-negative coverage (ie, gentamicin) often indicated for severe open fractures	IA
Neurosurgery				
CSF shunt procedures	*S. aureus*, *S. epidermidis*	Cefazolin 1 g every 8 hours × 3 doses or ceftriaxone 2 g × 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 × 1	Limited number of clinical trials comparing different treatment regimens	IB
CSF shunt procedures	*S. aureus*, *S. epidermidis*	Cefazolin 1 g every 8 hours × 3 doses or ceftriaxone 2 g × 1	No agents have been shown to be better than cefazolin in randomized comparative trials	IA
Craniotomy	*S. aureus*, *S. epidermidis*	Cefazolin 1 g × 1 or cefotaxime 1 g × 1	Vancomycin 1 g IV × 1 can be substituted for patients with penicillin allergy	IA

CSF, cerebrospinal fluid; DS, double strength.

[a]One-time doses are optimally infused at induction of anesthesia except as noted. Repeat doses may be required for long procedures. See the text for references.

[b]Strength of recommendations: Category IA: Strongly recommended and supported by well-designed experimental, clinical, or epidemiologic studies. Category IB: Strongly recommended and supported by some experimental, clinical, or epidemiologic studies and strong theoretical rationale. Category II: Suggested and supported by suggestive clinical or epidemiologic studies or theoretical rationale.

Gastrointestinal 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.[4]

Gastroduodenal Surgery

Insignificant numbers of bacteria usually are found in the stomach and duodenum because of their acidity. The rate of SSIs in gastroduodenal surgery generally is low, so procedures in this region can be classified as clean. The risk for an SSI in this population increases with any condition that can lead to bacterial overgrowth, such as obstruction, hemorrhage, or malignancy, or increasing the pH of gastroduodenal secretions with concomitant acid suppression therapy. Antimicrobial prophylaxis is of clinical benefit only in this high-risk population. In most cases, a single IV dose of cefazolin will provide adequate prophylaxis.[10] 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, depending on whether an established infection is present.

Use of antibiotic prophylaxis for percutaneous endoscopic gastrostomy placement is also warranted. Postoperative peristomal infection can occur in up to 30% of patients and a systematic review of 12 trials involving 1,271 patients found a significant reduction in peristomal infections with antimicrobial prophylaxis (OR 0.36, 95% CI 0.26-0.50).[42] A single dose of cefazolin given 30 minutes preoperatively is preferred over longer regimens.

There are few well-designed clinical trials of antimicrobial prophylaxis in bariatric surgery (ie, Roux en Y gastric bypass, gastric banding, sleeve gastrectomy). However, given that obesity is a consistently identified risk factor for SSIs, guidelines do promote antimicrobial prophylaxis with cefazolin as this is the agent that has been most studied.[43] Dosing is still controversial, but at higher doses is generally recommended based on greater volumes of distribution in morbidly obese patients.[10] Pharmacokinetic studies suggest that 2 g of cefazolin provided adequate tissue levels for 4.8 hours.[43]

Hepatobiliary Surgery

Although bile normally is sterile, and the SSI rate after biliary surgery is low, antibiotic prophylaxis is of benefit in this population. Bile contamination (bactobilia) can increase the frequency of SSIs and is present in many patients (eg, those with acute cholecystitis or biliary obstruction and those of advanced age).[41] In general, however, the correlation between bactobilia in surgical specimens and the subsequent pathogens implicated in an SSI is poor. The most frequently encountered organisms are *E. coli*, *Klebsiella* species, and enterococci. *Pseudomonas* is an uncommon finding in the absence of cholangitis. Most of the SSI literature on biliary tract surgery pertains to cholecystectomy while more recent trials pertain to laparoscopic procedures which have eclipsed the traditional open cholecystectomy because of a reduction in recovery time and hospital stay. The evidence in open cholecystectomy strongly supports the use of antimicrobial prophylaxis while the evidence for laparoscopic procedures is less impressive.[10] Trials comparing first-, second-, and third-generation cephalosporins have not demonstrated benefit over single-dose cefazolin prophylaxis even in high-risk patients (eg, age greater than 60 years, previous biliary surgery, acute cholecystitis, jaundice, obesity, diabetes, and common bile duct stones).[44] Ciprofloxacin and levofloxacin are effective alternatives for β-lactam-allergic patients undergoing open cholecystectomy.[45,46] In fact, oral levofloxacin appears to provide similar intraoperative gallbladder tissue concentrations.[46] For patients undergoing elective laparoscopic cholecystectomy, antibiotic prophylaxis has traditionally not been recommended but newer trials and systematic reviews are conflicting and assessments of current practice are reflective of this.[47,48] Detection of an active infection during surgery (eg, gangrenous gallbladder and suppurative cholangitis) is an indication for a course of postoperative therapeutic antibiotics. The risk for SSIs in cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt surgery may be reduced with a single prophylactic dose of ceftriaxone,[49] but not with single doses of shorter-acting cephalosporins.[50]

Appendectomy

Acute appendicitis can be broadly categorized as complicated (evidence of perforation, gangrene, peritonitis, or abscess formation) or uncomplicated. Complicated appendicitis should be treated as an active intra-abdominal infection. While appendectomy for uncomplicated appendicitis is more common it has been associated with SSI rates of 9% to 30% in the absence of antimicrobial prophylaxis. Randomized controlled trials do suggest that preoperative antimicrobials are effective at reducing this risk and should be administered in all cases.[51] Numerous antibiotic regimens, all with activity against gram-positive and gram-negative aerobes and anaerobic pathogens, are effective in reducing SSI incidence.[41] A cephalosporin with antianaerobic activity, such as cefoxitin or cefotetan, is recommended as first-line therapy; however, a comparative trial of cefoxitin and cefotetan suggests that cefotetan may be superior, possibly because of its longer duration of action.[52] Alternatively, cefazolin in combination with metronidazole is also effective. In patients with β-lactam allergy, metronidazole in combination with gentamicin is an effective regimen. Broad-spectrum antibiotics covering nosocomial pathogens (eg, *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 redosing if the procedure extends beyond 3 hours.

Colorectal Surgery

In the absence of adequate prophylactic therapy, the risk for SSI after colorectal surgery is high (5.4%-23.2%) because of the significant bacterial counts in fecal material present in the colon (frequently greater than 10^9 per gram).[53] Anaerobes and gram-negative aerobes predominate, but gram-positive aerobes also may play an important role. Reducing this bacterial load with a thorough bowel preparation regimen (4 L of polyethylene glycol solution or 90 mL of sodium phosphate solution administered orally the day before surgery) is controversial; however, 99% of US surgeons in a survey routinely use mechanical preparation.[54] The presumed value of a mechanical bowel preparation goes beyond its effect on SSIs as it is also thought to facilitate bowel manipulation, enable safe passage of surgical instruments, and allow for intraoperative colonoscopy if needed. A randomized trial of 380 patients undergoing elective colorectal surgery suggests that SSIs are not reduced by preoperative mechanical bowel preparation.[55] This finding was confirmed in two meta-analyses showing that mechanical bowel preparation does not reduce the risk of anastomotic leakage or other complications, including postoperative infection.[56,57] Despite this new evidence, mechanical bowel preparations continue to be a standard of practice prior to elective bowel surgery.

Risk factors for SSIs include age over 60 years, hypoalbuminemia, poor preoperative bowel preparation, corticosteroid therapy, malignancy, and operations lasting longer than 3.5 hours.[10] Antimicrobial prophylaxis reduced mortality from 11.2% to 4.5% in a pooled analysis of trials comparing antimicrobial prophylaxis with no prophylaxis for colon surgery.[58] Effective antibiotic prophylaxis consisting of an oral and IV regimen reduces even further the risk for an SSI. A Cochrane review comparing oral, IV, and combination regimens found that while each one was more effective at reducing SSI than placebo, combination therapy (oral and IV) was superior to oral regimens alone (OR 0.52 [0.35, 0.76]) and IV regimens alone (OR 0.55 [0.43, 0.71]).[59] This finding was confirmed by a systematic review of 14 trials, and now clinical practice guidelines from the American Society of Colon and Rectal Surgeons recommends the combination of oral antibiotics and mechanical bowel preparation preoperatively in addition to intravenous antibiotics at the time of surgery.[53,60]

Several oral regimens designed to reduce bacterial counts in the colon have been studied.[41] The combination of 1-g neomycin and 1-g erythromycin base given orally 19, 18, and 9 hours preoperatively is the regimen most commonly used in the United States.[60] Neomycin is poorly absorbed but provides intraluminal concentrations that are high enough to effectively kill most gram-negative aerobes. Oral erythromycin is only partially absorbed but still produces concentrations in the colon that are sufficient to suppress common anaerobes. If surgery is postponed, the antibiotics must be readministered to maintain efficacy. Optimally, the bowel preparation regimen (if used) should be completed prior to starting the oral antibiotic regimen. This is of particular concern because most procedures now are performed electively on a “same-day surgery” basis. In this case, the bowel preparation regimen is self-administered by the patient at home on the day prior to hospital admission, and compliance cannot be monitored carefully.

Single-dose cephalosporins are the most used and studied preoperative IV antimicrobial. Cefoxitin or cefotetan is used most commonly, but other second- and some third-generation cephalosporins also are effective.[61] The role of metronidazole in combination with cephalosporin therapy is unclear. Only retrospective evidence suggests that the addition of metronidazole to a cephalosporin or extended-spectrum penicillin provides additional benefit.[62] Until this finding is confirmed in prospective studies, metronidazole should be reserved for combination therapy with cephalosporins with poor anaerobic coverage (eg, cefazolin). At this time, the evidence recommending the addition of metronidazole to cephalosporins with anaerobic activity (eg, cefotaxime, cefoxitin, and ceftriaxone) is insufficient.[63] For β-lactam-allergic patients, perioperative doses of gentamicin and metronidazole have been used. Postoperative antibiotics generally are unnecessary in the absence of any untoward events or findings during surgery. IV antibiotics are required for colostomy reversal and rectal resection because enterally administered antibiotics will not reach the distal segment that is to be reanastomosed or resected.[64]

Gastrointestinal Endoscopy

Despite the large number of endoscopic procedures performed each year, the rate of postprocedural infection is relatively low. The highest bacteremia rates have been reported in patients undergoing esophageal dilation for stricture or sclerotherapy for management of esophageal varices. Although postprocedural bacteremia can occur in as many as 22% of patients, the bacteremia usually is transient (less than 30 minutes) and rarely results in clinically significant infection. Therefore, antimicrobial prophylaxis is routinely recommended only for high-risk patients (eg, patients with prosthetic heart valves, a history of endocarditis, systemic-pulmonary shunt, synthetic vascular graft less than 1-year-old, complex cyanotic congenital heart disease, obstructed bile duct, or liver cirrhosis, as well as immunocompromised patients) undergoing high-risk procedures (eg, stricture dilation, variceal sclerotherapy, and endoscopic retrograde cholangiopancreatography, ERCP).[65] 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 or cefazolin). A meta-analysis of antimicrobial prophylaxis for endoscopic placement of percutaneous feeding tubes also suggests that a single preoperative dose of antibiotics reduces the risk of postoperative infection compared with no antibiotic (6.4% vs 24%).[66] Consensus guidelines have adopted this recommendation and suggest a single dose of cefazolin within 30 minutes prior to the procedure.[65]

Urologic Surgery

Preoperative bacteriuria is the most important risk factor for development of an SSI after urologic surgery. All patients should have a preoperative urinalysis and should receive therapeutic antibiotics if bacteriuria is detected. Patients undergoing clean urologic procedures with sterile urine preoperatively are at low risk for developing an SSI, and antimicrobial prophylaxis is not recommended.[10] Antibiotic prophylaxis is recommended for all patients undergoing transurethral resection of the prostate or bladders tumors, shock-wave lithotripsy, percutaneous renal surgery, or ureteroscopy.[67] The exact incidence of SSIs in this population is obscured by the frequent use of postoperative urinary catheters and the subsequent risk of bacteriuria. *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, but the ability to administer fluoroquinolones orally rather than IV makes antimicrobial prophylaxis with ciprofloxacin easier and less expensive.[68] First- or second-generation cephalosporins are considered the antimicrobial agents of choice for patients undergoing open or laparoscopic procedures involving entry into the urinary tract and any urologic surgical procedures involving the intestine, rectum, vagina, or implanted prosthesis.[67] The evidence supporting antimicrobial prophylaxis for the removal of external urinary catheters, cystography, urodynamic studies, simple cystourethroscopy, and open or laparoscopic urologic procedures that do not involve entry into the urinary tract is not as evident. Only patients considered to have risk factors (patients of advanced age; those with anatomic anomalies, poor nutritional history, externalized catheters, colonized endogenous/exogenous material, or distant coexistent infection; smokers; immunocompromised patients; and those who are hospitalized for a prolonged stay) should receive antimicrobial prophylaxis.[67]

Obstetric and Gynecologic Surgeries

Cesarean Section

Cesarean section is the most frequently performed surgical procedure in the United States.[10] Prophylactic antibiotics are given to prevent endometritis, the most commonly occurring SSI. In the past, antibiotics were recommended for only high-risk patients, including those with premature membrane rupture or those not receiving prenatal care. Several large trials, as well as a meta-analysis of 95 trials, have shown benefit in administering prophylactic antibiotics to all women undergoing emergent or elective cesarean section regardless of their underlying risk factors.[69] Cefazolin remains the drug of choice despite the wide spectrum of potential pathogens, and a single 2-g dose for patients weighing 80 kg or more and a single 1-g dose for patients weighing less than 80 kg is recommended.[70] For patients with a β-lactam allergy, preoperative metronidazole is an acceptable alternative.[69] In women undergoing nonelective cesarean section, a composite outcome of endometritis, wound infection, or other infection occurring within 6 weeks was 6.1% in women who received extended spectrum coverage with azithromycin plus cefazolin versus 12% in those who received cefazolin alone.[71] This study makes a strong argument for extending the spectrum of coverage with azithromycin in addition to the standard cephalosporin regimen for patients undergoing nonelective cesarean section.

During a cesarean section, unlike other surgical procedures, the most appropriate timing of antibiotic administration has been a source of controversy. 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 infection and induce antimicrobial resistance. The most recent CDC guidelines suggest that high-quality evidence supports antimicrobial administration at the time of the initial incision instead of at the time of umbilical cord clamping.[4] A meta-analysis of seven randomized controlled trials reports a 43% reduction in postpartum endometritis without an increase in neonatal sepsis or antimicrobial resistance.[4]

Hysterectomy

The most important factor affecting the incidence of SSI after hysterectomy is the type of procedure performed. Vaginal hysterectomies are associated with a high rate of postoperative infection when performed without the benefit of prophylactic antibiotics because of the polymicrobial flora normally present at the operative site.[72] As with cesarean sections, cefazolin is the drug of choice for vaginal hysterectomies despite the wide spectrum of possible pathogens.[72] The American College of Obstetricians and Gynecologists (ACOG) recommends a single dose of either cefazolin or cefoxitin.[73] For patients with a β-lactam allergy, a single preoperative dose of either metronidazole or doxycycline also is effective.[73]

Prophylactic antibiotics are recommended for abdominal hysterectomy despite the lack of bacterial contamination from the vaginal flora. Single-dose cefotetan was superior to single-dose cefazolin,[74] and the investigators suggested that cefotetan should be the drug of choice for abdominal hysterectomies. However, other investigators suggested that either agent is appropriate, provided 24 hours of antimicrobial coverage is not exceeded.[10] The ACOG guidelines suggest that first- (such as cefazolin), second- (such as cefotetan), or third-generation cephalosporins can be used for prophylaxis.[73] Metronidazole plus an aminoglycoside or fluoroquinolone is also effective and can be used if patients are allergic to β-lactam antibiotics. Antibiotic prophylaxis may not be required in laparoscopic gynecologic surgery or tubal microsurgery.[75] As with other surgical procedures, perioperative events and findings may require the use of therapeutic antibiotics after surgery.

Head-and-Neck Surgery

The use of prophylactic antibiotics during head-and-neck surgery depends on the procedure type. Clean procedures (per NRC definition), such as thyroidectomy, lymph node excision, and simple tooth extraction, are associated with a low incidence of SSI. Antimicrobial prophylaxis is not recommended for these procedures. Head-and-neck surgeries involving an incision through a mucosal layer are associated with a higher risk for SSI but antimicrobial prophylaxis is not always associated with a reduction in SSI (ie, adenoidectomy, tonsillectomy, and septoplasty).[10] The normal flora of the mouth is polymicrobial; both anaerobes and gram-positive aerobes predominate. Although typical doses of cefazolin usually are ineffective for anaerobic infections, a 2-g dose produces concentrations high enough to inhibit these organisms. A single dose of clindamycin is adequate for prophylaxis in maxillofacial surgery unless the procedure lasts longer than 4 hours, when a second dose should be administered intraoperatively.[76] The greatest evidence for antimicrobial prophylaxis is in head-and-neck cancer resection surgeries. 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. Ampicillin/sulbactam is preferred to clindamycin to cover aerobic, anaerobic, and gram-negative bacteria in clean–contaminated oncologic surgery.[77] Topical therapy with clindamycin, amoxicillin–clavulanate, and ticarcillin–clavulanate has been described in small trials, but the exact role of topical antibiotics is not defined.[78] Antimicrobial prophylaxis is not indicated for endoscopic sinus surgery without nasal packing.[36]

Cardiothoracic Surgery

Although cardiac surgery generally is considered a clean procedure, antibiotic prophylaxis lowers SSI incidence.[41] The substantial morbidity related to an SSI in this population, coupled with the routine implementation of prosthetic devices, further justifies the routine use of prophylaxis.[79] Patients who develop SSIs after coronary artery bypass graft surgery have a mortality rate of 22% at 1 year compared with 0.6% for those who do not develop an SSI.[80] Risk factors for developing an SSI after cardiac surgery include obesity, renal insufficiency, connective tissue disease, reexploration for bleeding, and poorly timed administration of antibiotics.[79] Skin flora pathogens predominate; gram-negative organisms are rare.

Cefazolin has been studied extensively and is considered the drug of choice. Although several studies and a meta-analysis advocate the use of second-generation cephalosporins (eg, cefuroxime) rather than cefazolin, various methodologic flaws in these studies have limited the extrapolation of these results to practice. Cefazolin was as effective as cefuroxime in a large, randomized trial of 702 patients undergoing open heart surgery and thus remains the standard of care.[81] Both patient weight and timing of cefazolin administration relative to surgery must be considered when developing a dosing strategy. Patients weighing greater than 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.[77] 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.[82]

7 Routine vancomycin administration may be justified in hospitals having a high incidence of MRSA or when sternal wounds are to be explored surgically for possible mediastinitis. However, a large comparative trial enrolling almost 900 patients in a single center with a high prevalence of MRSA infections found that both cefazolin and vancomycin had similar efficacy in preventing SSI in patients undergoing cardiac surgery that required sternotomy.[83] Mediastinitis constitutes a failure of a prior prophylactic regimen. Continued postoperative vancomycin should be guided by culture and sensitivity data.[37] Subsequent antibiotic therapy is guided by intraoperative findings.

Since *S. aureus* is routinely identified as the most common pathogen in SSIs after cardiac surgery, several studies have investigated alternative methods for preoperative eradication including nasal mupirocin administration (ie, twice daily for 5 days preoperatively) and chlorhexidine body wash (ie, daily preoperatively for up to 5 days). A bundled approach (ie, more than one intervention implemented together) in addition to preoperative antimicrobials appears to further reduce the risk of postoperative SSI in both cardiac and orthopedic surgeries.[11,84]

Pulmonary resection is associated with significant SSI risk, and prophylactic antibiotics have an established role in preventing postoperative infectious morbidity. Pleuropulmonary infections are much more common than wound infections, and pathogenic organisms likely migrate from the oral cavity or pharynx.[85] First-generation cephalosporins are inadequate; 48 hours of cefuroxime is preferred. A regimen of ampicillin–sulbactam is superior to first-generation cephalosporins, but further studies are required before this agent can be recommended as first-line prophylactic therapy.[86]

Vascular Surgery

Vascular surgery, like cardiac surgery, generally is considered clean by NRC criteria. Although vascular graft infections occur infrequently (3%-5%), the associated morbidity and mortality are extensive because treatment often requires surgical graft removal along with therapeutic antibiotic therapy.[87] Prophylactic antibiotics are of benefit, particularly for procedures involving the abdominal aorta, lower extremities, or the implantation of prosthetic devices. Cefazolin is regarded as the drug of choice. Twenty-four hours of prophylaxis with cefazolin is adequate; longer courses may lead to bacterial resistance.[88] For patients with β-lactam allergy, 24 hours of oral ciprofloxacin was effective.[87]

Orthopedic Surgery

Most orthopedic surgery is clean by definition; thus, prophylactic antibiotics generally are indicated only when prosthetic materials (eg, pins, plates, and artificial joints) are implanted.[23] A late-occurring infectious complication in this surgical population can result in substantial morbidity and may lead to prosthesis failure and subsequent removal. Staphylococci species are the most frequently encountered pathogens; gram-negative aerobes are infrequent. The use of cefazolin is supported by substantial evidence in the literature and therefore is the prophylactic agent of choice. Vancomycin, although effective, is not recommended for routine use unless a patient has a documented history of a serious allergy to β-lactams, or the propensity for MRSA infections at a particular institution necessitates its use. The current recommended duration of prophylaxis for joint replacement and hip fracture surgery is 24 hours.[10] Antibiotic-impregnated cement and beads have been used to lower SSI rates, but conclusive data regarding their efficacy are lacking.[23]

Duration of prophylaxis for the surgical repair of long bone fractures depends on the nature of the fracture. Multiple doses of prophylactic antibiotics offer no advantage over a single preoperative dose for repair of closed bone fractures and is more cost effective.[89,90] Patients suffering open (compound) fractures are particularly susceptible to infection because bacterial contamination almost always has occurred already. Under these circumstances, the use of antibiotics is presumptive. In this setting, cefazolin often is combined with an aminoglycoside, but controlled trials are lacking.[91] A clinical trial comparing clindamycin and cloxacillin suggests that clindamycin is superior and may be appropriate as monotherapy for Gustilo type I and II open fractures but not for type III fractures, for which added gram-negative activity is recommended.[92] Duration of antibiotic therapy is highly variable and depends on surgical findings during debridement, results of intraoperative cultures, and clinical status. A prospective trial and subsequent systematic review comparing short (less than 24 hours) and long (greater than 24 hours) courses of antimicrobial prophylaxis for severe trauma suggests that longer courses of antibiotics do not offer additional benefit and may be associated with the development of resistant infections.[93] However, established joint infections and osteomyelitis require an extended course of therapeutic antibiotics.

As in cardiac surgery, there is evidence to support the use of preoperative intranasal mupirocin and chlorhexidine body wash for patients colonized with *S. aureus*. For elective procedures, patients would be instructed to administer these at home in the days prior to the surgery. This bundled approach appears to further reduce the risk of postoperative SSI in addition to preoperative antimicrobials.[11,84]

Neurosurgery

The rates of SSI after clean neurosurgical operations (ie, craniotomy, spinal procedures) are low; however, the morbidity and mortality of central nervous system SSI, should they occur, are high. Preoperative antibiotics are effective at reducing SSI rates and are recommended even in clean procedures.[94,95] While many antimicrobials have been studied, a single dose of cefazolin is what is recommended.[10]

Procedures involving cerebrospinal fluid (CSF) shunt placement should be considered separately because this procedure involves placement of a foreign body and is associated with higher infection rates. A study of 780 patients undergoing neurosurgical procedures that included shunt surgery reported that single doses of cefotaxime and trimethoprim–sulfamethoxazole were equally effective in preventing SSIs.[96] Most studies of procedures involving a shunt have been small in size and do not consistently show lower infection rates with antibiotic prophylaxis, although the results of a systematic review and meta-analysis suggest that a significant improvement in the incidence of shunt infection with 24 hours of systemic antibiotics (ie, cefazolin) and the use of antibiotic-impregnated catheters independently.[97]

SSIs associated with spinal surgery are rare but devastating when they occur. The use of antimicrobial prophylaxis in this setting is warranted and recommended.[93] Large randomized, controlled trials are lacking, but cefazolin is the antibiotic recommended most commonly. Cephalosporin penetration into the vertebral disk has been questioned. Some small studies suggest that the addition of gentamicin, which has better penetration, might be warranted; however, there is a paucity of clinical trials comparing these two regimens.[98]

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. Although interventions to maintain normothermia intraoperatively provide supplemental oxygen in the perioperative period, and aggressively control perioperative glucose show a significant reduction in SSI, they cannot be generalized to all types of surgeries. However, given the simplicity and low cost of these interventions, many clinicians consider applying these measures outside of the studied population(s).

Core body temperature can fall by 1°C to 1.5°C 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 tension, and an increased risk of SSI. Efforts to maintain intraoperative normothermia should be exercised and may include the use of warming blankets and IV fluid warmers to maintain core body temperature between 36°C and 38°C. One prospective trial of 200 patients undergoing colorectal surgery found that maintenance of normothermia reduced postoperative infection rates along with other morbidity parameters, including length of stay.[99] CDC guidelines promote maintaining normothermia with strong recommendation based on moderate- to high-quality evidence.[4]

Low oxygen 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 activity. Administration of high concentrations of oxygen (80% via ventilator or 12 L/min via a nonrebreather mask) reduced postoperative infection rates significantly in a multicenter randomized trial of 500 patients undergoing colorectal surgery.[100] Supplemental oxygen during the intraoperative and immediate postoperative periods is recommended even in patients with normal pulmonary function.[4]

Diabetes and poor glucose control are well-known risk factors for SSI. The increased risk of infection is thought to be due to both macrovascular (vasculopathy and venoocclusive disease) and microvascular (subtle immunologic deficiencies, including neutrophil dysfunction and reduced complement and antibody activity) complications. Aggressive control of perioperative blood glucose not only decreases the incidence of SSI in diabetics and nondiabetics but is also a better predictor of SSI risk than long-term glucose control (eg, as measured by hemoglobin A1C).[7,101] Perioperative blood glucose levels should be checked in all patients regardless of diabetes status and glucose targets of 6.1-8.3 mmol/L (110-150 mg/dL) are recommended.[4] In cardiac surgery the recommended target is <10 mmol/L (180 mg/dL).[7]

Prophylactic antibiotics are only effective when therapeutic concentrations in the surgical field are maintained for the entire duration of the surgery. While consideration of drug half-life in the context of the duration of surgery has been discussed earlier in this chapter, other patient-related factors may influence the effectiveness of antibiotic prophylaxis and warrant consideration when choosing a prophylactic regimen (Table 146-7).

TABLE 146-7

Strategies for Implementing an Institutional Program to Ensure Appropriate Use of Antimicrobial Prophylaxis in Surgery

1. **Educate:** Develop an educational program that enforces the importance and rationale of timely antimicrobial prophylaxis. Make this educational program available to all healthcare practitioners involved in the patient's care.
2. **Standardize the ordering process:** Establish a protocol (eg, a preprinted order sheet) that standardizes antibiotic choice according to current published evidence, formulary availability, institutional resistance patterns, and cost.
3. **Standardize the delivery and administration process:** Use system that ensures antibiotics are prepared and delivered to the holding area in a timely fashion. Standardize the administration time to <1 hour preoperatively. Designate responsibility and accountability for antibiotic administration. Provide visible reminders to prescribe/administer prophylactic antibiotics (eg, checklists). Develop a system to remind surgeons/nurses to readminister antibiotics intraoperatively during long procedures.
4. **Provide feedback:** Follow up with regular reports of compliance and infection rates.

Obese patients require larger doses of prophylactic antibiotics to maintain therapeutic drug levels when compared to nonobese patients. Patients with a body mass index greater than 40 kg/m^2 are more likely to have subtherapeutic concentrations at the end of surgery with cefazolin 1 g preoperatively (and intraoperative for surgeries greater than 3 hours) and thus should receive 2 g doses.[102] Underlying disease states that may affect antibiotic metabolism and/or elimination should be considered when developing a prophylactic regimen. For example, patients with thermal burn and spinal cord injuries eliminate certain classes of antibiotics, primarily the aminoglycosides and β-lactams, at unusually high rates compared with controls and will need more frequent intraoperative dosing. Conversely, individuals with renal failure may need less frequent dosing of renally cleared antibiotics. For example, while intraoperative dosing for cefazolin should be every 3 to 4 hours in patients with normal renal function, this interval should be extended to 8 hours for patients with creatinine clearances of less than 50 mL/min (0.83 mL/s). Individuals who are aggressively fluid resuscitated pre- or intraoperatively or those undergoing cardiac bypass may have altered antibiotic disposition related to increased volume of distribution and reduced total body clearance and may need larger doses (ie, 2-g cefazolin).

EVALUATION OF THERAPEUTIC OUTCOMES

When evaluating the outcome of surgical antibiotic prophylaxis, it is important to differentiate any potential SSI from other postoperative infection or complication. Although fever and leukocytosis are common in the immediate postoperative period, they typically resolve with prompt ambulation, timely removal of invasive devices, prevention and/or resolution of atelectasis through optimal respiratory care, and effective analgesia. It is important to remember that the emergence of distal infections, such as pneumonia, does not constitute a failure of surgical prophylaxis. Prophylaxis should be as short as possible because prolonged prophylactic regimens may contribute to the selection of resistant organisms and may make any infection more difficult to treat.

Surgical site appearance is the most important determinant of the presence of an infection. Drainage of pus from the incision accompanied by redness, warmth, and pain or tenderness is highly suggestive of an SSI. By definition, any surgical site that requires incision and drainage by the surgeon is considered infected regardless of appearance. Failure to heal and wound dehiscence also are seen with SSIs, although the surgical technique and nutritional status may be important contributing factors.

The presentation of signs and symptoms consistent with an SSI in relation to previous surgery is an important consideration when evaluating therapeutic outcomes after surgical prophylaxis. 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. Thus, the true incidence of SSI can be determined only by completing comprehensive postdischarge surveillance. All studies investigating the efficacy of surgical prophylaxis must include adequate postdischarge follow-up to be able to thoroughly assess the success of any prophylactic regimen.

ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
ASA	American Society of Anesthesiologists
CDC	Centers for Disease Control and Prevention
CSF	cerebrospinal fluid
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-sensitive *Staphylococcus aureus*
NNIS	National Nosocomial Infections Surveillance System
NRC	National Research Council
SENIC	Study on the Efficacy of Nosocomial Infection Control
SSI	surgical site infection
WHO	World Health Organization

REFERENCES

1. Hollingsworth JM, Krein SL, Ye Z, et al. Opening of ambulatory surgery centers and procedure use in elderly patients: data from Florida. *Arch Surg* 2011;146:187–193. [PubMed: 21339431]

2. National Hospital Discharge Survey. Available at: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Datset_Documentation/NHDS/NHDS_2010_Documentation.pdf. Accessed October 19, 2015.

3. Alexander JW, Solomkin JS, Edwards MJ. Updated recommendations for control of surgical site infections. *Ann Surg.* 2011;253:1082–1093.

[PubMed: 21587113]

4. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg.* 2017;152(8):784–791. 10.1001/jamasurg.2017.0904. 28467526.

5. Hendrick TL, Anastacio MM, Sawyer RG. Prevention of surgical site infection. *Expert Rev Anti Infect Ther.* 2006;4:223–233. [PubMed: 16597204]

6. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty*. 2012;27(8 Suppl):61–5.e1. 10.1016/j.arth.2012.02.022.22554729.

7. Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. *J Am Coll Surg.* Jan 2017;224(1):59–74. 10.1016/j.jamcollsurg.2016.10.029. 27915053.

8. Stryja J, Sandy-Hodgetts K, Collier M et al. Surgical site infection: preventing and managing surgical site infection across health care sectors. *J Wound Care*. 2020;29(2)(Suppl 2b):S1–S69.

9. Cruse PJE, Foord R. A five-year prospective study of 23,649 surgical wounds. *Arch Surg.* 1973;107:206–210. [PubMed: 4719566]

10. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm.* 2013;70:195–283. [PubMed: 23327981]

11. Martin ET, Kaye KS, Knott C et al. Diabetes and risk of surgical site infection: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol.* 2016;37(1):88–99. https://doi.org/10.1017/ice.2015.249. [PubMed: 26503187]

12. Drapeau CMJ, Pan A, Bellacosa C, et al. Surgical site infections in HIV-infected patients: results from an Italian prospective multicenter observational study. *Infection.* 2009;37:455–460. [PubMed: 20358638]

13. Dionigi R, Rovera F, Dionigi G, et al. Risk factors in surgery. *J Chemother.* 2001;13:6–11. [PubMed: 11936382]

14. Haley RW, Culver DH, Morgan WM, et al. Identifying patients at high risk of surgical wound infection: a simple multivariate index of patient susceptibility and wound contamination. *Am J Epidemiol.* 1985;127:206–215.

15. Wilson AP, Hodgson B, Liu M, et al. Reduction in wound infection rates by wound surveillance with postdischarge follow-up and feedback. *Br J Surg.* 2006;93:630–638. [PubMed: 16550635]

16. NNIS. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004 issued October 2004. *Am J Infect Control.* 2004;32:470–485. [PubMed: 15573054]

17. Owens WD, Felts JA, Spitznagel EL. ASA physical status classifications: a study of consistency of ratings. *Anesthesiology.* 1978;49:239–243. [PubMed: 697077]

18. van Walraven C, Musselman R, et al. The Surgical Site Infection Risk Score (SSIRS): A model to predict the risk of surgical site infections. *PLoS ONE.* 2013;8(6):e67–167. https://doi.org/10.1371/journal.pone.0067167.

19. Elek SD, Conen PE. The virulence of *Staphylococcus pyogenes* for man: A study of the problems of wound infection. *Br J Exp Pathol.* 1958;38:573–586.

20. Burke JF. Identification of the sources of staphylococci contaminating the surgical wound during operation. *Ann Surg.* 1963;158:898–904. [PubMed: 14074082]

21. Kaiser AB, Kernodle DS, Parker RA. Low-inoculum model of surgical wound infection. *J Infect Dis.* 1992;166:393–399. [PubMed: 1634811]

22. Esposito S. Immune system and surgical site infection. *J Chemother.* 2001;13:12–16. [PubMed: 11936355]

23. De Lalla F. Antibiotic prophylaxis in orthopedic prosthetic surgery. *J Chemother.* 2001;13:48–53. [PubMed: 11936379]

24. Halwani M, Solaymani-Dodaran M, Grundman H, et al. Cross transmission of nosocomial pathogens in an adult intensive care unit: incidence and risk factors. *J Hosp Infect.* 2006;63:39–46. [PubMed: 16517009]

25. Kim DH, Spencer M, Davidson SM, et al. Institutional prescreening for detection and eradication of methicillin-resistant *Staphylococcus aureus* in patients undergoing elective orthopaedic surgery. *J Bone Joint Surg Am.* 2010;92:1820–1826. [PubMed: 20610773]

26. Munoz P, Burrillo A, Bouza E. Criteria used when initiating antifungal therapy against *Candida* spp. in the intensive care unit. *Int J Antimicrob Agents.* 2000;15:83–90. [PubMed: 10854803]

27. Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev.* Feb 9 , 2017;2:CD003543. 10.1002/14651858.CD003543.pub4. 28178770.

28. Sartelli M, Duane TM, Catena F, et al. Antimicrobial stewardship: a call to action for surgeons. *Surg Infect (Larchmt).* Dec 2016;17(6):625–631. 10.1089/sur.2016.187. 27828764.

29. Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical wound infection. *N Engl J Med.* 1992;326:281–286. [PubMed: 1728731]

30. Weber WP, Mujagic E, Zwahlen M, et al. Timing of surgical antimicrobial prophylaxis: a phase 3 randomised controlled trial *Lancet Infect Dis.* Jun 2017;17(6):605–614. 10.1016/S1473-3099(17)30176-728385346.

31. Hawn MT, Richman JS, Vicks CC, et al. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. *JAMA Surg.* 2013;148:649–657. [PubMed: 23552769]

32. Zelenitzky SA, Ariano RE, Harding GKM, et al. Antibiotic pharmacodynamics in surgical prophylaxis: an association between intraoperative antibiotic concentrations and efficacy. *Antimicrob Agents Chemother.* 2002;46:3026–3030. [PubMed: 12183263]

33. Goldman DA, Hopkins CC, Karchmer AW. Cephalothin prophylaxis in cardiac valve surgery: a prospective, double-blind comparison of two-day and six-day regimen. *J Thorac Cardiovasc Surg.* 1977;73:470–479. [PubMed: 402508]

34. Zanetti G, Flanagan HL Jr, Cohn LH, et al. Improvement of intraoperative antibiotic prophylaxis in prolonged cardiac surgery by automated alerts in the operating room. *Infect Control Hosp Epidemiol.* 2003;24:79.

35. Branch-Elliman W, O'Brien W, Strymish J, Itani K, Wyatt C, Gupta K. Association of duration and type of surgical prophylaxis with antimicrobial-associated adverse events. *JAMA Surg.* 2019;154(7):590–598. doi: 10.1001/jamasurg.2019.0569.

36. Weed HG. Antimicrobial prophylaxis in the surgical patient. *Med Clin North Am.* 2003;27:59–75.

37. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination: is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. *JAMA.* 2001;285:2498–2505. [PubMed: 11368703]

38. Gemmel CG, Edwards DI, Fraise AP, et al. Guidelines for the prophylaxis and treatment of methicillin *Staphylococcus aureus* (MRSA) infections in the UK. *J Antimicrob Chemother.* 2006;57:589–608. [PubMed: 16507559]

39. Wong RS, Cheng G, Chang NP, et al. Use of cefoperazone still needs a caution for bleeding from induced vitamin K deficiency. *Am J Hematol.* 2006;81:76. [PubMed: 16369967]

40. Frighetto L, Marra CA, Stiver HG, et al. Economic impact of standardized orders for antimicrobial prophylaxis program. *Ann Pharmacother.* 2000;34:154–160. [PubMed: 10676821]

41. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis.* 2004;38:1706–1715. [PubMed: 15227616]

42. Lipp A, Lusardi G. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy. *Cochrane Database Syst Rev.* 2013;11:CD005571.

43. Ferraz AAB, Santa-Cruz F, Edmiston CE Jr., et al. Antibiotic prophylaxis in bariatric surgical procedures: is there an ideal antimicrobial agent? *Surg Infect* 2020;Oct:654–658.

44. Jewesson PJ, Stiver G, Wai A, et al. Double-blind comparison of cefazolin and ceftizoxime for prophylaxis against infections following elective biliary tract surgery. *Antimicrob Agents Chemother.* 1996;40:70–74. [PubMed: 8787882]

45. Agrawal CS, Sehgal R, Singh RK, Gupta AK. Antibiotic prophylaxis in elective cholecystectomy: a randomized, double-blinded study comparing ciprofloxacin and cefuroxime. *Ind J Physiol Pharmacol.* 1999;43:501–504.

46. Swoboda S, Oberdorfer K, Klee F, et al. Tissue and serum concentrations of levofloxacin 500 mg administered intravenously or orally for antibiotic prophylaxis in biliary surgery. *J Antimicrob Chemother.* 2003;51:459–462. [PubMed: 12562723]

47. Matsui Y, Satoi S, Hirooka S, Kosaka H, Kawaura T, Kitawaki T Reappraisal of previously reported meta-analyses on antibiotic prophylaxis for low-risk laparoscopic cholecystectomy: an overview of systematic reviews. *BMJ Open.* Mar 16 , 2018;8(3):e016666. 10.1136/bmjopen-2017-01666629549197.

48. Gomez-Ospina JC, Zapata-Copete JA, Bejarano M, García-Perdomo HA. Antibiotic prophylaxis in elective laparoscopic cholecystectomy: a systematic review and network meta-analysis. *J Gastrointest Surg.* Mar 19 , 2018. 10.1007/s11605-018-3739-429556974.

49. Gulberg V, Deibert P, Ochs A, et al. Prevention of infectious complications after transjugular intrahepatic portosystemic shunt in cirrhotic patients with a single dose of ceftriaxone. *Hepatogastroenterology.* 1999;46:1126–1130. [PubMed: 10370679]

50. Deibert P, Schwartz S, Olschewski M, et al. Risk factors and prevention of early infection after implantation or revision of transjugular intrahepatic portosystemic shunts: results of a randomized study. *Dig Dis Sci.* 1998;43:1708–1713. [PubMed: 9724157]

51. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendicectomy. *Cochrane Database Syst Rev.* 2005;3:CD001439.

52. Liberman MA, Greason KL, Frame S, Ragland JJ. Single-dose cefotetan or cefoxitin versus multiple-dose cefoxitin as prophylaxis in patients undergoing appendectomy for acute nonperforated appendicitis. *J Am Coll Surg.* 1995;180:77–80. [PubMed: 8000659]

53. Migaly J, Bafford AC, Francone TD, Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the use of bowel preparation in elective colon and rectal surgery. *Dis Colon Rectum.* Jan 2019;62(1):3–8. [PubMed: 30531263]

54. Zmora O, Wexner SD, Hajjar L, et al. Trend in preparation for colorectal surgery: survey of the members of the American Society of Colon and Rectal Surgeons. *Am Surg.* 2003;69:150–154. [PubMed: 12641357]

55. Zmora O, Mahajna A, Bar-Zakai B, et al. Colon and rectal surgery without mechanical bowel preparation: a randomized, prospective trial. *Ann Surg.* 2003;237:363–367. [PubMed: 12616120]

56. Cao F, Li J, Li F. Mechanical bowel preparation for elective colorectal surgery: updated systematic review and meta-analysis. *Int J Colorectal Dis.* 2012;27:803–810. [PubMed: 22108902]

57. Dahabreh IJ, Steele DW, Shah N, Trikalinos TA. Oral Mechanical Bowel Preparation for Colo-rectal Surgery. Comparative Effectiveness Review No. 128. Rockville, MD: Agency for Healthcare Research and Quality; April 2014. AHRQ Publication No. 14-EHC018-EF. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm. Accessed October 19, 2015.

58. Baum ML, Anish DS, Chalmers TC, et al. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. *N Engl J Med.* 1981;305:795–799. [PubMed: 7266633]

59. Nelson RL, Gladman E, Barbateskovic M. Antimicrobial prophylaxis for colorectal surgery. *Cochrane Database Syst Rev.* 2014;5:CD001181.

60. Battersby CLF, Hajibandeh S, Hajibandeh S. Oral antibiotics as adjunct to systemic antibiotics and mechanical bowel preparation for prevention of surgical site infections in colorectal surgery. Do we really need more trials? *Dis Colon Rectum.* Jun 2018;61(6):e341–e342. [PubMed: 29722733]

61. Fujita S, Saito N, Yamada T, et al. Randomized, multicenter trial of antibiotic prophylaxis in elective colorectal surgery: single dose vs 3 doses of a second-generation cephalosporin without metronidazole and oral antibiotics. *Arch Surg.* 2007;142:657–661. [PubMed: 17638804]

62. Mittelkotter U. Antimicrobial prophylaxis for abdominal surgery: is there a need for metronidazole? *J Chemother.* 2001;13:27–34. [PubMed: 11936375]

63. Kobayashi M, Mohri Y, Tonouchi H, et al. Randomized clinical trial comparing intravenous antimicrobial prophylaxis alone with oral and intravenous antimicrobial prophylaxis for the prevention of a surgical site infection in colorectal cancer surgery. *Surg Today.* 2007;37:383–388. [PubMed: 17468819]

64. Ghorra SG, Rzeczycki TP, Natarajan R, Pricolo VE. Colostomy closure: impact of preoperative risk factors on morbidity. *Am Surg.* 1999;65:266–269. [PubMed: 10075307]

65. ASGE Standards of Practice Committee. Antibiotic prophylaxis for GI endoscopy. *Gastrointest Endosc.* 2015;81:81–89. [PubMed: 25442089]

66. Sharma VK, Howden CW. Meta-analysis of randomized, controlled trials of antibiotic prophylaxis before percutaneous endoscopic gastrostomy. *Am J Gastroenterol.* 2001;96:1951–1952. [PubMed: 11419869]

67. Wolf JS Jr, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearles MS, Schaeffer AJ. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol.* 2008;179:1379–1390. [PubMed: 18280509]

68. Christiano AP, Hollowell CM, Kim H, et al. Double-blind, randomized comparison of single-dose ciprofloxacin versus intravenous cefazolin in patients undergoing outpatient endourologic surgery. *Urology.* 2000;55:182–185. [PubMed: 10688075]

69. Smaill FM, Grivell R. Antibiotic prophylaxis versus noprophylaxis for preventing infection after cesarean section. *Cochrane Database System Rev.* 2014;10 0.1002/14651858. Art. No.: CD007482.

70. Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 199: Use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol.* Sep 2018;132(3):e103–e119. [PubMed: 30134425]

71. Tita AT, Szychowski JM, Boggess K, et al. Adjunctive azithromycin prophylaxis for cesarean delivery. *N Engl J Med.* Sep 29 , 2016;375(13):1231–1241. 10.1056/NEJMoa160204427682034.

72. Guaschino S, De Santo D, De Seta F. New perspectives in antibiotic prophylaxis for obstetric and gynaecological surgery. *J Hosp Infect.* 2002;50(suppl A):S13–S16. [PubMed: 11993639]

73. ACOG Practice Bulletin No. 195: Prevention of infection after gynecologic procedures. *Obstet Gynecol.* Jun 2018;131(6):e172–e189. [PubMed: 29794678]

74. Hemsell DL, Johnson ER, Hemsell PG, et al. Cefazolin is inferior to cefotetan as single dose prophylaxis for women undergoing elective total abdominal hysterectomy. *Clin Infect Dis.* 1995;20:677–684. [PubMed: 7756495]

75. Sturlese E, Retto G, Pulia A, et al. Benefits of antibiotic prophylaxis in laparoscopic gynaecological surgery. *Clin Exp Obstet Gynecol.* 1999;26:217–218. [PubMed: 10668161]

76. Meuller SC, Henkel KO, Neumann J, et al. Perioperative antibiotic prophylaxis in maxillofacial surgery: penetration of clindamycin into various tissues. *J Craniomaxillofac Surg.* 1999;27:172–176. [PubMed: 10442308]

77. Van der Poorten V, Uyttebroek S, Robbins KT, et al. Perioperative antibiotics in clean-contaminated head and neck surgery: a systematic review and meta-analysis. *Adv Ther.* Apr 2020;37(4):1360–1380. [PubMed: 32141017]

78. Grandis JR, Vickers RM, Rihs JD, et al. Efficacy of topical amoxicillin plus clavulanate–ticarcillin plus clavulanate and clindamycin in contaminated head and neck surgery: effect of antibiotic spectra and duration of therapy. *J Infect Dis.* 1994;170:729–732. [PubMed: 8077738]

79. Roy MC. Surgical-site infections after coronary artery bypass graft surgery: discriminating site-specific risk factors to improve prevention efforts. *Infect Control Hosp Epidemiol.* 1998;19:229–233. [PubMed: 9605270]

80. Hollenbeak CS, Murphy DM, Koenig S, et al. The clinical and economic impact of deep chest surgical site infections following coronary artery bypass graft surgery. *Chest.* 2000;118:397–402. [PubMed: 10936131]

81. Curtis JJ, Boley TM, Walls JT, et al. Randomized, prospective comparison of first- and second-generation cephalosporins as infection prophylaxis for cardiac surgery. *Am J Surg.* 1993;166:734–737. [PubMed: 8273859]

82. Edwards FH, Egleman RM, Houck P, et al. The society of thoracic surgeons practice guidelines series: antibiotic prophylaxis in cardiac surgery, part 1: duration. *Ann Thorac Surg.* 2006;81:397–404. [PubMed: 16368422]

83. Finkelstein R, Rabino G, Masiah T, et al. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg.* 2002;123:326–332. [PubMed: 11828293]

84. Schweizer ML, Perencevich E, McDaniel J, et al. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. *BMJ.* 2013;346:f2743. [PubMed: 23766464]

85. Sok M, Dragas AZ, Erzen J, et al. Sources of pathogens causing pleuropulmonary infections after lung cancer resection. *Eur J Cardiothorac Surg.* 2002;22:23–27. [PubMed: 12103368]

86. Boldt J, Piper S, Uphus D, et al. Preoperative microbiologic screening and antibiotic prophylaxis in pulmonary resection operations. *Ann Thorac Surg.* 1999;68:208–211. [PubMed: 10421142]

87. Pratesi C, Russo D, Dorigo W, et al. Antibiotic prophylaxis in clean surgery: Vascular surgery. *J Chemother.* 2001;13:123–128. [PubMed: 11936356]

88. Terpstra S, Noorkhoek GT, Voesten HG, et al. Rapid emergence of resistant coagulase-negative staphylococci on the skin after antibiotic prophylaxis. *J Hosp Infect.* 1999;43:195–202. [PubMed: 10582186]

89. Slobogean GP, Kennedy SA, Davidson D, et al. Single- versus multiple-dose antibiotic prophylaxis in the surgical treatment of closed fractures: a meta-analysis. *J Orthop Trauma.* 2008;22:264–269. [PubMed: 18404036]

90. Slobogean PG, O'Brien PJ, Brauer CA. Single-dose versus multiple-dose antibiotic prophylaxis for the surgical treatment of closed fractures: a cost-effective analysis. *Acta Orthop.* 2010;81:256–262. [PubMed: 20148647]

91. Gillespie WJ, Walenkamp G. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures. *Cochrane Database Syst*

Rev. 2001;1:CD000244.

92. Vasenius J, Tulikoura I, Vainionpaa S, Rokkanen P. Clindamycin versus cloxacillin in the treatment of 240 open fractures: a randomized, prospective study. *Ann Chir Gynaecol.* 1998;87:224–228. [PubMed: 9825068]

93. Shaffer WO, Baisden JL, Fernand R, Matz PG. An evidence-based clinical guideline for antibiotic prophylaxis in spine surgery. *Spine J.* Oct 2013;13(10):1387–1392. 10.1016/j.spinee.2013.06.030.23988461.

94. Barker FG II. Efficacy of prophylactic antibiotics against meningitis after craniotomy: a meta-analysis. *Neurosurgery.* 2007;60:887–894. [PubMed: 17460524]

95. Watters WC 3rd, Baisden J, Bono CM, et al. Antibiotic prophylaxis in spine surgery: an evidence-based clinical guideline for the sue of prophylactic antibiotics in spine surgery. *Spine J.* 2009;9:142–146. [PubMed: 18619911]

96. Whitby M, Johnson BC, Atkinson RL, et al. The comparative efficacy of intravenous cefotaxime and trimethoprim/sulfamethoxazole in preventing infection after neurosurgery: a prospective, randomized study. Brisbane Neurosurgical Infection Group. *Br J Neurosurg.* 2000;14:13–18. [PubMed: 10884878]

97. Ratilal B, Costa J, Sampaio C. Antibiotic prophylaxis for surgical introduction of intracranial ventricular shunts: a systematic review. *J Neurosurg Pediatr.* 2008;1:48–56. [PubMed: 18352803]

98. Riley LH 3rd. Prophylactic antibiotics for spine surgery: description of a regimen and its rationale. *J South Orthop Assoc.* 1998;7:212–217. [PubMed: 9781898]

99. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med.* 1996;334:1209–1215. [PubMed: 8606715]

100. Greif R, Akca O, Horn EP, et al. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. Outcomes Research Group. *N Engl J Med.* 2000;342:161–167. [PubMed: 10639541]

101. Kao LS, Meeks D, Moyer VA, Lally KP. Peri-operative glycaemic control regimens for preventing surgical site infections in adults. *Cochrane Database Syst Rev.* 2009;3:CD006806.

102. Ho VP, Nicolau DP, Dakin GF, et al. Cefazolin dosing for surgical prophylaxis in morbidly obese patients. *Surg Infect (Larchmt).* 2012;13:33–37. [PubMed: 22316145]

SELF-ASSESSMENT QUESTIONS

1. A patient undergoing a cholecystectomy for acute cholecystitis requires:

   A. No antibiotic therapy

   B. Prophylactic antibiotic therapy

   C. Presumptive antibiotic therapy

   D. Therapeutic antibiotic therapy

2. According to the National Research Council classification of surgical site infection, antibiotic therapy is *not* required for:

   A. Clean procedures

B. Clean–contaminated procedures

C. Contaminated procedures

D. A and B

3. Which of the following is not considered patient-specific risk factors for surgical site infections?

A. Smoking history

B. Preoperative nutritional status

C. Male gender

D. Diabetes

4. Which of the following statements about preoperative nutrition is *true*?

A. Preoperative dietary supplementation with glutamine reduces the risk of postoperative surgical site infections.

B. Preoperative dietary supplementation with arginine reduces the risk of postoperative surgical site infections.

C. Preoperative dietary supplementation with omega-3 fatty acids reduces the risk of postoperative surgical site infections.

D. No dietary supplements have been shown to decrease postoperative surgical site infection.

5. According to the National Nosocomial Infection Surveillance System, which one of the following organisms is ***most often*** isolated from surgical site infections?

A. *Streptococcus pneumonia*

B. *Staphylococcus aureus*

C. *Escherichia coli*

D. *Enterococci* sp.

6. The Center for Disease Control recommends that vancomycin should be substituted for a cephalosporin for surgical prophylaxis when:

A. Methicillin-resistant *S. aureus* is suspected

B. "Contaminated" and "dirty" procedures are expected

C. Patients with a documented history of a life-threatening allergy to penicillins or cephalosporins.

D. The surgical procedure involves implantation of any prosthetic device.

E. A and C.

7. Which one of the following statements regarding prophylactic antimicrobial regimens is *false*?

A. Therapeutic antimicrobials for unrelated infections can be used in place of a prophylactic antimicrobial regimen, provided the antibiotic used has appropriate antimicrobial activity.

B. Bactericidal concentrations of antibiotics must be delivered to the surgical site prior to the initial incision.

C. Bactericidal concentrations of antibiotics must be maintained throughout the duration of the surgery.

D. Antimicrobials should be administered with anesthesia or within 60 minutes prior to the initial incision.

8. Intraoperative redosing of antimicrobials are required for surgical procedures longer than:

A. 5 half-lives of the antibiotic used for prophylaxis

B. 2 hours

C. 2.5 half-lives of the antibiotic used for prophylaxis

D. 6 hours

9. With respect to gastrointestinal surgeries, third-generation cephalosporins are considered to be effective prophylactic regimens for:

A. Cholecystectomies

B. Gastroduodenal surgeries

C. Colorectal surgeries

D. All of the above

10. Regarding colorectal surgery, which one of the following statements is *true*?

A. Mechanical bowel preparation (ie, with polyethylene glycol) is an effective way to reduce bacterial load in the colon.

B. Most surgeons report routinely using a mechanical bowel preparation in addition to antibiotics prior to elective colorectal surgery.

C. Mechanical bowel preparation (ie, with polyethylene glycol) is an effective way to reduce surgical site infection risk after elective colorectal surgery.

D. All of the above.

E. A and B only.

11. Prophylactic antimicrobial therapy for gastrointestinal endoscopy is recommended for:

A. All patients as postprocedure bacteremia is common

B. No patient as the risk of postprocedure infection is low

C. High-risk procedures including colonoscopy

D. High-risk patients including those with prosthetic heart valves

12. Which one of the following statements about hysterectomies is *false*?

A. Cefazolin is the prophylactic drug of choice for vaginal hysterectomies.

B. Abdominal hysterectomies are associated with a higher rate of surgical site infections when compared to vaginal hysterectomies.

C. It is unnecessary to provide more than 24 hours of prophylactic antimicrobial coverage for abdominal hysterectomies.

D. Metronidazole is a reasonable alternative to a cephalosporin for penicillin-allergic patients undergoing a hysterectomy.

13. Screening and preoperative eradication of *S. aureus* with intranasal mupirocin and chlorhexidine body wash has been shown to reduce surgical site infections:

A. Only in cardiac surgery

B. Only in orthopedic surgery

C. Only in neurosurgery

D. Both cardiac and orthopedic surgeries

14. Patients suffering an open compound limb fracture:

    A. Requires no more than 24 hours of prophylactic antibiotics

    B. Requires no more than a single dose of prophylactic antibiotics

    C. Requires a course of antibiotics for "presumptive" infection

    D. None of the above

15. Non-antimicrobial strategies to reduce surgical site infections include all of the following, except:

    A. Permissive hypothermia intraoperatively

    B. High concentrations of oxygen administration intraoperatively

    C. Protocolized aseptic technique

    D. Perioperative normoglycemia

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** For a patient with acute cholecystitis that requires surgical intervention one must presume that the surgical site is contaminated, and the risk of active infection is high. Therefore, a presumptive course of antimicrobials is warranted. If culture results or diagnostic imaging confirm an active infection, then therapeutic (and culture directed) antimicrobial therapy would be warranted.

2. **A.** Clean procedures have the lowest relative risk of postoperative surgical site infections and typically do not require prophylactic antimicrobials.

3. **C.** Unlike gender, smoking history, nutritional status, and diabetes have all been identified as risk factors for surgical site infections.

4. **D.** Although malnutrition has been identified as a risk factor for surgical site infections, perioperative dietary supplementation has not been shown to reduce this risk.

5. **B.** Skin flora is the most common source of wound and surgical site bacterial contamination and staphylococcal species are the most common bacterial pathogens found in skin flora.

6. **E.** Beta-lactam antibiotics are the preferred agents for surgical site infection prevention unless resistant gram-positive organisms are suspected (ie, methicillin-resistant *S. aureus*) or the patient has a documented and serious allergy to penicillins or cephalosporins. Understanding resistance patterns at your institution will help assess this risk related to resistant organisms.

7. **A.** Therapeutic antimicrobials for unrelated indications should not be relied upon for surgical prophylaxis even if their spectrum of bacterial coverage would be sufficient for surgical prophylaxis. Issues of dose and timing of administration are critical to the efficacy of surgical prophylaxis. Prophylactic antimicrobials should ideally be administered within 60 minutes prior to the initial incision. It is more practical to schedule the prophylactic antibiotic prior to the surgery than to schedule the surgery according to the administration times of the therapeutic antimicrobial regimen.

8. **C.** Because different prophylactic antimicrobials are indicated for different surgical procedures it makes more sense to consider the duration of therapeutic serum concentrations at the site of the infection rather than an arbitrary or absolute time trigger. This is best estimated using the half-

life of the antimicrobial. At 2.5 half-lives serum concentrations will have dropped more than 80% from baseline and should be the trigger for redosing.

9. **C.** Compared with first- and second-generation cephalosporins, third-generation cephalosporins have increased activity against gram-negative organisms including most pathogenic enteric gram negatives. The risk of surgical site infections caused by gram-negative organisms is higher with colorectal surgeries than gastroduodenal procedures or cholecystectomies and thus warrant better gram-negative coverage with third-generation cephalosporins.
10. **E.** Despite the widespread use of mechanical bowel preparations prior to colorectal surgery they have never been shown to reduce the risk of surgical site infections. They do, however, reduce bacterial load in the colon and allow for easier bowel manipulation and instrumentation.
11. **D.** Prophylactic antimicrobials for gastrointestinal endoscopy is only indicated for high-risk patients, including those with prosthetic heart valves.
12. **B.** Vaginal hysterectomies are associated with a greater risk of surgical site infections when compared to abdominal hysterectomies because of the polymicrobial flora and risk of contamination at the surgical site.
13. **D.** Preoperative attempts to eradicate *S. aureus* from the skin and nares to reduce surgical site infections has only been shown to be effective in orthopedic and cardiac surgery.
14. **C.** The risk of direct contamination and subsequent surgical site infections after repair of an open compound limb fracture is significantly higher than that of a closed fracture. Therefore in these cases infection should be presumed.
15. **A.** Intraoperative hypothermia should be avoided when possible as this has been shown to increase the risk of surgical site infections.