Antimicrobial Prophylaxis for Ambulatory Surgery

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Learning Objectives

1. Classify a patient's requirement for endocarditis prophylaxis according to risk factors.
2. Evaluate a patient's requirement for pharmacologic prophylaxis by assessing the risk of surgical site infection (SSI).
3. Design a prophylactic regimen according to local epidemiology, type of surgery, and patient characteristics.
4. Assess SSIs for patient outcomes and quality measurement purposes.

Introduction

Since 1970, when the first ambulatory surgery center was created, the number of such centers has steadily increased. By the early 1990s, surgical procedures performed in ambulatory centers surpassed those in the inpatient setting, according to the Ambulatory Surgery Center Association (ASCA 2011). Surgical site infections (SSIs) occur when a pathogenic organism gains access to the surgical wound and multiplies, causing local and sometimes systemic signs and symptoms.

Surgical site infections complicate surgery and result in significant morbidity and excess health care costs. In the 1960s, the National Academy of Sciences National Research Council developed a standard classification scheme for surgical wounds that was based on the risk of intraoperative bacterial contamination. Surgical wounds are classified into four categories (clean, clean-contaminated, contaminated, and dirty). Antibiotics are used to prevent infections at or around the surgical site for clean, clean-contaminated, and contaminated wounds. Antibiotics are considered treatment instead of prophylaxis when used for dirty surgical procedure in which infection is already established. Antibiotic use is not without risk. Benefits must be weighed against the risk of drug toxicity, superinfection, selection of resistant organisms, and cost.

Epidemiology and Classification of SSIs

Surgical site infections occur in about 5% of cases, depending on the surgical procedure and patient risk factors. Surgical site infections increase morbidity and extend the duration of hospitalization. They are the second most commonly reported hospital-associated infection and are associated with an additional cost of $1.6 billion for the estimated 26.6 million inpatient surgical procedures performed annually in the United States (de Lissovoy 2009;

Baseline Knowledge Statements

Readers of this chapter are presumed to be familiar with the following:

- Infection rate according to the National Research Wound Classification
- Assessment of antibiotic prophylaxis in a direct patient care setting
- Patient assessment skills for evaluating skin and soft tissue infections

Additional Readings

The following free resources are available for readers wishing additional background information on this topic.

- 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.
- Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. Circulation 2007;116:1736-54.

Abbreviations in This Chapter

IE	Infective endocarditis
NNIS	National Nosocomial Infections Surveillance system
SSI	Surgical site infection

Klevens 2007; NNIS 2004). The incidence of SSIs in ambulatory surgery centers may be lower than in health care institutions. However, monitoring of ambulatory surgery is insufficient for appropriate comparisons to be made.

The most widely recognized definition of infection is that devised by Horan and colleagues and adopted by the Centers for Disease Control and Prevention (CDC) (Horan 1992). It splits SSIs into three groups: superficial, deep incisional, and organ/space, depending on the site and the extent of infection. Surgical site infections include infectious lesions to the surgical wound and to tissues involved in the operation (e.g., soft tissue, organs and deep space, bones, joints, meninges).

Only infections occurring within 30 days of surgery (or within 1 year for implants) should be classified as SSIs.

Pathophysiology

Surgical wounds are assessed routinely and frequently to ensure proper healing and rapid intervention in case complications develop. Wound healing will generally occur by primary closure. The surgeon will bring the wound edges close together and facilitate closure by mechanical means such as sutures, staples, wound adhesive, or adhesive paper strips. These wounds will normally seal and dry out within 48 hours, and they will heal within 8–14 days. The terms *inflammation*, *tissue formation*, and *tissue remodeling* are used to describe the different phases of the healing process.

On occasion, surgical incisions are allowed to heal by delayed primary intention; in this process, nonviable tissue is removed, and the wound is initially left open. Wound edges are brought together at about 4–6 days, before granulation tissue is visible. Healing by secondary intention occurs when the wound is left open—usually because of the presence of infection, excessive trauma, or skin loss—and the wound edges come together naturally by means of granulation and contraction. Improper healing and some complications can lead to wound dehiscence (i.e., opening up of the wound). Infection is a primary cause, among others, of wound dehiscence. Other primary causes include mechanical stress, and local inflammation and edema leading to excessive exudate.

Bacterial contamination has long been identified as a major determinant of infection and serves as the basis in wound classification. Tremendous efforts are put into aseptic technique in the operating room with the aim of reducing contamination as much as possible. Antibiotic prophylaxis has helped further reduce the risk of SSI in selected procedures without succeeding at eliminating it. Development of SSIs is influenced by complex interactions between host defenses, microbial factors (e.g., degree of bacterial contamination during surgery, virulence of the infecting organism), and procedure-related events (e.g., degree of trauma to the host tissue, implantation of foreign material). In this setting, patient- and procedure-related factors are the most important contributors to SSI development.

Risk factors for postoperative site infection can be classified according to procedure-specific factors and patient characteristics. Bacterial contamination can occur from exogenous sources (e.g., the operative team, instruments, airborne organisms) or from endogenous sources (e.g., microflora from the patient's skin or respiratory, genitourinary, or gastrointestinal tract). Infection control procedures to minimize all sources of bacterial contamination, including patient and surgical team preparation, operative technique, and incision care, are compiled in the CDC guidelines for SSIs (Anderson 2008).

The risk of postoperative wound infection is influenced by host factors such as those listed in Box 1-1. In addition, the longer the surgical procedure, the greater the likelihood of developing a postoperative wound infection, presumably because of the greater amount of bacterial contamination occurring over time.

In clean surgery, the predominant organisms associated with infection are gram-positive bacteria and, more specifically, *Staphylococcus* spp., most likely from the patient's own flora. In contaminated surgery, organisms associated with infection are commonly related to the normal flora of the internal organ entered during surgery. *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter* spp., and *Klebsiella* spp. are among the gram-negative bacteria most commonly associated with infection. Fungi such as *Candida* spp. are encountered rarely, but the incidence of fungal infection is rising. Although direct inoculation from the

Box 1-1. Patient Risk Factors for Surgical Site Infection

Colonization with microorganisms
Comorbid states
- Diabetes mellitus
- Glycemic control in patients with diabetes

Immunosuppressive therapy
Ischemia
Malnutrition
Obesity
Oxygenation and body temperature during the procedure
Remote infection
Tobacco use

patient's own colonized flora is probably the most common mechanism, many different sources and types of contamination have been identified (e.g., surgical material and instruments, hematogenous seeding from a distant infectious or colonized foci, operating room staff).

Assessing Risk

Measuring and predicting infection risk determines which patients benefit from antibiotic prophylaxis. The CDC study on the Efficacy of Nosocomial Infection Control developed an index that includes the level of wound contamination and three other criteria according to procedure- and patient-related factors. Modification of this tool has led to the National Nosocomial Infections Surveillance system (NNIS) risk index, which considers the patient's preoperative assessment (American Anesthesiology Assessment), the level of contamination of the procedure, the duration of the procedure, and the use of a laparoscope (NNIS 2004). This last criterion was added because of the associated decreased incidence of infection with the introduction of laparoscopic procedures. Indexes like these are particularly useful for comparing performance between institutions and public reporting. Given these risk factors for infection, deciding whether a given patient should receive antimicrobial prophylaxis depends on several factors.

Evaluation of the level of infection risk is based on the NNIS risk index system. This system can be summarily understood by performing three steps (Figure 1-1). The first step is to determine the surgical wound class. Surgical wounds of class II, III, or IV are counted as 1 point for the NNIS risk index system. Class I surgical wounds, which includes clean surgeries, should not be attributed a point in this step. The second step is to determine the American Society of Anesthesiology preoperative assessment

Step 1: Wound Class Scoring System			
Class	**Wound type**	**NNIS Risk Index Points**	**Step Score Totals**
I	Clean	0	
II	Clean–contaminated	1	
III	Contaminated	1	
IV	Dirty	1	
Step 2. ASA Preoperative Scoring System			
ASA Preoperative Assessment		**NNIS Risk Index Points**	
1. Patient with normal health		0	
2. Patient with mild systemic disease		0	
3. Patient with non-incapacitating severe systemic disease		1	
4. Patient with life-threatening incapacitating systemic disease		1	
5. Moribund patient not expected to survive 24 hours		1	
Step 3. Standard Duration of the Operation (T point) of Selected Procedures			
Operation		**T point (hours)**	
Coronary artery bypass graft		5	
Craniotomy		4	
Joint prosthesis surgery		3	
Herniorrhaphy		2	
Appendectomy		1	
Limb amputation		1	
Cesarean section		1	
Cumulative Step Scores			

Figure 1-1. National Nosocomial Infections Surveillance risk index system for predicting surgical site infections. The total number achieved with this scoring system is then compared with a standardized scale based on SSI rates observed in large cohort studies.

ASA = American Society of Anesthesiology; NNIS = National Nosocomial Infections Surveillance system.

score. One point is assigned if the patient has an American Society of Anesthesiology preoperative assessment score of 3, 4, or 5. Patients in normal health or with mild systemic disease do not score a point. The third step is to determine whether the duration of the operation exceeds the standard time (75th percentile) as determined by the NNIS database. Surgical procedures lasting longer than standard times are assigned 1 point. The total number achieved with this scoring system is then compared with a standardized scale based on SSI rates observed in large cohort studies. According to the NNIS risk index system, the risk of infection can then be predicted.

Principles of Antibiotic Prophylaxis for Surgery

Goals of Prophylaxis

Antibiotics to prevent infection are targeted to patients at high risk of infection, patients in whom an infection would have catastrophic consequences, and patients who have undergone surgical procedures to insert implants or prosthetic material. The main objective is to minimize the risk of surgical infection by decreasing the bacterial load at the incision site. Antibiotics can play a pivotal role in preventing infections in patients at risk. However, benefits must be weighed against the possibility of a superinfection or drug-related adverse event.

Pharmacologic Strategies

Although most surgical procedures are performed on an outpatient basis, the majority of evidence has been accumulated in the inpatient setting. It is generally thought that ambulatory care centers perform procedures that can be safely conducted in less than 90 minutes and that do not require an overnight stay for recovery and monitoring, as defined by the Centers for Medicare & Medicaid Services (CMS). Therefore, patient- and procedure-related factors differ, and some principles (e.g., multidosing) in cardiovascular surgery are less applicable.

Overall, clean surgeries are at low risk of infection and do not require prophylaxis. On the other end of the spectrum, patients with a load of contamination (dirty wounds) or infection should be considered for treatment of infection, not prophylaxis. Prophylaxis should be given in cardiovascular, neurologic, orthopedic, and thoracic surgical procedures because of potential complications should an SSI occur. No other clean surgeries require prophylaxis. Parameters to be considered when using antibiotics for prophylaxis in surgery are presented in Box 1-2.

The patient undergoing a procedure not recommended for prophylaxis can still receive antibiotics if the surgeon believes the patient to be at particularly high risk of an SSI. In this case, the criteria used for risk assessment should be recorded. The most critical factors in the prevention of postoperative infections, although difficult to quantify, are the sound judgment and proper technique of the surgeon and surgical team, as well as the general health and concurrent disease states of the patient. Other factors that should be assessed include comorbidities such as diabetes, nicotine use, immunosuppressive therapy, age, obesity, low albumin levels, and malnutrition. Modifiable factors such as glycemic control and smoking cessation should be optimized.

The selection of a prophylactic regimen should be based on the spectrum of activity of the agents and the most likely pathogens associated with the given surgical procedure, pharmacokinetic characteristics (e.g., half-life), adverse event profile, selective pressure for bacterial resistance, and cost of the antibiotic. These principles are usually adapted into the guidelines and recommendations according to local bacterial resistance patterns. At the bedside, agent selection should also be adapted according to patient characteristics including allergies, risk of specific adverse events, bacterial resistance colonization status, and procedure-related events.

Optimal prophylaxis ensures that adequate concentrations of an appropriate antibiotic are present in the serum and tissue during the entire time the surgical wound is open and at risk of bacterial contamination. In general, the dosage of an antibiotic for prophylaxis is the same as that required for treatment of infection. Higher doses may be required in patients who are obese, depending on the antibiotic used. Infusion of antibiotics should be started within 60 minutes before incision. However, vancomycin and quinolones require longer infusion times and therefore should be initiated 120 minutes before surgical incision. Antibiotics should be re-dosed in prolonged surgery or if there is major blood loss (i.e., more than 1500 mL). This should occur at 1–2 half-lives of the prophylactic antibiotic. For example, a second dose of cefazolin should be given if the procedure lasts more than 4 hours. Re-dosing is most likely not required in ambulatory surgery. Additional doses after surgery are generally not required.

Nonpharmacologic Strategies

The goal of nonpharmacologic strategies is to eliminate preventable events by decreasing and avoiding inoculation of bacteria into the wound. Aseptic techniques, hair

Box 1-2. Considerations in Antibiotic Prophylaxis in Surgery

- Indication of antibiotic prophylaxis
- Choice of antibiotic agent
- Dosing of antibiotic
- Route of administration
- Timing of administration prior to incision
- Redosing of antibiotic during the procedure
- Duration of antibiotic prophylaxis

removal with clippers only when necessary, and minimal use of drains during surgery are some of the infection control strategies (Mangram 1999). Improving host factors to contain any contaminating bacteria by different methods is the second sphere of intervention. This includes resolving malnutrition, achieving smoking cessation, and achieving diabetes control before surgery and different perioperative interventions such as glycemic control; maintaining normothermia, hydration, and oxygenation; and minimizing hematomas, devitalized tissue, and dead space.

Type and Management of Prophylaxis

Endocarditis Prophylaxis

Use of antibiotics for endocarditis prevention has undergone a paradigm shift. The perspective of applying evidence in decision-making has forced experts to revisit the role of antibiotics in this case. Experts and associations no longer recommend prophylaxis in gastrointestinal and genitourinary procedures. Prophylaxis has been recommended according to the underlying principles listed in Box 1-3. It is now being recognized that infective endocarditis (IE) is much more likely to develop from frequent exposure to random bacteremias associated with daily activities than from those associated with a dental, gastrointestinal tract, or genitourinary tract procedure.

The risk of antibiotic-associated adverse events generally outweighs the benefits of IE prophylaxis, given that only a few, if any, IE cases may be prevented with antibiotics. Lack of efficacy of prophylaxis in humans has led experts and associations to stop recommending prophylaxis for most patients and procedures. The National Institute for Health and Clinical Excellence recommends no antibiotics for any patient or intervention, whereas the European Society of Cardiology and the American Heart Association (AHA) recommend antibiotics only for patients at high risk (Habib 2009; NICE 2008; Wilson 2007). According to the AHA guidelines, prophylaxis is deemed reasonable only for the indications shown in Figure 1-2 and the procedures shown in Table 1-1. Given this change in practice, patients should be reminded to maintain optimal oral health and hygiene to reduce the incidence of bacteremia; this is more important than prophylactic antibiotics in dental procedures for reducing the risk of IE. The incidence of IE caused by viridans streptococci seems to have remained stable in adults and children after these guidelines were published (Desimone 2012; Pasquali 2012).

A single dose of oral amoxicillin remains the drug of choice for most procedures. Intravenous or intramuscular ampicillin, cefazolin, or ceftriaxone can be given to patients unable to take oral medication. For penicillin-allergic patients, cephalexin, clindamycin, or a macrolide (azithromycin or clarithromycin) can be used. Intravenous or intramuscular cefazolin, ceftriaxone, or clindamycin can be used for patients with penicillin allergy who are unable to take oral medication. However, cephalosporins should be avoided in individuals with a history of severe penicillin allergy (anaphylaxis, angioedema, or urticaria). In patients already receiving long-term antibiotic therapy, an agent from a different class should be selected to minimize the risk of encountering bacterial resistance. Intramuscular injections should be avoided in patients taking anticoagulation agents. In these circumstances, the oral route is preferable, with intravenous administration reserved for when oral intake is not possible.

Box 1-3. Historical Underlying Principles for Recommending Prophylaxis to Prevent IE

- IE is a devastating disease, with mortality reaching 100% if left untreated.
- Prevention is preferable to treatment.
- Patients with underlying predisposing cardiac conditions develop IE.
- Patients undergoing invasive dental, gastrointestinal tract. and genitourinary tract procedures commonly develop bacteremia with organisms associated with IE.
- Antibiotics have been shown effective in preventing IE in animal models.

IE = infective endocarditis.

Prophylaxis for Surgical Procedures

Dental Procedures

Most oral and maxillofacial surgical procedures are considered clean and do not require antibiotic prophylaxis. However, some surgical procedures may be at higher risk of infection (e.g., third molar extractions); the role of antibiotics in these procedures remains controversial and is the subject of a planned review by the Cochrane collaboration. In addition to usual patient and procedure risk factors, prophylaxis is suggested according to the degree of molar inclusion and therefore the access ostectomy necessary for extraction of the impacted tooth, according to several authors. Some evidence supports a preoperative dose for the prevention of infection in patients receiving dental implants.

Facultative anaerobic gram-positive cocci continue to be the most prevalent bacteria in oral SSIs, with *Streptococcus viridans* as the predominant pathogen. Strict anaerobic gram-negative rods, mainly *Porphyromonas* and *Prevotella* spp., are also found. Strict anaerobic gram-positive cocci (*Peptostreptococcus* spp.) and other gram-negative anaerobic bacilli such as *Fusobacterium* spp. are also sometimes identified, mainly in polymicrobial infections. A single oral dose (2 g) of amoxicillin remains the drug of choice if any antibiotics are to be considered. Clindamycin 600 mg orally once can be used as an alternative in penicillin-allergic patients. The usual principles of prophylaxis apply,

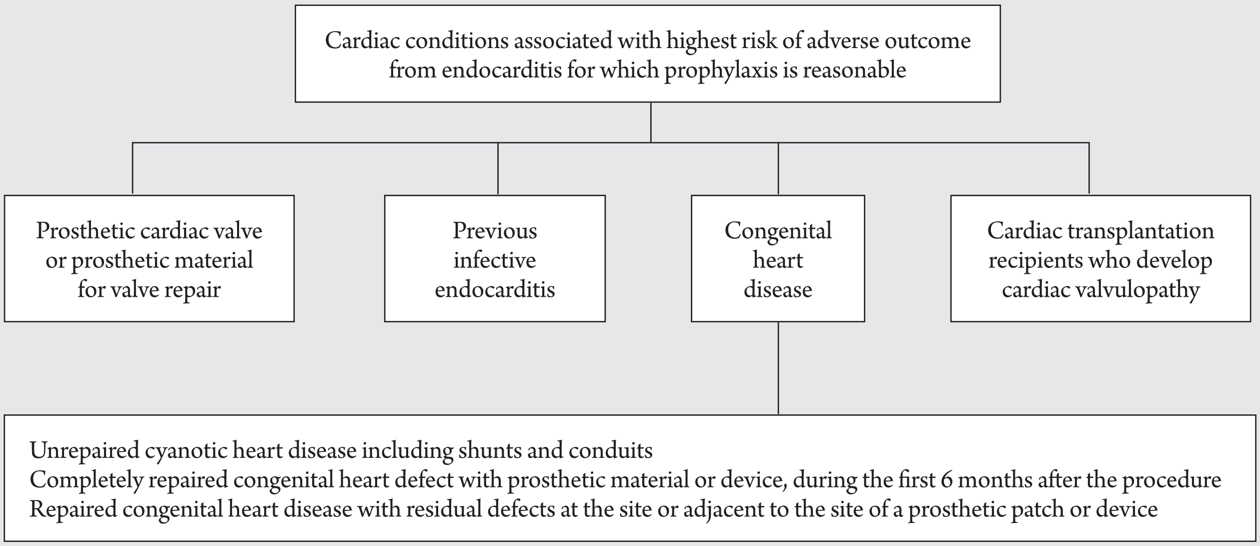

Figure 1-2. Cardiac conditions requiring antimicrobial prophylaxis for prevention of infective endocarditis.

Information from Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;116:1736-54.

Table 1-1. Recommendations for Prophylaxis in Patients at High Risk of Adverse Outcomes from Infective Endocarditis

Procedure	Conditions for Prophylaxis	Conditions Not Requiring Prophylaxis
Dental	All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa	Routine anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa
Respiratory tract	Invasive procedures requiring incision or biopsy of the respiratory mucosa (e.g., tonsillectomy and adenoidectomy)	Bronchoscopy unless the procedure involves incision of the respiratory tract mucosa
Cardiac or vascular	Preoperative dental evaluation so that required dental treatment is completed whenever possible before cardiac valve surgery or replacement or repair of congenital heart disease	
Gastrointestinal tract (e.g., diagnostic esophagogastro-duodenoscopy or colonoscopy)	Prophylactic antibiotics solely to prevent endocarditis are not recommended	
Genitourinary tract	Prophylactic antibiotics solely to prevent endocarditis are not recommended	
Infected cutaneous or musculoskeletal tissues	Treat the infected site; prophylaxis solely to prevent endocarditis is not recommended	

including administration within a 1-hour window before incision for an oral antibiotic dose or within 30 minutes of an intravenous antibiotic dose. This can be challenging in a busy dental clinic, where patients have control of timing and are unclear on precise scheduling, as opposed to an operating room where the surgeon or anesthesiologist take direct action.

Antibiotics are considered appropriate for clean-contaminated interventions such as repair of compound fractures and orthognathic, oncologic, reconstructive, and cervical surgery. Associated pathogens vary according to the contaminated areas penetrated. The usual pathogens found in the oral cavity are as mentioned previously. Agent selection may need to provide broader activity such as amoxicillin/clavulanate when other gram-negative bacteria including *E. coli* or *Klebsiella* spp. or resistant organisms are involved, depending on the type of surgery.

Gastrointestinal Procedures

Because colonization patterns vary with the wide range of surgical sites and techniques, it is difficult to make broad recommendations that apply to the gastrointestinal system. The associated pathogens and risks according to surgical methods and sites should be recognizable to determine the indication of prophylaxis and agent selection. A general guide is provided in Box 1-4.

Clinicians also should be aware of the risk of gastric contents contaminating and complicating surgery even before the incision is made. If a rupture or breach of membrane integrity is suspected, antibiotics should be given before the rupture or breach is confirmed. For example, laparoscopic removal of an inflamed appendix is a clean surgery with small risk and normally does not require pharmacologic preventive measures. However, rupture of the appendix can be unpredictable and difficult to identify because of nonspecific presenting symptoms. Therefore, prophylaxis is recommended for all patients and is to be continued as treatment if there is a major breach in technique or if preoperative contamination is discovered during the procedure.

A single dose of cefazolin 1 g intravenously 30 minutes before incision is suitable for most upper gastrointestinal procedures because it provides adequate coverage for associated gram-negative enteric pathogens. Clindamycin 900 mg intravenously can be used for penicillin-allergic patients. For appendectomy and colorectal surgery, cefoxitin 2 g intravenously and, as alternatives, gentamicin 2 mg/kg intravenously or cefazolin combined with metronidazole 500 mg intravenously or clindamycin are preferred because anaerobic pathogens (e.g., *Bacteroides fragilis*) are also involved. Oral nonabsorbable agents (combination of neomycin and erythromycin) are often substituted for systemic agents in colorectal surgery. Administered for 12–24 hours before incision, antibiotic prophylaxis is meant to decrease the large bacterial load.

Urologic Procedure

Most procedures involving the urinary tract are considered clean-contaminated. Bacteriuria increases the likelihood of bacterial invasion. In the absence of preexisting bacterial colonization, there is no evidence that prophylaxis should extend beyond 24 hours after a procedure. Some procedures (e.g., cystography, urodynamic study, simple cystourethroscopy) do not require prophylaxis in the absence of bacterial growth.

At the other end of the spectrum, antimicrobials are considered therapeutic when aimed at sterilizing the field where an existing infection or colonization is present (e.g., bacteriuria at the time of endoscopic procedure, devitalized tissue, colonized stone). A coexisting infection can be difficult to eradicate before surgery (e.g., in the treatment of a patient with an indwelling urinary catheter or an infected urinary stone). The goal of antibiotics is therefore to decrease bacterial load. Several different agents provide adequate coverage of *E. coli* as a uropathogen. Single-dose cephalosporins, fluoroquinolones, trimethoprim/sulfamethoxazole, and aminoglycosides are generally equally efficacious, well tolerated, and inexpensive.

Box 1-4. Antibiotic Prophylaxis Indications in Gastrointestinal Surgery

Prophylaxis recommended:
- Esophageal surgery mainly in the presence of obstruction
- Stomach and duodenal surgery
- Gastric bypass
- Small intestine surgery
- Hepatobiliary surgery (bile duct, pancreas, liver, open gallbladder)
- Appendectomy (perforated, necrotic, or gangrenous appendix must be treated)
- Colorectal surgery

Consider prophylaxis for patients at high risk[a]:
- Laparoscopic gallbladder surgery
- Biliary tract surgery
- Splenectomy
- Therapeutic endoscopic procedures

Prophylaxis not recommended:
- Low-risk gastroduodenal surgery
- Low-risk biliary surgery
- Hernia repair
- Abdominal open or laparoscopic surgery with mesh (e.g., gastric banding or rectopexy)
- Diagnostic endoscopic procedures

[a]Patients at high risk include those with intraoperative cholangiography, bile spillage, conversion to laparotomy, acute cholecystitis/pancreatitis, jaundice, pregnancy, immunosuppression, or insertion of prosthetic devices.

Pivotal Study That May Change Practice

Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med 2010;362:9-17.

Setting: High-level nasal carriers of *S. aureus* have up to a 6-fold increased risk of developing health care–associated infections compared with non- and low-level carriers. Decolonization with intranasal mupirocin is effective in preventing *S. aureus* infections in long-term patients undergoing hemodialysis, but not in nonsurgical patients. In surgical patients, researchers did not show the conclusive efficacy of such intervention.

Design: Nine hundred eighteen patients with nasal carriage of *S. aureus* on screening were randomized in this double-blind placebo-controlled trial designed to evaluate the efficacy of mupirocin-chlorhexidine in preventing SSIs. Patients received either 2% mupirocin ointment applied twice daily in combination with a once-daily total body wash with chlorhexidine gluconate soap (40 mg/mL) or equivalent placebo ointment and placebo soap for 5 days. Patients were followed for *S. aureus* infections for 6 weeks after discharge from the hospital.

Outcomes: Of the 917 patients included in the analysis, 49 had hospital-associated *S. aureus* infections: 17 (3.4%) in the mupirocin–chlorhexidine group and 32 (7.7%) in the placebo group (relative risk with mupirocin-chlorhexidine, 0.42; 95% confidence interval, 0.23–0.75). The cumulative incidence of health care–associated *S. aureus* infections was significantly lower in the mupirocin-chlorhexidine group than in the placebo group. The time to infection with *S. aureus* was significantly shorter in the placebo group than in the mupirocin-chlorhexidine group (p=0.005). The mean duration of hospitalization was significantly shorter in the mupirocin-chlorhexidine group than in the placebo group (crude estimate, 12.2 vs. 14.0 days; p=0.04). All-cause in-hospital mortality did not differ between groups.

Impact: Rapid detection of *S. aureus* nasal carriage, followed by immediate decolonization before surgical intervention, significantly decreased the risk of hospital-acquired *S. aureus* infection and mean duration of hospital stay by almost 2 days. Broad application of topical mupirocin for *S. aureus* decolonization has resulted in increased local resistance rates and subsequent failures of this intervention. Targeting patients who may benefit most, as in the surgical population, could delay the emergence of resistance. In addition, because methicillin-resistant *S. aureus* is becoming so prevalent, β-lactams are used less and less frequently to the advantage of other antimicrobials at increased adverse events and cost.

Aminopenicillins are now compromised because of widespread resistance to this class.

Musculoskeletal Procedures

Orthopedic surgery is a clean surgery with low infection rates; it does not require prophylaxis except when internal fixation devices (prosthetics, nails, plates, screws, and wires) are implanted (Gillespie 2010). Antibiotics play a role in prevention in the latter because an SSI is associated with extensive morbidity. The most common pathogens of SSIs in ambulatory bone and joint surgery are *Staphylococcus aureus* (35.5%), followed by coagulase-negative staphylococci (12.9%) and enterococci (12.8%) (Gastmeier 2012). A single dose or up to 24 hours of cefazolin 1 g intravenously provides adequate coverage. Vancomycin 1 g intravenously is considered for allergic patients or if there is risk of methicillin-resistant *S. aureus* infection. Screening for *S. aureus* nasal colonization, followed by subsequent decolonization, could be particularly important in prevention (Bode 2010).

Another concern in orthopedic surgery is the seeding of implanted material already in place after transient bacteremia caused by surgery at a different site. Infection of prosthetics is a major complication that results in significant morbidity and expense. According to the American Academy of Orthopaedic Surgeons, antibiotic prophylaxis can be considered for patients who have previous joint replacement infections or who are at high risk of hematogenous seeding of an artificial joint (e.g., immunosuppressed or immunocompromised patients; patients with diabetes, obesity, smoking, malnourishment, malignancy, megaprostheses). The use of an antibiotic in a second procedure to prevent infection of material implanted in a first procedure is termed *secondary prophylaxis*. Concepts are similar to those of IE prevention. The American Dental Association has provided a long list of situations that cause transient bacteremia, which might lead to infection of artificial joints. However, significant knowledge gaps remain that require further assessment before clear recommendations can be provided for this type of secondary antibiotic prophylaxis.

Other Procedures (Cardiovascular, Neurologic)

Although the incidence of postoperative wound infection for cardiothoracic and neurosurgery procedures is low (less than 5%), the devastating consequences of postoperative endocarditis (after valve replacement), mediastinitis or sternal osteomyelitis (after sternotomy), or meningitis warrant antimicrobial prophylaxis. These clean surgical procedures require substantial operative time and prolonged recovery. Therefore, most are performed within hospitals and are beyond the scope of this chapter.

Optimizing Antibiotic Prophylaxis

The objectives in managing antimicrobial prophylaxis are to decrease infectious complications after surgery with minimal adverse effects, minimize selective pressure for bacterial resistance, and lower cost. Pharmacists assess antibiotic prophylactic regimens in direct patient care settings and when developing guidelines for different procedures and surgical specialties. Steps for assessment include indications for prophylaxis, choice of antibiotic, dosing, timing of administration, re-dosing during the surgical procedure, and duration of prophylaxis.

Antibiotic stewardship strategies have improved the appropriate use of antibiotics for prophylaxis in surgery. Antibiotic prophylactic measures are influenced by many factors, including individual knowledge, attitudes, beliefs, and practice; team communication and allocation of responsibilities; and institutional support for promoting and monitoring practice. Interventions for improvement are focused on the education of practitioners; standardization of the ordering, delivery, and administration processes; and provision of feedback on performance as measured by infection rates and compliance with improvements.

The Surgical Care Improvement Project, a national multidisciplinary initiative developed by CMS, aims at improving surgical care. Reducing SSIs is among the targeted goals of this initiative. Prophylactic antimicrobials that are received within 1 hour before surgical incision, selected in compliance with published guidelines, and discontinued within 24 hours of surgery end time are three performance measures included in this quality improvement process.

In collaboration with other health care providers, pharmacists should be responsible for optimizing the indication, timing, choice, and duration of antimicrobial surgical prophylaxis. Educating surgical, anesthesia, and nursing staff, while being supported by policy changes that standardize the ordering, delivery, and administration process, all of which are initiated by pharmacists, can improve appropriate use with considerable cost avoidance. Postdischarge surveillance and feedback are also essential in reducing SSIs.

Patient Monitoring

Surgical site infections involving the incision site are defined as either superficial (involving the skin and subcutaneous fat) or deep incisional (involving fascia and muscle). Organ/space infection is defined as a third category. Clinically, local signs and symptoms such as purulent drainage, pain, tenderness, swelling, redness, or heat at the incision site are suggestive of a superficial infection. An abscess or wound dehiscence is suggestive of a deep infection. Assessment tools such as the CDC definitions, the ASEPSIS scale, and the Southampton Wound Assessment Scale are used to accurately identify and classify SSIs for monitoring (Bruce 2001). Superficial incisional SSIs occur within 30 days of the procedure and involve only the skin or subcutaneous tissue around the incision. Signs and symptoms include pain or tenderness, localized swelling, and redness or heat, and the SSI may require deliberate opening by a surgeon.

Deep incisional SSIs occur within 30 days of a procedure or up to 1 year in the presence of implants; are related to the procedure; and involve deep soft tissues such as the fascia and muscles. Purulent drainage from the incision can be used as an indicator for infection. However, purulent drainage cannot be used as an indication for deep incisional infections because it is not easily observed unless aided by radiologic techniques or exploratory surgery. Deep incisions that spontaneously dehisce or that require deliberate opening, in the presence of localized pain, tenderness, or fever, are used as evidence of infection. The presence of an abscess found on direct or radiologic examination is also sufficient for the diagnosis of infection.

Practice Points

Antibiotic prophylaxis for surgical procedures is assessed for indication, choice, dosing, timing, route of administration, and duration.

Local resistance patterns should be considered when developing guidelines on the choice of antimicrobials.

Decolonization of *S. aureus* nasal carriers may be efficacious at reducing SSIs.

Prophylaxis for IE is now targeted only to high-risk patients undergoing specific dental, respiratory tract, and cardiovascular interventions.

Concepts similar to IE prophylaxis are being developed to prevent hematogenous seeding of noncardiac prosthetic implants, but they require further evaluation before broad application.

Interventions to optimize antibiotic prophylaxis for surgical procedures should focus on:

- Educating practitioners
- Standardizing the ordering, delivery, and administrative process
- Providing feedback on performance as measured by infection rates and compliance with improvements

Patient Education

Patients should be informed of SSI risks and complication rates associated with the type of surgery they will undergo. Appropriateness of antibiotic prophylaxis, benefits, and related adverse events should be discussed in sufficient detail to allow informed decision-making. This is particularly crucial for patients no longer requiring IE prophylaxis according to the criteria of the recent AHA guideline. Adverse event monitoring by the patient should focus on allergies and diarrhea associated with the antibiotic and *Clostridium difficile*. Adherence to the scheduling of oral antibiotics requires appropriate counseling to avoid errors in administration timing. Patients should also be able to recognize signs and symptoms of infection and seek immediate medical attention when systemic symptoms occur.

Conclusion

Surgical procedures are now predominantly performed in the ambulatory care setting. Antibiotic prophylaxis for surgical procedures plays a pivotal role in preventing SSIs in addition to the control of patient- and procedure-related factors. Indiscriminate antibiotic use, however, increases the risk of adverse events and superinfections and will eventually fail with the emergence of resistance. From a professional perspective, it is the pharmacist's responsibility to ensure the appropriate use of antimicrobials. The pharmacist also has the ability to individualize therapy to patient characteristics and risk factors for infection. Time and energy should be focused on this subject because it is a primary contributor to overall antibiotic use.

References

Ambulatory Surgery Center Association. Ambulatory Surgery Centers: A Positive Trend in Health Care. 2011.
Internet Link

Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. Infect Control Hosp Epidemiol 2008;29(suppl 1):S51.
Pub Med Link

Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med 2010;362:9-17.
Pub Med Link

Bruce J, Russell EM, Mollison J, et al. The quality of measurement of surgical wound infection as the basis for monitoring: a systematic review. J Hosp Infect 2001;49:99-108.
Pub Med Link

de Lissovoy G, Fraeman K, Hutchins V, et al. Surgical site infection: incidence and impact on hospital utilization and treatment costs. Am J Infect Control 2009;37:387.
Pub Med Link

Desimone DC, Tleyjeh IM, Correa de Sa DD, et al. Incidence of infective endocarditis caused by viridans group streptococci before and after publication of the 2007 American Heart Association's endocarditis prevention guidelines. Circulation 2012;126:60-4.
Pub Med Link

Gastmeier P, Breier AC, Sohr D, et al. Prevention of surgical site infections—results from 14 years of KISS. Trauma Berufskrankheit 2012;14:110-4 [German].
Internet Link

Gillespie WJ, Walenkamp GH. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures. Cochrane Database Syst Rev 2010;17:CD000244.
Pub Med Link

Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Eur Heart J 2009;30:2369-413.
Pub Med Link

Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Am J Infect Control 1992;20:271-4.
Pub Med Link

Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care associated infections and deaths in U.S. hospitals, 2002. Public Health Rep 2007;122:160-6.
Pub Med Link

Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250-78.
Pub Med Link

National Institute for Health and Clinical Excellence (NICE). Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. Clinical guidance. Report No. 64. London: NICE, 2008.
Internet Link

National Nosocomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32:470-85.
Pub Med Link

Pasquali Sk, He X, Mohamad Z, et al. Trends in endocarditis hospitalizations at US children's hospitals: impact of the 2007 American Heart Association antibiotic prophylaxis guidelines. Am Heart J 2012;163:894-9.
Pub Med Link

Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;116:1736-54.
PubMed Link

Self-Assessment Questions

Questions 1–5 pertain to the following case.
C.F. is a 65-year-old man (height 70 inches, weight 135 kg) who is being evaluated for right lower quadrant abdominal pain. He presented with a history of nausea, loss of appetite, and fever for the past 48 hours. There are no signs of infection or rupture of the appendix. His medical history includes hypertension, coronary artery disease, and hypothyroidism. He is admitted for a laparoscopic resection of the appendix, a 1-hour intervention.

1. In determining the indication for antibiotic prophylaxis, which one of the following best categorizes C.F.'s surgical wound?
   - A. Clean.
   - B. Clean-contaminated.
   - C. Contaminated.
   - D. Dirty.

2. Which one of the following best justifies prophylactic antibiotics for C.F.?
   - A. Surgical removal of the appendix is associated with a high risk of infection.
   - B. The appendix may be ruptured, therefore requiring antibiotic administration before surgery.
   - C. Antibiotic prophylaxis is necessary because the risk of infection is low, with a low risk of complications if an infection were to arise.
   - D. Antibiotic prophylaxis is required because the prosthetic material (mesh and sutures) that will be implanted can easily become infected.

3. Which one of the following dosing regimens is most appropriate for C.F.?
   - A. Cefazolin 2 g intravenously with metronidazole 500 mg intravenously once.
   - B. Proceed without antibiotic prophylaxis.
   - C. Vancomycin 15 mg/kg of total body weight intravenously once and every 12 hours for 24 hours.
   - D. Clindamycin 900 mg intravenously and gentamicin 2 mg/kg intravenously once and every 8 hours for 24 hours.

4. C.F.'s surgeon usually prescribes cefazolin 2 g intravenously every 8 hours for 72 hours in patients undergoing this type of surgery. Which one of the following is best to recommend for C.F.?
   - A. No intervention is required because the usual regimen is appropriate.
   - B. Reduce prophylaxis to one dose because there is no benefit to further doses.
   - C. No prophylaxis should be given because it puts the patient at risk of *Clostridium difficile* diarrhea.
   - D. Prolong the duration of prophylaxis because of the risk of an appendix rupture and abscess formation.

5. Which one of the following patient counseling points would be most important to give C.F. after his surgery?
   - A. Consult a physician, should he develop diarrhea.
   - B. Monitor vital signs, including respiratory rate, heart rate, and blood pressure, every 4 hours.
   - C. He should be able to recognize the signs and symptoms of a surgical site infection (SSI).
   - D. Consult a physician if he develops abdominal pain.

Questions 6–9 pertain to the following case.
D.J. is a 67-year-old man scheduled to undergo elective root canal dental surgery in 2 weeks. The tooth is decaying with damage to the root but does not present any signs of infection or abscess. D.J.'s medical history includes coronary artery disease, type 2 diabetes mellitus, paroxysmal atrial fibrillation, aortic stenosis, aortic valve replacement, rheumatic fever (in childhood), and a stroke (2 years ago). He has never had infective endocarditis (IE).

6. Which one of the following is best to recommend regarding antibiotic prophylaxis for IE in D.J.?
   - A. He should have it because he has significant cardiac disease (coronary artery disease, aortic stenosis, rheumatic fever).
   - B. He should have it because the dental procedure is sufficient risk in itself to require prophylaxis.
   - C. He should have it because he has both the cardiac diseases and the dental procedure risks.
   - D. He should receive a full treatment course of antibiotics.

7. Which one of the following is best to recommend for D.J.?
   - A. Amoxicillin 2 g orally once.
   - B. Cefazolin 1 g intravenous once.
   - C. Azithromycin 500 mg orally once.
   - D. Clindamycin 600 mg orally once.

8. Which one of the following best delineates when D.J. should take his medication?

A. 90 minutes before the procedure as instructed by medical staff.
B. 1 hour before the procedure.
C. 30–60 minutes before the dental appointment.
D. As instructed by the dentist.

9. D.J. remembers that he once developed a severe allergy after taking penicillin. In addition, his oral dysphagia has made it difficult for him to take oral medication. Which one of the following is now most appropriate as prophylaxis for D.J.?

A. Ceftriaxone 1 g intramuscularly once.
B. Moxifloxacin 400 mg intravenously once.
C. Clindamycin 600 mg intraveinously once.
D. Cefazolin 1 g intravenously once.

10. A few months later, D.J. is to undergo routine dental cleaning. Which one of the following is best to recommend regarding antibiotic prophylaxis for IE?

A. Prophylaxis should be given because he has significant cardiac disease (aortic valve replacement).
B. Prophylaxis is required because the dental procedure is sufficient risk in itself to require prophylaxis.
C. Prophylaxis should be given because he has both the cardiac diseases and the dental procedure risks.
D. No prophylaxis is required because the dental procedure presents minimal risk.

Questions 11–13 pertain to the following case.

J.B. is a 58-year-old woman (height 61 inches, weight 71 kg) who presents with hydronephrosis, abdominal pain, and hematuria related to a kidney stone. She has had some kidney stones in the past; these were treated with fluid intake and symptomatic control. J.B. currently has no signs or symptoms of infection. A single 2.8-cm kidney stone is found on computed tomography (CT). She will undergo tubeless percutaneous lithotomy for removal of the stone. Cultures before the procedure are positive and indicative of an infected stone. Results show *Escherichia coli* x 10^7 CFU/L, which is susceptible to trimethoprim/sulfamethoxazole, gentamicin, and piperacillin/tazobactam and resistant to cefazolin and ciprofloxacin. Her SCr is 160 mg/dL, and her WBC count is within normal limits.

11. Which one of the following is best to recommend for J.B.?

A. No prophylaxis is required.
B. Administer a single dose of prophylaxis.
C. Treat for asymptomatic bacteriuria, with the first dose given before surgery.
D. Treat for a urinary tract infection before surgery.

12. J.B.'s surgeon decides that she needs treatment. Which one of the following is best to recommend for J.B.?

A. Ciprofloxacin.
B. Trimethoprim/sulfamethoxazole.
C. Nitrofurantoin.
D. Gentamicin.

13. Which one of the following regimens would be best to recommend for J.B.?

A. A single dose of prophylaxis preoperatively.
B. 48 hours of antibiotic prophylaxis.
C. A dose preoperatively, followed by 3 days of treatment.
D. A 7-day treatment.

14. A 55-year old man is scheduled to undergo tubeless percutaneous lithotomy. He presents with minimal risk factors for infection and has no bacterial growth on a preoperative urine mid-stream clean-catch sample. Which one of the following would best to recommend for this patient?

A. No prophylaxis required.
B. A single dose of prophylaxis.
C. A dose of prophylaxis before surgery, with 5 days of prophylaxis after surgery.
D. 72 hours of antibiotic prophylaxis.

15. A 62-year-old woman (height 65 inches, weight 70 kg) presents with a 6-cm-long, 3-cm-wide, 2-cm-high mass on the right wrist. She mentions having slight discomfort on occasion; however, she is seeking surgery mainly because of its appearance. After evaluation, the patient is scheduled for elective soft tissue surgery for excision of a cyst. Which one of the following is most appropriate to recommend for this patient regarding prophylaxis?

A. No prophylaxis required.
B. Cefazolin 1 g intravenously once 30 minutes before incision.
C. Cefuroxime 750 mg intravenously once before incision and every 8 hours for three doses.
D. Vancomycin 1 g intravenously once 60 minutes before incision.

Questions 16 and 17 pertain to the following case.

T.R., a 19-year-old man, is an avid skateboarder. He presents to the outpatient clinic with minor lacerations and pain to the right hand after a fall. Radiography shows a shattered radial head requiring a prosthetic replacement. J.C. has already had several fractured bones requiring repair, as well as a total hip joint replacement related to his hobbies.

16. Which one of the following is best to recommend regarding prophylaxis for T.R.?

A. No prophylaxis required.
B. Cefazolin 1 g intravenously once 30 minutes before incision.
C. Ceftriaxone 1 g intravenously once and every 24 hours for 7 days.
D. Vancomycin 1 g intravenously once 60 minutes before incision.

17. Two weeks after the procedure, T.R. consults you for unusual pain at the surgical site. You suspect an SSI. Which one of the following parameters would be most likely to prompt a medical evaluation?

    A. No fever is present.
    B. Spontaneous wound dehiscence.
    C. Stitches removed by the patient.
    D. Normal function of the limb.

18. After seeing several patients with an SSI, you begin to wonder whether antibiotic prophylaxis can be optimized for the health care services provided in your area. Which one of the following criteria provides the most information on the quality of antimicrobial use?

    A. Administration of antibiotic prophylaxis when indicated.
    B. Administration of antibiotic prophylaxis 30–60 minutes before incision.
    C. Determination of patients at risk of infection before surgery.
    D. Incidence of SSIs occurring within 1 year after surgery.

Learner Chapter Evaluation: Antimicrobial Prophylaxis.

As you take the posttest for this chapter, also evaluate the material's quality and usefulness, as well as the achievement of learning objectives. Rate each item using this 5-point scale:

- Strongly agree
- Agree
- Neutral
- Disagree
- Strongly disagree

1. The content of the chapter met my educational needs.
2. The content of the chapter satisfied my expectations.
3. The author presented the chapter content effectively.
4. The content of the chapter was relevant to my practice and presented at the appropriate depth and scope.
5. The content of the chapter was objective and balanced.
6. The content of the chapter is free of bias, promotion, or advertisement of commercial products.
7. The content of the chapter was useful to me.
8. The teaching and learning methods used in the chapter were effective.
9. The active learning methods used in the chapter were effective.
10. The learning assessment activities used in the chapter were effective.
11. The chapter was effective overall.

Use the 5-point scale to indicate whether this chapter prepared you to accomplish the following learning objectives:

12. Classify a patient's requirement for endocarditis prophylaxis according to risk factors.
13. Evaluate a patient's requirement for pharmacologic prophylaxis by assessing the risk of surgical site infection (SSI).
14. Design a prophylactic regimen according to local epidemiology, type of surgery, and patient characteristics.
15. Assess SSIs for patient outcomes and quality measurement purposes.
16. Please provide any specific comments related to any perceptions of bias, promotion, or advertisement of commercial products.
17. Please expand on any of your above responses, and/or provide any additional comments regarding this chapter: