

Antibiotics in the Surgical Patient

James T. Dwyer DO, FACOI

Objectives

- Define current prophylactic recommendations for the use of antibiotics in the surgical patient
- List current antibiotics available and alternative antimicrobials, in addition to pharmacokinetic considerations for the surgical patient
- Verbalize considerations for the continued use of antibiotics in the post-surgical patient

Introduction

- Approximately 23 million surgical procedures are performed per year in the U.S.
- Post operative infection rate = 6%
- > 1 million surgical wound infections/year
- 25% of all nosocomial infections are related to surgical wounds

- Surgical wound infections increase health care costs by about 1.5 billion dollars/year
- Prophylactic antibiotics have been shown to decrease the risk of infection for many procedures and represents an important component of optimal management of the surgical patient.

- Controversies regarding prophylactic antibiotic use include:
 - Selection of antibiotic therapy
 - Duration of antibiotic therapy
 - Development of bacterial resistance
 - Role of newly developed antibiotics
- Factors resulting in failure of prophylaxis:
 - Inadequate timing of antibiotic
 - Failure to readminister antibiotic for prolonged procedures

Patient Risk Factors

- Extremes of age
- Nutritional status
- Obesity
- Diabetes
- Tobacco use
- Co-existent remote body site infections
- Altered immune system
- Corticosteroid therapy
- Recent surgical procedure
- Length of preoperative hospitalization
- Colonization with microorganisms

Definitions

- **Prophylaxis**
 - Administration of an antibiotic prior to contamination of previously sterile tissues or fluids (the use of antimicrobials for dirty and contaminated procedures is not considered prophylaxis)
- **Presumptive therapy**
 - Administration of an antibiotic when there is a strong possibility, yet unproven infection
- **Treatment**
 - Administration of an antibiotic when an established infection has been identified

“Dirty Procedures”

- Established infection
- Therapeutic course of antibiotics is required and is no longer considered prophylaxis
- Significant bacterial spillage from a ruptured viscus
- Requires antibiotic with broad spectrum activity

Ideal Agent

- Prevent surgical site infections
- Prevent surgical site infection related morbidity and mortality.
- Reduce the duration and cost of health care
- Produce no adverse effects
- Minimize consequences for the microbial flora for the patient or the hospital
- Agent should be active against pathogens most likely to contaminate the wound
- Given in an adequate dosage and at a time that ensures adequate tissue concentration during the period of potential contamination
- Safe
- Administered for the shortest effective period to minimize adverse effects, development of resistance, and cost.

Understanding Antibiotics

- Pharmacokinetics/Metabolism/Excretion/ Safety in pregnancy
- Methods of Administration
- Dosing intervals
- Mechanisms of action
- Tissue distribution
- Length of therapy
- Concurrent medications and medical conditions
- Risk and Benefits

Antibiotic Selection

- Nose
 - S. Aureus *, Pneumococcus, Meningococcus
- Skin
 - S. Aureus*, S. Epidermidis
- Mouth/Pharynx
 - Streptococci, Pneumococcus, E. Coli, Bacteroides, Fusobacterium, Peptostreptococcus
- Urinary Tract
 - E. Coli, Proteus, Klebsiella, Enterobacter

- GI Tract/Colon,
 - E. Coli, Klebsiella, Enterobacter, Bacteroides spp., Peptostreptococcus, Clostridia
- Biliary Tract
 - E. Coli, Klebsiella, Proteus, Clostridia
- Vagina
 - Streptococci, Staph spp., E. Coli, Bacteroides spp., Peptostreptococcus
- Upper Respiratory Tract
 - Pneumococcus, H. Influenzae

The Most Common

- Cefazolin/Cefotetan/Cefoxitin
- Vancomycin (only G+ coverage)
 - Can add Genatamicin/Aztreonam/Fluroquinolone to broaden coverage
- Clindamycin + aminoglycoside or aztreonam

ANTIMICROBIAL PREOPERATIVE PROPHYLAXIS GUIDELINES

CATEGORY	PROCEDURE	ADULT DOSAGE*	
Abdominal	Gastroduodenal surgery in patients with hemorrhage, cancer, obstruction, or other high-risk features	Cefazolin 1–2 g IV preoperatively <i>or</i> Clindamycin 600 mg plus gentamicin 120 mg IV preoperatively	
	Gastric bypass	Cefazolin 1–2 g IV preoperatively	
	Percutaneous gastrostomy	Cefazolin 1–2 g IV preoperatively	
	Biliary tract (including ERCP) in patients who have acute symptoms, jaundice, or other high-risk features or who have had previous surgery	Cefazolin 1–2 g IV preoperatively <i>or</i> Gentamicin 80 mg IV preoperatively and q 8 h for 3 doses	
	Appendectomy (without perforation)	Cefoxitin, cefotetan, or cefmetazole 1–2 g IV preoperatively and q 6 h for 3 doses <i>or</i> Metronidazole 500 IV mg plus gentamicin 1.5 mg/kg IV preoperatively	
	Colorectal surgery, elective	Neomycin 1 g plus erythromycin base 1 g po at 1, 2, and 11 PM on the day before surgery ± parenteral drugs listed below for emergency colorectal surgery	
	Colorectal surgery, emergency		Cefoxitin, cefotetan, or cefmetazole 2 g IV preoperatively and q 4 h for 3 doses <i>or</i> Metronidazole 500 mg IV plus gentamicin 1.7 mg/kg IV preoperatively and q 8 h for 3 doses

ANTIMICROBIAL PREOPERATIVE PROPHYLAXIS GUIDELINES

Cardiac	Median sternotomy, coronary artery bypass graft surgery, valve surgery, or pacemaker insertion	Cefazolin 2 g IV preoperatively and q 4–6 h intraoperatively <i>or</i> Cefuroxime 1.5 g IV preoperatively and q 4–6 h intraoperatively <i>or</i> Vancomycin 1 g IV preoperatively
Neurosurgery	Craniotomy, high-risk only (eg, reexplorations, microsurgery, entry into sinuses or nasopharynx)	Vancomycin 1 g IV plus gentamicin 1.5 mg/kg IV preoperatively <i>or</i> Cefazolin 1 g IV preoperatively
	CSF shunt placement—only in hospitals with high infection rates (15–20%)	Trimethoprim 160 mg IV plus sulfamethoxazole 800 mg IV preoperatively and q 12 h for 3 doses <i>or</i> Vancomycin 10 mg plus gentamicin 3 mg injected into a cerebral ventricle

ANTIMICROBIAL PREOPERATIVE PROPHYLAXIS GUIDELINES

CATEGORY	PROCEDURE	ADULT DOSAGE*
Noncardiac thoracic	Pneumonectomy, lobectomy, other resections, or esophageal surgery	Cefazolin 1–2 g IV preoperatively and q 6 h for 24 h <i>or</i> Vancomycin 1 g IV preoperatively
Obstetric-gynecologic	Cesarean delivery, high-risk only (eg, premature rupture of membranes)	Cefazolin 1 g IV after clamping cord and q 6 h for 2 doses
	Abortion, 2nd-trimester instillation	Cefazolin 1 g IV preoperatively and q 6 h for 2 doses
	Abortion, 1st trimester in patients with a history of pelvic inflammatory disease, gonorrhea, or multiple partners	Penicillin G 1–2 million units IV preoperatively and 3 h later <i>or</i> Doxycycline 100 mg po before the procedure and 200 mg 1/2 h afterward
	Hysterectomy, vaginal or abdominal	Cefazolin 1 g IV preoperatively and q 6 h for 2 doses <i>or</i> Doxycycline 200 mg IV preoperatively
Ophthalmic	Extraction of lens, with or without insertion of prosthesis	Gentamicin, tobramycin, or neomycin-gramicidin-polymyxin B drops over 2–24 h plus cefazolin 100 mg subconjunctivally at the end of the procedure

ANTIMICROBIAL PREOPERATIVE PROPHYLAXIS GUIDELINES

Orthopedic	Arthroplasty, including replacements	Cefazolin 1–2 g IV preoperatively and q 6 h for 3 doses <i>or</i> Vancomycin 1 g IV preoperatively
	Open reduction of fractures	Cefazolin 1 g IV preoperatively and as a single postoperative dose
	Lower-extremity amputation (nonischemic)	Cefoxitin 2 g IV preoperatively and q 6 h for 4 doses
Otolaryngologic	Major head and neck surgery involving mucosa of the oral cavity or pharynx	Cefazolin 1–2 g IV preoperatively and q 8 h for 2 doses <i>or</i> Clindamycin 600–900 mg IV ± gentamicin 1.5 mg/kg IV preoperatively and q 8 h for 2 doses
Urologic	Prostatectomy if bacteriuria is present	Cefazolin 1 g IV preoperatively or another drug selected based on susceptibility tests
	Penile prosthesis insertion	Cefazolin 1 g IV preoperatively

ANTIMICROBIAL PREOPERATIVE PROPHYLAXIS GUIDELINES

CATEGORY	PROCEDURE	ADULT DOSAGE*
Vascular	Lower-extremity or abdominal arterial surgery or lower-extremity amputation for ischemia	Cefazolin 1–2 g IV preoperatively and q 6 h for 24 h <i>or</i> Vancomycin 1 g IV preoperatively and 12 h after the procedure

*Drugs, dosages, routes, and frequencies given represent current expert recommendations. Cefazolin remains highly favored because of its spectrum of bactericidal activity, long half-life, low cost, and low toxicity. Alternatives are primarily for patients with β -lactam allergies.

± = with or without.

Adapted from Kemodle DS, Kaiser AB: Postoperative infections and antimicrobial prophylaxis. In *Principles and Practice of Infectious Diseases*, ed 5, edited by GL Mandell, JE Bennett, and R Dolin. New York, Churchill Livingstone, 2000, pp. 3186–3187 and from Antimicrobial prophylaxis in surgery. *The Medical Letter* 37:79–82, 1995.

Antimicrobial Selection

- Development of Resistance
 - MRSA
 - 49.2% of surgical wound infections (2008)
(National Healthcare Safety Network)
 - Concern for VRSE/VRSA
 - VRE
 - 33% (2007)
 - Routine use of Vancomycin antimicrobial prophylaxis is not recommended for any procedure
 - Agent of choice when a cluster or high rate (>20%) of surgical wound infections in a institution isolate MRSA/CoAg (-) Staph spp.

- Patient Colonization

- Bacterial flora most affected (but not limited to)
 - » C. Difficile
 - » Enterococci
 - » Pseudomonas spp.
 - » Serratia spp.

Universal screening of patients for MRSA/VRE is controversial

Administration

- Intravenously
 - Produces rapid, reliable and predictable serum and tissue concentration
- Orally
- Topically

Timing of the initial dose

- Preoperative administration within 2 hours prior to the incision decreased the risk of surgical site infections to 0.59% from:
 - 3.8% (2 – 24 hours) prior to the incision
- Overall the recommended timing should be with 60 minutes of the surgical incision
 - (Vancomycin/Fluoroquinolones should begin within 60 – 120 minutes prior to incision)

Dosing

- Pharmacokinetic
- Pharmacodynamic properties
- Patient factors
 - Obesity has been recognized as a risk factor for surgical site infection; therefore “normal” dosing may be inadequate
- No conclusive recommendation for weight-based dosing for prophylaxis in adults

Redosing

- If a short acting agent is used, antibiotic should be redosed if the procedure extends beyond 3 hours
- Prolonged and excessive bleeding
- Anything that may shorten the half-life of the antimicrobial (eg. extensive burns)
- Not warranted if the half-life is prolonged (renal failure/insufficiency)

Duration

- For most procedures:
 - 24 hours or less
- Cardiothoracic
 - Up to 48 hours
- Ophthalmic
 - Duration not clearly established
- No data to support the continuation of antimicrobial prophylaxis until all drains, invasive lines or indwelling catheters are removed

Irrigations/Topicals/Washes

- Topicals generally only used in ophthalmic procedures
- Limited good data on the use of topicals, irrigations and washes
- Mupirocin decolonization?
- There is some interest in the use of topical Gentamicin or Vancomycin in cardiothoracic procedures to prevent mediastinitis, but data is still limited

Mechanical Bowel Prep

- No longer recommended for routine use in elective procedures
- No benefit for the use of MBP without oral or appropriate IV antimicrobials in elective colorectal procedures

Endocarditis Prophylaxis

- Procedures resulting in bacteremia increasing at risk patients for the development of endocarditis
- Who should receive:
 - Patients with artificial heart valves
 - Patients who have had heart repairs using prosthetic material (does not include coronary artery stents)
 - Patients with a prior history of endocarditis
 - Certain unrepaired or incompletely repaired congenital heart defects
 - Heart transplant patients who have now developed valvular disease

- Prophylaxis is recommended only for:
 - Dental procedures involving manipulation of the gums or roots of teeth
 - Procedures of the respiratory tract
 - Procedures involving infected tissue

- Prophylaxis is no longer recommended for procedures of the gastrointestinal or genitourinary systems.
- It is worth noting that the current guidelines do not recommend prophylaxis for:
 - Most patients with aortic or mitral valve disease (including MVP)
 - Patients with hypertrophic cardiomyopathy

- Merck Manual On-Line Library. Care of the Surgical Patient: Antimicrobial Preoperative Prophylaxis Guidelines. May,2009.
- Kritchevsky SB, Braun BI, Busch AJ et al. “The Effect of a Quality Improvement Collaborative to Improve Antimicrobial Prophylaxis in Surgical Patients: a Randomized Trial. Annals of Internal Medicine. 2008;149:472-80.
- Weber WP, Marti WR, Zwahlen M et al. “The Timing of Surgical Antimicrobial Prophylaxis”. Annals of Surgery. 2009;250:10-16.
- Frumin J, Gallagher JC. “Allergic Cross-Sensitivity between Penicillin, Carbapenems, and Monobactam Antibiotics: What are the Chances”. Annals of Pharmacotherapy. 2009;43:304-15.
- Draft Therapeutic Guideline on Antimicrobial Prophylaxis in Surgery. Executive summary. 10/2010.