ANTIBIOTIC PROPHYLAXIS IN SURGERY

SUMMARY

Antimicrobial prophylaxis is used to reduce the incidence of postoperative wound infections. Patients undergoing procedures associated with high infection rates, those involving implantation of prosthetic material, and those in which the consequences of infection are serious should receive perioperative antibiotics. Treatment, rather than prophylaxis, is indicated for procedures associated with obvious preexisting infection (i.e. abscess, pus, or necrotic tissue). Cephalosporins (such as cefazolin) are appropriate first line agents for most surgical procedures, targeting the most likely organisms while avoiding broad-spectrum antimicrobial therapy that may lead to the development of antimicrobial resistance. Duration of prophylaxis should not exceed 24 hours.

RECOMMENDATIONS

- **Level I**
  - A single preoperative dose of antibiotic is preferred as it is as effective as a full 5-day course of post-operative therapy assuming an uncomplicated procedure.
  - Prophylactic antibiotics should be administered within 1 hour prior to incision.
  - Complicated-contaminated or dirty procedures should receive additional post-operative antibiotic coverage.

- **Level II**
  - Prophylactic antibiotics should target the anticipated organisms.
  - For the majority of procedures, prophylaxis should not exceed 24 hours.
  - Prophylaxis is unnecessary if the patient is already receiving antibiotics that cover likely pathogens.
  - The timing of antibiotic administration should be adjusted to maximize prophylactic efficacy.
  - During prolonged procedures, antibiotic prophylaxis should be re-administered every 4 hours (with the exception of vancomycin, aminoglycosides, and fluoroquinolones).

- **Level III**
  - Re-administration of prophylactic antibiotics is recommended for each 1500 mL of blood loss or hemodilution.

INTRODUCTION

Surgical site infections (SSI's) account for approximately 15% of nosocomial infections and are associated with prolonged hospital stays and increased costs. Infection develops when endogenous flora are translocated to a normally sterile site. Seeding of the operative site from a distant site of infection can also occur (especially in patients with a prosthesis or other implant). Factors influencing the development of SSI's include bacterial inoculum and virulence, host defenses, perioperative care, and intraoperative management. Unfortunately, an increasing number of resistant pathogens, such as methicillin-resistant

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

Approved 10/17/06
Revised 03/13/12

Staphylococcus aureus (MRSA) and *Candida spp.*, are commonly implicated in surgical wound infections. For patients who have demonstrated recent infection with MRSA or vancomycin-resistant *Enterococcus* (VRE), prophylaxis with clindamycin, vancomycin, linezolid (Zyvox®), or quinupristin/dalfopristin (Synercid®) should be considered based on available culture susceptibilities (1-3,5).

The goal of prophylactic antibiotics is to reduce the incidence of postoperative wound infection. It is important to recognize the difference between *prophlyaxis* and *empiric* therapy. *Prophylaxis* is indicated for procedures associated with high infection rates, those involving implantation of prosthetic material, and those in which the consequences of infection are serious. The antibiotic should cover the most likely contaminating organisms and be present in the tissues when the initial incision is made. Therapeutic concentrations should be maintained throughout the procedure. *Empiric* therapy is the continued use of antibiotics after the operative procedure based upon the intraoperative findings. Empiric antibiotic therapy is addressed in a separate guideline. Inappropriate prophylaxis is characterized by unnecessary use of broad-spectrum agents and continuation of therapy beyond the recommended time period. These practices increase the risk of adverse effects and promote emergence of resistant organisms.

The traumatically injured patient represents a population in which antibiotics cannot be given before bacterial contamination occurs. An important principle of antibiotic prophylaxis is violated, raising the issue of whether or not antimicrobial administration in these patients truly represents prophylaxis. As a result, both short and long-term regimens have been advocated. Numerous studies have been conducted to identify the optimal duration of therapy in this population.

The Joint Commission on Accreditation of Healthcare Organizations and the Centers for Medicaid and Medicare Services (CMS) mandate reporting of the following performance measures on a monthly basis. Compliance with reporting these performance measures is directly linked to CMS reimbursement. The performance measures currently mandated are as follows:

1. Prophylactic antibiotics must be administered to the patient within 1 hour prior to surgical incision.
2. Prophylactic antibiotics must be discontinued within 24 hours from the end of surgery.

The procedures included in the CMS standards included coronary artery bypass grafting (CABG), cardiac surgery, hip arthroplasty, knee arthroplasty, colon surgery, hysterectomy, and vascular surgery. Patients who have a documented infection at the time of surgery or within 48 hours post-operatively are excluded from the 24 hours rule. Additionally, post-cardiothoracic surgery patients are allowed up to 48 hours of post-operative antibiotic therapy (5,6,8).

LITERATURE REVIEW

Numerous studies have been performed investigating the utility of prophylactic antibiotics in surgery. A wide variety of antibiotics, either singly or in combination, have been evaluated. With regards to surgical prophylaxis, the data from these studies support several recurring themes:

- A single preoperative dose of antibiotic is preferred as it is as effective as a full 5-day course of post-operative therapy assuming an uncomplicated procedure (1,2,11,13).
- Prophylactic antibiotics should target the anticipated organisms (1,2,13).
- Complicated-contaminated or dirty procedures should receive additional post-operative coverage (1,2,5,11,13,14,26).
- During prolonged procedures, antibiotic prophylaxis should be re-administered every 4 hours (1-5).
- Prophylactic antibiotics should be administered within 1 hour prior to incision (1-6).

The chart below summarizes the recommendations of several prospective, randomized controlled studies as well as several systematic literature reviews addressing the use of prophylactic antibiotics in various surgical procedures (8-29).

Procedure	Likely Pathogens	Recommended Antibiotic[a]	Penicillin Allergy [a,c]	Recommended Duration
Cardiothoracic Surgery	*Staph epi, Staph aureus, Streptococcus, Corynebacteria,* enteric-Gram-negative bacilli	Cefazolin 1g	Clindamycin 600mg	48 hours
General Surgery				
• Appendectomy (non-perforated)	Enteric Gram(-) bacilli	Cefoxitin 1g OR Cefotetan 1g	Clindamycin 600mg + Gentamicin 2mg/kg OR Cefazolin 1g+ Metronidazole 500mg	Single dose
• Colorectal surgery	Enteric Gram(-) bacilli, *Enterococcus*, anaerobes	Cefoxitin 1g OR Cefotetan 1g	Clindamycin 600mg + Gentamicin 2mg/kg OR Cefazolin 1g + Metronidazole 500mg	Single dose
• High-risk[b] esophageal, gastro-duodenal or biliary surgery	Enteric Gram(-) bacilli, Gram(+) cocci	Cefazolin 1g	Clindamycin 600 mg + Gentamicin 2mg/kg OR Cefazolin 1g + Metronidazole 500mg	Single dose
• Penetrating abdominal trauma	Enteric Gram(-) bacilli, *Enterococcus*, anaerobes	Cefoxitin 1g OR Cefotetan 1g	Clindamycin 600mg + Gentamicin 2mg/kg OR Cefazolin 1g + Metronidazole 500mg	24 hours
Gynecologic Surgery				
• C-section	*Staph epi, Staph aureus*, Group B *Strep, Enterococcus*	Cefazolin 2g	Clindamycin 900mg + Gentamicin 2mg/kg	Single dose
• Hysterectomy	Enteric Gram(-) bacilli, Group B *Strep, Enterococcus*	Cefazolin 1g	Clindamycin 600mg + Gentamicin 2mg/kg	Single dose
Head & Neck Surgery	Anaerobes*, Staph aureus*, Gram(-) bacilli	Clindamycin 600mg OR Ampicillin/sulbactam 3g	Clindamycin 600mg	24 hours
Neurosurgery				
• Clean	*Staph aureus, Staph epi*	Cefazolin 1g	Clindamycin 600mg	Single dose
• Skull fracture, CSF leak	Anaerobes, *Staph epi, Staph aureus*	Cefazolin 1g	Clindamycin 600mg	Single dose
• Penetrating trauma	*Staph, Strep,* Gram(-) bacilli*, anaerobes*	Cefoxitin 1g OR Cefotetan 1g	Clindamycin 600mg	5 days
• Spine	*Staph aureus, Staph epi*	Cefazolin 1g	Clindamycin 600mg	Single dose
Orthopedic Surgery				
• Closed fractures	*Staph epi, Staph aureus*	Cefazolin 1g	Clindamycin 600mg	Single dose
• Open fractures	*Staph, Strep*, Gram(-) bacilli, anaerobes	Cefazolin 1g + Gentamicin 2mg/kg[d]	Clindamycin 600mg + Gentamicin 2mg/kg	Grade I/II – 24 hours[e] Grade III – 48 hours[e]
Urologic Surgery				
• Genitourinary (high risk only)[f]	Gram(-) bacilli, *Enterococcus*	Cefazolin 1g	Ciprofloxacin 400mg	Single dose
Vascular Surgery	*Staph epi, Staph aureus*, Gram(-) bacilli, *Enterococcus*	Cefazolin 1g	Clindamycin 600mg	24 hours

[a] Antibiotic dose recommendations are for intravenous administration. Doses recommended are for patients with adequate renal function.
[b] High-risk patients include those with: age > 70 years, acute cholecystitis, nonfunctioning gallbladder, obstructive jaundice, common bile duct stones, morbid obesity, esophageal obstruction, decreased gastric acidity or motility.
[c] Clindamycin 600mg or vancomycin 1g may be used in patients with documented penicillin or cephalosporin allergies.
[d] Cefazolin should be used alone for Grade I and II open fractures. Gentamicin should be added for Grade III open fractures.
[e] Duration of antibiotics after closure of fractures.
[f] Genitourinary High Risk Criteria: positive urine culture (or unavailable urine culture), preoperative urinary catheter, and/or transrectal prostatic biopsy.

Approved 10/17/06
Revised 03/13/12

Recommendations for re-dosing antibiotics:

Delay in time to surgical incision:

In order for a case to pass core measure auditing, parenteral antibiotic surgical prophylaxis should begin within 60 minutes prior to incision so that the drug is distributed to tissues prior to the initial incision. The most effective way to achieve this is to administer the drug immediately prior to induction of anesthesia. Vancomycin and ciprofloxacin are the only exceptions to this rule and both should be given 60 to 120 minutes prior to induction of anesthesia. Antimicrobial re-dosing recommendations are described below(1-5).

Antibiotic	**Dosing Procedure (delays > 60 minutes from start of antibiotic infusion and incision)**
Cefazolin, Cefuroxime, Cefotetan, Cefoxitin, Ampicillin/sulbactam	Repeat pre-op dose
Clindamycin	Repeat pre-op dose
Metronidazole	Repeat pre-op dose
Gentamicin	Do ***NOT*** repeat dose
Antibiotic	**Dosing Procedure (delays > 120 minutes from start of antibiotic infusion and incision)**
Vancomycin	Delay *less* than 8 hours: • Give an additional 500mg vancomycin IV*
	Delay *greater* than 8 hours: • Serum creatinine less than or equal to 2 mg/dL: Repeat pre-op dose* • Serum creatinine greater than 2 mg/dL: Give an additional 500 mg vancomycin IV*
Ciprofloxacin	Repeat pre-op dose

*Vancomcyin should not be infused faster than 1g over 1 hour

Lengthy surgical procedures and blood loss during surgery:

If the surgical procedure is prolonged ≥ 4 hours, antibiotics should be re-administered to ensure adequate antimicrobial concentrations at the site of infection throughout the entire case (1-5). For most agents re-dosing is recommended every 4 hours during surgery, but the medication half-life and usual dosage interval should be considered. A table regarding the recommended time to re-dose prophylactic antibiotics (for patients with adequate renal function) is described below. For patients with impaired renal function, re-dosing is left to the discretion of the surgeon. Re-administration of prophylactic antibiotics is recommended for each 1500 mL of blood loss or hemodilution (3).

Drug	**Recommended Re-dosing Interval**
Cefazolin, Cefuroxime, Cefotetan, Cefoxitin, Ampicillin/sulbactam, Clindamycin	4 hours
Ciprofloxacin	6 hours
Gentamicin, Metronidazole	8 hours
Vancomycin	12 hours

Patients receiving antibiotic treatment prior to surgery:

When patients are receiving antibiotic therapy for treatment of infection prior to surgery, administering additional antibiotics for prophylaxis may not be necessary due to similar spectrum of activity. Ensuring adequate antibiotic concentrations at the incision site at the time of cut is still important. Therefore, adherence to the recommendations regarding the re-dosing of antibiotics above in the “delay in time to surgical incision” chart is recommended (1-5).

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