10

Antibiotics and perioperative infections

Michael James D.O., M.S.

Assistant Professor of Anesthesiology and Critical Care Medicine

Elizabeth A. Martinez* M.D., M.H.S

Associate Professor of Anesthesiology and Critical Care Medicine, and Surgery

Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medicine,
600 N. Wolfe Street, Meyer 296, Baltimore, MD 21287, USA

Surgical site infections remain a significant contributor to postoperative morbidity and mortality. It is estimated that 500,000 patients suffer from this complication annually. Among other interventions, appropriate administration of prophylactic antibiotics has been shown to decrease the risk of perioperative infections. The goal of prophylactic antibiotic administration is to decrease the risk of contamination of the wound from skin flora in the case of clean procedures, and to add coverage of organisms that are anticipated to contaminate the surgical field, as in open bowel procedures. The purpose of this review is to summarize the guiding principles of perioperative antibiotic administration including selection, timing, redosing, and discontinuation. In addition, special topics including likely organisms for classes of surgical procedures, endocarditis prophylaxis, and management strategies for patients with allergies will be reviewed.

Key words: surgical site infections; surgical antimicrobial prophylaxis; surgical care improvement project; endocarditis prophylaxis; beta-lactam allergy.

INTRODUCTION: BACKGROUND OF SURGICAL SITE INFECTIONS

Surgical site infections (SSIs) are an especially important type of healthcare-acquired infection because of the increased morbidity, mortality, and cost that they impart on patients and the healthcare system.[1–4] The estimated incidence of SSIs is approximately 500,000 cases annually in the U.S., and these range in severity from the superficial, requiring minimal intervention, to those that require re-operation (e.g. muscle

* Corresponding author. Tel.: +1 410 955 9080; Fax: +1 410 955 8978.
  E-mail addresses: mjames12@jhmi.edu (M. James), emartine@jhmi.edu (E.A. Martinez).

and skin flap closure for deep mediastinal wound infections following cardiac surgery).[5]

Prevention of SSIs has become a national focus because of the impact and burden of such infections and the poor compliance with practices recommended to decrease the risk of SSIs. The Centers for Medicare and Medicaid Services (CMS) and the Joint Commission (JCAHO) have made this issue a national priority. The Surgical Care Improvement Project (SCIP) is a national quality partnership of organizations (CMS, JCAHO) focused on improving surgical care by reducing surgical complications. The SCIP goal is to reduce the incidence of surgical complications, including infections, by 25% nationally by the year 2010 through implementation of key interventions that have been shown to decrease SSIs.[6] These evidence-based measures include appropriate use of antibiotics (selection, timing and discontinuation), appropriate hair removal, perioperative normothermia, and glycemic control in cardiac surgical patients. Provider and hospital performance of these process measures is being reported publicly and is a component of pay-for-performance programs.[6]

The remainder of this review will focus on perioperative antimicrobial prophylaxis (AMP).

Practice points

- Many of the national performance measures are under the domain of the anesthesiologist. (Appropriate antibiotic administration, maintenance of normothermia, and glycemic control in cardiac surgical patients).

BACKGROUND AND PRINCIPLES OF PROPHYLACTIC ANTIBIOTIC ADMINISTRATION

In healthcare, prophylactic measures can be divided between primary prophylaxis (to prevent the development of a disease) and secondary prophylaxis (whereby the disease has already developed and the patient is protected against worsening of this process).[7] In surgical patients, the use of AMP is generally for the *primary prevention of contamination and development of a wound infection*.[5] For most SSIs, the pathogen sources are the endogenous flora (skin, mucous membranes, or hollow viscera).[8]

Surgical AMP consists of a brief course of antibiotics that begins before the start of a surgical procedure (before incision); it should be discontinued very shortly postoperatively, if continued after the procedure at all. It is not intended to sterilize the tissues or prevent against all possible contaminants, but rather prevent against the dominant skin, or site-specific, flora. The CDC has outlined basic principles of surgical AMP and these are summarized in Table 1.[8–10]

Four components are important to appropriate administration of perioperative AMP and include appropriate antibiotic (1) selection, (2) timing, (3) redosing, and (4) discontinuation. The principles discussed in this review focus on prophylaxis, rather than treatment of a previously diagnosed infection whose management may continue into the perioperative period.

Table 1. CDC Principles guiding maximization of safety and effectiveness of surgical antimicrobial prophylaxis (AMP).[8–10]

1. Use AMP for those procedures that carry a risk of perioperative infection, or when the consequences of an infection are great, and have evidence to support that administration of AMP reduces the risk of SSIs.
2. Select the agent that is safe, inexpensive, preferably bactericidal, and that most narrowly covers the most likely organisms causing SSI in that patient population.
3. Administer the antibiotic such that the bactericidal concentration of the agent is established in serum and tissues by the time the skin incision is made.
4. Maintain adequate /therapeutic levels until the incision is closed.

ANTIBIOTIC SELECTION

Spectrum

The antibiotic used for prophylaxis needs to cover the common organisms that would most likely cause an SSI. In other words, specific types of procedures are known to be associated with specific microorganisms, and antibiotics have clear profiles of the organisms they will effectively cover. ([Tables 2 and 3](#)) *Staphylococci* and *Streptococci*

Table 2. Procedure type, Likely SSI Pathogens.[5,8,12]		
Operations	Likely pathogens[1]	Appropriate antibiotic (if PCN allergic)
Placement of all grafts, prostheses or implants; Cardiac; Neurosurgery; Breast; Vascular	S. *aureus*; coag (-) staph	Cefazolin (Vancomycin or clindamycin)[1]
Orthopedic (± hardware/implant)	S. *aureus*; coag (-) staph; GNR	Cefazolin (Vancomycin or clindamycin)[1]
Noncardiac thoracic	S. *aureus*; coag (-) staph; GNR; Streptococcus pneumoniae	Cefazolin (Vancomycin or clindamycin)[1]
GI (non-duodenal)	GNR; anaerobes	Cefotetan (Clindamycin; ± gent)
Gastroduodenal	GNR; anaerobes; oral anaerobes	Cefotetan (Clindamycin; ± gent)
Head & neck (major with oropharyngeal incision)	S. *aureus*, streptococci, oropharyngeal anareobes	Clindamycin plus gent; Cefazolin probably adequate[2]
Obstetric/Gynecologic	GNR; Enterococci, Group B strep; anaerobes	Cefazolin (clindamycin)
Urologic	GNR	Cefazolin; High risk: ciprofloxacin

S. *aureus, Staphylococcus aureus;* Coag (-) staph: Coagulase negative staphylococci; GNR: Gram negative bacilli (rods); gent, gentamicin; GI, gastrointestinal

Adapted with permission: 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 Apr;20(4):250-78, University of Chicago Press.

[1] Consideration may be made to substitute vancomycin for clindamycin when hardware/implants are used, including sternal wires.

[2] Guideline in Mayhall et al.[5]

Class	Spectrum of coverage	Activity (at recommended doses)	Recommended dosage (intraoperative)	Elimination half Life (hours)
Table 3. Appropriate Antibiotic Selection Considerations.				
Penicillins				
Ampicillin-sulbactam (Unasyn)	Gram (+), Gram (−) and Anaerobes Dosage adjustment of renal impairment CrCl 20-40 ml/min, dose decrease of 30% CrCl <20 ml/min, Dose decrease by 30% and increase re-dose interval to every 8 hours Beta-lactamase inhibitor broadens coverage	Bactericidal	3 g IV every 4 h	1.2—1.3
Cephalosporin (1st-generation)				
Cefazolin (Ancef, Kefzol)	Drug of choice for surgical prophylaxis not involving the GI tract Staphylococcal and enterococcal Streptococcus, E.coli, Klebsiella, P. mirabilis	Bactericidal	2 g IV every 2—4 h	1.8
Cephalosporin (2nd-generation)				
Cefotetan (Cefotan)	Prophylactic coverage for abdominal, pelvic, colorectal and cesarean section Gram (−) and anaerobic (Bacteroides and Clostridium sp.) Improved Gram (−) coverage over cefazolin	Bactericidal	2 g IV every 8 h	3—4.6
Cefoxitin (Mefoxin)	Prophylactic coverage for abdominal, pelvic, colorectal and cesarean section Gram (−) and anaerobic (Bacteroides and Clostridium sp.) Improved Gram (−) coverage over cefazolin	Bactericidal	2 g IV every 6 h	1.2—1.3
Macrolides				
Azithromycin (Zithomax)	Gram (−) including atypical organisms	Bacteriostatic	500 mg IV once	40
Lincomycins				
Clindamycin (Cleocin)	Gram (+) coverage including Staphylococcus aureus Anaerobic coverage including Bacteroides fragilis	Bacteriostatic	600 mg IV every 6 h	2.4—3

Table 3 (continued)				
Class	Spectrum of coverage	Activity (at recommended doses)	Recommended dosage (intraoperative)	Elimination half Life (hours)
Monobactams				
Aztreonam (Azactam)	Gram (−) coverage only, including Pseudomonas	Bactericidal	1-2 g IV every 8 h	1.5−2.1
Quinolones (second-generation)				
Ciprofloxacin (Cipro)	Gram (−) coverage, Quinolone of choice for Pseudomonas Contra-indicated in Pregnancy and pediatric patients	Bactericidal	400 mg IV once	4
Glycopeptides				
Vancomycin (Vancocin)	Drug of choice for MRSA Gram (+) coverage only, no Gram (−) or anaerobic coverage	Bactericidal	1 g IV every 12 h	4−6
Miscellaneous				
Metronidazole (Flagyl)	Anaerobic coverage including Bacteroides fragilis Relative contra-indication in first trimester of pregnancy	Bactericidal	500 mg IV every 8 h	7−8

are the most common organisms of concern for most procedures, whereas anaerobes and Enterobacteriaceae are common for GI cases. Many published guidelines for AMP[5,6,11–15] are available for development of local antibiotic guidelines; local sensitivity profiles also should be taken into account.

Toxicity

The penicillins and cephalosporins are effective agents because they selectively inhibit the growth of susceptible microorganisms with minimal detriment to the patient.

Activity

An ideal prophylactic antibiotic is bactericidal rather than bacteriostatic. Bactericidal agents imply bacterial killing and subsequent reduction in potential inoculum size at the surgical site. Bacteriostatic agents inhibit cell growth but do not produce cell death or a reduction in bacterial population. Static agents require innate host defenses to be intact for cell destruction and do not prevent resumed bacterial growth once serum or tissue levels have diminished (Table 3).[10]

Dosing

The dose selection for antibiotics is based on patient weight. The antibiotic must attain adequate serum and tissue levels, and recommendations for dosing are made based on

the expected volume of distribution of the specific agent. It is important to note that the most commonly used prophylactic agents, the cephalosporins, require dose adjustment for weights above 75 kg. Increasingly, adult patients are larger than 75 kg. Our local antibiotic recommendations are to administer 2 g of cefazolin or cefotetan for *all* of our adult patients, as even this higher dose, which is frequently administered only two to three times for most surgical procedures, has low risk of complications. Vancomycin is also adjusted for weight (1.25 g for patients who are >70 kg, and 1.5 g if >100 kg).

Practice points

- AMP should target the most likely organisms that will cause SSIs.
- The ideal AMP agent is bactericidal and has low toxicity.
- Antibiotic dose needs to be adjusted for weight.

Special considerations

Patients with beta-lactam allergies

Hypersensitivity reactions to antimicrobial agents represent a therapeutic challenge to the selection of appropriate surgical prophylaxis. Hypersensitivity reactions to beta-lactams typically manifest as drug fever, maculopapular rash, or urticaria (hives) and anaphylaxis.[16] It is important to note that hypersensitivity reactions are stereotyped and that there is generally no progression with repeated exposure.[16] In other words, once a reaction occurs on primary exposure it will typically not progress on re-exposure (e.g. gastrointestinal disturbance does not progress to anaphylaxis, nor does maculopapular rash progress to anaphylaxis); however, hives may carry increased risk of progression to true anaphylaxis.

Most patients provide remote or vague histories of a reaction to a beta-lactam agent that cannot be substantiated further. The positive predictive value of the clinical history has been estimated at a mere 14%.[17] Others report symptoms that are not characteristic of true allergy, instead representing expected (e.g. "red man" syndrome with rapid vancomycin administration) or idiosyncratic side effects (e.g. gastrointestinal intolerance or idiopathic cutaneous reactions). History consistent with *true allergy* (urticaria, pruritus, angioedema, bronchospasm, hypotension, or arrhythmia) or of a serious drug reaction (drug-induced hypersensitivity syndrome, drug fever, or toxic epidermolysis) is the key information to obtain. In general, patients who report a drug fever or rash can safely be given a beta-lactam.[16] In addition, cephalosporins are well tolerated in most patients with a positive clinical history and negative penicillin skin testing, with reported frequency of reaction at 1.7%.[17] Patients with hives/urticaria or previous anaphylactic reaction (hypersensitivity type I reaction) should receive *neither* a beta-lactam nor cephalosporin. Although the cross-reactivity is low (estimated <2%), the risk is significant. If there is any doubt as to the type of skin reaction, assume it is urticaria.[18]

Skin testing will detect only allergen specific IgE antibodies that produce type I hypersensitivity reactions. In addition, the rates of false-positive and false-negative results to skin testing are not insignificant.[17,19,20] Although there is interest in limiting the use of vancomycin and broad-spectrum antibiotics for prophylaxis, no compelling evidence to date supports pre-operative skin testing in penicillin-allergic patients. Therefore, it

is important to know what antibiotics have shown no cross-allergenicity with penicillins or beta-lactams. These include aminoglycosides, tetracyclines, macrolides, clindamycin, chloramphenicol, metronidazole, vancomycin, linezolid, daptomycin, tigecycline, quinolones, nitrofurantoin and monobactams.[16]

Intra-operative "test dosing" is not well studied. Some practitioners will administer a small initial dose before injection of the full prophylactic dose. This practice is not supported by the literature and will not prevent potential anaphylaxis. Importantly, anaphylaxis *is not dose dependent*, and the test dose can result in anaphylaxis (up to 1 h after dose) and acute hemodynamic collapse.

Practice points

- History of a true allergy or serious drug reaction after exposure to a beta-lactam is an absolute contraindication to administration of a beta-lactam or cephalosporin
- Anaphylaxis is not dose dependent and can occur up to 1h after exposure.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

With the increasing prevalence of colonization with MRSA[21,22], providers are questioning whether patients should receive vancomycin as prophylaxis. The Hospital Infection Control Practices Advisory Committee recommends that "high" levels of local rates of MRSA should influence local antibiotic selection for prophylaxis.[8] However, there is no consensus of what this threshold is. Furthermore, there is no evidence that routine use of vancomycin for prophylaxis in institutions with high rates of MRSA will decrease SSIs more than use of agents such as cefazolin.[15] It is recommended that vancomycin be considered the appropriate antimicrobial agent for prophylaxis for individual patients who are colonized with MRSA.[15,23]

Given these recommendations, the limitations of vancomycin should be considered. Vancomycin has only Gram-positive coverage, unlike cefazolin which also has Gram-negative coverage. Furthermore, it is a more complicated agent to administer in the perioperative setting as it requires administration over at least 1 h because of the risk of histamine release and "red man" syndrome. There is no clear evidence to determine when vancomycin would be the optimal agent; therefore, the decision should be specific to the patient and situation. The Society of Thoracic Surgeons recommends a *single preoperative dose* of vancomycin in addition to cefazolin when the patient is colonized with MRSA for patients undergoing cardiothoracic procedures.[24]

Practice points

- Vancomycin has not been shown to decrease the rates of SSIs in institutions with high MRSA colonization rates.
- Vancomycin has only Gram-positive coverage
- Vancomycin should be considered for patients who are colonized with MRSA or when there is a high-rate of local MRSA SSIs (not just colonization).

Infective endocarditis (IE) prophylaxis

The American Heart Association has outlined practice guidelines for the prevention of IE; these were substantially revised in 2007.[25] Full review of these guidelines is recommended for all anesthesia providers.

The most significant change is that IE prophylaxis recommendations are now based on the patient's *risk of adverse outcomes* should they develop IE, rather than on his/her lifelong risk of developing this entity. The groups of patients that remain at highest risk of adverse outcomes are those with a prosthetic valve, prior endocarditis, congenital heart disease, or cardiac transplant recipients with cardiac valvulopathy.[25] Patients with mitral valve prolapse are not included in this list because their *risk of adverse outcomes* is not increased, despite their high risk of development.

It is recommended that these *highest risk patients* receive prophylaxis for only a very small subset of procedures. In general, patients who are receiving recommended SSI prophylaxis will *not require additional antibiotics* for IE. In other words, the likely organisms that might cause endocarditis are covered by the routinely recommended prophylactic antibiotics. The specific procedures highlighted in the guidelines and recommended IE prophylaxes are: (1) high-risk dental procedures-Amoxicillin as first line to cover *Strep viridans*, with cefazolin or clindamycin for penicillin-allergic patients. (2) Invasive respiratory procedures-the same agents are recommended as for dental procedures, unless the infection is suspected to be caused by *S. aureus;* then an anti-staphylococcal penicillin (oxacillin), or vancomycin if the organism is MRSA, should be used.

It is important to note that antibiotic prophylaxis is *not recommended in GI and GU* procedures solely for the purpose of IE prevention. Of course such patients should still receive the standard surgical prophylaxis regimen if it is an invasive procedure. The guidelines support consideration of an agent that would be active against *Enterococci* (penicillin or vancomycin). Our local guidelines suggest the use of vancomycin instead of clindamycin for high-risk GI procedures in penicillin-allergic patients.

Practice points

- Routine surgical AMP should cover most IE pathogens.
- Antibiotics are not indicated for GI and GU procedures solely for the prevention of IE.
- Mitral valve prolapse is no longer an indication for IE prophylaxis.

TIMING AND REDOSING OF PROPHYLACTIC ANTIBIOTICS

The goal of appropriately timed AMP is to achieve adequate serum and tissue levels of antibiotic before incision and to maintain these throughout the procedure. An adequate antibiotic level is defined as a concentration higher than the minimum inhibitory concentration (MIC) of the suspected pathogens *in the surgical wound at the time of incision.*[26] Multiple studies support administration of AMP close to the time of incision, and prior to it, to achieve the desired protective benefit.[26–30]

The SCIP measure is that the infusion of the first antimicrobial dose should begin within 60 min before incision, or within 120 min for vancomycin and fluoroquinolones

(since these require a slow infusion).[6,15] Bratzler et al[15] reported an alarmingly low 56% compliance with appropriate timing of AMP among a national sample of patients. Current opinion as to the goal of infusion completion favors completion prior to incision; however there is currently no consensus in this regard.[15] General principles and supporting evidence for antibiotic action and timing, including redosing, are discussed below.

Pharmacologic considerations

The beta-lactam antimicrobials (i.e. penicillin, cephalosporin, monobactam and carbapenem) are time-dependent killers. Their bactericidal effect is directly proportional to the amount of time the concentration of the antibiotic at the surgical site is above the MIC of the organisms[10] most likely to contaminate the wound (the area under the curve). Intra-operative redosing is based on the elimination half-life and maintenance of serum concentrations above the MIC for continued effect. The MIC for common organisms will vary based on local sensitivity patterns. These data are provided through the microbiology laboratory and should be reviewed before developing a local selection algorithm for surgical prophylaxis. Cefazolin is an example of a time dependent killing agent (Figure 1). It is re-dosed every 4 h based on the elimination half-life of 1.8 h. Serum concentrations are highest 10–15 min after intravenous administration and steadily decline to levels at or below the MIC breakpoint at the 4-hour mark. Based on the available MICs for standardized organisms, an intra-operative re-dosing scheme can be formulated based on the elimination half-life. Below the MIC breakpoint, reliable bacterial killing is not sustained and wound contamination may occur. Vancomycin, clindamycin, and the macrolide family work through similar mechanisms.

An alternate mechanism through which antimicrobials exert their effect is known as concentration-dependent killing. Antimicrobials with concentration-dependent pharmacodynamics include the aminoglycosides, fluoroquinolones, and metronidazole. Maximization of bactericidal effects is dependent on achieving peak serum
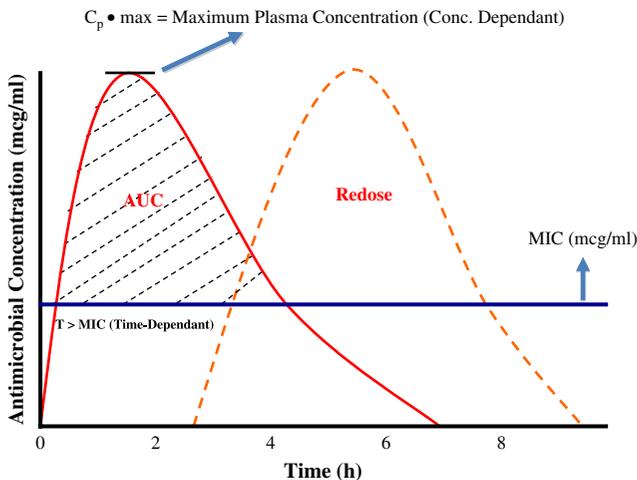

Figure 1. Representation of Pharmacodynamic Pattern Over a Concentration-time Profile.

concentrations rather than total time above the predicted MIC.[10] Many concentration-dependent antimicrobials exhibit additional post-antibiotic effects that allow prolonged killing or suppressive effects after the serum concentration has dissipated.

Evidence for timing of AMP

In 1992, the landmark study by Classen et al[26] described the association between timing of prophylactic antibiotics and infection rates. Patients undergoing clean or clean-contaminated surgical procedures were prospectively monitored for antibiotic timing and the incidence of SSI. They showed that if antibiotics were *not* given in the pre-procedure time window, defined as 0–2 h before incision in this study, the relative risk of infection was 2.4 times the baseline if given 0–2 hours after incision, 5.8 times the risk if given 2–24 hours pre-incision, and 6.7 times the risk if given 3–24 hours post-incision.[26] Another recent study by van Kasteren et al[31] demonstrated the same U-shaped relationship between timing and SSI incidence, with the lowest rates of infection associated with the immediate pre-incision timing and higher rates if administered too early or too late.[31,32] Current recommendations are that the anesthesia provider be responsible for the administration of the prophylactic antibiotic to optimize timing. Such practices have resulted in improved performance with this process measure.

Special considerations

Obstetrics

Nearly all published obstetric trials since 1978 have administered the antimicrobial agent immediately after the umbilical cord is clamped. Before that time, AMP was administered pre-operatively. This change followed the publication of a single prospective trial demonstrating that AMP administered after the umbilical cord was clamped was as effective in decreasing maternal morbidity as AMP given prior to the procedure.[33]

In 2007, a prospective, randomized, double-blind, placebo-controlled trial compared patients given cefazolin 15–60 min prior to incision for cesarean section with controls who received cefazolin at the time of umbilical cord clamping. This study showed a significantly lower total infectious morbidity in the study group, with a relative risk of 0.4 (95% CI, 0.18 to 0.87), and no increase in neonatal morbidity. In 2007, our local practice was changed, with a goal of administering AMP 30 minutes prior to incision.

Procedures with use of tourniquet

As the goal of prophylactic antibiotics is to attain adequate tissue levels, consideration must be made for the timing of tourniquet inflation (which occurs before incision). Studies have suggested that administration of a cephalosporin within 30 sec before tourniquet inflation may be adequate; however, given the variation in cephalosporin absorption, some authors suggest waiting 5 min before tourniquet inflation.[34,35]

> ### Practice points
>
> - Surgical AMP should be administered <60 min before incision, or <120 min for vancomycin and fluoroquinolones, with infusion complete before incision.
> - The anesthesiologist should be responsible for administering the antibiotics to optimize appropriate timing.
> - Consider administering AMP prior to incision for Caesarean sections.
> - AMP needs to be administered before inflation of a tourniquet.

Redosing of AMP

The goal of administering antibiotics intraoperatively is to maintain adequate serum and tissue levels during the highest risk period, which is while the incision is open. Observational studies have shown that repeated intraoperative dosing of an antibiotic with a short half-life is associated with a decreased risk of SSI.[36–39] Redosing of antibiotics should be based on the specific antibiotic's half-life and the patient's creatinine clearance.[5,40,41] It is therefore recommended that during the time the skin incision remains open, AMP should be redosed at 2-times the half-life. The inclusion of antibiotic redosing as a SCIP measure is being considered. This measure will be based on the specific agent's serum half-life.

Swoboda and colleagues[41] found that increased clearance of antimicrobial prophylaxis might occur during procedures with high blood loss. Our local recommendations include a caveat for redosing of cefazolin, cefotetan, and ampicillin/sulbactam when intraoperative blood loss is ≥1500 cc.

DISCONTINUATION OF PROPHYLACTIC ANTIBIOTICS

There are no data to support a prolonged course of prophylactic antibiotics. In fact, many studies show no added benefits of postoperative doses, possibly because the highest risk period is while the incision is open.[29,42] Furthermore, there are risks of prolonged antibiotic usage such as the development of drug resistant pathogens and *Clostridium difficile*.

The national measure is discontinuation of AMP within 24 h after surgery end time, except for cardiac surgery, which has been approved for up to 48 h of coverage, although no strong data support this extension.[43]

> ### Practice points
>
> - While the incision is open, antibiotics should be redosed based on their respective half-lives. Redosing is recommended at 2-times the half-life.
> - Consider redosing cephalosporins and penicillins when the patient has significant blood loss.

Practice points

- Data do not support prolonged use of AMP.
- AMP should be discontinued in less than 24 h for all procedures (<48 h for cardiac surgical procedures).
- To meet the 24 h measure patients should receive two doses of cefazolin, cefotetan, or clindamycin or one dose of vancomycin postoperatively.

SUMMARY

Anesthesia providers should take ownership of the administration of surgical AMP. They need to become familiar with the goals of AMP, which are: to administer the *appropriate* AMP in a timely fashion (≤60 min before incision (or ≤120 min) for vancomycin/fluoroquinolones), to *redose* during the procedure based on the agents half-life, and to *discontinue* AMP in a timely fashion. Furthermore, we must improve the process (or system) of our AMP delivery by adopting practices of highly reliable systems that include decreasing the complexity (guidelines, availability of AMP agents) and introducing redundancies (reminders, checklists) into this process.[44,45] In order to improve local performance, and deliver these best practices to all patients, providers should work with their infectious disease and surgical colleagues to develop a local guideline for the selection of antibiotics (and make certain this is readily available in the operating room), encourage discussion of antibiotic selection and timing during the pre-procedure time out, and write anticipated times of redosing on the "white board," or use other types of reminders (kitchen timers, computer reminders). And finally – in order to improve performance with these measures it is imperative that providers have feedback on their performance[46] in order to make change, and that there be sharing of ideas between surgical teams and collaboration within and across hospitals.[47] Our experience, and the experience of others[47], suggest that these interventions are successful at improving local compliance with these SCIP performance measures.

Research agenda

- Research is needed to evaluate how to best translate these evidence-based process measures into practice and close the gap between best evidence and best practice.
- Prospective randomized trials to evaluate the risks-benefits of broad use of vancomycin in patients who are colonized with MRSA.
- Prospective randomized trial to evaluate the risk-benefits of preoperative penicillin skin-testing.

REFERENCES

1. Nelson RM & Dries DJ. The economic implications of infection in cardiac surgery. *Annals of Thoracic Surgery* 1986 Sep; **42**(3): 240–246.
2. Perencevich EN, Sands KE, Cosgrove SE et al. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerging Infectious Diseases* 2003 Feb; **9**(2): 196–203.

3. Taylor GJ, Mikell FL, Moses HW et al. Determinants of hospital charges for coronary artery bypass surgery: the economic consequences of postoperative complications. *American Journal of Cardiology* 1990 Feb 1; **65**(5): 309–313.

4. Malangoni MA, Cheadle WG, Dodson TF et al. New opportunities for reducing risk of surgical site infection. *Surgical Infections (Larchmt)* 2006; **7**(Suppl. 1): S23–S39. Roundtable discussion.

5. Mayhall CG. *Hospital epidemiology and infection control.* 3rd edn. Philadelphia: Lippincott Williams & Wilkins, 2004.

*6. Surgical Care Improvement Project: infection, www.medqic.com.

7. Wikipedia: prophylaxis, www.wikipedia.com. accessed Feb 1, 2008.

*8. Mangram AJ, Horan TC, Pearson ML et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infection Control and Hospital Epidemiology* 1999 Apr; **20**(4): 250–278. quiz 279–280.

9. Mangram AJ. A brief overview of the 1999 CDC guideline for the prevention of surgical site infection. centers for disease control and prevention. *Journal of Chemotherapy* 2001 Nov; **13 Spec No 1**(1): 35–39.

10. Mandell GL, Douglas RG, Bennett JE & Dolin R. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases.* 6th edn. New York: Elsevier/Churchill Livingstone, 2005.

*11. Treatment guidelines from the medical letter. *Antimicrobial Prophylaxis for Surgery* 2006; **4**(52): 83.

12. ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery. *American Society of Health-System Pharmacists* 1999 Sep 15; **56**(18): 1839–1888.

13. De Lalla F. Perioperative antibiotic prophylaxis: a critical review. *Surgical Infections (Larchmt)* 2006; **7**(Suppl 2): S37–S39.

14. Auwaerter P. 2007. Available from: http://www.hopkins-abxguide.org. Accessed 3/2008, 2008

*15. Bratzler DW & Houck PM. Surgical infection prevention guideline writers workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *American Journal of Surgery* 2005 Apr; **189**(4): 395–404.

*16. Cunha BA. Antibiotic selection in the penicillin-allergic patient. *The Medical Clinics of North America* 2006 Nov; **90**(6): 1257–1264.

17. 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: The Journal of the American Medical Association* 2001 May 16; **285**(19): 2498–2505.

18. Robinson JL, Hameed T & Carr S. Practical aspects of choosing an antibiotic for patients with a reported allergy to an antibiotic. *Clinical Infectious Diseases* 2002 Jul 1; **35**(1): 26–31.

19. Arroliga ME & Pien L. Penicillin allergy: consider trying penicillin again. *Cleveland Clinic Journal of Medicine* 2003 Apr; **70**(4): 313–314. 317–8, 320–1 passim.

20. Gruchalla RS & Pirmohamed M. Clinical practice. Antibiotic allergy. *New England Journal of Medicine* 2006 Feb 9; **354**(6): 601–609.

21. Fridkin SK, Hageman JC, Morrison M et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *New England Journal of Medicine* 2005 Apr 7; **352**(14): 1436–1444.

22. Klevens RM, Morrison MA, Nadle J et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA: The Journal of the American Medical Association* 2007 Oct 17; **298**(15): 1763–1771.

*23. Bratzler DW & Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clinical Infectious Diseases* 2004 Jun 15; **38**(12): 1706–1715.

24. Engelman R, Shahian D, Shemin R et al. The society of thoracic surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part II: antibiotic choice. *Annals of Thoracic Surgery* 2007 Apr; **83**(4): 1569–1576.

*25. 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 Oct 9; **116**(15): 1736–1754.

*26. Classen DC, Evans RS, Pestotnik SL et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *New England Journal of Medicine* 1992 Jan 30; **326**(5): 281–286.

27. Burke JF. Preventive antibiotics in surgery. *Postgraduate Medicine* 1975 Sep; **58**(3): 65–68.

28. Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* 1961 Jul; **50:** 161–168.
29. DiPiro JT, Vallner JJ, Bowden Jr. TA et al. Intraoperative serum and tissue activity of cefazolin and cefoxitin. *Archives of Surgery* 1985 Jul; **120**(7): 829–832.
30. Stone HH, Hooper CA, Kolb LD et al. Antibiotic prophylaxis in gastric, biliary and colonic surgery. *Annals of Surgery* 1976 Oct; **184**(4): 443–452.
31. van Kasteren ME, Mannien J, Ott A et al. Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor. *Clinical Infectious Diseases* 2007 Apr 1; **44**(7): 921–927.
32. Dellinger EP. Prophylactic antibiotics: administration and timing before operation are more important than administration after operation. *Clinical Infectious Diseases* 2007 Apr 1; **44**(7): 928–930.
33. Gordon HR, Phelps D & Blanchard K. Prophylactic cesarean section antibiotics: maternal and neonatal morbidity before or after cord clamping. *Obstetrics & Gynecology* 1979 Feb; **53**(2): 151–156.
34. Bannister GC, Auchincloss JM, Johnson DP & Newman JH. The timing of tourniquet application in relation to prophylactic antibiotic administration. *The Journal of Bone and Joint Surgery. British Volume* 1988 Mar; **70**(2): 322–324.
35. Friedman RJ, Friedrich LV, White RL et al. Antibiotic prophylaxis and tourniquet inflation in total knee arthroplasty. *Clinical Orthopaedics and Related Research* 1990 Nov; **260:** 17–23.
36. Morita S, Nishisho I, Nomura T et al. The significance of the intraoperative repeated dosing of antimicrobials for preventing surgical wound infection in colorectal surgery. *Surgery Today* 2005; **35**(9): 732–738.
*37. Zanetti G, Giardina R & Platt R. Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. *Emerging Infectious Diseases* 2001 Sep–Oct; **7**(5): 828–831.
38. Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *American Surgeon* 1997 Jan; **63**(1): 59–62.
39. Ohge H, Takesue Y, Yokoyama T et al. An additional dose of cefazolin for intraoperative prophylaxis. *Surgery Today.* 1999; **29**(12): 1233–1236.
40. Bergamini TM & Polk Jr. HC. Pharmacodynamics of antibiotic penetration of tissue and surgical prophylaxis. *Surgery Gynecology & Obstetrics* 1989 Mar; **168**(3): 283–289.
41. 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. *Journal of Antimicrobial Chemotherapy* 2003 Feb; **51**(2): 459–462.
42. McDonald M, Grabsch E, Marshall C & Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Australian and New Zealand Journal of Surgery* 1998 Jun; **68**(6): 388–396.
43. Edwards FH, Engelman RM, Houck P et al. The society of thoracic surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, Part I: duration. *Annals of Thoracic Surgery* 2006 Jan; **81**(1): 397–404.
44. Berenholtz SM, Pronovost PJ, Lipsett PA et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Critical Care Medicine* 2004 Oct; **32**(10): 2014–2020.
45. Pronovost P, Needham D, Berenholtz S et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *New England Journal of Medicine* 2006 Dec 28; **355**(26): 2725–2732.
46. Pronovost PJ, Berenholtz SM, Goeschel CA et al. Creating high reliability in health care organizations. *Health Services Research* 2006 Aug; **41**(4 Pt 2): 1599–1617.
*47. Dellinger EP, Hausmann SM, Bratzler DW et al. Hospitals collaborate to decrease surgical site infections. *American Journal of Surgery* 2005 Jul; **190**(1): 9–15.