



## Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project

Dale W. Bratzler, D.O., M.P.H.\*, Peter M. Houck, M.D., for the Surgical Infection Prevention Guideline Writers Workgroup

*Oklahoma Foundation for Medical Quality, Inc., 14000 Quail Springs Pkwy., Suite 400, Oklahoma City, OK 73134-2627, USA*

---

### Abstract

In January 2003, leadership of the Medicare National Surgical Infection Prevention Project hosted the Surgical Infection Prevention Guideline Writers Workgroup meeting. The objectives were to review areas of agreement among the published guidelines for surgical antimicrobial prophylaxis, to address inconsistencies, and to discuss issues not currently addressed. The participants included authors from most of the published North American guidelines for antimicrobial prophylaxis and several specialty colleges. The workgroup reviewed currently published guidelines for antimicrobial prophylaxis. Nominal group process was used to draft a consensus paper that was widely circulated for comment. The consensus positions of the workgroup include that infusion of the first antimicrobial dose should begin within 60 minutes before surgical incision and that prophylactic antimicrobial agents should be discontinued within 24 hours of the end of surgery. This advisory statement provides an overview of other issues related to antimicrobial prophylaxis including specific suggestions regarding antimicrobial selection.

*Keywords:* Antibiotics; Postoperative complications; Practice guidelines; Surgical site infection

---

Surgical site infections (SSIs) are the second most common cause of nosocomial infections [1,2]. Up to 2% to 5% of patients undergoing clean extra-abdominal operations and up to 20% undergoing intra-abdominal operations will develop an SSI [3, Available at: <http://www.ahrq.gov/clinic/ptsafety/pdf/ptsafety.pdf>. Accessed: December 8, 2003]. The Centers for Disease Control and Prevention (CDC) estimates that approximately 500,000 SSIs occur annually in the United States [4]. Patients who develop SSIs are up to 60% more likely to spend time in an intensive care unit, five times more likely to be readmitted to the hospital, and to have twice the mortality rate compared with patients without an SSI [5]. Health care costs are substantially increased in patients who develop SSIs [1,5–8].

In August 2002, the Centers for Medicare and Medicaid Services (CMS) and the CDC implemented the National Surgical Infection Prevention (SIP) Project [9]. The goal of

the project is to decrease the morbidity and mortality associated with postoperative SSIs by promoting appropriate selection and timing of administration of prophylactic antimicrobial agents. A panel of experts in surgical infection prevention, hospital infection control, and epidemiology developed 3 performance measures for national surveillance and quality improvement [9]. These measures are as follows: (1) the proportion of patients who have parenteral antimicrobial prophylaxis initiated within 1 hour before the incision; (2) the proportion of patients who are given a prophylactic antimicrobial agent that is consistent with currently published guidelines; and (3) the proportion of patients whose prophylactic antimicrobial is discontinued within 24 hours of the end of surgery. For the purposes of national surveillance, the project focuses on operations commonly performed on Medicare patients and for whom there is no controversy about the need for antimicrobial prophylaxis. These include coronary artery bypass grafting; other open-chest cardiac surgery (excluding transplant surgery); vascular surgery including aneurysm repair, thromboendarterectomy, and vein bypass; general abdominal colorectal surgery; hip and knee arthroplasty (excluding revisions); and abdominal and vaginal hysterectomy [9].

Several guidelines for antimicrobial prophylaxis in sur-

---

This article is being reprinted with permission from The University of Chicago Press. Original citation: Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis* 2004;38:1706–1715.

\* Corresponding author. Tel.: +1-405-840-2891; fax: +1-405-840-1343.

*E-mail address:* [dbratzler@okqio.sdps.org](mailto:dbratzler@okqio.sdps.org)

Table 1  
Summary of published guidelines on antimicrobial prophylaxis for operations targeted for surveillance in the National Surgical Infection Prevention Project [9]

| Operations                        | Prophylactic antibiotic recommendation*  | Comments   |
|-----------------------------------|--|--|
| Cardiothoracic surgery            | Cefazolin†, ‡, §, ¶, #<br>Cefuroxime§,   , ¶<br>Cefamandole§<br><br>If $\beta$ -lactam allergy:<br>vancomycin†, ‡, §,   , ¶<br>clindamycin#  | Most of the guidelines agree that duration of prophylaxis for cardiac surgery should not exceed 24 hours. The ASHP suggests continuation of prophylaxis for cardiothoracic surgery for up to 72 hours; however, the authors suggest that prophylaxis for $\leq 24$ hours may be appropriate.§,**<br><br>Cefamandole is not available in the United States.   |
| Vascular surgery                  | Cefazolin†, ‡, §,   , ¶<br>Cefuroxime¶<br>If $\beta$ -lactam allergy:<br>Vancomycin†, ‡, §,   , ¶, #<br>Vancomycin with or without gentamicin§<br>Clindamycin#                         |  |
| Colon surgery                     | Oral:<br>Neomycin plus erythromycin base†, ‡, §,   , ¶<br>Neomycin plus metronidazole¶<br><br>Parenteral:<br>Cefoxitin or cefotetan†, ‡, §,   , ¶<br>Cefazolin plus metronidazole  , ¶ | Currently, none of the guidelines address antimicrobial prophylaxis for those patients with documented $\beta$ -lactam allergy.<br><br>Cefmetazole is not available in the United States.†,§<br><br>Although a recent study indicates that the combination of oral prophylaxis with parenteral antimicrobial prophylaxis may result in lower wound infection rates, this is not specified in any of the published guidelines [86]. |
| Hip or knee arthroplasty          | Cefazolin†, ‡, §,   , ¶<br>Cefuroxime¶<br>If $\beta$ -lactam allergy:<br>Vancomycin†, ‡, §,   , ¶<br>Clindamycin#  | Although not addressed in any of the published guidelines, the workgroup recommends that the prophylactic antimicrobial be completely infused before inflation of a tourniquet.<br>Cefuroxime is recommended for patients undergoing total hip arthroplasty.   |
| Vaginal or abdominal hysterectomy | Cefazolin†, ‡, §,   , ¶, ††<br>Cefotetan§,   , ¶, ††<br>Cefoxitin§,   , ¶, ††<br>Cefuroxime¶   | Metronidazole monotherapy is recommended in the ACOG Practice Bulletin as an alternative to cephalosporin prophylaxis for patients undergoing hysterectomy††<br><br>Trovaflaxacin, while still available in the United States, is recommended on a limited basis only.¶  |

ACOG = American College of Obstetricians and Gynecologists; ASHP = American Society of Health-System Pharmacists; HICPAC = Hospital Infection Control Practices Advisory Committee; SIP = Surgical Infection Prevention.

\* The antibiotics in this column are currently used to assess quality of care on the national performance measure on the proportion of patients who receive prophylactic antimicrobials consistent with current recommendations in the National SIP Project.

† Surgical Infection Society Antimicrobial Agents Committee [10].

‡ Infectious Diseases Society of America Quality Standards Subcommittee of the Clinical Affairs Committee [11].

§ ASHP Commission on Therapeutics [12].

|| Medical Letter on Drugs and Therapeutics [14].

¶ The Sanford Guide to Antimicrobial Therapy, 2003 [16].

# HICPAC [13] recommends either clindamycin or vancomycin as alternatives for gram-positive bacterial coverage if a patient is unable to receive a cephalosporin because of  $\beta$ -lactam allergy.

\*\* The ASHP recommendation for duration of prophylaxis for cardiothoracic surgery was based on expert opinion, and the authors suggest that prophylaxis for 24 hours may be appropriate [12].

†† ACOG Committee on Practice Bulletins [15].

gery have been published [10–16]. Although there is considerable agreement in recommendations for antimicrobial selection and timing (Table 1), inconsistencies exist, and several important issues are not addressed. In January 2003, leadership of the National SIP Project hosted a meeting of the Surgical Infection Prevention Guideline Writers Workgroup (Appendix). Authors from most of the North American guidelines and representatives of several additional specialty societies interested in surgical infection prevention attended. The objectives of the meeting were to review areas

of agreement, to address issues of inconsistency, and to discuss issues not currently addressed in published guidelines.

This advisory statement summarizes the workgroup's meeting and subsequent discussions, provides an overview of current guidelines on antimicrobial prophylaxis, and provides expert consensus on issues that are inconsistent or not addressed in the guidelines. Specific recommendations regarding the national performance measures and antimicrobial prophylaxis for operations targeted in the National SIP

Project are discussed. This article is not meant to be an exhaustive review of the literature of antimicrobial prophylaxis for surgery because published guidelines provide such reviews, and the workgroup discussions were generally limited to operations being evaluated in the national project.

## General Recommendations

### *Timing of antimicrobial first dose*

The goal of antimicrobial prophylaxis is to achieve serum and tissue drug levels for the duration of the operation that exceed the minimum inhibitory concentration for organisms likely to be encountered during the operation. As early as 1961, Burke [17] demonstrated that experimental incisions contaminated with *Staphylococcus aureus* could not be distinguished from incisions that had not been contaminated when antimicrobial agents were administered before the incision. He found that antimicrobial agents were effective in decreasing lesion size if administered no later than 3 hours after bacterial contamination was introduced. In 1969, Polk and Lopez-Mayor [18] reported a randomized trial of antimicrobial prophylaxis in patients undergoing elective gastrointestinal tract surgery that demonstrated a significant decrease in the frequency of wound and intra-abdominal sepsis among treated patients. In 1976, Stone et al [19] demonstrated the lowest SSI rates in patients undergoing gastrointestinal, biliary, and colon operations when antimicrobial agents were administered within 1 hour before incision. Administration of first antimicrobial dose after surgery resulted in SSI rates almost identical to those in patients who did not receive prophylaxis [19]. Ideally, the antimicrobial agent should be administered as near to the incision time as possible to achieve low SSI rates [17–25]. Based on published evidence, the workgroup endorsed the national performance measure that infusion of the first antimicrobial dose should begin within 60 minutes before incision. However, when a fluoroquinolone or vancomycin is indicated, the infusion should begin within 120 minutes before incision to prevent antibiotic-associated reactions. Although research has demonstrated that administration of the antimicrobial agent at the time of anesthesia induction is safe and results in adequate serum and tissue drug levels at the time of incision, there was no consensus that the infusion must be complete before incision. Whenever a proximal tourniquet is required, however, the entire antimicrobial dose should be administered before the tourniquet is inflated.

### *Duration of antimicrobial prophylaxis*

The majority of published evidence demonstrates that antimicrobial prophylaxis after wound closure is unnecessary, and most studies comparing single- with multiple-dose prophylaxis have not shown benefit of additional doses [3,10–14,26–28]. Prolonged use of prophylactic antimicro-

bial agents is associated with emergence of resistant bacterial strains [29–31]. For the majority of operations being evaluated in the National SIP Project, the guidelines cited in this article recommend that prophylaxis end within 24 hours after the operation. The one exception is the preferred regimen of antimicrobial prophylaxis for cardiothoracic surgery recommended by the American Society of Health-System Pharmacists (ASHP). It includes continuation of prophylaxis for up to 72 hours [12]. This ASHP recommendation was based on expert opinion, and the authors suggest that prophylaxis for  $\leq 24$  hours may be appropriate [12]. Based on published evidence, the workgroup endorsed the national performance measure that prophylactic antimicrobial agents should be discontinued within 24 hours of the end of surgery.

## Beta-Lactam Allergy

### *Screening for allergy*

Although many patients have documented drug allergies in their medical records, symptoms or circumstances of these are rarely documented. Several studies have demonstrated that the incidence of true drug “allergy” is lower than that recorded in medical records [32–34]. Because beta-lactam antimicrobial agents often represent agents of choice for prophylaxis, the medical history should be adequate to determine if the patient likely had a true allergy (eg, urticaria, pruritus, angioedema, bronchospasm, hypotension, or arrhythmia) or serious adverse drug reaction (eg, drug-induced hypersensitivity syndrome, drug fever, or toxic epidermal necrolysis) [35].

In operations for which cephalosporins represent appropriate prophylaxis, alternate antimicrobial agents should be given to those with a high likelihood of past serious adverse reaction or allergy based on patient history or diagnostic tests such as skin testing. However, the incidence of adverse reactions to cephalosporins in patients with reported penicillin allergy is rare, and penicillin skin tests do not predict the likelihood of allergic reactions to cephalosporins in patients reporting penicillin allergy. Practical approaches to patients with a history of antibiotic allergy have been previously published [35–37].

### *Antimicrobial choice for beta-lactam allergy*

Recommendations for confirmed beta-lactam allergy are provided in the discussion of specific operations that follow. In operations where prophylaxis is directed primarily at gram-positive cocci—such as orthopedic operations with joint replacement; cardiothoracic operations; or general, vascular, and neurosurgical operations with implants—alternatives to cephalosporins for beta-lactam allergy are vancomycin and clindamycin [13]. The decision to use vancomycin or clindamycin should involve examination of local antimicrobial resistance patterns and institutional incidence

of infections caused by organisms such as *Clostridium difficile* and *Staphylococcus epidermidis* [38]. Based on antimicrobial spectrum, vancomycin and clindamycin are appropriate alternatives to beta-lactams, although few data exist to support the use of either for routine prophylaxis.

### **Methicillin-Resistant *Staphylococcus aureus***

The Hospital Infection Control Practices Advisory Committee guideline suggests that “high” levels of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in an institution should influence the use of vancomycin for prophylaxis [13]. However, there is no consensus about what constitutes high levels of methicillin resistance. In addition, there is no evidence that routine use of vancomycin for prophylaxis in institutions with perceived high rates of MRSA will decrease SSIs more than agents such as cefazolin. In a study of cardiac surgery in an institution with a perceived high rate of MRSA, Finkelstein et al [39] randomized 885 patients to prophylaxis with cefazolin or vancomycin. There was no difference in SSI rates between the 2 groups (9.0% cefazolin vs. 9.5% vancomycin,  $P = .8$ ). However, patients who received cefazolin and later developed an SSI were more likely to be infected with MRSA. Patients who developed an SSI after vancomycin prophylaxis were more likely to be infected with methicillin-sensitive *Staphylococcus aureus*. The choice of antimicrobial changed the flora of infections that occurred but did not alter infection rates. Similarly, Manian et al [40] recently demonstrated that 2 postoperative factors (postoperative antibiotic treatment >1 day and discharge to a long-term care facility) were associated with development of MRSA SSIs. Lack of vancomycin use for prophylaxis was not associated with risk of MRSA SSI [40].

For patients with known MRSA colonization, vancomycin should be considered the appropriate antimicrobial agent for prophylaxis. The Society for Healthcare Epidemiology of America recently recommended routine surveillance cultures at the time of admission for patients at high-risk for carriage of MRSA [41]. Rates of MRSA colonization may be greater in patients who have previously spent >5 days in an institutional setting including long-term or acute care [41–44].

### **Limitation of Additional Agents**

The goal of antimicrobial prophylaxis is to prevent infection of the wound with the most probable organisms to be encountered for that type of operation. For most operations, a single antimicrobial is sufficient to prevent SSIs. However, there may be cases where an unlikely contaminant is present or suspected (eg, there is coexisting infection) in which additional coverage is necessary. For clean procedures, it is recommended to treat or remove other sources of infection before an elective operation [13]. If it is not possible to postpone the operation, antimicrobial pro-

phylaxis specific for the suspected bacteria and appropriate for the surgical site is recommended.

Intranasal mupirocin has been studied in a variety of operations to evaluate impact on SSIs. Although the use of intranasal mupirocin has been effective at decreasing nasal carriage of *Staphylococcus aureus*, the majority of studies do not demonstrate a decrease in SSI rates [45–47].

### **Antimicrobial Dosing**

Limited published data exist on appropriate antimicrobial dosing for prophylaxis. The drug should be given in an adequate dose based on patient weight, adjusted dosing weight, or body mass index, and administration should be repeated intraoperatively if the operation is still continuing two half-lives after the first dose to ensure adequate antimicrobial levels until wound closure. In a study of obese patients undergoing gastroplasty, blood and tissues levels of cefazolin were consistently below the minimum inhibitory concentration for gram-positive and -negative organisms in patients who received a 1-g dose before surgery [48]. Those patients receiving 2 g cefazolin had a lower incidence of SSI than those receiving a 1-g dose [48]. Studies of patients undergoing gastrointestinal, biliary, and cardiac operations have demonstrated that repeat dosing of short-half-life antimicrobial agents is associated with lower SSI rates [49–51]. Suggested initial dose, infusion time, and time to redosing for commonly recommended prophylactic antimicrobial agents are summarized in Table 2.

### **Nonantimicrobial Methods of Preventing Infection**

Recent data suggest that attention to intraoperative temperature control and supplemental oxygen administration, along with aggressive fluid resuscitation, may decrease infection rates [52–55]. Additional research is required before definitive recommendations can be made [56]. Considerable evidence exists that aggressive perioperative blood sugar control with intravenous insulin in patients undergoing cardiac operations decreases SSI rates [57–59]. The risk of SSI appears to be related to the presence of hyperglycemia rather than to a diagnosis of diabetes mellitus.

### **Specific Antimicrobial Recommendations**

Published evidence exists to support the use of many different prophylactic antimicrobial regimens other than those included in this advisory statement or existing guidelines. However, factors such as cost, half-life, safety, and antimicrobial resistance favor the use of older, relatively narrow-spectrum agents. The use of newer, broad-spectrum drugs, ie, frontline therapeutic agents, should be avoided in surgical prophylaxis to decrease emergence of bacterial strains that are resistant to these antimicrobial agents.

Table 2  
Suggested initial dose and time to redosing for antimicrobials commonly used for surgical prophylaxis [88–90]

| Antimicrobial     | Half-life normal renal function (h)                              | Half-life end-stage renal disease (h)    | Recommended infusion time (min)                     | Standard intravenous dose (g)          | Weight-based dose recommendation* (mg)         | Recommended redosing interval† (h) |
|-------------------|--|--|---|--|--|------------------------------------|
| Aztreonam         | 1.5–2  | 6  | 3–5‡  | 1–2                                    | Maximum 2 g (adults)                           | 3–5                                |
| Ciprofloxacin     | 3.5–5  | 5–9                                      | 60  | 400 mg                                 | 400 mg   | 4–10                               |
| Cefazolin         | 1.2–2.5  | 40–70                                    | 3–5‡<br>15–60§                                      | 1–2                                    | 20–30 mg/kg<br>1 g < 80 kg<br>2 g ≥ 80 kg      | 2–5                                |
| Cefuroxime        | 1–2  | 15–22                                    | 3–5‡<br>15–60§                                      | 1.5                                    | 50 mg/kg                                       | 3–4                                |
| Cefamandole       | 0.5–2.1  | 12.3–18                                  | 3–5‡<br>15–60§                                      | 1                                      |  | 3–4                                |
| Cefoxitin         | 0.5–1.1  | 6.5–23                                   | 3–5‡<br>15–60§                                      | 1–2                                    | 20–40 mg/kg                                    | 2–3                                |
| Cefotetan         | 2.8–4.6  | 13–25                                    | 3–5‡<br>20–60§                                      | 1–2                                    | 20–40 mg/kg                                    | 3–6                                |
| Clindamycin       | 2–5.1  | 3.5–5.0¶                                 | 10–60<br>(Do not exceed 30 mg/min)                  | 600–900 mg                             | <10 kg: at least 37.5 mg<br>≥10 kg: 3–6 mg/kg  | 3–6                                |
| Erythromycin base | 0.8–3  | 5–6                                      | NA  | 1 g orally 19, 18, 9 h before surgery  | 9–13 mg/kg                                     | NA                                 |
| Gentamicin        | 2–3  | 50–70                                    | 30–60   | 1.5 mg/kg#                             | See footnote#                                  | 3–6                                |
| Neomycin          | 2–3 hours (3% absorbed under normal gastrointestinal conditions) | 12–≥24                                   | NA  | 1 gm orally 19, 18, 9 h before surgery | 20 mg/kg                                       | NA                                 |
| Metronidazole     | 6–14   | 7–21 no change                           | 30–60   | 0.5–1                                  | 15 mg/kg (adult) 7.5 mg/kg on subsequent doses | 6–8                                |
| Vancomycin        | 4–6  | 44.1–406.4 (Cl <sub>cr</sub> <10 mL/min) | 1 g ≥60 min (use longer infusion time if dose <1 g) | 1.0                                    | 10–15 mg/kg (adult)                            | 6–12                               |

DW = dosing weight; IBW = ideal body weight; NA = not applicable.

\* Weight-based doses are primarily from published pediatric recommendations.

† For procedures of long duration, antimicrobials should be redosed at intervals of 1 to 2 times the half-life of the drug. The intervals in the table were calculated for patients with normal renal function.

‡ Dose injected directly into vein or running intravenous fluids.

§ Intermittent intravenous infusion.

|| In patients with a serum creatinine 5 to 9 mg/dL.

¶ The half-life of clindamycin is the same or slightly increased in patients with end-stage renal disease compared with patients with normal renal function.

# If the patient's weight is 30% above their ideal body weight, dosing weight can be determined as follows: DW = IBW + 0.4 (total body weight-IBW).

### Gynecologic and obstetric surgery

For abdominal or vaginal hysterectomy, cefotetan is preferred, but reasonable alternatives are cefazolin or cefoxitin [10–12,14–16,60]. Metronidazole monotherapy is included in the American College of Obstetricians and Gynecologist's Practice Bulletin as an alternative for patients undergoing hysterectomy, although it may be less effective as a single agent for prophylaxis [15]. In cases of beta-lactam allergy, the work-group recommends the use of 1, of the following regimens: clindamycin combined with gentamicin, aztreonam, or ciprofloxacin; metronidazole combined with gentamicin or ciprofloxacin; or clindamycin monotherapy. Levofloxacin, 750 mg, given once can be substituted for ciprofloxacin.

Patients undergoing cesarean section can be divided into low- and high-risk groups for postoperative infection [61]. High-risk patients include cesarean deliveries after rupture of the membranes, onset of labor, or both, and patients who undergo emergency operations for which preoperative cleansing may have been inadequate. Although antimicrobial prophylaxis is recommended for both risk groups, the benefits are greatest for high-risk patients. A narrow-spectrum antimicrobial regime similar to that recommended for hysterectomy provides adequate prophylaxis [62,63]. In the United States, the antimicrobial is usually not administered until the umbilical cord is clamped. Although there is no evidence to support the delay in administration, it is standard



practice and is preferred by neonatologists because of concern of masking septic manifestations in the neonate [64].

#### *Orthopedic total joint (hip and knee) arthroplasty*

The preferred antimicrobial for prophylaxis in patients undergoing hip or knee arthroplasty is either cefazolin or cefuroxime [10–12,14,16]. Vancomycin or clindamycin may be used in patients with serious allergy or adverse reactions to beta-lactam agents. Several studies comparing short- versus long-duration antimicrobial prophylaxis for total joint arthroplasty have shown no advantage to prolonged prophylaxis [3,65–70]. The workgroup recommends that antimicrobial prophylaxis be discontinued within 24 hours after the end of the operation [3,10–12,14,16,65–70]. If a proximal tourniquet is used, the antimicrobial should be completely infused before inflation.

There is no evidence that continuing antimicrobial agents until all catheters and drains are removed will lower infection rates. However, the use of drains has been associated with numerous complications including infection, drain retention, and soft tissue problems [71–73]. The necessity of drains for total joint arthroplasty is controversial [72–80]. With time, there is increased bacterial colonization of the drain tip and migration of skin organisms into the wound [81–83].

Despite the potential benefits of antibiotic-impregnated bone cement for joint arthroplasty, controversies remain regarding its use. There are no established guidelines for use of these agents for prophylaxis. Commercially available, preblended antibiotic bone cements are indicated only for use in the second stage of a 2-stage revision for total joint arthroplasty after elimination of active infection. These products are not currently approved for prophylaxis.

#### *Cardiothoracic and vascular surgery*

The recommended antimicrobial agents for cardiothoracic and vascular operations include cefazolin or cefuroxime [10–12,14,16]. For patients with serious allergy or adverse reaction to beta-lactam agents, vancomycin is appropriate, and clindamycin may be an acceptable alternative [13]. The workgroup acknowledged the concern of some cardiovascular surgeons about discontinuing the antimicrobial before all invasive lines and drains are removed. Although a number of studies have found no advantage of long- over short-duration prophylaxis during cardiothoracic surgery, the consequences of deep sternal infections or infected prostheses are devastating. Longer-duration prophylaxis has been associated with higher rates of resistant organisms when SSI occurs [29]. The consensus of the workgroup is that prophylaxis lasting  $\leq 24$  hours is acceptable and that there is no evidence showing that giving antimicrobial agents for longer periods of time will decrease SSI rates. Table 3 Pending a systematic review of the literature by its Committee on Evidence-based Medicine, the Society of Thoracic Surgeons currently recommends

that antimicrobial prophylaxis be continued for 24 to 48 hours.

#### *Colorectal surgery*

Antimicrobial prophylaxis for colorectal operations can consist of an oral antimicrobial bowel preparation, preoperative parenteral antimicrobial, or a combination of both. Recommended oral prophylaxis consists of neomycin plus erythromycin, or neomycin plus metronidazole, started no more than 18 to 24 hours before surgery along with a mechanical bowel preparation. Cefotetan or cefoxitin are recommended for parenteral prophylaxis [10–12,14,16]. The combination of parenteral cefazolin and metronidazole is also recommended as a cost-effective alternative [84,85]. Although a recent study suggested that the combination of oral prophylaxis with parenteral antimicrobial prophylaxis might result in lower SSI rates, this is not specified in any published guideline [86]. A survey of colorectal surgeons found that combination oral and parenteral prophylaxis is common practice in the United States [87]. For patients with confirmed allergy or adverse reaction to beta-lactam agents, use of one of the following regimens is recommended: clindamycin combined with gentamicin, aztreonam, or ciprofloxacin; or metronidazole combined with gentamicin or ciprofloxacin. Levofloxacin, 750 mg, given once can be substituted for ciprofloxacin.

#### **Conclusion**

Optimal prophylaxis ensures that adequate concentrations of an appropriate antimicrobial are present in the serum, tissue, and wound during the entire time that the incision is open and at risk for bacterial contamination. The antimicrobial agent should be active against bacteria that are likely to be encountered in the particular type of operation and should be safe for the patient and economical for the hospital. The selection and duration of antimicrobial prophylaxis should have the smallest impact possible on the normal bacterial flora of the patient and the microbiologic ecology of the hospital.

In this advisory statement, the Surgical Infection Prevention Guideline Writers Workgroup attempted, as they did with their own individual guidelines, to address the need for effective, safe, economical prophylaxis that does not promote antimicrobial-resistant bacteria. The advice included in this report will fit most patients at the majority of facilities. However, sound clinical judgment must be exercised to recognize those unusual cases in which an alternative approach is necessary. Many of the studies that have supported the development of antimicrobial prophylaxis guidelines are quite old, and antimicrobial susceptibility patterns change with time. Clinicians must continue to evaluate current literature and carefully examine susceptibility patterns within their own institutions.

Table 3  
Summary of the Surgical Infection Prevention Guideline Writers Workgroup consensus positions

| Principals and antibiotic selection   | Consensus position  |
|---------------------------------------|---|
| General principles                    |   |
| Antibiotic timing                     | Infusion of the first antimicrobial dose should begin within 60 minutes before the surgical incision is made.*  |
| Duration of prophylaxis               | Prophylactic antimicrobials should be discontinued within 24 hours of the end of surgery.   |
| Screening for $\beta$ -lactam allergy | For those operations for which the cephalosporins represent the most appropriate antimicrobials for prophylaxis, the medical history should be adequate to determine if the patient has a history of allergy or serious adverse antibiotic reaction. Alternative testing strategies (eg, skin testing) may be useful in patients with reported allergy [35–37]. |
| Antimicrobial dosing                  | The initial antimicrobial dose should be adequate based on the patient's weight, adjusted dosing weight, or body mass index. An additional dose of antimicrobial should be given intraoperatively if the operation is still continuing two half-lives after the initial dose.†  |
| Antibiotic selection                  |   |
| Abdominal or vaginal hysterectomy     | Cefotetan is preferred; cefazolin or ceftioxin are alternatives; metronidazole monotherapy.‡<br><br>If $\beta$ -lactam allergy:<br>Clindamycin combined with gentamicin or ciprofloxacin§ or aztreonam<br>Metronidazole combined with gentamicin or ciprofloxacin§<br>Clindamycin monotherapy   |
| Hip or knee arthroplasty              | Cefazolin or cefuroxime<br>If $\beta$ -lactam allergy:<br>Vancomycin<br>Clindamycin   |
| Cardiothoracic and vascular surgery   | Cefazolin or cefuroxime<br><br>If $\beta$ -lactam allergy:<br>Vancomycin<br>Clindamycin   |
| Colon surgery                         | Oral antimicrobial prophylaxis:<br>Neomycin plus erythromycin base<br>Neomycin plus metronidazole<br>Parenteral antimicrobial prophylaxis:<br>Cefotetan or ceftioxin<br>Cefazolin plus metronidazole<br>If $\beta$ -lactam allergy:<br>Clindamycin combined with gentamicin or ciprofloxacin§ or aztreonam<br>Metronidazole with gentamicin or ciprofloxacin§   |

\* In those settings where a fluoroquinolone or vancomycin is indicated, the infusion of the first antimicrobial dose should begin within 120 minutes before the incision.

† See Table 2.

‡ Metronidazole monotherapy is included in the American College of Obstetricians and Gynecologist's Practice Bulletin as an alternative to beta-lactams for patients undergoing hysterectomy although it may be less effective as a single agent for prophylaxis [15].

§ Levofloxacin 750 mg given once may be substituted for ciprofloxacin.

## Required Disclaimer

The analyses on which this publication is based were performed under Contract No. 500-99-P619 entitled "Utilization and Quality Control Peer Review Organization for the State of Oklahoma," sponsored by the CMS, Department of Health and Human Services. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the United States Government. The authors assume full responsibility for the accuracy and completeness of the ideas presented. This article is a direct result of the Health Care Quality Improvement Program initiated by CMS, which has encouraged identification of

quality-improvement projects derived from analyses of patterns of care and therefore required no special funding on the part of this contractor. Ideas and contributions to the authors concerning experience in engaging with issues presented are welcomed.

## Appendix

*Members of the Surgical Infection Prevention Guideline Writers Workgroup*

*American Academy of Orthopaedic Surgery:* Jason H. Calhoun, M.D., University of Missouri, Columbia, MO;  
*American College of Obstetricians and Gynecologists:* Va-

nessa Dalton, M.D., M.P.H., University of Michigan, Ann Arbor, MI; *American College of Surgeons*: Christopher Daly, M.D., Duquesne University, Pittsburgh, PA; *American Geriatrics Society*: Robert A. Bonomo, M.D., Cleveland Department of Veterans Affairs Medical Center, Cleveland, OH; *American Society of Health-System Pharmacists*: Keith M. Olsen, Pharm.D., University of Nebraska Medical Center, Omaha, NE; *CDC*: Chesley Richards, M.D., M.P.H., National Center for Infectious Diseases, Atlanta, GA; *Healthcare Infection Control Practices Advisory Committee*: James T. Lee, M.D., Ph.D., Saint Paul, MN; *CMS*: Peter Houck, M.D., Seattle, WA; *Infectious Diseases Society of America*: E. Patchen Dellinger, M.D., University of Seattle, WA, and Peter Gross, M.D., Hackensack University Medical Center, Hackensack, NJ; *The Medical Letter*: Gianna Zuccotti, M.D., M.P.H., New York, NY; *National Surgical Infection Prevention Quality Improvement Organization Support Center*: Dale W. Bratzler, D.O., M.P.H., Karina Carr, R.N., C.P.H.Q., Michele Clark, A.B.C., and Lisa Red, M.S.H.A., Oklahoma Foundation for Medical Quality, Oklahoma City, OK; *Society for Healthcare Epidemiology of America*: William R. Jarvis, M.D., Atlanta, GA; *Society of Thoracic Surgeons*: Fred H. Edwards, M.D., University of Florida, Jacksonville, FL; *Surgical Infection Society*: Donald E. Fry, M.D., University of New Mexico, Albuquerque, NM; *VHA, Inc.*: John A. Hitt, M.D., VHA Mountain States, Denver, CO.

## Acknowledgments

*The following organizations have endorsed this advisory statement*: American Academy of Orthopaedic Surgeons; American Association of Critical Care Nurses; American Association of Nurse Anesthetists; American College of Surgeons; American College of Osteopathic Surgeons; American Geriatrics Society; American Society of Anesthesiologists; American Society of Colon and Rectal Surgeons; ASHP; American Society of PeriAnesthesia Nurses; Ascension Health; Association of periOperative Registered Nurses; Association for Professionals in Infection Control and Epidemiology; Infectious Diseases Society of America; The Medical Letter; Premier, Inc.; Society for Healthcare Epidemiology of America; Society of Thoracic Surgeons; Surgical Infection Society. *The following organizations have had the opportunity to review and provide comment on this advisory statement*: American College of Obstetricians and Gynecologists; American Hospital Association; CDC; Joint Commission on Accreditation of Healthcare; VHA, Inc.

## References

- [1] Burke JP. Infection control—a problem for patient safety. *N Engl J Med* 2003;348:651–656.
- [2] National Nosocomial Infections Surveillance. Data summary from October 1986–April 1996, issued May 1996. A report from the National Nosocomial Infections Surveillance (NNIS) System. *Am J Infect Control* 1996;24:380–388.
- [3] Auerbach AD. Prevention of surgical site infections. In: Shojania KG, Duncan BW, McDonald KM, et al., editors. *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Evidence Report/Technology Assessment No. 43. AHRQ Publication No. 01-E058, Rockville, MD: Agency for Healthcare Research and Quality; 2001:221–244.
- [4] Wong ES. Surgical site infection. In: Mayhall DG, editor. *Hospital Epidemiology and Infection Control*. 2nd ed. Philadelphia, PA: Lippincott; 1999: 189–210.
- [5] Kirkland KB, Briggs JP, Trivette SL, et al. The impact of surgical site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999;20: 725–730.
- [6] Martone WJ, Jarvis WR, Culver DH, et al. Incidence and nature of endemic and epidemic nosocomial infections. In: Bennett JV, Brachman PS, editors. *Hospital Infections*. 3rd ed. Boston: Little, Brown; 1992:577–596.
- [7] Hollenbeak CS, Murphy D, Dunagan WC, et al. Nonrandom selection and the attributable cost of surgical-site infections. *Infect Control Hosp Epidemiol* 2002;23:174–176.
- [8] Perencevich EN, Sands KE, Cosgrove SE, et al. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis* 2003;9:196–203.
- [9] <http://www.medqic.org/sip>. Accessed: January 21, 2004.
- [10] Page CP, Bohnen JM, Fletcher JR, et al. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. *Arch Surg* 1993; 128:79–88.
- [11] Dellinger EP, Gross PA, Barrett TL, et al. Quality standard for antimicrobial prophylaxis in surgical procedures. *Infectious Diseases Society of America. Clin Infect Dis* 1994;18:422–427.
- [12] American Society of Health-System Pharmacists. ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 1999;56:1839–1888.
- [13] 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;20:250–278.
- [14] Antimicrobial prophylaxis in surgery. *Med Lett Drugs Ther* 2001;43: 92–97.
- [15] ACOG Committee on Practice Bulletins. Antibiotic prophylaxis for gynecologic procedures. *ACOG Practice Bulletin No. 23*. Washington, DC: The American College of Obstetricians and Gynecologists; 2001.
- [16] Gilbert DN, Moellering RC, Sande MA. *The Sanford Guide to Antimicrobial Therapy*, 2003. 33rd ed. Hyde Park, Vermont: Antimicrobial Therapy, Inc.; 2003:123–124.
- [17] Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* 1961;50:161–168.
- [18] Polk HC Jr, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 1969; 66:97–103.
- [19] Stone HH, Hooper CA, Kolb LD, et al. Antibiotic prophylaxis in gastric, biliary and colonic surgery. *Ann Surg* 1976;184:443–452.
- [20] Polk HC Jr, Trachtenberg L, Finn MP. Antibiotic activity in surgical incisions. The basis for prophylaxis in selected operations. *JAMA* 1980;244:1353–1354.
- [21] DiPiro JT, Vallner JJ, Bowden TA, et al. Intraoperative serum and tissue activity of cefazolin and cefoxitin. *Arch Surg* 1985;120:829–832.
- [22] Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992;326:281–286.



- [23] Fukatsu K, Saito H, Matsuda T, et al. Influences of type and duration of antimicrobial prophylaxis on an outbreak of methicillin-resistant *Staphylococcus aureus* and on the incidence of wound infection. *Arch Surg* 1997;132:1320–1325.
- [24] Trick WE, Scheckler WE, Tokars JL, et al. Modifiable risk factors associated with deep sternal site infection after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2000;119:108–114.
- [25] Burke JP. Maximizing appropriate antibiotic prophylaxis for surgical patients: an update from LDS Hospital, Salt Lake City. *Clin Infect Dis* 2001;33(suppl 2):S78–S83.
- [26] Meijer WS, Schmitz PI, Jeekel J. Meta-analysis of randomized, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. *Br J Surg* 1990;77:283–290.
- [27] Kreter B, Woods M. Antibiotic prophylaxis for cardiothoracic operations. Meta-analysis of thirty years of clinical trials. *J Thorac Cardiovasc Surg* 1992;104:590–599.
- [28] McDonald M, Grabsch E, Marshall C, et al. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust N Z J Surg* 1998;68:388–396.
- [29] Harbarth S, Samore MH, Lichtenberg D, et al. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000;101:2916–2921.
- [30] Eggimann P, Pittet D. Infection control in the ICU. *Chest* 2001;120:2059–2093.
- [31] Hecker MT, Aron DC, Patel NP, et al. Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. *Arch Intern Med* 2003;163:972–978.
- [32] Tripp DM, Brown GR. Pharmacist assessment of drug allergies. *Am J Hosp Pharm* 1993;50:95–98.
- [33] Hung OR, Bands C, Laney G, et al. Drug allergies in the surgical population. *Can J Anaesth* 1994;41:1149–1155.
- [34] Pilzer JD, Burke TG, Mutnick AH. Drug allergy assessment at a university hospital and clinic. *Am J Health Syst Pharm* 1996;53:2970–2975.
- [35] Robinson JL, Hameed T, Carr S. Practical aspects of choosing an antibiotic for patients with a reported allergy to an antibiotic. *Clin Infect Dis* 2002;35:26–31.
- [36] Anne S, Reisman RE. Risk of administering cephalosporin antibiotics to patients with history of penicillin allergy. *Ann Allergy Asthma Immunol* 1995;74:167–170.
- [37] Solensky R. Hypersensitivity reactions to beta-lactam antibiotics. *Clin Rev Allergy Immunol* 2003;24:201–220.
- [38] Thomas C, Stevenson M, Riley TV. Antibiotics and hospital-acquired *Clostridium difficile*-associated diarrhoea: a systematic review. *J Antimicrob Chemother* 2003;51:1339–1350.
- [39] Finkelstein R, Rabino G, Mashiah T, et al. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg* 2002;123:326–332.
- [40] Manian FA, Meyer PL, Setzer J, et al. Surgical site infections associated with methicillin-resistant *Staphylococcus aureus*: do postoperative factors play a role? *Clin Infect Dis* 2003;36:863–868.
- [41] Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;24:362–386.
- [42] Arnold MS, Dempsey JM, Fishman M, et al. The best hospital practices for controlling methicillin-resistant *Staphylococcus aureus*: on the cutting edge. *Infect Control Hosp Epidemiol* 2002;23:69–76.
- [43] Farr BM, Jarvis WR. Would active surveillance cultures help control healthcare-related methicillin-resistant *Staphylococcus aureus* infections? *Infect Control Hosp Epidemiol* 2002;23:65–68.
- [44] Jernigan JA, Pullen AL, Flowers L, et al. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* at the time of hospital admission. *Infect Control Hosp Epidemiol* 2003;24:409–414.
- [45] Perl TM, Cullen JJ, Wenzel RP, et al. Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections. *N Engl J Med* 2002;346:1871–1877.
- [46] Laupland KB, Conly JM. Treatment of *Staphylococcus aureus* colonization and prophylaxis for infection with topical intranasal mupirocin: an evidence-based review. *Clin Infect Dis* 2003;37:933–938.
- [47] Suzuki Y, Kamigaki T, Fujino Y, et al. Randomized clinical trial of preoperative intranasal mupirocin to reduce surgical-site infection after digestive surgery. *Br J Surg* 2003;90:1072–1075.
- [48] Forse RA, Karam B, MacLean LD, et al. Antibiotic prophylaxis for surgery in morbidly obese patients. *Surgery* 1989;106:750–756.
- [49] Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg* 1997;63:59–62.
- [50] Ohge H, Takesue Y, Yokoyama T, et al. An additional dose of cefazolin for intraoperative prophylaxis. *Surg Today* 1999;29:1233–1236.
- [51] Zanetti G, Giardina R, Platt R. Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. *Emerg Infect Dis* 2001;7:828–831.
- [52] Kurz A, Sessler DI, Lenhardt RA. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *N Engl J Med* 1996;334:1209–1215.
- [53] Grief R, Akca O, Horn E-P, et al. Supplemental perioperative oxygen to reduce the incidence of surgical wound infection. *N Engl J Med* 2000;342:161–167.
- [54] Melling AC, Ali B, Scott EM, et al. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomized controlled trial. *Lancet* 2001;358:876–880.
- [55] Sessler DI, Akca O. Nonpharmacologic prevention of surgical wound infections. *Clin Infect Dis* 2002;35:1397–1404.
- [56] Pryor KO, Fahey TJ 3rd, Lien CA, et al. Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: a randomized controlled trial. *JAMA* 2004;291:79–87.
- [57] Zerr KJ, Furnary AP, Grunkemeier GL, et al. Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Ann Thorac Surg* 1997;63:356–361.
- [58] Furnary AP, Kerr KJ, Grunkemeier GL, et al. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg* 1999;67:352–360.
- [59] Latham R, Lancaster AD, Covington JF, et al. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol* 2001;22:607–612.
- [60] Hemsell DL, Johnson ER, Hemsell PG, et al. Cefazolin is inferior to cefotetan as single-dose prophylaxis for women undergoing elective total abdominal hysterectomy. *Clin Infect Dis* 1995;20:677–684.
- [61] American College of Obstetricians and Gynecologists. Prophylactic antibiotics in labor and delivery. ACOG practice bulletin no. 47. *Obstet Gynecol* 2003;102:875–882.
- [62] Faro S, Martens MG, Hammill HA, et al. Antibiotic prophylaxis: is there a difference? *Am J Obstet Gynecol* 1990;162:900–907.
- [63] Hopkins L, Smail F. Antibiotic prophylaxis regimens and drugs for cesarean section. *Cochrane Database Syst Rev*. 2000;(2):CD001136. Review.
- [64] Cunningham FG, Leveno KJ, DePalma RT, et al. Perioperative antimicrobials for cesarean delivery: before or after cord clamping? *Obstet Gynecol* 1983;62:151–154.
- [65] Pollard JP, Hughes SO, Scott JE, et al. Antibiotic prophylaxis in total hip replacement. *Br Med J* 1979;1:707–709.
- [66] Williams DN, Gustilo RB, Beverly R, et al. Bone and serum concentrations of five cephalosporin drugs. Relevance to prophylaxis and treatment in orthopedic surgery. *Clin Orthop* 1983;179:253–265.

- [67] Nelson CL, Green TG, Porter RA, et al. One day versus seven days of preventive antibiotic therapy in orthopedic surgery. *Clin Orthop* 1983;176:258–263.
- [68] Heydemann JS, Nelson CL. Short-term preventive antibiotics. *Clin Orthop* 1986;205:184–187.
- [69] Oishi CS, Carrion WV, Hoaglund FT. Use of parenteral prophylactic antibiotics in clean orthopaedic surgery. A review of the literature. *Clin Orthop* 1993;296:249–255.
- [70] Mauerhan DR, Nelson CL, Smith DL, et al. Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am* 1994;76:39–45.
- [71] Magee C, Rodeheaver GT, Golden GT, et al. Potentiation of wound infection by surgical drains. *Am J Surg* 1976;13:547–549.
- [72] Chandratreya A, Giannikas K, Livesley P. To drain or not to drain: literature versus practice. *J R Coll Surg Edinb* 1998;43:404–406.
- [73] Cobb JP. Why use drains. *J Bone Joint Surg* 1990;72:993–995.
- [74] Adalberth G, Bystrom S, Kolstad K, et al. Postoperative drainage of knee arthroplasty is not necessary: a randomized study of 90 patients. *Acta Orthop Scand* 1998;69:475–478.
- [75] Niskanen RO, Korkala OL, Haapala J, et al. Drainage is of no use in primary uncomplicated cemented hip and knee arthroplasty for osteoarthritis. A prospective randomized study. *J Arthroplasty* 2000;15:567–569.
- [76] Hadden WA, McFarlane AG. A comparative study of closed-wound suction drainage vs. no drainage in total hip arthroplasty. *J Arthroplasty* 1990;5(suppl):S21–S24.
- [77] Ritter MA, Keating EM, Faris PM. Closed wound drainage in total hip or total knee replacement. A prospective, randomized study. *J Bone Joint Surg* 1994;76:35–38.
- [78] Reilly TJ, Gradisar IA, Pagan W, et al. The use of postoperative suction drainage in total knee arthroplasty. *Clin Orthop* 1986;208:238–242.
- [79] Esler CN, Blakeway C, Fiddian NJ. The use of a closed-suction drain in total knee arthroplasty. A prospective randomised study. *J Bone Joint Surg* 2003;85:215–217.
- [80] Beer KJ, Lombardi AV, Mallory TH, et al. The efficacy of suction drains after routine total joint arthroplasty. *J Bone Joint Surg* 1991;73:584–587.
- [81] Drinkwater CJ, Neil MJ. Optimal timing of wound drain removal following total joint arthroplasty. *J Arthroplasty* 1995;10:185–189.
- [82] Willett KM, Simmons CD, Bentley G. The effect of suction drains after total hip replacement. *J Bone Joint Surg* 1988;70:607–610.
- [83] Raves JJ, Slifkin M, Diamond DL. A bacteriologic study comparing closed suction and simple conduit drainage. *Am J Surg* 1984;148:618–620.
- [84] Pavan MM, Malyuk DL. A cost effective approach to surgical antibiotic prophylaxis. *Can J Hosp Pharm* 1992;45:151–156.
- [85] Brown GR, Clarke AM. Therapeutic interchange of cefazolin with metronidazole for cefoxitin. *Am J Hosp Pharm* 1992;49:1946–1950.
- [86] Lewis RT. Oral versus systemic antibiotic prophylaxis in elective colon surgery: a randomized study and meta-analysis send a message from the 1990s. *Can J Surg* 2002;45:173–180.
- [87] Nichols RL, Smith JW, Garcia RY, et al. Current practices of preoperative bowel preparation among North American colorectal surgeons. *Clin Infect Dis* 1997;24:609–619.
- [88] McEvoy GK, editor. *AHFS Drug Information 2003*. 43rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2003.
- [89] Nissen D, editor. *Mosby's Drug Consultant*. 2nd ed. St. Louis, MO: Elsevier; 2003.
- [90] Anderson PO, Knoeben JE, Troutman WG, editors. *Handbook of Clinical Drug Data*. 10th ed. New York, NY: McGraw-Hill; 2002.