

ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery

The ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery,¹ which have provided practitioners with standardized effective regimens for the rational use of prophylactic antimicrobials, have been revised as described in this document on the basis of new clinical evidence and additional concerns. Recommendations are provided for adult and pediatric patients (1 to 21 years of age), including infants (one month to 2 years of age). Geriatric patients, newborns (premature and full-term), and patients with renal or hepatic dysfunction are not specifically addressed. Therefore, the guidelines may not be applicable to these patients, or certain adjustments to the recommendations may be necessary. The higher occurrence of resistant organisms and the importance of controlling health care costs are also considered.

Prophylaxis refers to the prevention of an infection and can be characterized as primary prophylaxis, secondary prophylaxis (suppression), or eradication. Primary prophylaxis refers to the prevention of an initial infection. Secondary prophylaxis refers to the prevention of recurrence or reactivation of a preexisting infection (e.g., prevention of the recurrence of a latent herpes simplex virus infection). Eradication refers to the elimination of a colonized organism to prevent the development of an infection (e.g., eliminating methicillin-resistant *Staphylococcus aureus* [MRSA] from the nares of health care workers). These guidelines focus on primary prophylaxis. Secondary prophylaxis and eradication are not addressed.

Guideline Development and Use

These guidelines were prepared by the Rocky Mountain Poison and Drug Center under contract to ASHP. The project was coordinated by a drug information pharmacist who worked with a multidisciplinary consortium of writers and consulted with six physicians on staff at the University of Colorado Health Sciences Center. The project coordinator worked in conjunction with an independent panel of eight clinical pharmacy specialists with expertise in either adult or pediatric infectious disease. The panel was appointed by ASHP. Panel members and contractors were required to disclose any possible conflicts of interest before their appointment. The guidelines underwent multidisciplinary field review to evaluate their validity, reliability, and utility in clinical practice. The final document was approved by the ASHP Commission on Therapeutics and the ASHP Board of Directors.

The recommendations in this document may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgment of the clinician and consideration of individual patient circumstances and available resources.

These guidelines reflect current knowledge (at the time of publication) on antimicrobial prophylaxis in surgery. Given the dynamic nature of scientific information and technology, periodic review, updating, and revision are to be expected.

Strength of Evidence for Recommendations. The primary literature from the previous ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery¹ was reviewed together with the primary literature between the date of the previous guidelines and August 1997, identified by a MEDLINE search. Particular attention was paid to study design, with greatest credence given to randomized, controlled, double-blind studies. Established recommendations by experts in the area (i.e., Centers for Disease Control and Prevention [CDC], American College of Obstetricians and Gynecologists [ACOG]) were also considered.

Guideline development included consideration of the following characteristics: validity, reliability, clinical applicability, flexibility, clarity, and a multidisciplinary nature as consistent with ASHP's philosophy on therapeutic guidelines.² Recommendations on the use of an antimicrobial are substantiated by the strength of evidence that supports the recommendation. The strength of evidence represents only support for or against prophylaxis and does not apply to the antimicrobial choice, dose, or dosage regimen. Studies supporting the recommendations for the use of an antimicrobial were classified as follows:

- Level I:** (evidence from large, well-conducted randomized, controlled clinical trials or a meta-analysis)
- Level II:** (evidence from small, well-conducted randomized, controlled clinical trials)
- Level III:** (evidence from well-conducted cohort studies)
- Level IV:** (evidence from well-conducted case-control studies)
- Level V:** (evidence from uncontrolled studies that were not well conducted)
- Level VI:** (conflicting evidence that tends to favor the recommendation)
- Level VII:** (expert opinion)

This system has been used by the Agency for Health Care Policy and Research, and ASHP supports it as an acceptable method for organizing strength of evidence for a variety of therapeutic or diagnostic recommendations.² Each recommendation was assigned a category corresponding to the strength of evidence that supports the use or nonuse of antimicrobial prophylaxis:

- Category A:** (levels I–III)
- Category B:** (levels IV–VI)
- Category C:** (level VII)

A category C recommendation represents a consensus of the expert panel based on the clinical experience of individual panel members and a paucity of quality supporting literature. In cases for which opinions were markedly divided, the recommendations indicate that a substantial number of panel members supported an alternative approach.

Pediatrics. Pediatric patients are subject to many prophylaxis opportunities that are similar to those for adults. Although pediatric-specific prophylaxis data are sparse, available data have been evaluated and are presented in this document. However, in most cases, the pediatric recommendations, including recommendations for infants, have been extrapolated from adult data.

Clinical studies to determine the optimal dosages of antimicrobials used for pediatric prophylaxis are essentially nonexistent. In contrast, there are sufficient pharmacokinetic studies for most agents used that appropriate pediatric dosages can be estimated that provide systemic exposure, and presumably efficacy, similar to that demonstrated in the adult efficacy trials. It is also common clinical practice to use antimicrobial prophylaxis in pediatric patients in a manner that is similar, if not identical, to that used in adults. Therefore, the pediatric dosages provided in these guidelines are based largely on pharmacokinetic equivalence and the generalization of the adult efficacy data to pediatric patients.^{3,4} Because pediatric trials have generally not been conducted, a strength of evidence has not been applied to these recommendations. With few exceptions (e.g., aminoglycoside dosages), pediatric dosages should not exceed the maximum adult recommended dosages. If dosages are calculated on a milligram-per-kilogram basis for children weighing more than 40–50 kg, the calculated dosage will exceed the maximum recommended dosage for adults; thus adult dosages should be used.

Resistance. The basis for guideline development was to recommend an effective antimicrobial with the narrowest spectrum of activity. Alternative antimicrobials were included on the basis of documented efficacy. Individual health systems must consider specific resistance patterns at their practice site when adopting these recommendations.

When considering the use of antimicrobials for prophylaxis, one must also take into account the risks of contributing to the development of antimicrobial resistance. In numerous studies of prophylaxis, both surgical^{5,6} and nonsurgical,^{7–16} attempts have been made to evaluate the impact of antimicrobial prophylaxis on the development of resistance. Numerous studies^{5,7–13} demonstrated an increase in resistance, yet other studies^{6,14–16} failed to demonstrate the emergence of resistance. Most of the studies demonstrating the development of resistance involved the use of broad-spectrum antimicrobials.^{5,7–13} Thus, currently recommended practice is to use narrow-spectrum antimicrobials for the shortest duration to reduce the likelihood of the development of antimicrobial resistance.

The frequency with which MRSA has been recovered from various infection sites has increased steadily throughout the United States.^{17–19} The frequency of methicillin resistance among staphylococcal strains rose from 2.4% in 1975 to 29% in 1991.¹⁹ CDC's National Nosocomial Infections Surveillance identified a rapid increase in vancomycin-resistant enterococci (VRE) from 0.3% in 1989 to 7.9% in 1993. The rate of high-level enterococcal resistance to penicillin and aminoglycosides increased simultaneously. The use of vancomycin has been reported consistently as a risk factor for infection and colonization with VRE and may increase the possibility of the emergence of vancomycin-resistant *S. aureus* or vancomycin-resistant *Staphylococcus epidermidis*.²⁰ In response, the Hospital Infection Control Practices Advisory Committee (HICPAC), with the support of other major organizations, developed measures for preventing and

controlling vancomycin resistance.²¹ The ASHP guidelines are consistent with the HICPAC recommendations. The following situations are appropriate or acceptable for use of vancomycin: prophylaxis of endocarditis (as recommended by the American Heart Association [AHA]) before certain procedures and for major surgical procedures involving implantation of prosthetic materials or devices (e.g., cardiac and vascular procedures, total hip replacement) at institutions with a high rate of infections due to MRSA or methicillin-resistant *S. epidermidis* (MRSE). Use of vancomycin for routine surgical prophylaxis should be discouraged (other than in a patient with a life-threatening allergy to β -lactam antimicrobials).

Cost. Pharmacoeconomic studies have been lacking or inadequate with regard to the prophylactic use of antimicrobials; therefore, a cost-minimization approach was employed in developing these guidelines. When antimicrobials have been shown to be equally efficacious and safe, the recommendation is based on the least expensive agent (on the basis of average wholesale price). The other antimicrobials are considered to be alternative agents. The recommendation of an antimicrobial is determined primarily by efficacy and secondarily by cost. Because of variations in cost from one health system to another, health systems must tailor the choice of antimicrobials to their individual acquisition costs.

Goals of Surgical Prophylaxis

Ideally, an anti-infective drug for surgical prophylaxis should achieve the following goals: (1) prevent postoperative infection of the surgical site, (2) prevent postoperative infectious morbidity and mortality, (3) reduce the duration and cost of health care (when the costs associated with the management of postoperative infection are considered, the cost-effectiveness of prophylaxis becomes evident),^{22,23} (4) produce no adverse effects, and (5) have no adverse consequences for the microbial flora of the patient or the hospital.²⁴ To achieve these goals, an anti-infective drug should be (1) active against the pathogens most likely to contaminate the wound, (2) given in an appropriate dosage and at a time that ensures adequate concentrations at the incision site during the period of potential contamination, (3) safe, and (4) administered for the shortest effective period to minimize adverse effects, development of resistance, and cost.²⁴ The benefits of preventing postoperative infection pertain to both outpatient and inpatient surgeries. Other guidelines on antimicrobial prophylaxis in surgery have been published.²⁵

Although prophylactic antimicrobials play an important part in reducing the rate of postoperative wound infection, other factors, such as the surgeon's experience, the length of the procedure, hospital and operating-room environments, and the underlying medical condition of the patient, have a strong impact on wound infection rates. Medical conditions associated with an increased risk of postoperative infection include extremes of age, undernutrition, obesity, diabetes, hypoxemia, remote infection, corticosteroid therapy, recent operation, chronic inflammation, and prior site irradiation.²⁶ Antimicrobial prophylaxis may be justified for any procedure if the patient has an underlying medical condition associated with a risk of wound infection or if the patient is immunocompromised (e.g., malnourished, neutropenic, receiving immunosuppressive agents). These variables should be considered in evaluations of infection-control problems.

Antimicrobial prophylaxis is beneficial in surgical procedures associated with a high rate of infection (clean-contaminated or contaminated operations), for implantation of prosthetic materials, and in any procedure in which postoperative infection, however unlikely, may have severe consequences. Other clean procedures that may warrant prophylaxis are breast procedures^{27,28} and hernia procedures,²⁷ although more data are needed.

The modified National Research Council wound classification criteria are as follows^{28,29}:

- Clean surgical procedures (primarily closed, elective procedures involving no acute inflammation, no break in technique, and no transection of gastrointestinal [GI], oropharyngeal, genitourinary [GU], biliary, or tracheobronchial tracts)
- Clean-contaminated procedures (procedures involving transection of GI, oropharyngeal, GU, biliary, or tracheobronchial tracts with minimal spillage or with minor breaks in technique; clean procedures performed emergently or with major breaks in technique; reoperation of clean surgery within seven days; or procedures following blunt trauma)
- Contaminated procedures (clean-contaminated procedures during which acute, nonpurulent inflammation is encountered or major spillage or technique break occurs; procedures performed within four hours of penetrating trauma or involving a chronic open wound)
- Dirty procedures (procedures performed when there is obvious preexisting infection [abscess, pus, necrotic tissue present]; preoperative perforation of GI, oropharyngeal, biliary, or tracheobronchial tracts; or penetrating trauma greater than four hours old)

Typically, prophylactic antimicrobials are not indicated for clean surgical procedures. However, prophylaxis is justified for procedures involving prosthetic placement because of the potential for severe complications if postoperative infections involve the prosthesis. Antimicrobial prophylaxis is justified for the following types of surgical procedures: cardiothoracic, GI tract (e.g., colorectal and biliary tract operations), head and neck (except clean procedures), neurosurgical, obstetric or gynecologic, orthopedic (except clean procedures), urologic, and vascular. The use of antimicrobials for dirty and contaminated procedures is not classified as prophylaxis but as treatment for a presumed infection; therefore, dirty and contaminated procedures are not discussed in these guidelines.³⁰

It is difficult to establish significant differences in efficacy between prophylactic antimicrobials and placebo when infection rates are low. A small sample size increases the likelihood of Type II error; therefore, there may be no apparent difference between the antimicrobial and placebo when in fact the antimicrobial has a beneficial effect.³¹ A valid study would be placebo controlled and randomized with a large enough sample in each group to avoid Type II error. A large sample is rarely achieved in well-controlled studies of surgical prophylaxis. Thus, some of the surgical prophylaxis efficacy data are at risk for Type II error. Because of this obstacle, prophylaxis is recommended in some cases because the complications of postoperative infection (e.g., removal of an infected device) necessitate precautionary measures despite the lack of statistical support.

Selection of Antimicrobial Agents

The selection of an appropriate antimicrobial agent for specific patients should take into account not only comparative efficacy but also adverse-effect profiles and patient drug allergies. A discussion of adverse-effect profiles of the antimicrobials is beyond the scope of these guidelines. There is little evidence to suggest that the newer antimicrobials, with broader antibacterial activity in vitro, result in lower rates of postoperative wound infection than older drugs whose spectrum of activity is narrower. Because most comparative studies have a small number of patients, a significant difference between antimicrobials cannot be detected; therefore, antimicrobial selection is based on cost, adverse-effect profile, ease of administration, pharmacokinetic profile, and antibacterial activity. The agent chosen should have activity against the most common surgical wound pathogens. For clean-contaminated operations, the agent of choice should be effective against common pathogens found in the GI and GU tracts. In clean operations, the gram-positive cocci—*S. aureus* and *S. epidermidis*—predominate. For most procedures, cefazolin should be the agent of choice because of its relatively long duration of action, its effectiveness against the organisms most commonly encountered in surgery, and its relatively low cost.

Specific recommendations for the selection of prophylactic antimicrobials for various surgical procedures are provided in Table 1. Equivalent pediatric dosages have been included in Table 2; however, these recommendations are based on data derived primarily from adult patients and from tertiary references.^{3,4,35} Neonatal (full-term and preterm) dosages are not provided. The reader is referred to Neofax for neonatal dosages.³⁶ There are few data on the use of surgical antimicrobial prophylaxis in the pediatric population. Available pediatric clinical data were evaluated and are presented in the efficacy section after the adult data.

Development of Colonization or Resistance. One factor that may influence the selection of cefazolin is the occurrence of surgical wound infections despite prophylaxis with cefazolin. An infection-control surveillance study of surgical wound infections implicated β -lactamase production as a possible cause of cefazolin and cefamandole failure.³⁹ β -lactamase-producing *S. aureus* isolates associated with the wound infections rapidly hydrolyzed cefamandole and cefazolin. Isolates of *S. aureus* taken from patients who had received cefazolin were more resistant than isolates taken from patients who had received cefamandole, and the cefazolin-associated isolates were capable of hydrolyzing cefazolin more rapidly. These findings may have important implications for the use of first-generation cephalosporins, particularly cefazolin, for surgical prophylaxis. However, the overall frequency of cefazolin failure as a result of resistance is low, and cefazolin continues to be the drug of choice. New studies comparing cefazolin with agents that are more resistant to β -lactamase, such as cefamandole and cefuroxime, may be needed.

A second factor that may discourage the selection of cefazolin is the recognition that MRSA and methicillin-resistant, coagulase-negative staphylococci are resistant to all cephalosporins. These organisms have been associated with infection after cardiothoracic, orthopedic, vascular, and cerebrospinal shunting procedures. This resistance pattern may influence drug selection in hospitals with a high frequency of such isolates. However, vancomycin use should be restricted because of the increase in vancomycin-resistant enterococci.

Table 1.

Recommendations for Surgical Antimicrobial Prophylaxis in Adults

Type of Surgery	Recommended Regimen ^a	Alternative Regimens ^a	Strength of Evidence ^p
Cardiothoracic	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for up to 72 hr ^{c,d}	Cefuroxime 1.5 g i.v. at induction of anesthesia and q 12 hr for up to 72 hr, cefamandole 1 g i.v. at induction of anesthesia and q 6 hr for up to 72 hr, vancomycin 1 g i.v. with or without gentamicin 2 mg/kg i.v. ^e	A
Gastrointestinal			
Gastroduodenal			
Procedures involving entry into the lumen of the gastrointestinal tract	Cefazolin 1 g i.v. at induction of anesthesia		A
Highly selective vagotomy, Nissen's fundoplication, and Whipple's procedure	Cefazolin 1 g i.v. at induction of anesthesia		C
Biliary tract			
Open procedure	Cefazolin 1 g i.v. at induction of anesthesia		A
Laparoscopic procedure	None		B
Appendectomy for uncomplicated appendicitis	Cefoxitin, cefotetan, or cefmetazole 1–2 g i.v. at induction of anesthesia	Piperacillin 2 g i.v. at induction of anesthesia; if patient is allergic to penicillin, metronidazole 500 mg i.v. plus gentamicin 2 mg/kg i.v. at induction of anesthesia	A
Colorectal	Neomycin sulfate 1 g plus erythromycin base 1 g p.o. (after mechanical bowel preparation is completed ^f) at 19, 18, and 9 hr before surgery; if oral route is contraindicated, cefoxitin, cefotetan, or cefmetazole 2 g i.v. at induction of anesthesia; for patients undergoing high-risk surgery (e.g., rectal resection), oral neomycin and erythromycin plus an i.v. cephalosporin		A
Head and neck			
Clean	None		B
With placement of prosthesis	Cefazolin 1 g i.v. at induction of anesthesia		C
Clean-contaminated	Cefazolin 2 g i.v. at induction of anesthesia and q 8 hr for 24 hr or clindamycin 600 mg i.v. at induction of anesthesia and q 8 hr for 24 hr	Addition of gentamicin 1.7 mg/kg i.v. to clindamycin regimen or of metronidazole 500 mg i.v. q 8 hr to cefazolin regimen is controversial; single-dose regimens might be preferable, but this approach is controversial	A
Elective craniotomy or cerebrospinal fluid shunting	Cefazolin 1 g i.v. at induction of anesthesia	Oxacillin 1 g or nafcillin 1 g i.v. at induction of anesthesia; vancomycin 1 g i.v. ^g	A
Obstetric or gynecologic			
Cesarean delivery ^h	Cefazolin 2 g i.v. immediately after clamping of umbilical cord		B (low risk), A (high risk)
Hysterectomy (vaginal, abdominal, or radical) ⁱ	Cefazolin 1 g i.v. or cefotetan 1 g i.v. at induction of anesthesia	Cefoxitin 1 g i.v. at induction of anesthesia	A
Ophthalmic	Topical neomycin–polymyxin B–gramicidin 1–2 drops or tobramycin 0.3% or gentamicin 0.3% 2 drops instilled before procedure ^f	Addition of tobramycin 20 mg by subconjunctival injection is optional	C
Orthopedic			
Clean, not involving implantation of foreign materials ^k	None		C
Hip fracture repair ^l	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 1 g i.v. ^g	A
Implantation of internal fixation devices ^l	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 1 g i.v. ^g	C
Total joint replacement	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 1 g i.v. ^g	A

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Table 1. (continued)
Recommendations for Surgical Antimicrobial Prophylaxis in Adults

Type of Surgery	Recommended Regimen ^a	Alternative Regimens ^a	Strength of Evidence ^b
Urologic (high-risk patients only ^m)	Trimethoprim 160 mg with sulfamethoxazole 800 mg p.o. or lomefloxacin 400 mg p.o. 2 hr before surgery (if oral agents used) or cefazolin 1 g i.v. at induction of anesthesia (if injection preferred)		A
Vascular ⁿ	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 1 g i.v. with or without gentamicin 2 mg/kg i.v. ⁹	A
Transplantation Heart	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 48–72 hr ^d	Cefuroxime 1.5 g i.v. at induction of anesthesia and q 12 hr for 48–72 hr, cefamandole 1 g i.v. at induction of anesthesia and q 6 hr for 48–72 hr, or vancomycin 1 g i.v. with or without gentamicin 2 mg/kg i.v. ^e	A
Lung and heart–lung, ^{o,p}	Cefazolin 1 g i.v. at induction of anesthesia and q 8 hr for 48–72 hr	Cefuroxime 1.5 g i.v. at induction of anesthesia and q 12 hr for 48–72 hr, cefamandole 1 g i.v. at induction of anesthesia and q 6 hr for 48–72 hr, or vancomycin 1 g i.v. ⁹	B
Liver	Cefotaxime 1 g i.v. plus ampicillin 1 g i.v. at induction of anesthesia and q 6 hr during procedure and for 48 hr beyond final surgical closure	Antimicrobials that provide adequate coverage against gram-negative aerobic bacilli, staphylococci, and enterococci may be appropriate	B
Pancreas and pancreas–kidney	Cefazolin 1 g i.v. at induction of anesthesia		B
Kidney	Cefazolin 1 g i.v. at induction of anesthesia		A

^aIf a short-acting agent is used, it should be readministered if the operation takes more than three hours. If an operation is expected to last more than six to eight hours, it would be reasonable to administer an agent with a longer half-life and duration of action or to administer a short-acting agent at three-hour intervals during the procedure. Readministration may also be warranted if prolonged or excessive bleeding occurs or there are factors that may shorten the half-life (e.g., extensive burns). Readministration may not be warranted in patients in whom the half-life is prolonged (e.g., patients with renal insufficiency or failure).

^bStrength of evidence that supports the use or nonuse of prophylaxis is classified as A (levels I–III), B (levels IV–VI), or C (level VII). Level I evidence is from large, well-conducted randomized, controlled clinical trials. Level II evidence is from small, well-conducted randomized, controlled clinical trials. Level III evidence is from well-conducted cohort studies. Level IV evidence is from well-conducted case–control studies. Level V evidence is from uncontrolled studies that were not well conducted. Level VI evidence is conflicting evidence that tends to favor the recommendation. Level VII evidence is expert opinion.

^cDuration is based on expert panel consensus. Prophylaxis for 24 hours or less may be appropriate.

^dThere is currently no evidence to support continuing antimicrobial prophylaxis until chest and mediastinal drainage tubes are removed.

^eAccording to Hospital Infection Control Practices Advisory Committee guidelines²¹ or American Heart Association recommendations for penicillin-allergic patients at high risk for endocarditis.³²

^fMechanical bowel preparation is required for nonobstructed patients undergoing elective operations.

^gAccording to Hospital Infection Control Practices Advisory Committee guidelines.²¹

^hThe American College of Obstetricians and Gynecologists (ACOG) considers the use of prophylaxis controversial in low-risk patients.³³ ACOG does not routinely recommend prophylaxis in low-risk patients because of concerns about adverse effects, development of resistant organisms, and relaxation of standard infection-control measures and proper operative technique.

ⁱAccording to ACOG guidelines, first-, second-, and third-generation cephalosporins can be used for vaginal, abdominal, and radical hysterectomies.³⁴

^jThe necessity of continuing topical antimicrobials postoperatively has not been established by data.

^kLaminectomy and knee, hand, and foot surgeries. The evaluated studies did not include arthroscopy and did not identify specific procedures, like carpal tunnel release; however, arthroscopy and other procedures not involving implantation are similar enough to be included with clean orthopedic procedures not involving implantation.

^lProcedures involving internal fixation devices (e.g., nails, screws, plates, wires).

^mHigh risk is defined as prolonged postoperative catheterization, positive urine cultures, or hospital infection rate of greater than 20%.

ⁿProphylaxis is not indicated for brachiocephalic procedures. Although there are no data, patients undergoing brachiocephalic procedures involving vascular prostheses or patch implantation (e.g., carotid endarterectomy) may benefit from prophylaxis.

^oPatients undergoing lung transplantation with negative pretransplant cultures should receive antimicrobial prophylaxis as appropriate for other types of cardiothoracic surgeries.

^pPatients undergoing lung transplantation for cystic fibrosis should receive 7–14 days of prophylaxis with antimicrobials selected according to pretransplant culture and susceptibility results. This may include additional antibacterial agents or antifungal agents.

Table 2.
Antimicrobial Regimens for Surgical Prophylaxis in Pediatric Patients^a

Type of Surgery	Preferred Regimen ^b	Alternative Regimens ^b
Cardiothoracic	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia and q 8 hr for up to 72 hr ^{c,d}	Cefuroxime 50 mg/kg i.v. at induction of anesthesia and q 8 hr for up to 72 hr, ^{c,d} vancomycin 15 mg/kg i.v. with or without gentamicin 2 mg/kg i.v. ^e
Gastrointestinal		
Gastroduodenal (procedures involving entry into the lumen of the gastrointestinal tract, highly selective vagotomy, Nissen's fundoplication, and Whipple's procedure)	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia	
Biliary tract		
Open procedures	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia	
Laparoscopic procedures	None	
Appendectomy for uncomplicated appendicitis	Cefoxitin 20–40 mg/kg i.v., cefotetan 20–40 mg/kg i.v., cefotaxime 25–50 mg/kg i.v., or ceftizoxime 25–50 mg/kg i.v. at induction of anesthesia	Piperacillin 50 mg/kg i.v. at induction of anesthesia; if patient is allergic to penicillin, metronidazole 10 mg/kg i.v. plus gentamicin 2 mg/kg i.v. at induction of anesthesia
Colorectal	Neomycin sulfate 20 mg/kg plus erythromycin base 10 mg/kg p.o. (after mechanical bowel preparation is completed) at 19, 18, and 9 hr before surgery; if oral route is contraindicated, cefoxitin or cefotetan 30–40 mg/kg i.v. at induction of anesthesia; for patients undergoing high-risk surgery (e.g., rectal resection), oral neomycin and erythromycin plus an i.v. cephalosporin	
Head and neck		
Clean	None	
With placement of prosthesis	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia	
Clean-contaminated	Cefazolin 30–40 mg/kg i.v. at induction of anesthesia and q 8 hr for 24 hr or clindamycin 15 mg/kg i.v. at induction of anesthesia and q 8 hr for 24 hr	Addition of gentamicin 2.5 mg/kg i.v. to clindamycin regimen or of metronidazole 10 mg/kg i.v. q 8 hr to cefazolin regimen is controversial; single-dose regimens might be preferable, but this approach is controversial
Elective craniotomy or cerebrospinal-fluid shunting	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia	Vancomycin 15 mg/kg i.v. ^f
Obstetric or gynecologic		
Cesarean delivery ^g	Cefazolin 2 g i.v. immediately after clamping of umbilical cord	
Hysterectomy (vaginal, abdominal, or radical) ^h	Cefazolin 1 g i.v. or cefotetan 1 g i.v. at induction of anesthesia	Cefoxitin 1 g i.v. at induction of anesthesia
Ophthalmic	Topical neomycin–polymyxin B–gramicidin 1–2 drops or tobramycin 0.3% or gentamicin 0.3% 2 drops instilled before procedure ⁱ	
Orthopedic		
Clean, not involving implantation of foreign materials ^j	None	
Hip fracture repair, ^k implantation of internal fixation devices, ^k total joint replacement	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 15 mg/kg i.v. ^f
Urologic procedures (high-risk patients only ^l)	Trimethoprim 6–10 mg/kg plus sulfamethoxazole 30–50 mg/kg p.o. 2 hr before surgery (if oral agents used) or cefazolin 20–30 mg/kg i.v. at induction of anesthesia (if injection preferred)	
Vascular procedures ^m	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia and q 8 hr for 24 hr	Vancomycin 15 mg/kg i.v. with or without gentamicin 2 mg/kg i.v. ^f
Transplantation		
Heart	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia and q 8 hr for 48–72 hr ^d	Cefuroxime 50 mg/kg i.v. at induction of anesthesia and q 8 hr for 48–72 hr, ^{c,d} vancomycin 15 mg/kg with or without gentamicin 2 mg/kg i.v. ^e

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Table 2. (continued)
Antimicrobial Regimens for Surgical Prophylaxis in Pediatric Patients^a

Type of Surgery	Preferred Regimen ^b	Alternative Regimens ^b
Transplantation		
Lung and heart–lung ^{n,o}	Cefazolin 20–30 mg/kg i.v. at induction of anesthesia and q 8 hr for 48–72 hr ^d	Cefuroxime 50 mg/kg i.v. at induction of anesthesia and q 8 hr for 48–72 hr, ^d vancomycin 15 mg/kg i.v. ^f
Liver	Cefotaxime 50 mg/kg i.v. plus ampicillin 50 mg/kg i.v. at induction of anesthesia and q 6 hr for 48 hr beyond final surgical closure	Antimicrobials that provide adequate coverage against gram-negative aerobic bacilli, staphylococci, and enterococci may be appropriate
Pancreas and pancreas–kidney	Cefazolin 20 mg/kg i.v. at induction of anesthesia	
Kidney	Cefazolin 20 mg/kg i.v. at induction of anesthesia	

^aThe recommendations included in this table have been extrapolated from adult data. The pediatric dosages are approximately equivalent to the adult dosages listed in Table 1. With few exceptions (aminoglycosides), pediatric dosages should not exceed the maximum dosage recommended for adults. Adult dosages should be used for children weighing more than 40–50 kg because a dosage calculated on a milligram-per-kilogram basis will exceed the maximum recommended dosage for adults.^{34,35} Dosages for neonates (full-term and preterm) are not provided. The reader is referred to Neofax for neonatal dosing.³⁶

^bIf a short-acting agent is used, it should be readministered if the operation takes more than three hours. If an operation is expected to last more than six to eight hours, it would be reasonable to administer an agent with a longer half-life and duration of action or to administer a short-acting agent at three-hour intervals during the procedure. Readministration may also be warranted if prolonged or excessive bleeding occurs or there are factors that may shorten the half-life (e.g., extensive burns). Readministration may not be warranted in patients in whom the half-life is prolonged (e.g., patients with renal insufficiency or failure).

^cDuration is based on expert panel consensus. Prophylaxis for 24 hours or less may be appropriate.

^dThere is currently no evidence to support continuing antimicrobial prophylaxis until chest and mediastinal drainage tubes are removed.

^eAccording to Hospital Infection Control Practices Advisory Committee guidelines²¹ or American Heart Association recommendations for penicillin-allergic patients at high risk for endocarditis.³² Pediatric cancer patients may require dosages greater than the standard dosage.^{37,38}

^fAccording to Hospital Infection Control Practices Advisory Committee guidelines.²¹

^gThe American College of Obstetricians and Gynecologists (ACOG) considers the use of prophylaxis controversial in low-risk patients.³³ ACOG does not routinely recommend prophylaxis in low-risk patients because of concerns about adverse effects, development of resistant organisms, and relaxation of standard infection-control measures and proper operative technique.

^hAccording to ACOG guidelines, first-, second-, and third-generation cephalosporins can be used for vaginal, abdominal, and radical hysterectomies.³⁴

ⁱThe necessity of continuing topical antimicrobials postoperatively has not been established by data.

^jLaminectomy and knee, hand, and foot surgeries. The evaluated studies did not include arthroscopy procedures and did not identify specific procedures, like carpal tunnel release; however, arthroscopy and other procedures not involving implantation are similar enough to be included with clean orthopedic procedures not involving implantation.

^kProcedures involving internal fixation devices (e.g., nails, screws, plates, wires).

^lHigh risk is defined as prolonged postoperative catheterization, positive urine cultures, or hospital infection rate of greater than 20%.

^mProphylaxis is not indicated for brachiocephalic procedures. Although there are no data, patients undergoing brachiocephalic procedures involving vascular prosthesis or patch implantation (e.g., carotid endarterectomy) may benefit from prophylaxis.

ⁿPatients undergoing lung transplantation with negative pretransplant cultures should receive antimicrobial prophylaxis as appropriate for other types of cardiothoracic surgeries.

^oPatients undergoing lung transplantation for cystic fibrosis should receive 7–14 days of prophylaxis with antimicrobials selected according to pretransplant isolates and susceptibilities. This may include additional antibacterial or antifungal agents.

The only situations in which vancomycin is appropriate for surgical prophylaxis are major surgical procedures involving the implantation of prosthetic materials or devices at institutions that have a high rate of infections caused by MRSA or MRSE or in patients who have a life-threatening allergy to β -lactam antimicrobials.²¹ A high rate of infection caused by MRSA is defined as >20% by our expert panel consensus. However, some institutions consider >10% to be a high MRSA infection rate and 20% to be a low infection rate for MRSE. Each institution is encouraged to develop guidelines for the proper use of vancomycin, as applicable to the institution. Consistent with the HICPAC recommendations, a single dose of vancomycin administered immediately before surgery is sufficient unless the procedure lasts more than six hours or major blood loss occurs, in which case the dose should be repeated.²¹ Prophylaxis should be discontinued after a maximum of two doses.

The use of antimicrobials for prophylaxis in surgery contributes to changes in individuals' and institutions' bacterial flora. Studies have demonstrated that the use of antimicrobials prophylactically can alter bacterial flora, leading to colonization or resistance^{5,40-45} although another study, which involved patients undergoing colorectal surgery, showed no effect on the emergence of resistant bacteria.⁶ The bacterial flora affected include, but are not limited to, *Clostridium difficile*, enterococci, *Pseudomonas* species, and *Serratia* species.

Colonization with *C. difficile* has been demonstrated with prophylaxis of more than 24 hours' duration⁴⁰ and single-dose prophylaxis.⁴¹ Colonization with *C. difficile* may lead to complications such as colitis. A retrospective review demonstrated that 55% of the *C. difficile*-associated colitis cases were associated with surgical patients receiving preoperative cephalosporins.⁴²

Surgical prophylaxis may be a contributing factor to the development of VRE. An increase in VRE infection has been demonstrated in solid-organ transplant patients.^{43,44} Although transplant patients receive multiple courses of antimicrobials, including vancomycin, throughout their hospital course, the use of prophylactic antimicrobials may contribute to the development of resistance. A descriptive report demonstrated higher VRE infection rates among patients on the organ transplantation service (13.2 infections per 1000 admissions) and the surgical intensive care unit (5.6 infections per 1000 admissions) compared with the medical intensive care unit (4.8 infections per 1000 admissions) and the internal medicine service (1.8 infections per 1000 admissions).⁴³ In a hospital surveillance study, 32 (10.4%) of the 307 patients in whom VRE were cultured were transplant recipients⁴⁴; 24 (75%) of 32 patients developed VRE within 30 days (mean time) of transplantation. In an infant-toddler surgical ward, colorectal prophylaxis was an independent risk factor for colonization with a β -lactamase-producing, gentamicin-resistant strain of *Enterococcus faecalis*.⁴⁵

The development of resistance to *Pseudomonas* species and *Serratia* species from the use of surgical prophylaxis has also been demonstrated.⁵ An increased rate of *Pseudomonas* and *Serratia* resistance to gentamicin was detected, with a subsequent decrease in resistance after gentamicin was removed from the prophylactic regimen for open-heart surgery.

Timing. Prophylaxis implies delivery of the drug to the operative site before contamination occurs. Thus, the anti-infective drug should be given before the initial incision to ensure its presence in an adequate concentration in the targeted tissues. A landmark study demonstrated that, in a guinea pig model,

antimicrobials administered before or around the time of *S. aureus* inoculation reduced the rate of infection, whereas administration after *S. aureus* exposure was less effective.⁴⁶ The effect of administering an antimicrobial in the fourth postoperative hour was no different from that seen in a control group. This was confirmed in a prospective clinical study that demonstrated that giving antimicrobials more than two hours before surgery was no more effective than giving no antimicrobials or postoperative antimicrobials alone.⁴⁷ By consensus, the ideal time of administration is within 30 minutes to one hour before the incision. For most procedures, scheduling administration at the time of induction of anesthesia ensures adequate concentrations during the period of potential contamination.³⁰ The exceptions are cesarean procedures, in which the antimicrobial should be administered after cross-clamping of the umbilical cord,^{48,49} and colonic procedures, in which oral antimicrobials should be administered starting 19 hours before the scheduled time of surgery.⁵⁰⁻⁵⁶

Duration. The shortest effective duration of antimicrobial administration for preventing postoperative infection is not known; however, postoperative antimicrobial administration is not necessary for most procedures.⁵⁷ For most procedures, the duration of antimicrobial prophylaxis should be 24 hours or less, with the exception of cardiothoracic procedures (up to 72 hours' duration) and ophthalmic procedures (duration not clearly established). The duration of cardiothoracic prophylaxis is based on expert panel consensus because the data do not delineate the optimal duration of prophylaxis. Prophylaxis for 24 hours or less may be appropriate for cardiothoracic procedures. At a minimum, antimicrobial coverage must be provided from the time of incision to closure of the incision. If a short-acting agent is used, it should be readministered if the operation extends beyond three hours in duration.⁵⁸ Readministration may also be warranted if prolonged or excessive bleeding occurs or there are factors that may shorten the half-life of the antimicrobial (e.g., extensive burns). Readministration may not be warranted in patients for whom the half-life is prolonged (e.g., patients with renal insufficiency or failure). If an operation is expected to last more than six to eight hours, it would be reasonable to administer an agent with a longer half-life and duration of action or to consider administering a short-acting agent at three-hour intervals during the procedure.

Route of Administration

Antimicrobials used for prophylaxis in surgery may be administered intravenously, orally, or topically. The preferred route of administration varies with the type of surgery, but, for a majority of procedures, intravenous administration is ideal because it produces reliable and predictable serum and tissue concentrations. Oral antimicrobials are often used for gut decontamination in elective colorectal operations and are an option in urologic procedures.

The use of topical antimicrobial agents, paste, and irrigations is beyond the scope of these guidelines. Intravenous and oral administration are the main focus of the guidelines, with the exception of ophthalmic procedures, for which topical administration is the primary route of administration.

Cardiothoracic Surgery

Background. Approximately 4 million cardiothoracic surgeries are performed annually in the United States.⁵⁹ Of

these, approximately 500,000 are coronary-artery bypass graft (CABG) procedures and approximately 600,000 are open-heart procedures. A relatively small number involve heart- or heart-lung transplants and repair of congenital heart defects in children.

Patients who have cardiac conditions such as prosthetic cardiac valves, previous bacterial endocarditis, acquired valvular dysfunction, hypertrophic cardiomyopathy, and mitral valve prolapse with valvular regurgitation are at risk for developing bacterial endocarditis when undergoing open-heart surgery. Few controlled trials have demonstrated a benefit of prophylaxis. However, because of the morbidity and mortality associated with bacterial endocarditis, the AHA recommends antimicrobial prophylaxis.³²

Mediastinitis and sternal wound infection are rare but serious complications of cardiothoracic surgery. The frequency of these infections with or without associated sternal dehiscence is 0.7% to 1.5%; however, the associated mortality rate is 13% to 33%.⁶⁰ Risk factors for these complications include chronic obstructive pulmonary disease, prolonged stay in the intensive care unit, respiratory failure, connective tissue disease, and male sex. Advanced age, lengthy surgery, and diabetes mellitus have also been identified as risk factors.⁶¹

Organisms. The primary intent of early antimicrobial prophylaxis in open-heart surgery was to reduce the frequency of postoperative endocarditis after valve repair. Early studies showed that coagulase-positive and coagulase-negative staphylococci were the primary pathogens infecting prosthetic valves.⁶²⁻⁶⁴ As a result, most early prophylactic regimens were directed against staphylococci, with semisynthetic penicillins and first-generation cephalosporins emerging as the drugs of choice. With the advent of the CABG procedure and an expansion in the number of cardiothoracic procedures performed in the United States, prophylaxis must cover a broader spectrum of aerobic gram-negative pathogens that cause wound infections postoperatively at the sternal incision and the saphenous vein harvest sites.⁶⁴⁻⁶⁷

Efficacy. The postoperative infection rate in clean cardiothoracic surgeries is intrinsically low, and the extent of superiority of one regimen over another is relatively small. Antimicrobial prophylaxis in cardiothoracic surgery is associated with a fivefold lower rate of postoperative wound infection compared with placebo (approximately 5% versus 20% to 25%).⁶⁸ Early placebo-controlled studies using a semisynthetic penicillin⁶⁹ or cephradine⁷⁰ were terminated early because of high infection rates in the placebo groups. Postoperative wound infection rates ranged from 9.1% to 54% in the placebo groups, compared with 0% to 6.7% in groups receiving antimicrobials. Since the routine administration of prophylactic antimicrobials for cardiothoracic surgeries, postoperative wound infection rates have ranged from 0.8% to 25%.

Choice. Cephalosporins were compared with antistaphylococcal penicillins as prophylactic agents for cardiothoracic surgery in five studies. The antistaphylococcal penicillins were used in combination with another penicillin, an aminoglycoside, or both in four of these studies.⁷¹⁻⁷⁵ In four of the five studies, there were fewer total wound infections in the cephalosporin-treated patients; however, none of the differences were significant.

Published trials comparing cefazolin, cefamandole, and cefuroxime as prophylactic antimicrobials for cardiothoracic

surgery have revealed fewer total infections in the second-generation cephalosporin-treated patients; however, none of the differences were significant.⁷⁶⁻⁸² Both sternal and total wound infection rates (sternal plus leg wound infection) ranged from 2.5% to 18.8% in cefazolin-treated patients and from 0% to 13.5% in cefamandole- or cefuroxime-treated patients. Total wound infection rates were lower in patients receiving the second-generation cephalosporin in seven of the eight comparison groups. Leg wound infection rates were lower in five of the eight second-generation cephalosporin treatment groups. Meta-analysis of these results did not yield significant differences between agents when sternal and leg wounds were analyzed separately.⁶⁸ In another study, in which cefazolin and cefamandole, both with the addition of gentamicin, were compared, there was a significantly lower rate of sternal and total wound infection in the cefamandole-gentamicin group.⁷⁷ Three randomized, prospective, double-blind studies did not favor the second-generation cephalosporins: One study demonstrated no clinically or statistically significant difference between cefazolin and cefuroxime prophylaxis in 702 patients undergoing heart surgery,⁸³ a second study showed that cefuroxime-treated patients developed more sternal wound infections than cefazolin-treated patients,⁸⁴ and a third study showed no difference in rates of postsurgical site wound infection among cefamandole, cefazolin, and cefuroxime.⁸²

In a study that compared second-generation cephalosporins, cefamandole was found to be superior to cefonicid in preventing perioperative infections.⁸⁵ No differences in total wound infection rates were found in another study in which cefuroxime was compared with ceftriaxone in 512 patients.⁷⁸ Vancomycin was superior to penicillin G in preventing total wound infections.⁸⁶

In summary, cefamandole and cefuroxime were each associated with a lower frequency of wound infection than cefazolin, although significant differences were not consistently demonstrated. There were no differences in wound infection rates in a study that compared cefazolin with ceftriaxone. In addition, no differences in outcome were seen in studies in which cefamandole was compared with cefuroxime. No differences were found between antistaphylococcal penicillin regimens (often used in combination with aminoglycosides or other penicillins) and single-agent first- or second-generation cephalosporin regimens. These results are further supported by the results of a 30-year meta-analysis.⁶⁸

Cephalosporins, as single agents, are at least as effective as combination regimens of antistaphylococcal penicillins and aminoglycosides and are much easier to administer. Cefazolin has been the traditional cephalosporin of choice. Further trials in a large number of patients would be required in order to demonstrate the superiority of cefamandole or cefuroxime.

There are limited data regarding the choice of an antimicrobial for penicillin-allergic patients undergoing cardiovascular procedures. Although vancomycin offers coverage against potential gram-positive pathogens, the addition of an aminoglycoside may be prudent when colonization and infection with gram-negative organisms are expected (such as a saphenous vein site).

Duration. The optimal duration of antimicrobial prophylaxis for cardiothoracic surgery was addressed by five studies, all using cephalothin as the prophylactic antimicrobial.^{66,87-90} Dosages and durations in the short-duration groups ranged from a single 1-g dose of cephalothin

(as the sodium) to 2 g every six hours for two days. Long treatment regimens ranged from 2 g of cephalothin preoperatively followed by 1 g every six hours for three days to 2 g every six hours for six days. Total wound infection rates were lower in the short-duration treatment groups in two of four studies, although the differences were not significant. In another randomized study, there was no significant difference between single-dose ceftriaxone and cefuroxime three times daily until the end of the second postoperative day.⁹⁰ The researchers concluded that a single dose of ceftriaxone was a viable alternative to cefuroxime for 48 hours as prophylaxis in cardiothoracic surgical procedures. A European randomized, prospective study in 844 evaluable patients demonstrated that a single dose of cefuroxime 20 mg/kg (as the sodium) at induction of anesthesia was as effective as the same dose at induction of anesthesia followed by 750 mg three times daily for three consecutive days.⁹¹

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing cardiovascular procedures. A survey indicated that the predominant practice in pediatric cardiovascular surgery is to use cefazolin for two days or less or until transthoracic medical devices are removed.⁹²

Recommendations. For patients undergoing cardiothoracic procedures, the recommended regimen is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia and every 8 hours for up to 72 hours. This duration is based on consensus of the expert panel because the data do not delineate the optimal duration of prophylaxis. Prophylaxis for 24 hours or less may be appropriate for cardiothoracic procedures. Currently there is no evidence to support continuing prophylaxis until chest and mediastinal drainage tubes are removed. Cefuroxime 1.5 g (as the sodium) intravenously at induction of anesthesia and every 12 hours for up to 72 hours or cefamandole 1 g (as the sodium) at induction of anesthesia and every six hours for up to 72 hours are suitable alternatives. Further studies are needed to demonstrate the efficacy of single-dose prophylaxis. Vancomycin 1 g (as the hydrochloride) intravenously over one hour, with or without gentamicin 2 mg/kg (as the sulfate) intravenously, should be reserved as an alternative on the basis of guidelines from HICPAC and AHA.^{21,32} (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing cardiothoracic procedures is cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for up to 72 hours. Cefuroxime 50 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for up to 72 hours is an acceptable alternative. Vancomycin 15 mg/kg (as the hydrochloride) intravenously over one hour, with or without gentamicin 2 mg/kg (as the sulfate) intravenously, should be reserved as an alternative on the basis of guidelines from HICPAC and AHA.^{21,32}

Gastroduodenal Surgery

Background. The gastroduodenal procedures considered in this document include resection with or without vagotomy for gastric or duodenal ulcers, resection for gastric carcinoma, revision required in order to repair strictures of the gastric outlet, and gastric bypass. Studies addressing

antimicrobial prophylaxis for gastroesophageal reflux disease procedures (Nissen's fundoplication), pancreaticoduodenectomy (Whipple's procedure), or highly selective vagotomy for ulcers could not be identified.

The stomach is an effective barrier to bacterial colonization; this is at least partially related to its acidity. The stomach and the duodenum typically contain small numbers of organisms (<10⁴ CFU/mL), the most common of which are streptococci, lactobacilli, diphtheroids, and fungi.^{93,94} Treatment with agents that increase gastric pH significantly increases the concentration of gastric organisms.^{95–97} Alterations in gastric and duodenal bacterial flora as a result of increases in gastric pH have the potential to increase the postoperative infection rate.^{98,99}

The risk of postoperative infection in gastroduodenal surgery depends on a number of factors. Patients who are at highest risk include those with achlorhydria, decreased gastric motility, gastric outlet obstruction, morbid obesity, gastric bleeding, or cancer.¹⁰⁰

Organisms. The most common organisms cultured from wound infections after gastroduodenal surgery are coliforms (*Escherichia coli*, *Proteus* species, *Klebsiella* species), staphylococci, streptococci, enterococci, and, occasionally, *Bacteroides* species.^{101–108}

Efficacy. In one large study, wound infection rates in patients not receiving antimicrobial prophylaxis were 6% after vagotomy and drainage, 13% after gastric ulcer surgery, 17% after surgery for gastric cancer, and 25% in patients with gastroduodenal bleeding.¹⁰⁹ Results of randomized, controlled trials clearly indicate that prophylactic antimicrobials are effective in decreasing postoperative infection rates in gastroduodenal surgery. Relative to other types of GI tract surgery, the number of clinical trials evaluating antimicrobial prophylaxis for gastroduodenal surgery is limited. The most common definition of wound infection used in those studies was the presence of purulent discharge. In placebo-controlled trials, infection rates ranged from 0% to 7% for patients receiving cephalosporins and from 21% to 44% for patients receiving placebo.^{102,103,105–107,110–112} The difference was significant in most studies.

No efficacy data are available on highly selective vagotomy, Nissen's fundoplication, or Whipple's procedure. Despite the lack of data, the expert panel supports the use of a single dose of cefazolin 1 g (as the sodium) intravenously for prophylaxis of these procedures.

Choice. No differences between first- and second-generation cephalosporins were found. The most frequently used agents were first-generation^{103,105,108,110–113} and second-generation^{101,102,104,106,107,113} cephalosporins. Ticarcillin,¹⁰⁸ amoxicillin-clavulanate,¹¹⁴ mezlocillin,¹⁰⁴ and ciprofloxacin^{101,115} were also evaluated. Relatively few studies have compared the efficacy of different agents in reducing postoperative infection rates. In comparative studies, ticarcillin (intravenous) and cephalothin (intravenous) were similarly effective,¹⁰⁸ as were ciprofloxacin (intravenous and oral) and cefuroxime (intravenous).¹⁰¹

Duration. Available data indicate that single-dose and multidose regimens are similarly effective. Two studies compared single- and multidose regimens of either cefamandole¹¹³ or amoxicillin-clavulanate.¹¹⁴ There was no significant difference in wound infection rates. No studies have evaluated the use of a single dose of a first-generation cephalosporin.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing gastroduodenal surgery.

Recommendation. Antimicrobial prophylaxis in gastroduodenal surgery should be considered for patients at highest risk for postoperative infections, such as patients with increased gastric pH (e.g., patients receiving histamine H₂-receptor antagonists), decreased gastric motility, gastric outlet obstruction, gastric bleeding, or cancer. Antimicrobials are not needed when the lumen of the intestinal tract is not entered.

A single dose of cefazolin 1 g (as the sodium) given intravenously at induction of anesthesia is recommended in procedures during which the lumen of the intestinal tract is entered. A single dose of cefazolin 1 g given intravenously at induction of anesthesia is recommended for highly selective vagotomy, Nissen's fundoplication, and Whipple's procedure. (Strength of evidence for prophylaxis = A when the lumen of the intestinal tract is entered.) (Strength of evidence for prophylaxis = C for highly selective vagotomy, Nissen's fundoplication, and Whipple's procedure.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing gastroduodenal surgery during which the lumen of the intestinal tract is entered, highly selective vagotomy, Nissen's fundoplication, and Whipple's procedure is a single dose of cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia.

Biliary Tract Surgery

Background. Biliary tract surgeries include cholecystectomy, exploration of the common bile duct, and choledochostomy. The overall risk of postoperative infection in biliary tract surgery is approximately 5% to 20%.¹¹⁶ The biliary tract is usually sterile; therefore, the risk of infection is low. However, it is generally accepted that patients with bacteria in the bile at the time of surgery are at higher risk of postoperative infection.^{117,118} Factors that place patients at a higher risk of infection include obesity, age greater than 70 years, an acute episode of cholecystitis or cholelithiasis within the previous six months, diabetes mellitus, or a history of obstructive jaundice or bile duct obstruction.^{116,119}

Organisms. The organisms most commonly associated with infection after biliary tract surgery include *E. coli*, *Klebsiella* species, and enterococci; less frequently, other gram-negative organisms, streptococci, or staphylococci are isolated. Anaerobes are occasionally reported, most commonly *Clostridium* species.^{117,119–128}

Efficacy. Data from randomized, controlled trials support the use of prophylactic antimicrobials in all patients undergoing biliary tract surgery. Significantly lower rates of postoperative wound infection have been demonstrated, even in patients at low risk.

Numerous studies have evaluated the use of prophylactic antimicrobials during biliary tract surgery. Although the definition of wound infection varied between studies, the presence of purulent discharge was the most common definition. First-generation^{121,127,129,138} second-generation,^{118–120, 122,123,126,133,135,136,138–143} and third-generation^{123,124,132,141} cephalosporins have been studied more extensively than other

antimicrobials. Limited data are available for ampicillin–gentamicin,¹⁴⁴ mezlocillin,¹⁴² piperacillin,¹³⁷ amoxicillin–clavulanate,¹⁴³ and ciprofloxacin.^{124,145}

Although many studies had an insufficient sample size to demonstrate a significant benefit of antimicrobial prophylaxis, a meta-analysis of 42 clinical trials that compared prophylactic antimicrobials with placebo demonstrated that active treatment significantly reduced the risk of wound infection.¹¹⁶ In that analysis, the overall wound infection rate was 15% in the control group. Wound infection rates were 9% lower in the antimicrobial treatment group than the control group. When patients were stratified by low or high risk and by early or late wound inspection (early in hospital or late at follow-up), antimicrobial prophylaxis was still effective in preventing wound infections in all groups, although the largest benefit was in high-risk patients with a later wound inspection.

Laparoscopic cholecystectomy has replaced open cholecystectomy as the standard of practice because of a reduction in recovery time and a shorter hospital stay. There have been few studies of antimicrobial prophylaxis for laparoscopic cholecystectomy. The studies that have addressed this procedure were not randomized, controlled studies. In one study at the Mayo Clinic, 95% of 195 patients received a preoperative dose of an antimicrobial, usually a first-generation cephalosporin. Erythema at the trocar site was noted in 6% of patients, and wound separation was noted in 5% of patients; however, no treatment was necessary.¹⁴⁶ A non-randomized study showed 14 infections in 228 patients who received antimicrobial prophylaxis and no infections in 188 patients who received only a chlorhexidine scrub before surgery.¹⁴⁷ The patients in this study were assigned to treatment groups according to the attending physician's treatment preference. In a study in the United Kingdom, cefuroxime 1.5 g (as the sodium) was administered at induction of anesthesia to 253 consecutive patients. At two weeks, 0.8% of patients had wound infections, 0.8% had chest infections, and 0.4% had an intra-abdominal abscess. No complications were noted at 12 months.¹⁴⁸ Current data do not support antimicrobial prophylaxis for laparoscopic cholecystectomies.

Choice. The data do not indicate a significant difference among first-, second-, and third-generation cephalosporins. Several studies have compared first-generation cephalosporins with second- or third-generation agents.^{127,132–136,138} With one exception,¹³⁶ there was no significant difference among agents. This was confirmed by a meta-analysis that found no significant difference among first-, second-, and third-generation cephalosporins.¹¹⁶ Other studies found no significant differences between ampicillin and cefamandole,¹²⁶ ciprofloxacin and ceftriaxone,¹²⁴ cefonicid and mezlocillin,¹⁴² cefuroxime with or without metronidazole and mezlocillin,¹⁴⁹ amoxicillin–clavulanate and mezlocillin,¹⁵⁰ amoxicillin–clavulanate and cefamandole,¹⁴³ and oral and intravenous ciprofloxacin and intravenous cefuroxime.¹⁴⁵

Duration. The effect of treatment duration on outcome has been evaluated. A single dose of a cephalosporin was compared with multiple doses in several studies; no significant differences were found.^{118,120,121,132,139–141,151} The largest study compared one dose of cefuroxime with three doses in 1004 patients with risk factors for infection who were undergoing biliary tract surgery.¹¹⁸ There was no significant difference in the rates of minor or major wound infection between the single- and multiple-dose groups.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing biliary tract surgery.

Recommendation. A single dose of cefazolin 1 g (as the sodium) administered intravenously at induction of anesthesia is recommended for open procedures in the biliary tract. (Strength of evidence for prophylaxis = A.) Antimicrobial prophylaxis is not recommended in laparoscopic cholecystectomies. (Strength of evidence against prophylaxis = B.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing open procedures in the biliary tract is a single dose of cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia.

Appendectomy

Background. Cases of appendicitis can be described as complicated or uncomplicated on the basis of the pathology. Patients with uncomplicated appendicitis have an acutely inflamed appendix. Complicated appendicitis usually includes perforated or gangrenous appendicitis, including peritonitis or abscess formation. However, in some studies patients with gangrenous appendicitis are considered to have uncomplicated disease because these patients generally have a lower infectious complication rate than patients with perforation. Because complicated appendicitis is treated as a presumed infection, it has not been addressed in these guidelines.

Approximately 80% of patients with appendicitis have uncomplicated disease.²⁴ Postoperative infection has been reported in 9–30% of patients with uncomplicated appendicitis who do not receive prophylactic antimicrobials.^{152–156} Postoperative infection was usually defined as purulent wound discharge with or without positive cultures. Laparoscopic appendectomy has been reported to produce similar or lower rates of infection as open appendectomy when antimicrobials are used; however, there have been no randomized, controlled studies.¹⁵⁷

Organisms. The most common microorganisms isolated from wound infections after appendectomy are anaerobic and aerobic gram-negative enteric organisms. *Bacteroides fragilis* is the most commonly cultured anaerobe, and *E. coli* is the most frequent aerobic, indicating that the bowel flora constitute a major source for pathogens.^{24,158,159} Aerobic and anaerobic streptococci, *Staphylococcus* species, and *Enterococcus* species also have been reported. *Pseudomonas aeruginosa* has been reported infrequently.

Efficacy. As a single agent, metronidazole was no more effective in appendectomy than placebo.^{152,155} Cefazolin was generally less effective than placebo, with postoperative infection rates above 10%.¹⁵³ This is likely due to its limited activity against anaerobes. Clindamycin was more effective than placebo, although the postoperative infection rate tended to be relatively high (17%).¹⁵³

Choice. Randomized, controlled trials have failed to identify an agent that is clearly superior to other agents in the prophylaxis of postappendectomy infectious complications. The second- and third-generation cephalosporins appear to have similar efficacy and are the recommended agents on the basis of cost and tolerability. Given the relatively equivalent efficacy between agents, a cost-minimization approach

is reasonable; the choice of agents should be based on local drug acquisition costs.

A wide range of antimicrobials have been evaluated for prophylaxis in uncomplicated appendicitis. The most commonly used agents were cephalosporins. In general, second-generation cephalosporins (cefoxitin, cefotetan) and third-generation cephalosporins (cefoperazone, cefotaxime) were effective, with postoperative infection rates of <5% in most studies.^{156,160–166} However, one study¹⁶⁵ showed that single-dose cefotetan was significantly more effective than single-dose cefoxitin, perhaps because of the longer half-life of cefotetan.

Piperacillin 2 g (as the sodium) was comparable to cefoxitin 2 g (as the sodium) in a well-controlled study.¹⁶⁶ Metronidazole was less effective than cefotaxime, with infection rates above 10%.¹⁶⁰ However, when metronidazole was combined with ampicillin¹⁶⁷ or gentamicin,^{162,168} the postoperative infection rates were 3% to 6%. Clindamycin was more effective than cefazolin, although the postoperative infection rate tended to be relatively high (17%).¹⁵³

Duration. In most of the studies of second- or third-generation cephalosporins or metronidazole combinations, a single dose^{160–162,165,166,168} or two or three doses^{156,163,167} were given. Although direct comparisons were not done, there was no discernible difference in postoperative infection rates between single-dose and multidose administration in most studies.

Pediatric Efficacy. Two pediatric studies demonstrated no difference in infection rates between placebo and antimicrobials: metronidazole, penicillin plus tobramycin, and piperacillin¹⁶⁹ and single-dose metronidazole and single-dose metronidazole plus cefuroxime.¹⁷⁰ As a single agent, metronidazole was no more effective than placebo in two double-blind studies that included children 10 years of age and older¹⁵² and 15 years of age and older.¹⁵⁵ In a randomized study that included pediatric patients, ceftizoxime and cefamandole demonstrated significantly lower infection rates and duration of hospitalization than placebo.¹⁷¹ Both cefoxitin and a combination of gentamicin and metronidazole were associated with a lower rate of postoperative infection in a randomized study that included pediatric patients less than 16 years of age.¹⁶² Second-generation cephalosporins (cefoxitin) and third-generation cephalosporins (cefoperazone, cefotaxime) were effective, with postoperative infection rates of <5% in two studies that included pediatric patients less than 12 years of age.^{156,162,163}

Recommendation. For uncomplicated appendicitis, the recommended regimen is a cephalosporin with anaerobic and aerobic activity (cefoxitin, cefotetan, cefmetazole) 1–2 g intravenously at induction of anesthesia. An alternative is piperacillin 2 g (as the sodium) intravenously. For penicillin-allergic patients, an alternative is metronidazole 500 mg plus gentamicin 2 mg/kg (as the sulfate) intravenously at the induction of anesthesia. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing procedures for uncomplicated appendicitis is a single intravenous dose of cefoxitin 20–40 mg/kg (as the sodium), cefotetan 20–40 mg/kg (as the disodium), or cefotaxime or ceftizoxime 25–50 mg/kg (as the sodium) at induction of anesthesia. An alternative is piperacillin 50 mg/kg (as the sodium) intravenously at induction of anesthesia. For penicillin-allergic patients, an alternative is metronidazole 10 mg/kg plus gentamicin 2 mg/kg (as the sulfate) intravenously at induction of anesthesia.

Colorectal Surgery

Background. Wound infections are a frequent complication of surgery of the colon or rectum. Other septic complications, such as fecal fistula, intra-abdominal abscesses, peritonitis, and septicemia, are serious concerns but much less common.¹⁷² Infectious complication rates range from 30% to 60% when antimicrobial prophylaxis is not used.^{24,173} Patients receiving appropriate antimicrobial prophylaxis have infection rates of <10%. A pooled analysis of clinical trials of antimicrobial prophylaxis in colon surgery also demonstrated that the use of antimicrobials significantly reduces mortality (11.2% for control versus 4.5% for treatment).¹⁷⁴ The type and duration of surgery can affect the risk of infection. Rectal resection is associated with a higher risk of infection than intraperitoneal colon resection.^{175,176} Surgeries lasting 3.5 hours or more are associated with a higher risk of infection than shorter procedures.²⁴ Other risk factors include impaired host defenses, age of >60 years, hypoalbuminemia, poor preoperative bowel preparation, bacterial contamination of the surgical wound,¹⁷⁷ corticosteroid therapy, and malignancy.¹⁷⁸

The removal of feces and intestinal fluid by mechanical preparation is considered a prerequisite for colorectal surgery. Mechanical preparation also reduces the high concentrations of bacteria in the bowel. Traditional three- to four-day regimens of clear liquids, cathartics, and enemas have been replaced by single-day lavage techniques.^{179–186}

The choice of antimicrobials for prophylaxis in colorectal surgery should be guided by the spectrum of activity of the agent. Agents should have activity against the anaerobic and aerobic flora of the bowel. There have been three main approaches to the prophylaxis of infections after colorectal surgery: oral agents, intravenous agents (usually cephalosporins), and combinations of oral and intravenous agents. Although numerous clinical trials have been conducted, the central issues of determining the most appropriate regimen (oral versus intravenous versus an oral–intravenous combination) and the optimal choice of antimicrobial have yet to be fully resolved.

Organisms. The infecting organisms in colorectal surgery are derived from the bowel lumen, where there are high concentrations of organisms. *B. fragilis* and other obligate anaerobes are the most frequently isolated organisms from the bowel, with concentrations 1,000 to 10,000 times higher than those of aerobes.¹⁸⁷ *E. coli* is the most common aerobe. *B. fragilis* and *E. coli* make up approximately 20% to 30% of the fecal mass. They are the most frequently isolated pathogens from infected wounds after colon surgery.¹⁸⁷

Efficacy. Results from randomized, controlled trials unequivocally support the use of prophylactic antimicrobials in all patients undergoing colorectal surgery. Postoperative infection rates tend to be lower when oral antimicrobials are used for prophylaxis than after the use of intravenous agents; therefore, oral antimicrobials are preferred.

Oral regimens. A variety of oral agents administered after mechanical bowel preparation have been evaluated for prophylaxis for colorectal surgery. The most common combinations have been an aminoglycoside (neomycin and, less often, kanamycin) plus an agent that will provide sufficient anaerobic activity, usually erythromycin^{50–56,188} or metronidazole.^{56,182,188–192} In placebo-controlled studies,^{6,50,188,192,193} the oral combination was significantly more effective than

placebo in reducing wound infections. Postoperative wound infection rates ranged from 0% to 11% with neomycin plus erythromycin^{50–56} and from 2% to 13% with neomycin and metronidazole.^{189–191} Combinations of neomycin and tetracycline,^{6,193} and neomycin and clindamycin¹⁸⁹ have also been used successfully, with postoperative wound infection rates of <10%. The use of metronidazole as a single agent appears to be less effective, with reported wound infection rates of 12% to 15%.^{194,195}

Oral antimicrobials have been compared with intravenous agents in a few studies. Oral neomycin plus oral erythromycin was significantly more effective than intravenous gentamicin and intravenous metronidazole⁵⁴ but was similarly effective as intravenous cefoxitin,⁵² intravenous cefamandole,⁵³ and intravenous ceftriaxone plus intravenous metronidazole.⁵⁵

Intravenous regimens. A wide range of intravenous antimicrobials have been evaluated for prophylaxis in colorectal surgery. Cephalosporins are the most common agents, usually administered as a single agent. First-generation cephalosporins produced inconsistent results.^{196–200} With one exception,¹⁹⁹ single-agent first-generation cephalosporins were generally ineffective, with postoperative wound infection rates ranging from 12% to 39%.^{196,197} This is not surprising given the lack of *B. fragilis* activity of these agents. Second-generation cephalosporins have been widely evaluated. In single-agent therapy, wound infection rates ranged from 0% to 17%^{176,198,201–209}; however, more than half of the studies found rates of >10%. Third-generation agents have been evaluated in a few trials; postoperative wound infection rates were 8% to 19% with single-agent use.^{205,210,211} In some studies, second- or third-generation cephalosporins were combined with other intravenous agents, most commonly metronidazole.^{201,209–212} However, in three of four studies, a combination of a second- or third-generation cephalosporin plus metronidazole was no more effective than the cephalosporin alone.^{201,209–211} Other intravenous agents that have been evaluated either alone or in combination include aminoglycosides,^{54,101,213–217} clindamycin,²¹³ ampicillin,^{214,218,219} ampicillin plus a β -lactamase inhibitor,^{216,220} doxycycline,^{218,221–223} ticarcillin plus a β -lactamase inhibitor,^{215,224} piperacillin,^{206,225} piperacillin plus a β -lactamase inhibitor,²²⁵ imipenem,²¹² and ciprofloxacin.¹¹⁵

Combination oral and intravenous regimens. Combinations of oral and intravenous antimicrobials have been used in an attempt to further reduce postoperative infection rates. Regimens include oral neomycin and erythromycin plus intravenous administration of a cephalosporin,^{52,175,176,197,198,226,227} metronidazole,^{228,229} or gentamicin plus clindamycin.²¹³ Postoperative wound infection rates in these studies ranged from 0% to 7%. With one exception,¹⁷⁵ there was no significant difference between oral neomycin–erythromycin plus an intravenous antimicrobial and oral neomycin–erythromycin alone.^{52,197,213,226} When combination oral and intravenous agents were compared with intravenous agents alone, combination therapy tended to be superior in four of five studies^{52,176,197,198,228}; the difference was significant in two of the studies.^{176,197} In one study,¹⁷⁶ the difference was even greater among patients undergoing rectal resection, a procedure associated with a high risk of infection. The postoperative wound infection rates after rectal resection were 23% and 11%, respectively, for patients receiving intravenous cefoxitin and cefoxitin plus oral neomycin and erythromycin.

Duration. Single and multiple doses were compared in several studies.^{203–205,211,219,222} However, only two of these

studies,^{219,222} compared single doses with multiple doses of the same antimicrobial. There was no significant difference in infection rates between single-dose and multidose administration, with only one exception. A single dose of cefotaxime plus metronidazole was significantly more effective than three doses of cefotaxime alone.²¹¹

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing colorectal surgery. The safety, efficacy, tolerability, and cost-effectiveness of intestinal lavage have been demonstrated in pediatric patients.^{230,231}

Recommendation. Patients undergoing colorectal surgery should receive mechanical bowel preparation. Numerous bowel preparations are available. Lavage solutions are contraindicated in patients with obstruction.

Oral neomycin sulfate 1 g and erythromycin base 1 g should be given after the bowel preparation is complete at 19, 18, and 9 hours before surgery. If the oral route is contraindicated, a single 2-g dose of an intravenous cephalosporin with both aerobic and anaerobic activity (e.g., cefoxitin, cefotetan, cefmetazole) should be given at induction of anesthesia. Because there is no demonstrable difference in efficacy among these cephalosporins, the choice should be based on local drug acquisition costs. In patients undergoing high-risk surgery, such as rectal resection, a combination of oral neomycin-erythromycin plus a cephalosporin administered intravenously is recommended. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. Pediatric patients undergoing colorectal surgery should undergo mechanical bowel preparation. Numerous bowel preparations are available. Lavage solutions are contraindicated in patients with obstruction. One regimen for pediatric patients is polyethylene glycol-electrolyte lavage solution given orally or by nasogastric tube at a rate of 25–40 mL/kg/hr until rectal effluent is clear.^{230,231}

Oral neomycin sulfate 20 mg/kg and erythromycin base 10 mg/kg should be given after the bowel preparation is complete at 19, 18, and 9 hours before surgery. If the oral route is contraindicated, a single 30–40 mg/kg intravenous dose of cefoxitin or cefotetan should be given at induction of anesthesia. In patients undergoing high-risk surgery, such as rectal resection, a combination of oral neomycin and erythromycin plus a cephalosporin administered intravenously is recommended.

Head and Neck Surgery

Background. Elective surgical procedures of the head and neck can be categorized as clean or clean-contaminated. Clean procedures include parotidectomy, thyroidectomy, and submandibular-gland excision. Clean-contaminated procedures include all procedures involving an incision through the oral or pharyngeal mucosa.²³² These vary considerably from tonsillectomy, adenoidectomy, and rhinoplasty to complicated tumor-debulking procedures requiring massive reconstruction.

In prospective, randomized, double-blind trials comparing placebo with antimicrobials in clean-contaminated surgeries, patients receiving placebo had postoperative wound infection rates of 36% to 78%.^{233–235} Antimicrobials are associated with dramatically lower rates of postoperative wound infection. Infection rates below 10% may be expected when appropriate antimicrobial prophylaxis is

given.^{233,234,236–241} Postoperative wound infection rates are affected by age, nutritional status, and the presence of concomitant medical conditions such as diabetes mellitus. The hospital course, including length of hospitalization before surgery, duration of antimicrobial use before surgery, length of surgery, and presence of implants, can also affect postoperative wound infection rates. If the patient has cancer, the stage of the malignancy before operation and preoperative radiation therapy must also be assessed.^{242–244}

Organisms. The normal flora of the mouth and the oropharynx are responsible for most infections that follow clean-contaminated head and neck procedures. The predominant oropharyngeal organisms include various streptococci (aerobic and anaerobic species), *S. epidermidis*, *Peptococcus*, *Peptostreptococcus*, and numerous anaerobic gram-negative bacteria, including *Bacteroides* species (but almost never *B. fragilis*) and *Veillonella*. Nasal flora include *Staphylococcus* species and *Streptococcus* species. Anaerobic bacteria are approximately 10 times more common than aerobic bacteria in the oropharynx. As a result, postoperative wound infections are primarily polymicrobial. Both aerobic and anaerobic bacteria are cultured from infected wounds in more than 90% of cases.^{245–248} It has been suggested that aerobic gram-negative bacteria are colonizers rather than pathogens in most patients.^{237,246}

Efficacy for Clean Procedures. Systemic administration of prophylactic antimicrobials has not proven effective in reducing wound infection rates in patients undergoing clean procedures of the head and neck; however, randomized, blinded studies have not been performed for clean procedures. A retrospective review of 438 patients undergoing clean procedures (parotidectomy, thyroidectomy, or submandibular gland excision) demonstrated that 80% of the patients had not received prophylactic antimicrobials; the associated wound infection rate was 0.7%. Patients receiving antimicrobials had a similar wound infection rate.²⁴⁹ Another retrospective cohort study of 192 patients who underwent surgery between 1976 and 1989 did not demonstrate any difference in infection rates between patients who did and patients who did not receive perioperative antimicrobials.²⁵⁰ However, the authors calculated that the excess cost due to patients who developed a postoperative wound infection was in excess of \$36,000 and that the cost of administering prophylaxis to 100 patients is less than this amount. These retrospective data alone do not justify prophylaxis. Other factors besides cost need to be considered, including the potential for resistance, adverse events, and prosthetic placement.

Pediatric Efficacy for Clean Procedures. No well-controlled studies have evaluated the effect of antimicrobial prophylaxis in the pediatric population undergoing clean surgical procedures of the head and neck.

Efficacy for Clean-Contaminated Procedures. Three double-blind, placebo-controlled trials established superiority of antimicrobials over placebo in clean-contaminated procedures.^{233,234,238} In one trial, 101 patients were randomly assigned to receive placebo every eight hours for four doses, cefazolin 500 mg (as the sodium) every eight hours for four doses, cefotaxime 2 g (as the sodium) every eight hours for four doses, or cefoperazone 2 g (as the sodium) every eight hours for four doses.²³⁴ Infection rates were 78% in

the placebo group, 33% in the cefazolin group, 10% in the cefotaxime group, and 9% in the cefoperazone group. The difference between each antimicrobial group and the placebo group was significant. The length of hospital stay for infected patients was twice that of noninfected patients. The second study demonstrated a wound infection rate of 12% with ampicillin plus cloxacillin, compared with 28% with placebo.²³⁸ Although the wound infection rate (27%) for cefamandole 2 g (as the sodium) followed by 1 g every eight hours for a total of three doses was relatively high compared with the previous studies, cefamandole did demonstrate superiority over placebo (wound infection rate of 55%).²³³ Another study involving cefoperazone, cefotaxime, and placebo demonstrated similar results.²³⁵

Choice. Various studies of prophylaxis for clean-contaminated procedures have demonstrated wound infection rates of less than 10% with clindamycin plus gentamicin,^{236,251} clindamycin plus amikacin,²⁵² cefazolin plus metronidazole,²⁴¹ cefuroxime alone,²⁵³ and cefuroxime plus metronidazole.²⁵³ A prospective, randomized, double-blind study compared clindamycin 600 mg (as the hydrochloride) intravenously for a total of four doses with clindamycin 600 mg plus gentamicin 1.7 mg/kg (as the sulfate) intravenously for a total of four doses in 104 patients undergoing clean-contaminated oncological head and neck surgery.²³⁷ The combination of gentamicin plus clindamycin demonstrated no significant advantage over clindamycin alone. The postoperative infection rate was 3.8% in both groups. The authors concluded that clindamycin alone appears effective as a prophylactic agent and that broad-spectrum antimicrobials such as ceftioxin may be unnecessary. Because clindamycin is not active against aerobic gram-negative bacteria, the authors concluded that these bacteria are probably colonizers rather than pathogens. This study suggests that aerobic gram-negative coverage (as provided by gentamicin) may be unnecessary. However, the study lacked sufficient power to show a difference among groups.

Cefazolin offers coverage against potential aerobic and anaerobic organisms, except *B. fragilis*, in clean-contaminated procedures of the head and neck. Although the need for coverage against *B. fragilis* has not been substantiated by the literature, some people consider the addition of metronidazole to cefazolin acceptable when colonization with *B. fragilis* is expected.

Dosage. Cefazolin 500 mg (as the sodium) three times daily for a total of one and five days demonstrated high infection rates (35% and 18%, respectively).²⁵¹ Another study showed similar results with cefazolin.²³⁶ Two major flaws with these studies were the dose (500 mg) and the administration time (three hours preoperatively).

In a randomized trial, cefazolin 2 g (as the sodium) was compared with moxalactam 2 g (as the disodium), each given one hour before surgery and three more times, for a total of four doses.²⁵⁴ Infection rates were not significantly different: 8.5% in the cefazolin group and 3.4% in the moxalactam group. A prospective, randomized multicenter trial compared the effectiveness of clindamycin 900 mg (as the hydrochloride) with that of cefazolin 2 g (as the sodium) before surgery and continued every 8 hours for a total of 24 hours in patients undergoing major procedures (pectoralis major myocutaneous flap reconstruction).²⁵⁵ Wound infections developed in 19.6% of patients in the clindamycin group and 21.6% of patients in the cefazolin group. This difference was not significant. These two trials demonstrated that, when administered at the appropriate time, cefazolin 2 g is effective.

In a prospective, double-blind trial, 159 patients were randomly assigned to receive amoxicillin 1750 mg (as the trihydrate) with clavulanic acid 250 mg (as clavulanate potassium), clindamycin 600 mg (as the hydrochloride) plus gentamicin 80 mg (as the sulfate), or cefazolin 2 g (as the sodium).²⁵⁶ All groups received a total of three intravenous doses (the cefazolin group received one 2-g dose followed by two doses of 1 g each). There was no significant difference in wound infection rates among these regimens.

Duration. There was no difference in efficacy between one day and five days of clindamycin plus gentamicin prophylaxis in a randomized, unblinded study.²⁵⁶ Other studies involving prophylaxis for a total duration of one day or less also demonstrated wound infection rates of 10% or less.^{235,237,239,240,251,253,254} Single-dose prophylaxis has not been studied.

Pediatric Efficacy for Clean-Contaminated Procedures.

No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing clean-contaminated surgery of the head and neck.

Recommendation. *Clean procedures.* Infection rates in clean head and neck surgical procedures are generally less than 2%. Antimicrobial prophylaxis is not justified in patients undergoing clean surgical procedures of the head and neck. If there is prosthetic placement, cefazolin 1 g (as the sodium) intravenously at induction of anesthesia is appropriate. (Strength of evidence against prophylaxis = B.) (Strength of evidence for prophylaxis with prosthesis placement = C.)

Clean-contaminated procedures. The preferred regimens for patients undergoing clean-contaminated head and neck procedures are cefazolin 2 g (as the sodium) intravenously at induction of anesthesia and every 8 hours for 24 hours or clindamycin 600 mg (as the hydrochloride) intravenously at induction of anesthesia and every 8 hours for 24 hours. The necessity of giving gentamicin with clindamycin or metronidazole with cefazolin remains controversial; if these combinations are selected, the dosages are gentamicin 1.7 mg/kg (as the sulfate) intravenously and metronidazole 500 mg intravenously every eight hours. Agents should be administered at induction of anesthesia. Prophylaxis should not exceed 24 hours. Single-dose regimens may be preferable, particularly when cost and the possibility of resistance are considered; however, this approach remains controversial. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. *Clean procedures.* Antimicrobial prophylaxis is not recommended in pediatric patients undergoing clean head and neck procedures unless there is prosthetic placement. In these cases, cefazolin 20–30 mg/kg (as the sodium) administered intravenously at induction of anesthesia is appropriate.

Clean-contaminated procedures. The recommended regimen for pediatric patients undergoing clean-contaminated head and neck procedures is cefazolin 30–40 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 24 hours or clindamycin 15 mg/kg (as the hydrochloride) intravenously, at induction of anesthesia and every 8 hours for 24 hours. The addition of gentamicin 2.5 mg/kg (as the sulfate) intravenously to clindamycin remains controversial, as does the addition of metronidazole 10 mg/kg intravenously every eight hours to cefazolin. Agents should be administered at induction of anesthesia. Single-dose regimens may be preferable, particularly when cost and the possibility of resistance are considered; however, this approach remains controversial.

Neurosurgery

Background. Clean neurosurgical procedures are those during which there is no break in surgical technique and no entry into the respiratory or GI tract. Clean procedures usually carry a risk of postoperative wound infection of less than 5%. In many hospitals the risk is 1% to 2%. It is therefore understandable that the use of injectable antimicrobials for such procedures is controversial. In addition, it is difficult to design clinical trials that could enable a distinction between infection rates of 2% and 5%. Clean-contaminated neurosurgical procedures (e.g., surgical approach through the nasopharynx or transphenoid sinus) are not addressed in these guidelines because there is a lack of data and there are no sufficiently similar procedures from which to extrapolate data.

Examples of clean neurosurgical procedures include elective craniotomy for the repair of aneurysms, correction of arteriovenous malformations, and removal of various types of brain tumors. There can be major differences (e.g., immune status, nutrition) between a person who undergoes elective surgery for a nonmalignant condition and a patient with cancer. These variables make clinical trial results difficult to interpret. Some craniotomies for ruptured aneurysms must be done on an emergency basis, and meticulous preparation of the skin cannot be ensured. Neurosurgical procedures after trauma occurring outside the hospital should never be included in comparative trials and would be considered contaminated surgery. Laminectomies (with or without the use of the operating microscope) are performed by orthopedic surgeons and neurosurgeons. Many studies include laminectomies and elective craniotomies in trials of clean neurosurgical procedures. The microscope introduces an additional source of potential contamination that should be considered. Laminectomies are addressed in this section and the orthopedic section.

Ventricular fluid-shunting procedures (ventriculo-peritoneal shunts), performed to control increased intracranial pressure in patients with hydrocephalus, have also been included in some clinical trials of clean neurosurgical procedures. Because this procedure involves the placement of a foreign body (pressure-release valve and tubing) in the cranium, another variable is introduced. Most infectious disease consultants believe that such shunting operations should be studied as a separate entity.²⁵⁸ Ventricular fluid-shunting procedures are also performed after serious head trauma and in some elective craniotomy procedures to drain cerebrospinal fluid (CSF) and lower intracranial pressure. The drains are left in place for varying lengths of time, ranging from 48 hours to seven days.

Postoperative central nervous system (CNS) shunt infections are associated with serious morbidity and mortality. The rate of infection is generally reported as 5% to 20%.^{259–261} Infections after surgery include meningitis, ventriculitis (most common infection), and, less frequently, wound infection.²⁵⁸ In most cases, antimicrobial therapy without shunt removal is not effective in eradicating the infecting organism.^{262–267} Therefore, shunt removal or replacement, in addition to intravenous antimicrobial therapy, is common practice.

Organisms. Data from most published clinical trials indicate that wound infections are primarily associated with gram-positive bacteria. *S. aureus* and coagulase-negative

staphylococci are responsible for more than 85% of such infections and are isolated in mixed cultures with other gram-positive bacteria in an additional 5% to 10% of cases. Gram-negative bacteria are isolated as the sole cause of postoperative neurosurgical wound infections in only 5% to 8% of cases.^{268–273} Therefore, most clinical trials of antimicrobial prophylaxis use a drug with primary activity against staphylococci: clindamycin, erythromycin, penicillinase-stable penicillins (oxacillin, nafcillin, and methicillin), first-generation cephalosporins, and vancomycin.

Staphylococci account for 75% to 80% of CNS and wound infections after shunting procedures. Gram-negative bacteria are responsible for only 10% to 20% of such infections.^{261,274–281}

Efficacy for Clean Neurosurgical Procedures. Although the efficacy of antimicrobials in lowering postoperative wound infection rates after elective craniotomy and laminectomy has not been demonstrated in a pivotal clinical trial, a single dose of an antimicrobial effective against *S. aureus* can be recommended. The strongest evidence supporting prophylaxis is a meta-analysis of eight prospective, randomized, placebo-controlled trials in craniotomy patients.²⁸² The following data also support prophylaxis.

Studies, mostly published before 1980, of prophylactic antimicrobials in clean neurosurgery cases were uncontrolled, nonrandomized, and retrospective.^{268,269,283–287} These studies seemed to favor some type of prophylactic regimen. In 1980, an excellent review of most of these studies concluded that a final recommendation regarding antimicrobial prophylaxis in clean neurosurgical procedures must await the results of controlled clinical trials.²⁸⁸ A randomized, non-blinded, clinical trial involving 402 cases (including craniotomy and spinal operations) demonstrated the superiority of antimicrobial prophylaxis (vancomycin and gentamicin with a streptomycin irrigation during the surgical procedure) in preventing infections compared with controls.²⁷¹

Prospective studies involving large numbers of patients have also demonstrated lower neurosurgical postoperative infection rates when antimicrobial prophylaxis is used.^{270,289–291} One such study in craniotomy, spinal surgery, and shunting procedures was stopped early because of an excessive number of wound infections in the placebo group.²⁷³

Choice. In a blinded study, 826 patients undergoing clean neurological procedures were randomly assigned to receive either a single dose of ceftizoxime 2 g (as the sodium) or a combination of a single dose of vancomycin 1 g (as the hydrochloride) and gentamicin 80 mg (as the sulfate).²⁹² Patients undergoing cranial, spinal, or transphenoidal neurosurgical procedures who were not undergoing placement of a shunt or another foreign body were included. The rate of primary and secondary wound infections was not different between the treatment groups. Ceftizoxime was better tolerated than the vancomycin-gentamicin combination. CSF and blood samples were obtained from 19 craniotomy patients. Ceftizoxime and gentamicin were detectable in all samples. Vancomycin was detectable in the serum in all cases but was undetectable in some CSF samples. The researchers concluded that ceftizoxime is as effective as the combination of gentamicin and vancomycin but is less toxic and has better CSF penetration.

A meta-analysis also did not demonstrate a significant difference between antimicrobial regimens.²⁸²

Duration. A meta-analysis did not demonstrate a significant difference between single-dose and multi-dose regimens for clean neurosurgical procedures.²⁸²

Pediatric Efficacy for Clean Neurosurgical Procedures.

A randomized, placebo-controlled, double-blind trial that included pediatric patients undergoing clean neurosurgical procedures was stopped prematurely because of an excessive number of wound infections in the placebo group.²⁷³ The overall rate of infection was 2.8% in the antimicrobial group and 11.7% in the placebo group.

Efficacy for CSF-Shunting Procedures. Because CNS infections after shunting procedures are responsible for substantial mortality and morbidity, especially in children, the possible role of prophylactic antimicrobials in such procedures has been the subject of numerous small, but well-conducted, randomized, controlled trials.²⁹³⁻³⁰⁰ Meticulous surgical and aseptic technique and short operation time were determined to be important factors in lowering infection rates after shunt placement. Although the number of patients studied in each trial was small, two meta-analyses of the data demonstrated that the use of antimicrobial prophylaxis in CSF-shunting procedures reduces the risk of infection by approximately 50%.^{301,302}

Choice. Because no antimicrobial has been demonstrated to have greater efficacy over the others for CSF-shunting procedures, a single dose of cefazolin appears to be the best choice.

Duration. In most studies, prophylaxis was continued for 24 to 48 hours postoperatively, but regimens of different durations were not compared for efficacy. There is a lack of data evaluating the continuation of extraventricular drains with and without antimicrobial prophylaxis.

Pediatric Efficacy for CSF-Shunting Procedures. A retrospective pediatric study of 1201 CSF-shunting procedures failed to demonstrate a significant difference in infection rates between patients who received antimicrobials (2.1%) and those who did not receive antimicrobials (5.6%). Two randomized, prospective studies that included pediatric patients did not demonstrate a significant difference in infection rates between the control group and the groups that received cefotiam³⁰⁰ or methicillin.²⁹⁷ A randomized, double-blind, placebo-controlled study that included pediatric patients undergoing ventriculoperitoneal shunt surgeries failed to demonstrate that the use of perioperative sulfamethoxazole-trimethoprim reduced the frequency of shunt infection.²⁹³

Other studies have demonstrated efficacy for prophylactic antimicrobials.^{295,303} A single-center, randomized, double blind, placebo-controlled trial of perioperative rifampin plus trimethoprim was performed in pediatric patients.³⁰³ Among patients receiving rifampin plus trimethoprim, the infection rate was 12%, compared with 19% in patients receiving placebo. The study was ended (because of the high infection rates) before significance could be achieved. Infection rates at the study institution had been 7.5% in the years before the study. An open randomized study institution that included pediatric patients demonstrated a lower infection rate in a group receiving oxacillin (3.3%) than in a control group (20%).²⁹⁵

Recommendation. A single dose of cefazolin 1 g (as the sodium) intravenously at induction of anesthesia is recommended for patients undergoing clean neurosurgical procedures or CSF-shunting procedures. Alternatively, a single

intravenous dose of one of the β -lactamase-stable penicillins might be used (oxacillin 1 g [as the sodium] or nafcillin 1 g [as the sodium]). Vancomycin 1 g (as the hydrochloride) intravenously over one hour should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.²¹ (Strength of evidence for prophylaxis for clean neurosurgical procedures = A.) (Strength of evidence for prophylaxis for CSF-shunting procedures = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing clean neurosurgical procedures or CSF-shunting procedures is a single dose of cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia. Vancomycin 15 mg/kg (as the hydrochloride) intravenously should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.^{21,32}

Cesarean Delivery

Background. Approximately 1 million infants are born by cesarean delivery in the United States annually.³⁰⁴ The rate of cesarean delivery has risen from 5% to 25% over the past two decades.³⁰⁵ Postpartum infectious complications are common after cesarean delivery. Endometritis (infection of the uterine lining) is usually identified by uterine tenderness and sometimes abnormal or foul-smelling lochia. Wound infection is usually defined as the presence of pus at the incision site. Although febrile morbidity, or temperature elevation in an asymptomatic patient, is often considered in evaluations of antimicrobial prophylaxis, it appears that this temperature elevation is often not associated with an identifiable infectious source or with symptoms specific for infection. It may occur in women with normal physical examination results and sometimes disappears without treatment. In controlled trials, increased temperature occurred with equal frequency in placebo and treatment groups.^{306,307} Moreover, women with febrile morbidity appear not to be those who later develop clinical infection. The presence or absence of febrile morbidity is not an appropriate indication of the efficacy of antimicrobial prophylaxis and therefore will not be considered in these guidelines.

Endometritis has been reported to occur in up to 85% of patients in high-risk populations.³⁰⁸ High-risk patients are defined as women who have not received prenatal care; who are poorly nourished; who have prolonged labor, especially in the presence of ruptured membranes; or who have undergone multiple vaginal examinations or frequent invasive monitoring. A majority of these women are of lower socioeconomic status. In contrast, women in upper or middle socioeconomic populations, who tend to be better nourished and to have received appropriate prenatal care, are at lower risk; the postpartum rate of endometritis in these patients ranges from 5% to 15%.

The factor most frequently associated with infectious morbidity in postcesarean delivery is prolonged labor in the presence of ruptured membranes. Intact chorioamniotic membranes serve as a protective barrier against bacterial infection. Rupture of the membrane exposes the uterine surface to bacteria from the birth canal. The vaginal fluid with its bacterial flora is drawn up into the uterus when it relaxes between contractions during labor. Women undergoing labor for six to eight hours or longer in the presence of ruptured membranes should be considered at high risk for developing endometritis.³⁰⁶ Other risk factors include systemic illness, poor hygiene, obesity, and anemia.

Organisms. The natural microflora of the vaginal tract are often involved in endometritis and include various aerobic and anaerobic streptococci, enterococci, staphylococci, enteric gram-negative bacilli, and anaerobic gram-negative bacteria such as *Bacteroides bivius*, *B. fragilis*, and *Fusobacterium* species.³⁰⁶ In contrast, the organisms causing wound infections after delivery most often are *S. aureus* and other staphylococci, streptococci, and Enterobacteriaceae. Anaerobes are also present but less commonly than with endometritis.³⁰⁹

Efficacy. Most investigations of the efficacy of prophylactic antimicrobials in cesarean delivery have been conducted in high-risk patients. There has been considerable controversy about the necessity for prophylaxis in low-risk women undergoing cesarean delivery.

Despite multiple clinical trials assessing the efficacy of broad-spectrum antimicrobials or multiple doses of antimicrobials for prophylaxis in cesarean delivery, the data support the use of narrow-spectrum agents, such as first-generation cephalosporins, administered as a single dose intravenously immediately after clamping of the umbilical cord.^{310,311}

Low-risk patients. Two early investigations showed significantly lower rates of postcesarean endometritis in low-risk patients with the use of prophylactic antimicrobials.^{312,313} Some authorities have dismissed these benefits, arguing that limited morbidity, theoretical risks, and excessive costs do not justify prophylaxis in these patients.³¹⁴

A randomized, prospective study compared the use of a 1-g dose of cefazolin (as the sodium) with no prophylaxis in 307 low-risk patients undergoing cesarean delivery.³¹⁵ The outcomes investigated were endometritis, wound infection, febrile morbidity, and use of antimicrobials for presumed or confirmed infection. The study showed significantly lower febrile morbidity and therapeutic antimicrobial use in the treatment group, although the sample was not large enough to enable a significant reduction in endometritis and wound infection to be detected.

A large-scale prospective study in more than 1800 low-risk women who underwent cesarean delivery was conducted from 1980 to 1982.³¹⁶ Although prophylaxis was uncontrolled for, endometritis and wound infection rates were significantly lower (0.7% and 0.2%, respectively in the group receiving prophylaxis than the group not receiving prophylaxis (2.1% and 2%, respectively). A case-control study, including the prospective data and women at high risk, determined that patients undergoing a first-time cesarean delivery were five times more likely to develop endometritis than those who had had a cesarean delivery in the past. On the basis of certain assumptions, the investigators calculated that more than \$9 million could be saved annually by administering prophylaxis to low-risk patients. The cost of adverse effects was considered negligible. Thus, antimicrobial prophylaxis may be appropriate for low-risk cesarean deliveries.

However, ACOG considers the use of prophylaxis to be controversial in low-risk patients.³³ ACOG does not routinely recommend prophylaxis in low-risk patients because of concerns about adverse effects, development of resistant organisms, and relaxation of standard infection-control measures and proper operative technique.

High-risk patients. There have been more than 40 placebo-controlled, prospective trials evaluating the efficacy of prophylactic antimicrobials in cesarean delivery, most of which have been carried out in high-risk populations. A

meta-analysis of these data, which combined high- and low-risk patients undergoing both emergency and elective cesarean deliveries, suggests that the rate of serious infections and endometritis is 75% lower and the rate of wound infections 65% lower among antimicrobial-treated patients than control patients.³¹⁷

Choice. Although more than 20 different drugs have been used alone or in combination for antimicrobial prophylaxis during cesarean delivery, most obstetricians currently use either a penicillin or a cephalosporin.³¹⁸ ACOG recommends a first-generation cephalosporin, with extended-spectrum agents reserved for treatment rather than prophylaxis.³³

In a large-scale study involving more than 1600 high-risk patients, several single-dose regimens, including cefazolin 2 g (as the sodium) or piperacillin 4 g (as the sodium), were comparably effective.³¹⁹ This provides two disparate choices, with drugs that offer differing spectra of activity with roughly equivalent efficacy. Two large-scale, randomized, double-blind trials offer a potential solution to this dilemma.^{320,321} Both studies involved hundreds of high-risk patients and compared cefazolin, which has poor *Bacteroides* coverage, with cefoxitin or moxalactam, which has excellent *Bacteroids* coverage. In both studies, cefoxitin and moxalactam were slightly less effective than cefazolin in preventing endometritis, although the differences did not reach significance.

In another study of nearly 350 high-risk women undergoing cesarean delivery, a two-dose regimen of cefoxitin or piperacillin was given starting immediately after the cord was clamped.³²² Despite its superior in vitro activity against enterococci, *P. aeruginosa*, and several enteric gram-negative bacillary species, piperacillin was found to be no more effective than cefoxitin.

Timing. Unlike other surgical procedures for which antimicrobials are ideally administered just before incision, administration of antimicrobials in cesarean delivery is usually delayed until after cord clamping. This is done principally to avoid suppression of the infant's normal bacterial flora. Although toxicity in the infant is of potential concern, a majority of drugs used for this procedure (primarily β -lactams) have a documented record of safety in the treatment of infections during pregnancy, and many are used in the treatment of neonatal sepsis. ACOG and the American Academy of Pediatrics recommend administration of prophylactic antimicrobials after cord clamping.^{33,34}

The issue of timing was addressed in three controlled trials. A large, randomized trial in 642 women undergoing cesarean delivery⁴⁹ and a smaller randomized, placebo-controlled study⁴⁸ demonstrated no difference in infectious complications, regardless of whether the antimicrobials were given preoperatively or after the cord was clamped. In the larger study, infants who were not exposed to antimicrobial agents in utero required significantly fewer evaluations for neonatal sepsis. A third case-control study demonstrated that a second- or third-generation cephalosporin given before incision was superior to cefazolin given as three 1-g doses starting immediately after cord clamping.³²³ Thus, antimicrobials provide effective prophylaxis, even when given after clamping of the umbilical cord.⁴⁹

Duration. Most recent trials of antimicrobial prophylaxis for cesarean delivery have assessed the efficacy of a single dose versus multiple doses (usually up to 24 hours). Early studies used regimens that lasted as long as five or six days. Two prospective, randomized studies found that a five-day course of a cephalosporin was no more efficacious than a 24-hour

course.^{324,325} A third study, by contrast, found that a three-day course of ampicillin was significantly more effective than three doses of ampicillin.³²⁶ The explanation for this difference is unclear. The efficacy of several types of β -lactam antimicrobials given in various regimens to nearly 1600 patients was assessed in an open, randomized, comparative study.³¹⁹ One group of patients was given three doses of cefazolin, and the two other groups received a single dose of cefazolin, either 1 or 2 g (as the sodium). One dose of cefazolin 2 g was superior to three doses of cefazolin 1 g. One dose of cefazolin 1 g was no different than three doses of cefazolin 1 g. It does not seem necessary to extend prophylaxis beyond a single dose. These data also suggest that cefazolin 2 g is more efficacious than cefazolin 1 g.

Pediatric Efficacy. No well-controlled studies have evaluated the effect of antimicrobial prophylaxis for low- or high-risk adolescents undergoing cesarean delivery.

Recommendation. The recommended regimen for all women (low and high risk) undergoing cesarean delivery is a single dose of cefazolin 2 g (as the sodium) intravenously immediately after clamping of the umbilical cord. (Strength of evidence for prophylaxis for low-risk women = B.) (Strength of evidence for prophylaxis for high-risk women = A.)

Pediatric Dosage. The recommended regimen for low- and high-risk adolescents undergoing cesarean delivery is a single dose of cefazolin 2 g (as the sodium) intravenously immediately after clamping of the umbilical cord.

Hysterectomy

Background. Hysterectomy is second only to cesarean delivery as the most frequently performed major gynecologic operation in the United States, with approximately 590,000 hysterectomies being performed annually. Although there appears to be a downward trend in the rate since the mid-1980s, it is not yet known whether a true decline has occurred because of recent changes in the National Hospital Discharge Survey sampling method.³²⁷

Uterine fibroid tumors account for 30% of all presurgical diagnoses leading to hysterectomy; other common diagnoses are dysfunctional uterine bleeding, genital prolapse, endometriosis, chronic pelvic pain, pelvic inflammatory disease, endometrial hyperplasia, and cancer.³²⁷ The proportion of patients undergoing concurrent unilateral or bilateral oophorectomy increases with age; this procedure is performed in approximately two thirds of women over the age of 60 years who undergo hysterectomy.³⁰⁹

Hysterectomy may be performed by a transvaginal or transabdominal approach. During a vaginal hysterectomy, the uterus and, occasionally, one or two fallopian tubes, the ovaries, or a combination of ovaries and fallopian tubes are removed through the vagina. No abdominal incision is made. Because the procedure is performed in an organ that is normally colonized with bacteria, it is associated with a high risk of postoperative infection. Abdominal hysterectomy involves removal of the uterus and, in some cases, one or both fallopian tubes, the ovaries, or a combination of ovaries and fallopian tubes. Because bacterial contamination associated with this procedure is minimal, postoperative infection rates in women receiving no antimicrobial prophylaxis have often been lower than those in women undergoing vaginal hysterectomy.^{328–333} Radical hysterectomy, which entails removal of the uterus, fallopian tubes, and ovaries and extensive

stripping of the pelvic lymph nodes, is performed in patients with extension of cervical cancer. Many factors increase the risk of postoperative infection. Nonetheless, because of the low rate of contamination associated with this procedure, the need for prophylaxis has not been established.

Infections after hysterectomy include operative site infections: vaginal cuff infection, pelvic cellulitis, and pelvic abscess. Wound infections are usually diagnosed by the presence of pus or a purulent discharge.³⁰⁷

Risk factors for infection after vaginal or abdominal hysterectomy include longer duration of surgery, young age, diabetes, obesity, peripheral vascular disease, collagen disease, anemia, poor nutritional status, and previous history of postsurgical infection.^{309,328,334,335} The depth of subcutaneous tissue is also a significant risk factor for transabdominal hysterectomy.³³⁶ Factors that increase the risk of postoperative infection in women undergoing radical hysterectomy for cervical cancer include extended length of surgery, blood loss and replacement, presence of malignancy, prior radiation therapy, obesity, and presence of indwelling drainage catheters.^{337,338}

Organisms. The vagina is normally colonized with a wide variety of bacteria, including gram-positive and gram-negative aerobes and anaerobes. The normal flora of the vagina include staphylococci, streptococci, enterococci, lactobacilli, diphtheroids, *E. coli*, anaerobic streptococci, *Bacteroides* species, and *Fusobacterium* species.^{307,339} Postoperative vaginal flora differ from preoperative flora; enterococci, gram-negative bacilli, and *Bacteroides* species increase postoperatively. Postoperative changes in flora may occur independently of prophylactic antimicrobial administration and are not by themselves predictive of postoperative infection.^{307,340,341} Postoperative infections associated with vaginal hysterectomy are frequently polymicrobial; enterococci, aerobic gram-negative bacilli, and *Bacteroides* species are isolated most frequently. Postoperative wound infections after abdominal and radical hysterectomy are also polymicrobial; gram-positive cocci and enteric gram-negative bacilli predominate, and anaerobes are also frequently isolated.^{341,342}

Efficacy for Vaginal Hysterectomy. The rate of postoperative infection (wound and pelvic sites) in women administered placebo or no prophylactic antimicrobials ranges from 14% to 57%.^{328–333,335,340,343–354} A number of antimicrobial agents, including clindamycin,³⁵⁵ metronidazole,^{331,354,356,357} penicillins,^{307,345,353,355,357–360} ampicillin,^{345,361,362} tetracycline derivatives,^{333,352,363} streptomycin,³⁴⁵ and first-generation,^{328–330,344,347,351,353,356,358,360,361,364–367} second-generation,^{307,349,350,357–359,363} and third-generation^{355,367} cephalosporins have been studied as perioperative prophylaxis for vaginal hysterectomy. Overall, the use of antimicrobials markedly reduces the frequency of postoperative infection after vaginal hysterectomy to a generally acceptable rate of less than 10%.

Choice. Cephalosporins are the most frequently used antimicrobials for prophylaxis in vaginal hysterectomy. Cefazolin is the drug of choice. Cefazolin has been associated with postoperative infection rates ranging from 0% to 12%.^{346,347,351,368–370} Postoperative infection rates with various second- and third-generation cephalosporins have ranged between 0% and 16%.^{349,350,355,357–359,363,371} Studies directly comparing different cephalosporins have shown no significant differences in rates of infection.^{372–381} Studies directly comparing the first-generation cephalosporins with second- or third-generation cephalosporins indicate that

first-generation cephalosporins (primarily cefazolin) are equivalent to second- and third-generation agents.^{367–370,382}

In light of the organisms encountered in the vaginal canal and comparative studies conducted among different classes of cephalosporins, the expert panel considers cefazolin and cefotetan appropriate first-line choices for prophylaxis during vaginal hysterectomy and cefoxitin a suitable alternative. The ACOG guidelines support the use of a first-, second-, or third-generation cephalosporin for prophylaxis.³⁸³

Duration. The trend in recent years has been toward use of single-dose regimens of antimicrobials, administered immediately before surgery. Studies comparing single doses of one antimicrobial with multidose regimens of a different antimicrobial have shown the two regimens to be equally effective.^{346,356,363,368–371,373–379,384–392} Although there have been few comparative trials involving single-dose cefazolin,^{346,370} clinical experience indicates that this regimen is effective for most women. In addition, the drug's relatively long serum half-life (1.8 hours) suggests that a single dose would be sufficient. The exception is when the procedure lasts three hours or longer or if blood loss exceeds 1500 mL, in which case a second dose is warranted.

Efficacy for Abdominal Hysterectomy. At least 25 placebo-controlled or nonantimicrobial-controlled studies involving abdominal hysterectomy have been performed.^{328–333,342,347,348,351–354,360,393–403} First- and second-generation cephalosporins and metronidazole have been studied more widely than any other agents. A meta-analysis of 25 controlled, randomized trials demonstrated the efficacy of antimicrobial prophylaxis with any of these agents in the prevention of postoperative infections.⁴⁰⁴ The infection rate was 21.1% with placebo or no prophylaxis and 9.0% with any antimicrobial. Cefazolin was significantly more effective than placebo or no prophylaxis, with an infection rate of 11.4%.

Choice. Studies comparing second-generation cephalosporins and comparing second- and third-generation cephalosporin regimens have not shown significant differences in rates of serious infections.^{376,387–392,405–407} Few comparisons have been made between second-generation cephalosporins and cefazolin. Cefazolin has been at least as effective in preventing infectious complications as third-generation cephalosporins.^{369,384,399,408} However, in one double-blind, controlled study, the risk of major operative site infection requiring antimicrobial therapy was significantly higher with cefazolin (11.6%; relative risk, 1.84; 95% confidence interval, 1.03–3.29) than with cefotetan (6.3%).³³⁴ A total of 511 women undergoing abdominal hysterectomy participated in this study and received a single dose of cefazolin 1 g (as the sodium) or cefotetan 1 g (as the disodium).

In light of the organisms involved in infectious complications from abdominal hysterectomy and the lack of superior efficacy demonstrated in comparative trials, the expert panel considers cefazolin or cefotetan an appropriate choice for prophylaxis and cefoxitin a suitable alternative. The ACOG guidelines state that first-, second-, and third-generation cephalosporins can be used for prophylaxis.³⁸³

Duration. A 24-hour antimicrobial regimen has been shown to be as effective as longer courses of prophylaxis for abdominal hysterectomy,^{400,409} and many single-dose prophylaxis regimens have proved as effective as multidose regimens.^{369,371,376,385,387–392,410} Single doses of cefotetan, ceftizoxime, or cefotaxime appear to be as effective as multiple doses of cefoxitin.^{380,387,388,390–392,406}

Efficacy for Radical Hysterectomy. Six small prospective, placebo-controlled trials evaluated the impact of antimicrobial prophylaxis on wound infection rates after radical hysterectomy.^{337,411–414} Rates of infection in the placebo groups ranged from 17% to 87%. In all six trials, the frequency of postoperative infection was lower with antimicrobial prophylaxis. Infection rates in antimicrobial-treated patients ranged from 0% to 64% (but generally from 0% to 15%). The antimicrobial agents used were cefoxitin, cefamandole, mezlocillin, and doxycycline. In one study in which cefamandole was given by injection and by intraperitoneal irrigation, postoperative infection rates were less than 4%.⁴¹¹

Choice. There is a lack of data comparing first- and second-generation cephalosporins. The optimal choice for prophylaxis has not been determined, but second-generation cephalosporins have demonstrated efficacy.^{337,411,413} Because similar approaches are used in abdominal and radical hysterectomy and in light of the results of a recent study (described in Efficacy for abdominal hysterectomy),³³⁴ a single dose of cefotetan may be applicable to radical hysterectomy procedures.

Appropriate cephalosporins identified by the expert panel members are cefazolin and cefotetan; an alternative is cefoxitin. The ACOG guidelines state that first-, second-, and third-generation cephalosporins can be used for prophylaxis.³⁸³

Duration. The optimal duration of antimicrobial prophylaxis for radical hysterectomy has not been established. The duration of prophylaxis ranged from one dose⁴¹⁴ to four days.^{337,413} A 24-hour regimen of mezlocillin appears to be as effective as other antimicrobial regimens of longer duration.⁴¹² A prospective, randomized study demonstrated no difference between a single dose of piperacillin plus tinidazole and a multidose (three-dose) regimen of the two drugs.⁴¹⁵

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in adolescents undergoing vaginal, abdominal, or radical hysterectomy.

Recommendation. The recommended regimen for women undergoing vaginal hysterectomy, abdominal hysterectomy, or radical hysterectomy is a single intravenous dose of cefazolin 1 g (as the sodium) or cefotetan 1 g (as the disodium) at induction of anesthesia. An alternative is cefoxitin 1 g (as the sodium) intravenously at induction of anesthesia. (Strength of evidence for prophylaxis for vaginal hysterectomy = A.) (Strength of evidence for prophylaxis for abdominal hysterectomy = A.) (Strength of evidence for prophylaxis for radical hysterectomy = A.)

Pediatric Dosage. The recommended regimen for adolescent women undergoing vaginal hysterectomy, abdominal hysterectomy, or radical hysterectomy is a single dose of cefazolin 1 g (as the sodium) or cefotetan 1 g (as the disodium) intravenously at induction of anesthesia. An alternative is cefoxitin 1 g (as the sodium) intravenously at induction of anesthesia.

Ophthalmic Surgeries

Background. Ophthalmic procedures include cataract extractions, vitrectomies, keratoplasties, implants, glaucoma operations, strabotomies, and retinal detachment repair. Most of the available studies involve cataract procedures.^{416–427}

There is a low rate of postoperative ophthalmic infection (bacterial endophthalmitis),^{417,418,424,428} but this is a devastating complication that may lead to an early loss of light sense and eventual loss of the eye if the infection is not eradicated.^{420,424,425} Possible risk factors for developing postoperative ophthalmic infections include poor surgical technique, “weak ocular tissue” (not defined by the author), and multiple ophthalmic operations.⁴²⁰ The duration of follow-up in studies that determined the postoperative endophthalmitis rate ranged from less than one week to 12 days^{416,421,424,429}; 97% of cases of postoperative endophthalmitis occurred within the first 7 days of the 12-day follow-up period.⁴¹⁶ However, the appropriate duration of follow-up is not established.

Organisms. Approximately 90% of postoperative ophthalmic infections are caused by *S. aureus* or *S. epidermidis*.^{420,425,430} The other organisms identified are *Streptococcus pneumoniae*, *Acinetobacter* species, and *P. aeruginosa*.⁴³⁰ Virulent pathogens such as *P. aeruginosa*, *Bacillus cereus*, and *S. aureus* can cause eye destruction within 24 hours.⁴³¹

Efficacy. Numerous studies have evaluated the effectiveness of prophylactic regimens in eradicating bacteria and reducing bacterial count on the conjunctivas, lower eyelid, eyelashes, and inner canthus (corner of the eye) preoperatively and postoperatively. There is a lack of controlled trials in the literature. The following studies had many flaws, including retrospective or uncontrolled design, inadequate follow-up, lack of confirmation of infection with cultures, difficulties in distinguishing between bacterial endophthalmitis and aseptic postoperative inflammation, inadequate aseptic surgical techniques, and inadequate preoperative and postoperative care.

Studies have shown that topical antimicrobials reduce ocular flora.^{419,421,422,425,427} The studies evaluating bacteria eradication do not provide definitive antimicrobial choices, dosages, or duration of treatment because elimination of ophthalmic flora does not equate with a lower rate of infections. Although up to 95% of eye cultures are positive, few develop into infections.^{420–422,425} Ciprofloxacin, norfloxacin, and ofloxacin have demonstrated antibacterial activity against organisms (staphylococcal and gram-negative organisms, in particular *Pseudomonas* species) that cause postoperative endophthalmitis,^{432–435} but they cannot be recommended because of a lack of trials using fluoroquinolones prophylactically.

Choice. There have been no controlled efficacy studies supporting a particular choice of antimicrobial prophylaxis for ophthalmic surgeries. Because of the very low rate of infections (0.05% to 0.82%),^{416–418,424,428,436} an enormous patient population would be required to allow determination of the most effective antimicrobial. The most efficacious antimicrobial cannot be determined from the available data because of study flaws.

A series of 16,000 cataract-extraction procedures demonstrated an infection rate of 0.6% (6 infections per 1,000 cases) with the use of an ointment containing neomycin 0.5% (as the sulfate), polymyxin B 0.1% (as the sulfate), and erythromycin 0.5% compared with 0.02% (3 infections per 15,000 cases) with the use of an ointment containing chloramphenicol 0.4%, polymyxin B 0.1% (as the sulfate), and erythromycin 0.5%.⁴¹⁷ Although these infection rates appear to favor chloramphenicol over neomycin, the superiority of chloramphenicol cannot be concluded because of limitations in the study design.

An open-label, nonrandomized, parallel trial demonstrated a lower rate of culture-proven endophthalmitis (0.06%) in a suite of operating rooms that used povidone-iodine preparation than in a similar suite that used topical silver protein solution (0.24%).⁴³⁶ The intraocular procedures included vitrectomy, extracapsular cataract extraction, phacoemulsifications, secondary intraocular lens procedure, trabeculectomy, and penetrating keratoplasty. Recommendations cannot be made for the use of povidone-iodine as a single agent because of limitations of the study design (open-label, nonrandomized, without placebo control) and the surgeon’s continued use of “customary” prophylactic antimicrobials (not identified) before, during, and after the procedure.

Prophylactic antimicrobials were administered during alternating cases in a series of 974 patients undergoing cataract extraction, glaucoma operations, corneal transplant, and pupillary membrane needling.⁴²⁴ The prophylactic antimicrobial regimen was a subconjunctival combination of penicillin G 100,000 units and 3.3% streptomycin. There were seven postoperative infections (1.4%) among patients who had not received antimicrobials, compared with one infection (0.2%) among patients who received subconjunctival antimicrobials. In a follow-up series in which antimicrobials were used routinely in 1480 consecutive cases, the rate of infection was 0.14%. Organisms causing the postoperative infections in patients who received prophylactic antimicrobials were penicillin- and streptomycin-resistant *Proteus vulgaris* and *P. aeruginosa* and penicillin-sensitive *S. aureus* in a penicillin-allergic patient who received subconjunctival streptomycin only.

Route. The most often studied routes of administration are preoperative topical application and perioperative subconjunctival injection. Human data directly comparing administration routes have not been reported. Animal data demonstrated that topical application was highly effective in eliminating *Staphylococcus* and *Pseudomonas* species from the cornea but that antimicrobials administered periocularly or by intravenous injection did not significantly reduce the number of *Staphylococcus* or *Pseudomonas* organisms in the cornea.⁴³⁷ Local reactions during the early postoperative period have been reported more frequently in eyes receiving subconjunctival antimicrobials than those in which no antimicrobials were used. These reactions, consisting of conjunctival hyperemia and chemosis (chemical action transmitted through a membrane) at the site of injection, usually subsided within two to four days. No systemic or serious local effects from the injections were reported.⁴²⁴ Subconjunctival injections have been administered perioperatively or postoperatively because of the practicality of administering ophthalmic injections in a sedated and anesthetized patient. The ideal circumstance would be subconjunctival administration preoperatively once anesthesia is induced.

A concurrent series of 6618 patients undergoing cataract extraction were randomly assigned to receive periocular penicillin G 500,000 units or no periocular injection.⁴²⁹ All patients were administered topical antimicrobials: chloramphenicol 0.5% and sulfamethazine 10% 15 to 20 hours before surgery, an unidentified ophthalmic antimicrobial ointment the day before surgery, polymyxin B 5000 units/mL (as the sulfate) and neomycin 2.5 mg/mL (as the sulfate) at the end of the procedure, an unidentified ophthalmic antimicrobial ointment the first day postoperatively, and sulfamethazine 5% solution for approximately another six days postoperatively starting the second postoperative day. The infection

rate was 0.15% with the combination of topical antimicrobials and periocular penicillin, compared with 0.45% with only topical antimicrobials. Other routes, including intraocular antimicrobials and antimicrobial-soaked collagen shields,⁴³⁸ are not widely accepted at this time because of the lack of safety and efficacy data. Topical only is the most common route of administration because of ease of administration, lack of complications, high efficacy in eliminating bacterial flora, and low cost.

Duration and timing. The available data do not specifically address duration and timing of antimicrobial administration. In studies to determine infection rates, the duration of preoperative antimicrobials ranged from one to five days. Postoperative topical antimicrobial regimens ranged from no postoperative antimicrobials to administration of antimicrobials until the time of patient discharge (approximately seven days).^{416,424,429} The following data may provide some guidance. A series of 2508 cataract extraction procedures demonstrated that penicillin ophthalmic ointment had to be applied every two to three hours for three to eight days to eliminate pathogenic staphylococci from the conjunctiva and the eyelids.⁴²⁵ Two consecutive patient groups undergoing open lacrimal surgery were retrospectively reviewed.⁴³⁹ Both groups received topical antimicrobial drops (not further defined). The infection rate was 1.6% (2 of 128 patients) in the group that received postoperative antimicrobials and 7.9% (12 of 152 patients) in the group that did not receive postoperative antimicrobials. The study was not designed to determine the best postoperative antimicrobial, but, in a majority of cases, cephalexin 250 mg orally four times daily for five days was used. Although this study demonstrated a five-fold lower rate of infection with postoperative antimicrobials, recommendations for postoperative antimicrobial prophylaxis cannot be made until controlled studies are performed. Duration and timing cannot be extrapolated from general surgery (non-ophthalmic) data because of the lack of data on antimicrobial pharmacokinetics in the eye (e.g., duration, distribution, and elimination from the aqueous humor). Recommendations on timing and duration are based solely on expert opinion.

Despite the lack of well-controlled trials, the consequences of bacterial endophthalmitis support the use of prophylactic antimicrobials. No definitive studies have delineated superiority of antimicrobial route, timing, or duration. The suggested antimicrobials are relatively similar in cost.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing ophthalmic surgery.

Recommendation. The prophylactic antimicrobials used in ophthalmic procedures should provide coverage against *Staphylococcus* species and gram-negative organisms, in particular *Pseudomonas* species. The necessity of continuing topical antimicrobials postoperatively has not been established. The frequency of administration is based on usual treatment regimens.

Antimicrobials that are appropriate include commercially available neomycin–polymyxin B–gramicidin solution one or two drops topically and tobramycin 0.3% or gentamicin 0.3% solution two drops topically before the procedure. Continuation of antimicrobials postoperatively is not supported by data. Addition of a subconjunctival antimicrobial, tobramycin 20 mg (as the sulfate), is optional. (Strength of evidence for prophylaxis = C.)

Pediatric Dosage. The recommendations for the use of topical antimicrobials in pediatric patients undergoing ophthalmic procedures are the same as for adults. Subconjunctival tobramycin cannot be recommended because there is a lack of pediatric data and dosages cannot be extrapolated from the insufficient adult data.

Orthopedics

Background. Antimicrobial prophylaxis will be discussed for total joint-replacement surgery, repair of hip fractures, implantation of internal fixation devices (screws, nails, plates, and pins), and clean orthopedic procedures (not involving replacement or implantations). Open (compound) fractures are often associated with extensive wound contamination and are virtually always managed with empirical antimicrobial therapy and surgical debridement. This practice is viewed as treatment rather than prophylaxis.⁴⁴⁰ Although antimicrobials are given to patients with prosthetic joints who undergo dental procedures to reduce the likelihood of prosthesis infection,⁴⁴¹ this practice has not been sufficiently studied and is beyond the scope of these guidelines.

Postoperative wound infection is one of the more frequent complications of orthopedic surgery, and it often has devastating results,⁴⁴² frequently requiring removal of the implanted hardware and a prolonged course of antimicrobials for cure. Although early studies did not support the routine use of prophylactic antimicrobials,^{443,444} these studies were flawed by an improper choice of agent(s), inappropriate dosage or route of administration, or failure to institute therapy until well beyond the time of the initial surgical incision. Later work has established that antimicrobial prophylaxis is indicated in some types of orthopedic procedures.^{442,445–452}

Organisms. Organisms that make up the skin flora are the most frequent causes of postoperative infections in orthopedic surgery. The pathogens involved in total joint replacement are *S. epidermidis* (40% of infected patients), *S. aureus* (35%), gram-negative bacilli (15%), anaerobes (5%), and others (5%).²⁴

Clean Orthopedic Procedures Not Involving Implantation of Foreign Materials

Background. The need for antimicrobial prophylaxis in clean orthopedic procedures is not well established.^{452,453} Included in this category are knee, hand, and foot surgeries and laminectomy with and without fusion. These procedures do not normally involve the implantation of foreign materials. The evaluated data do not include arthroscopy procedures and do not identify specific procedures, like carpal tunnel release; however, arthroscopy and other procedures not involving implantation are similar enough to be included with clean orthopedic procedures not involving implantation. The risks of wound infection and long-term sequelae are quite low for procedures not involving implantation. The duration of procedures may be a risk factor, with longer procedures having higher infection rates; the difference was significant in one study⁴⁵³ but not in another.⁴⁵² Neither study formally evaluated procedures performed on the feet of patients with diabetes. Diabetic patients are at a higher risk for infection, and their infections are typically polymicrobial;

therefore, recommendations for procedures performed on the feet of patients with diabetes cannot be extrapolated from the following efficacy data.

Efficacy. The most extensive investigation of the efficacy of antimicrobial prophylaxis in clean orthopedic procedures was performed in the early 1970s.⁴⁵² In a randomized, double-blind, prospective study, the efficacy of cephaloridine was compared with that of placebo in reducing postoperative wound infection in more than 1500 patients undergoing clean orthopedic procedures (internal fixation device involvement was not identified). Infection rates for the two groups differed significantly: 5% with placebo and 2.8% with perioperative cephaloridine. Drug fever (loosely defined as fever occurring on the day the study drug was administered) was noted in 34 antimicrobial-treated patients and 14 placebo recipients.

Given the small difference in infection rates between groups and the lack of serious long-term sequelae from postoperative infections associated with these procedures, many authorities have questioned the need for antimicrobial prophylaxis. Attempts to correlate infection rate with the type of clean orthopedic procedure or with certain patient characteristics (e.g., age, disease) have been unsuccessful. Although one study demonstrated that prophylaxis with cefamandole was more effective than placebo when procedures were longer than two hours, prophylaxis was not more effective than placebo in procedures shorter than two hours.⁴⁵³ These results were not consistent with those of the previously discussed study,⁴⁵² whose series was much larger and failed to demonstrate a difference in infection rates with procedures lasting longer than two hours.

The low rate of infection, coupled with the absence of serious morbidity as a consequence of postoperative infection, does not justify the expense or potential for toxicity and resistance associated with routine use of antimicrobial prophylaxis in this setting.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing clean orthopedic procedures.

Recommendation. Antimicrobial prophylaxis is not recommended for patients undergoing clean orthopedic procedures not involving implantation of foreign materials. (Strength of evidence against prophylaxis = C.)

Pediatric Dosage. Antimicrobial prophylaxis is not recommended for pediatric patients undergoing clean orthopedic procedures not involving implantation of foreign materials.

Hip Fracture Repair and Other Orthopedic Procedures Involving the Implantation of Internal Fixation Devices

Background. Data support the use of antimicrobial prophylaxis for hip fracture repairs. In contrast, there is a lack of data to support the use of prophylaxis for procedures other than hip fracture repairs that involve the implantation of internal fixation devices (e.g., high tibial osteotomy and ligament reconstruction). When internal fixation procedures involve the implantation of foreign bodies such as nails, screws, plates, and wires, postoperative infection can produce extensive morbidity—prolonged and repeated hospitalization, sepsis, persistent pain, and device replacement^{442,454}—and possible

death. No cost analysis is available to support the use of prophylaxis for any orthopedic procedure; however, the assumed costs for the associated morbidity may be adequate to justify prophylaxis. Consequently, antimicrobial prophylaxis is frequently used, even though the infection rate is low. For example, the frequency of infection after hip fracture repair with or without prophylaxis is generally less than 5%.^{442,450}

Efficacy. Hip fracture repair. The efficacy of antimicrobial prophylaxis in hip fracture repair was studied in three double-blind, randomized, placebo-controlled trials.^{442,450,455} One study demonstrated a significant difference in postoperative wound infections after hip fracture repair in patients receiving placebo (4.8%, or 7 of 145 patients) and patients given nafcillin 0.5 g (as the sodium) intramuscularly every six hours for two days (0.8%, or 1 of 135 patients).⁴⁴² Some prostheses were used, but a majority of patients had pin or plate implantation. The duration of follow-up was one year. There was no difference in the frequency of infected wound hematomas between the two groups.

In another study involving 307 patients with hip fractures, a significant difference was demonstrated for major postoperative wound infection rates: 4.7% in the placebo group compared with 0.7% in patients given preoperative cephalothin 1 g (as the sodium) intravenously and every 4 hours thereafter for 72 hours.⁴⁵⁰ The duration of follow-up was not identified. Patients who received cephalothin for prophylaxis tended to be colonized with cephalothin-resistant organisms (in urine, sputum, and blood).

Despite having a small sample size (127 patients) and an unusually high rate of wound infection in the control group, one study showed prophylaxis to be beneficial in preventing postoperative wound infection compared with no prophylaxis.⁴⁵¹ In contrast to the previously described studies, a randomized, double-blind, single-hospital study involving 352 patients undergoing hip fracture fixation failed to show a significant difference between four doses of cefazolin, one dose of cefazolin, and placebo.⁴⁵⁵ These regimens did not differ in efficacy even when both treatment groups were combined and compared with the placebo group. Although hip fracture repairs are associated with low infection rates, results from these three studies^{442,450,451} and the morbidity and costs associated with infectious complications in hip fracture repair support the use of short-term prophylactic antimicrobials. The long-term benefits of prophylaxis have not been determined.

Procedures other than hip surgery involving implantation of internal fixation devices. The evidence supporting antimicrobial prophylaxis for the implantation of internal fixation devices is not as strong for nonhip surgeries as for hip replacement or repair. In a randomized, double-blind study of 122 patients undergoing open reduction and internal fixation of closed ankle fractures, no difference was demonstrated between cephalothin 1 g (as the sodium) intravenously every six hours for a total of four doses and placebo.⁴⁵⁶ However, the sample was too small. Despite the lack of studies evaluating prophylaxis for procedures involving the implantation of internal fixation devices, consideration of antimicrobial use is warranted, especially in complicated procedures, because of the associated morbidity and assumed costs of infections involving implanted devices.

Choice. Studies comparing antimicrobials are lacking. The antimicrobials that have been studied most often for prophylaxis in orthopedic surgery are first-generation

cephalosporins. First-generation cephalosporins (particularly cefazolin) are the most suitable agents for orthopedic prophylaxis because their spectrum of activity includes *Staphylococcus* species and gram-negative bacilli (such as *E. coli*), they have desirable pharmacokinetic characteristics (adequate bone penetration),⁴⁵⁷ and they are easy to administer, low in cost, and safe. Second- and third-generation cephalosporins offer no major advantages over first-generation agents. Second- and third-generation cephalosporins are more expensive; furthermore, indiscriminate use is likely to promote resistance, particularly among nosocomial gram-negative bacilli. Therefore, the use of a second- or third-generation cephalosporin as orthopedic surgical prophylaxis should be avoided. The increasing prevalence of MRSA warrants discriminate use of alternative antimicrobials. No studies have evaluated vancomycin as a prophylactic agent in orthopedic procedures. However, vancomycin has adequate activity against the most common pathogens involved and would be an acceptable alternative under certain circumstances.²¹ Only patients with a serious β -lactam allergy or patients in institutions with a high rate of infection due to MRSA or MRSE should be administered vancomycin.

Duration. One study evaluated the duration of therapy in patients undergoing orthopedic surgery. A double-blind, randomized study compared one day of cefuroxime alone with one day of cefuroxime followed by oral cephalexin for a total of six days in 121 evaluable patients undergoing implantation surgery for intertrochanteric hip fracture repair.⁴⁵⁸ This study, combined with the total joint-replacement studies, supports a duration of 24 hours or less.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing hip fracture repair or implantation of internal fixation devices.

Recommendation. Despite the lack of substantial data, the use of antimicrobial prophylaxis in hip fracture repair and in other orthopedic procedures involving the implantation of internal fixation devices may be substantiated by the morbidity (possible removal of an infected internal fixation device) and costs associated with infectious events. The recommended regimen is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia and continued every 8 hours for 24 hours. Vancomycin 1 g (as the hydrochloride) intravenously over one hour should be reserved as an alternative agent on the basis of previously outlined guidelines from HICPAC.²¹ (Strength of evidence for prophylaxis for hip fracture repair = A.) (Strength of evidence for prophylaxis for implantation procedures = C.)

Pediatric Dosage. Despite the lack of substantial data, the use of antimicrobial prophylaxis in hip fracture repair and in other orthopedic procedures involving the implantation of internal fixation devices may be substantiated by the morbidity (possible removal of an infected internal fixation device) and costs associated with infectious events. The recommended regimen for pediatric patients is cefazolin 20–30 mg/kg (as the sodium) intravenously at the induction of anesthesia and every 8 hours for 24 hours. Vancomycin 15 mg/kg (as the hydrochloride) intravenously should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.^{21,32}

Total Joint Replacement

Background. It is estimated that more than 200,000 hip or knee replacements are performed each year in North America.⁴⁵⁹ The frequency of infections complicating hip, knee, elbow, or shoulder replacement is low, ranging from 0.6% to 11%.⁴⁵⁴ With the introduction of antimicrobial prophylaxis and the use of “ultraclean” operating rooms, the infection rate has declined substantially, generally to less than 1%.^{447,448,454} The two main types of infectious complications of total joint arthroplasty are superficial and deep infections of the prosthesis. Infections of the joint prosthesis may occur early (less than one year after the procedure) or late (occurring after the first year). Infection after joint arthroplasty can be disastrous, frequently requiring removal of the prosthesis and a prolonged course of antimicrobials for cure. An analysis of the costs associated with operations in Europe demonstrated that 90% of the total expense was associated with keeping the patient in a hospital bed.⁴⁶⁰ The stay for joint revision was much longer than the stay for primary joint replacement.

A 1992 survey documented low use of antimicrobial-impregnated bone cement and cement beads in the United States (for fewer than one procedure per month); a majority of the antimicrobial-impregnated cement was used in community hospitals.⁴⁶¹ Total hip arthroplasty, total knee arthroplasty, and chronic osteomyelitis were the most common indications for use. A wide variety of antimicrobials are used in these products, a majority of which have not been adequately studied in the clinical setting. Inadequate quality control during mixing and use has been identified. Prophylaxis with antimicrobial-impregnated bone cement and cement beads is not recommended. Readers are referred to a review of this topic for additional information about tissue penetration, clinical application, and safety.⁴⁶²

Efficacy. A majority of studies that have evaluated prophylactic antimicrobials in joint-replacement surgery have been conducted in patients undergoing total hip arthroplasty. There is a lack of data involving elbow and shoulder arthroplasty; however, these procedures are similar enough to justify inclusion with total hip arthroplasty.

A double-blind, randomized, placebo-controlled trial involving 2137 hip replacements in 2097 patients evaluated the efficacy of prophylactic cefazolin.⁴⁴⁷ Cefazolin 1 g (as the sodium) was given before surgery and continued every six hours for a total of five days. After a two-year follow-up period, a significant difference in the rate of “hip infection” was found between the placebo group and the cefazolin group (3.3% and 0.9%, respectively). When these results were further analyzed for the type of operating-room environment, a significant difference was observed only when surgery was carried out in a conventional operating room. Antimicrobial prophylaxis did not significantly reduce infection when hip replacement surgery was performed in a “hypersterile” (laminar airflow) operating room (1.3% with placebo versus 0.8% with cefazolin). This study was well designed in that sufficient numbers of patients were enrolled to reduce the probability of Type I and Type II errors in terms of the efficacy of prophylaxis.

Choice. (Readers are also referred to Procedures other than hip surgery involving implantation of internal fixation devices.) Cefazolin has been compared with cefuroxime⁴⁶³ and cefonicid.⁴⁶⁴ A double-blind multicenter study of 1354 patients undergoing total joint (hip or knee) arthroplasty compared

intravenous cefuroxime 1.5 g (as the sodium) preoperatively followed by 750 mg every eight hours for a total of three doses with intravenous ceftazidime 1 g (as the sodium) preoperatively followed by 1 g every eight hours for a total of nine doses.⁴⁶³ The preoperative doses were administered 50 to 60 minutes before incision. Follow-up assessments were performed at two to three months and one year after the procedure. An intention-to-treat analysis demonstrated no significant difference in the wound infection rate between cefuroxime (3%) and ceftazidime (3%). All three late wound infections (identified at one-year follow-up) developed in the ceftazidime group. The second trial was a double-blind, randomized, controlled trial that compared three doses of ceftazidime with three doses of cefonicid in 102 patients undergoing joint replacement or insertion of a metallic device for fixation.⁴⁶⁴ The median duration of follow-up was 106 to 109 days. There were six postoperative infections among 52 patients in the ceftazidime group and no infections among the 50 patients in the cefonicid group. This difference was significant. However, three of the six infections in the ceftazidime group were urinary tract infections.

Antimicrobials incorporated in bone cement is a viable method for prophylaxis. However, there are limited clinical data on the use of this method. One prospective, randomized clinical trial performed in two centers involved 401 patients undergoing total joint arthroplasty. Intravenous cefuroxime was compared with cefuroxime in bone cement.⁴⁶⁵ All patients were followed for two years. The overall rate of deep infection (infection extending to the deep fascia, with persistent wound discharge or joint pain, positive or negative cultures from deep tissues, and delay in wound healing) was 1%. No significant difference was demonstrated between the two groups. There were no late deep infections (deep infection present for at least three months and occurring up to two years after the operation). Another prospective, randomized, controlled study that compared gentamicin-impregnated bone cement with systemic antimicrobials (cloxacillin, dicloxacillin, cephalexin, or penicillin) had similar results.⁴⁶⁶ Antimicrobial bone cement has not been shown to be superior to intravenous antimicrobials.

The impact of ultraclean operating rooms on deep infection after joint-replacement surgery was evaluated in more than 8000 hip or knee operations.⁴⁴⁸ A significantly lower rate of deep infection was observed with the use of ultraclean operating rooms than with conventional rooms (0.6% versus 1.5%, respectively). Although not strictly controlled in this study, the use of prophylactic antimicrobials (primarily flucloxacillin) was associated with an even lower rate of deep infection of the prosthesis.

Taken together, studies reported in the medical literature suggest that a short course of antimicrobial prophylaxis can significantly reduce the rate of postoperative infection, particularly late, deep-seated infection, in joint-replacement surgery. Although infectious complications are infrequent, the consequences of an infected joint prosthesis can be devastating. The use of ultraclean operating rooms significantly reduces the rate of deep infection after joint-replacement surgery, regardless of whether antimicrobials are given.^{447,448} Because such operating environments are not widely available, antimicrobial prophylaxis using agents with activity primarily against *S. aureus* is indicated in patients undergoing joint-replacement surgery.

Duration. Two studies demonstrate that prophylactic antimicrobials are essential in total joint replacement, but the studies are not particularly helpful in guiding duration of use.^{446,447} Studies involving total hip replacement have used

antimicrobials for 12 hours to 14 days postoperatively.^{442,445-451,467} A duration of 24 hours was supported in a randomized trial of 358 patients undergoing total hip arthroplasty, total knee arthroplasty, or hip fracture repair that compared one day with seven days of either nafcillin or ceftazidime.⁴⁶⁷ The difference in infection rates between groups was not significant. The timing and duration of prophylaxis for total joint replacement have not been established, although there is general agreement that the first dose should be given about 30 minutes before the initial incision and the second dose given intraoperatively if the procedure takes more than three hours. The duration of prophylaxis remains controversial,²⁴ although the available data do not support prophylaxis beyond 24 hours.

A discussion of whether prophylaxis should be continued until postoperative surgical drainage tubes are removed is outside the scope of these guidelines; however, drainage tubes carry the risk of infection and thus are a variable in postoperative infections. There is a lack of data evaluating the risk of infection with and without continued antimicrobial prophylaxis in patients with surgical drainage tubes still in place. Continuation of antimicrobials may be warranted until the tubes are removed; however, there are no available data to support continuing prophylaxis.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of antimicrobial prophylaxis in pediatric patients undergoing total joint replacement.

Recommendation. The recommended regimen for patients undergoing total hip, elbow, knee, or shoulder replacement is ceftazidime 1 g (as the sodium) intravenously at induction of anesthesia and every 8 hours for 24 hours. Although continuing prophylaxis until drainage tubes are removed may be warranted, there is currently no evidence to support this practice. Vancomycin 1 g (as the hydrochloride) intravenously over one hour should be reserved as an alternative agent on the basis of previously outlined guidelines from HICPAC.²¹ (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing total hip, elbow, knee, or shoulder replacement is ceftazidime 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 24 hours. Vancomycin 15 mg/kg (as the hydrochloride) intravenously should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.^{21,32}

Urologic Surgery

Background. The efficacy of antimicrobial prophylaxis in urologic surgery has been investigated in many clinical trials, particularly in patients undergoing prostatectomy through the urethra, more commonly known as transurethral resection of the prostate (TURP).^{385,468-488} Many patients undergoing resection of bladder tumors have also been studied.^{470,489} Non-TURP transurethral procedures, like urethral dilatation and stone extraction, involve the same organisms and risk factors as TURP. Therefore, any transurethral procedure is similar enough to be included with TURP. Prostatectomy can also be performed through the perineum (perineal) and into the bladder (suprapubic). However, perineal procedures may involve different organisms on the basis of the proximity to the anus. There is a lack of studies addressing perineal prostatectomy;

therefore, the following recommendations do not include perineal prostatectomy. *S. aureus* may be the only organism causing infection after suprapubic procedures. However, there is a lack of studies, so the following recommendations do not include suprapubic procedures.

The most common infectious complication after urologic surgery is bacteriuria, the frequency of which has varied from 0% to 54% in reported studies. More serious infections, including bacteremia, are rare after TURP. Risk factors for infection after urologic surgery include age over 60 years, prolonged preoperative hospital stay, and wound contamination.⁴⁹⁰ Bacteriuria before open prostatectomy has also been identified as a risk factor for postoperative wound infection in patients with or without an indwelling catheter.⁴⁹¹ Other factors that contribute to postoperative complications are the length of postoperative catheterization and the mode of irrigation (closed versus open). No significant correlation between infection rate and diagnosis of benign prostate hyperplasia or prostate carcinoma has been identified.⁴⁸⁰ Therefore, neither of these diagnoses is considered a risk factor. The major objective of prophylaxis is the prevention of bacteremia and surgical wound infection and secondarily the prevention of postoperative bacteriuria.²⁴ The benefits of preventing postoperative bacteriuria are unknown; however, a majority of studies have regarded postoperative bacteriuria, regardless of the presence or absence of infectious signs and symptoms, as a postoperative complication. Therapeutic antimicrobials directed at the appropriate pathogens and for the appropriate duration should be used in patients with preoperative urinary tract infection.

Organisms. *E. coli* is the most common isolate in patients with postoperative bacteriuria; however, other gram-negative bacilli and enterococci also cause infection.

Efficacy. A wide range of antimicrobial regimens, including cephalosporins,^{385,469,471,473,475,477,479,480,483,484,486–489} aminoglycosides,^{468,474,481,482} carbenicillin,^{470,472} piperacillin–tazobactam,⁴⁸⁷ trimethoprim–sulfamethoxazole,^{473,476,486} nitrofurantoin,⁴⁷⁸ and fluoroquinolones,^{485,488,492–494} have been evaluated.

Four studies did not demonstrate a difference in the frequency of postoperative bacteriuria when prophylactic antimicrobials were compared with controls.^{469–472} The postoperative bacteriuria rate was 10% or less for the control groups and 6% or less for the prophylactic antimicrobial groups. In eight studies, the rate of postoperative bacteriuria was 25% in the control groups and 5% or less in the antimicrobial groups.^{474–476,478–482} These studies included only patients with sterile urine preoperatively. Postoperative bacteriuria was defined as greater than 10⁵ CFU/mL. In most of the studies, patients who received antimicrobial prophylaxis did not have fewer febrile episodes or shorter hospital stays than control patients.

Choice. No single antimicrobial regimen appears superior. Broad-spectrum antimicrobials, such as aminoglycosides or second- and third-generation cephalosporins, are no more effective than first-generation cephalosporins or oral agents (trimethoprim–sulfamethoxazole or nitrofurantoin). One prospective, randomized study demonstrated that norfloxacin is effective in preventing stricture formation after TURP.⁴⁸⁵ This study is relevant in that bacterial infection is believed to be the partial cause of stricture formation. Other trials have demonstrated the efficacy of lomefloxacin, another fluoroquinolone, for antimicrobial prophylaxis in urologic surgical procedures. One open-label, randomized trial showed that oral lomefloxacin is effective in preventing

postsurgical bacteriuria after visual laser ablation of the prostate.⁴⁹⁴ Additional studies indicated that oral lomefloxacin is as effective as intravenous cefotaxime or cefuroxime in the prevention of infections after transurethral surgical procedures.^{488,492,493} Other fluoroquinolones may provide the same benefit as lomefloxacin; however, there are no efficacy data at this time to support recommendation of these agents.

Duration. In a large number of the trials, prophylaxis was continued for up to three weeks postoperatively.^{468,470,472,474–476,478,480} The most recent studies suggest that continuation of prophylaxis after the preoperative dose is unnecessary.^{385,479,481–486,495} However, one study suggests that giving one dose of cefotaxime one hour before catheter removal instead of at the induction of anesthesia may be beneficial.⁴⁹⁶

Pediatric Efficacy. Most urologic studies evaluated prophylaxis for TURP or resection of bladder tumors, and pediatric patients therefore would be unlikely to have been included.

Recommendation. Considering the low risk of serious infection after urologic surgery, antimicrobial prophylaxis should be considered only in patients at high risk of postoperative bacteriuria (patients likely to require prolonged postoperative catheterization and patients with a positive urine culture) or in hospitals with infection rates of greater than 20%. Low-risk patients do not appear to benefit from the use of perioperative antimicrobials. If oral antimicrobials are used, a single dose of trimethoprim 160 mg with sulfamethoxazole 800 mg or lomefloxacin 400 mg (as the hydrochloride) should be administered two hours before surgery. If an injectable agent is preferred, cefazolin 1 g (as the sodium) intravenously at induction of anesthesia is recommended. Continuation of antimicrobial prophylaxis postoperatively is not recommended. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. Prophylaxis for urologic surgery in pediatric patients should be considered only in patients at high risk of postoperative bacteriuria (e.g., patients likely to require prolonged postoperative catheterization and patients with a positive urine culture) or in hospitals with infection rates of greater than 20%. If oral antimicrobials are used, a single dose of trimethoprim 6–10 mg/kg with sulfamethoxazole 30–50 mg/kg two hours before surgery is recommended. If an injectable agent is preferred, a single dose of cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia is recommended. Fluoroquinolones are not recommended in pediatric patients.

Vascular Surgery

Background. Infection after vascular surgery often is associated with extensive morbidity and mortality. Postoperative infection is particularly devastating if it involves the vascular graft material. As a result, antimicrobial prophylaxis is widely used with surgical revascularization.⁴⁹⁷ Patients undergoing brachiocephalic procedures do not appear to benefit from antimicrobial prophylaxis. Although there are no data, patients undergoing brachiocephalic procedures (e.g., carotid endarterectomy) involving vascular prosthesis or patch implantation may benefit from prophylaxis. Risk factors for postoperative surgical wound infection in patients undergoing vascular surgery include lower-extremity surgery, delayed surgery after hospitalization, diabetes mellitus, and a history of vascular surgery.⁴⁹⁸ Another risk factor is short duration of antimicrobial prophylaxis, which was

defined as a 1.5-g dose of intravenous cefamandole (as the nafate) at induction of anesthesia and 750 mg of cefamandole four and eight hours after the first dose.⁴⁹⁸

Organisms. The predominant organisms involved include *S. aureus*, *S. epidermidis*, and enteric gram-negative bacilli. At some institutions, MRSA could be an organism of concern.

Efficacy. Prophylactic antimicrobials decrease the rate of infection after procedures involving the lower abdominal vasculature and procedures required for dialysis access. The duration of follow-up for late wound complications was at least once after hospital discharge (not further defined) for most studies,⁴⁹⁰⁻⁵⁰¹ one month,^{498,502,503} six months,⁵⁰⁴ and up to three years.⁵⁰⁵

In the first randomized, prospective, double-blind placebo-controlled study in patients undergoing peripheral vascular surgery ($n = 462$), the infection rate was significantly lower with cefazolin than placebo (0.9% and 6.8%, respectively).⁴⁹⁹ Four deep graft infections were observed in the placebo group; none occurred in the patients who received cefazolin. No infections were observed in patients who underwent brachiocephalic ($n = 103$), femoral artery ($n = 56$), or popliteal ($n = 14$) procedures. Cefazolin-susceptible *S. aureus* was the predominant pathogen; however, gram-negative aerobic bacilli, coagulase-negative staphylococci, and enterococci were also isolated.

In a subsequent controlled trial, intravenous cephradine, topical cephradine, or both were evaluated in patients undergoing peripheral vascular surgery.⁵⁰⁵ The infection rate was significantly different between the cephradine groups (less than 6%) and the control group (25%). There were no significant differences in the infection rate among the groups that received cephradine, regardless of route. Ten of 16 infected patients grew *S. aureus*; *E. coli* and other gram-negative bacilli were infrequently associated with infection.

Patients undergoing vascular-access surgery for hemodialysis also benefit from the administration of antistaphylococcal antimicrobials.⁵⁰⁴ Two of 19 cefamandole-treated patients and 8 of 19 placebo recipients developed an infection after undergoing polytetra-fluoroethylene vascular-access grafts.

Choice. More recent studies have demonstrated that cefazolin remains the preferred cephalosporin for use in vascular surgery.^{500,501} There was no significant difference in infection rates between cefazolin and cefuroxime in patients undergoing abdominal aortic and lower-extremity peripheral vascular surgery⁵⁰⁰ or between cefazolin and cefamandole in patients undergoing aortic or infrainguinal arterial surgery.⁵⁰¹

There are limited data regarding the choice of an antimicrobial for penicillin-allergic patients undergoing vascular procedures. Although vancomycin offers coverage against potential gram-positive pathogens, the addition of an aminoglycoside may be prudent when colonization and infection with gram-negative organisms are expected. Given the lack of data regarding vancomycin as a single agent, definitive conclusions are not possible.

Duration. A prospective, randomized, double-blind study compared infection rates of a one-day and a three-day course of cefuroxime with placebo in patients undergoing peripheral vascular surgery.⁵⁰² The infection rates were 16.7%, 3.8%, and 4.3% in the placebo, one-day, and three-day groups, respectively. The difference in the infection rates between the one-day and three-day groups was not

significant. A prospective study that analyzed risk factors for surgical wound infection after vascular surgery found that patients randomly assigned to receive a short course of antimicrobial prophylaxis, defined as 1.5 g of cefamandole (as the nafate) at induction of anesthesia followed by 750 mg of cefamandole four and eight hours after the first dose, were more likely to develop surgical wound infection than patients randomly assigned to receive a longer course of antimicrobial prophylaxis, defined as 1.5 g of cefamandole (as the nafate) at induction of anesthesia and 750 mg every 6 hours for 48 hours after surgery.⁴⁹⁸

Route. The question of oral versus intravenous treatment was addressed in a multicenter, randomized, double-blind, prospective trial in 580 patients undergoing arterial surgery involving the groin.⁵⁰³ Patients received two doses of ciprofloxacin 750 mg orally or three doses of cefuroxime 1.5 g intravenously on the day of surgery. The wound infection rate within 30 days of surgery was 9.2% (27 patients) in the ciprofloxacin group and 9.1% (26 patients) in the cefuroxime group. Although oral ciprofloxacin was shown to be as effective as intravenous cefuroxime in one study, this study did not address the well-founded concern about resistance developing with routine use of fluoroquinolones⁵⁰⁶; therefore, intravenous cefazolin remains the first-line agent for this indication. The study did, however, demonstrate the need for more studies regarding efficacy of oral agents for postoperative prophylaxis.

Pediatric Efficacy. No well-controlled studies have evaluated the efficacy of surgical prophylaxis in pediatric patients undergoing vascular surgery.

Recommendation. The recommendation for patients undergoing vascular surgery is cefazolin 1 g (as the sulfate) intravenously at induction of anesthesia and every 8 hours for 24 hours. Vancomycin 1 g (as the hydrochloride) intravenously over one hour, with or without gentamicin 2 mg/kg (as the sulfate) intravenously, should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.²¹ Although there are no data, patients undergoing brachiocephalic procedures involving vascular prosthesis or patch implantation (e.g., carotid endarterectomy) may benefit from prophylaxis. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing vascular surgery is cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 24 hours. Vancomycin 15 mg/kg (as the hydrochloride) intravenously over one hour, with or without gentamicin 2 mg/kg (as the sulfate) intravenously, should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.²¹ Although there are no data, patients undergoing brachiocephalic procedures involving vascular prosthesis or patch implantation (e.g., carotid endarterectomy) may benefit from prophylaxis.

Solid Organ Transplantation

Few well-designed, prospective, comparative studies of antimicrobial prophylaxis have been conducted in patients undergoing solid organ transplantation, and no formal recommendations are available from professional organizations or expert consensus panels. As a result, multiple regimens are in use at different

transplant centers. A recent survey of four major U.S. centers performing combined pancreas–kidney transplantation identified four different prophylactic regimens using from one to four different drugs for two to seven days postoperatively.⁵⁰⁷

The recommendations given for each of the solid organ transplant procedures represent an attempt to provide guidelines for safe and effective surgical prophylaxis based on the best available literature. These recommendations will undoubtedly vary considerably from protocols in use at various transplantation centers around the United States.

Heart Transplantation

Background. Heart transplantation has emerged as a standard therapeutic option for selected patients with end-stage cardiac disease. Approximately 4000 heart transplants are performed worldwide each year, including approximately 100 in children less than 16 years of age.⁵⁰⁸ Survival rates after heart transplantation are approximately 79% at one year and 65% at five years, illustrating the tremendous progress that has been made over the past two decades. Infection continues to be an important cause of morbidity and mortality after heart transplantation and is the major cause of death in approximately 15%, 40%, and 10% of patients at <1 month, 1–12 months, and >12 months posttransplant, respectively.

Despite the large number of heart transplantation surgeries performed, few studies have specifically examined postoperative infection rates in this population. General cardiothoracic surgery has been associated with surgical wound infection rates of 9% to 55% in the absence of antimicrobial prophylaxis.^{69,70,88} Because heart transplantation is similar to other cardiothoracic surgeries, similar considerations regarding the need for antimicrobial prophylaxis apply (see Cardiothoracic surgery).⁵⁰⁹

Organisms. Similar to other types of cardiothoracic surgery, coagulase-positive and coagulase-negative staphylococci are the primary pathogens that cause surgical wound infection after heart transplantation. *S. aureus* was the cause of all wound infections in one study involving heart transplantation.⁵¹⁰

Efficacy. In an open-label, noncomparative study, the wound infection rate was 4.5% among 96 patients administered cefotaxime plus flucloxacillin preoperatively and for 72 hours after surgery.⁵¹⁰ This rate of infection was similar to that seen in other cardiothoracic, non-heart-transplantation procedures in which antimicrobial prophylaxis was used. Although antimicrobial prophylaxis appears to be effective in significantly reducing infection rates, no randomized, controlled trials have specifically addressed the use of antimicrobial prophylaxis in heart transplantation.

Choice. Antimicrobial prophylaxis for heart transplantation is similar to that used for other types of cardiothoracic procedures.⁵⁰⁹ First- and second-generation cephalosporins are considered to be equally efficacious and are the preferred agents. There appear to be no significant differences in efficacy among prophylactic regimens using agents such as cefazolin, cephalothin, cefuroxime, and cefamandole.⁵¹¹ The use of antistaphylococcal penicillins, either alone or in combination with aminoglycosides or cephalosporins, has not been demonstrated to provide efficacy superior to that of cephalosporin monotherapy (see Cardiothoracic surgery).

Duration. On the basis of data concerning other cardiothoracic procedures, prophylactic regimens of 48 to 72 hours' duration appear similar in efficacy to longer regimens.

Pediatric Efficacy. There are no data specifically addressing antimicrobial prophylaxis for heart transplantation in pediatric patients. Pediatric patients should be treated according to recommendations for other types of cardiothoracic procedures.

Recommendation. On the basis of data for other types of cardiothoracic surgery, antimicrobial prophylaxis is indicated for all patients undergoing heart transplantation. The recommended regimen is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia and every 8 hours for 48 to 72 hours. Currently there is no evidence to support continuing prophylaxis until chest and mediastinal drainage tubes are removed. Cefuroxime 1.5 g (as the sodium) intravenously at induction of anesthesia and every 12 hours for 48 to 72 hours and cefamandole 1 g (as the nafate) intravenously at induction of anesthesia and every 6 hours for 48 to 72 hours are acceptable alternatives. Further studies are needed to demonstrate the efficacy of single-dose prophylaxis. Vancomycin 1 g (as the hydrochloride) intravenously with or without gentamicin 2 mg/kg (as the sulfate) should be reserved as an alternative agent on the basis of previously outlined guidelines from HICPAC and AHA.^{21,32} (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing heart transplantation is cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 48 to 72 hours. Cefuroxime 50 mg/kg (as the sodium) at induction of anesthesia and every 8 hours for 48 to 72 hours is an acceptable alternative. Vancomycin 15 mg/kg (as the hydrochloride) intravenously with or without gentamicin 2 mg/kg (as the sulfate) should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC and AHA.^{21,32}

Lung and Heart–Lung Transplantation

Background. Lung transplantation has become an accepted mode of therapy for a variety of end-stage, irreversible lung diseases. The most common diseases for which lung transplantation is performed are chronic obstructive pulmonary disease, emphysema associated with α_1 -antitrypsin deficiency, cystic fibrosis, idiopathic pulmonary fibrosis, and primary pulmonary hypertension.⁵¹² Approximately 1000 single-lung, bilateral-lung, and heart–lung transplants are performed in the United States every year.^{508,512} National survival rates after lung transplantation are approximately 70% at one year and 50% at five years; differences in rates between single-lung and double-lung transplants are not significant.⁵⁰⁸ Survival rates after heart–lung transplants are somewhat lower: approximately 60% at one year and 40% at five years.

Bacterial, fungal, and viral infections are the most common complications and causes of death within the first 90 days after lung or heart–lung transplantation.^{512–514} Bacterial infections, particularly surgical wound infections and pneumonia, are common in the immediate postoperative period. The frequent occurrence of bacterial pneumonias is directly related to the procedure being performed. Thus antimicrobial prophylaxis is routinely administered to patients undergoing lung or

heart–lung transplantation with the aim of preventing bacterial pneumonia as well as wound infection. Although much has been published about general infectious complications associated with lung transplantation, there are no data specifically addressing the optimal prophylactic antimicrobial regimens. Fungal and viral infections are late complications not directly associated with the surgical procedure. Prophylaxis of these infections is beyond the scope of this document.

Organisms. Similar to other cardiothoracic surgeries, coagulase-positive and coagulase-negative staphylococci are the primary pathogens that cause wound infection after lung transplantation. Patients undergoing lung transplantation are also at risk for bacterial pneumonia due to colonization or infection of the lower and upper airways of the donor, the recipient, or both.⁵¹² The donor lung appears to be a major route of transmission of pathogens; 75% to 90% of bronchial washings from donor organs are positive for at least one bacterial organism.^{515,516}

Organ recipients may also be the source of infection of the transplanted organ. This is particularly true in patients with cystic fibrosis because of the frequent presence of *P. aeruginosa* in the upper airways and sinuses before transplantation.⁵¹⁴ These pathogens are often highly resistant to antimicrobials because of the frequent administration of broad-spectrum agents during the previous course of the disease. Multiresistant strains of *Burkholderia (Pseudomonas) cepacia* and *Stenotrophomonas maltophilia* may be a problem in cystic fibrosis patients in some transplant centers.^{514,517}

Infections with *Candida* and *Aspergillus* species are also common after lung transplantation. The occurrence of early *Candida* infections has been associated with colonization of the donor lung before transplantation.^{516,518}

Efficacy. No randomized, controlled trials regarding antimicrobial prophylaxis for lung transplantation have been conducted. The rate of bacterial pneumonia within the first two weeks after surgery has reportedly been decreased from 35% to approximately 10% by routine antimicrobial prophylaxis.^{519–521} Improvements in surgical technique and postoperative patient care may also be important factors in the apparently lower rates of pneumonia after lung transplantation.

Choice. No formal studies have addressed optimal prophylaxis for patients undergoing lung transplantation. Antimicrobial prophylaxis for lung and heart–lung transplantation should generally be similar to that for other cardiothoracic procedures (see Cardiothoracic surgery). First- and second-generation cephalosporins are considered to be equally efficacious and are the preferred agents for these procedures. However, prophylactic regimens should be modified to include coverage for any potential bacterial pathogens that have been isolated from the recipient's airways or the donor lung.⁵¹² Patients with end-stage cystic fibrosis should receive antimicrobials on the basis of the known susceptibilities of pretransplant isolates, particularly *P. aeruginosa*.

It has been suggested that antifungal prophylaxis should be considered when pretransplant cultures reveal fungi in the donor lung.⁵¹² Because of the serious nature of fungal infections in the early posttransplant period and the availability of relatively nontoxic antifungal agents, prophylaxis with fluconazole should be considered when *Candida* is isolated from the donor lung and itraconazole should be considered when *Aspergillus* is isolated.⁵¹² Amphotericin B may also be

considered.⁵²² No antifungal prophylaxis is necessary in the absence of positive fungal cultures from the donor lung.

Duration. No well-conducted studies have addressed the optimal duration of antimicrobial prophylaxis for lung transplantation. In the absence of positive cultures from the donor or the recipient, prophylactic regimens of 48 to 72 hours' duration are probably similar in efficacy to longer regimens.⁵²² In patients with positive pretransplant cultures from donor or recipient organs or patients with positive cultures posttransplant, prophylaxis should be continued for longer. Antimicrobial prophylaxis should be appropriately modified according to the specific organisms isolated and antimicrobial susceptibilities. It has been recommended that prophylactic regimens be continued for 7 to 14 days postoperatively in transplant recipients with positive cultures, particularly patients with cystic fibrosis and previous *P. aeruginosa* infection.^{512,514,522}

Pediatric Efficacy. There are few data specifically concerning antimicrobial prophylaxis for lung transplantation in pediatric patients. Pediatric patients should be treated according to recommendations for other types of cardiothoracic procedures and as previously discussed for adult lung transplantation.⁵²²

Recommendation. On the basis of data from other types of cardiothoracic surgery, all patients undergoing lung transplantation should receive antimicrobial prophylaxis because of the high risk of infection. Patients with negative pretransplant cultures should receive antimicrobial prophylaxis as appropriate for other types of cardiothoracic surgeries. The recommended regimen is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia and every 8 hours for 48 to 72 hours. There is no evidence to support continuing prophylaxis until chest and mediastinal drainage tubes are removed. Cefuroxime 1.5 g (as the sodium) intravenously at induction of anesthesia and every 12 hours for 48 to 72 hours and cefamandole 1 g (as the nafate) intravenously at induction of anesthesia and every 6 hours for 48 to 72 hours are acceptable alternatives. Further studies are needed to demonstrate the efficacy of single-dose prophylaxis. Vancomycin 1 g (as the hydrochloride) intravenously should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.²¹

The prophylactic regimen should be modified to provide coverage against any potential pathogens (e.g., *P. aeruginosa*) isolated from the donor lung or the recipient. Prophylactic regimens directed against *P. aeruginosa* may include one or two drugs with activity against this pathogen, although two-drug therapy is recommended for prophylaxis and is mandatory should prophylaxis fail and an actual infection develop. The regimen may also include antifungal agents such as fluconazole if donor lung cultures are positive for *Candida* and itraconazole if cultures are positive for *Aspergillus*. The following doses would be appropriate: fluconazole 200–400 mg intravenously or orally, or itraconazole 200 mg orally as tablet or suspension. If the use of amphotericin B is desired, doses of 0.1–0.25 mg/kg intravenously may be used. Patients undergoing lung transplantation for cystic fibrosis should receive 7 to 14 days of prophylaxis with antimicrobials selected according to pretransplant culture and susceptibility results. (Strength of evidence for prophylaxis = B.)

Pediatric Dosage. As used for other cardiothoracic procedures, the recommended regimen for pediatric patients

undergoing lung or heart–lung transplantation is cefazolin 20–30 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 48 to 72 hours. Cefuroxime 50 mg/kg (as the sodium) intravenously at induction of anesthesia and every 8 hours for 48 to 72 hours is an acceptable alternative. Vancomycin 15 mg/kg (as the hydrochloride) intravenously should be reserved as an alternative on the basis of previously outlined guidelines from HICPAC.²¹ If these regimens require modification for potential pathogens isolated from the donor or the recipient, the dosages are as appropriate for the specific agent(s) chosen. Patients undergoing lung transplantation for cystic fibrosis should receive 7 to 14 days of prophylaxis with antimicrobials selected according to pretransplant isolates and susceptibilities. These antimicrobials may be antibacterial or antifungal agents.

Liver Transplantation

Background. Liver transplantation is a life-saving procedure for many patients with end-stage hepatic disease for whom there are no other medical or surgical options. Approximately 6000 liver transplants are performed worldwide each year, with one- and five-year survival rates of 76% and 65%, respectively.^{523,524} Infection remains a major cause of morbidity and mortality in liver transplant recipients. Infections may occur in 42% to 83% of patients within three months of transplantation and are the cause of death in 4% to 23% of patients; these rates are highly variable and do not seem to have substantially changed in spite of advances in surgical technique and medical management.^{523–529}

Liver transplantation is often considered to be the most technically difficult of the solid organ transplant procedures. Surgical procedures longer than 8 to 12 hours have been consistently identified as one of the most important risk factors for early infectious complications, including wound infections, intra-abdominal infections, and biliary tract infections.^{523,527,529} Other important risk factors for infectious complications include previous hepatobiliary surgery, high pretransplantation serum bilirubin concentration, and surgical complications such as anastomotic leakage. In spite of the high rate of infections directly related to the transplantation procedure, there are few well-controlled studies concerning optimal antimicrobial prophylaxis in this setting.

Organisms. The pathogens most commonly associated with early wound and intra-abdominal infections are those derived from the normal flora of the intestinal lumen and the skin. Aerobic gram-negative bacilli, including *E. coli*, *Klebsiella* species, *Enterobacter* species, and *Citrobacter* species, are common causes of wound and intra-abdominal infections and account for up to 65% of all bacterial pathogens.^{523,524,527,529–531} Infections due to *P. aeruginosa* may also occur but are much less frequent in the early postoperative period. *P. aeruginosa* is most commonly associated with late pneumonias, vascular infections, and secondary bacteremias.^{523,524,527,529}

Enterococci are particularly common pathogens and may be responsible for 20% to 46% of wound and intra-abdominal infections. *S. aureus* and coagulase-negative staphylococci are also common causes of postoperative wound infections.^{524,525,527–529} Although *Candida* species commonly cause late infections, they are less frequent causes of early postoperative infections.

Efficacy. In evaluating the efficacy of prophylactic regimens, it is important to differentiate between early infections (variously defined as those occurring within 14 to 30 days after surgery) and late infections (those occurring >30 days after surgery). Infections occurring in the early postoperative period are most commonly associated with biliary, vascular, and abdominal surgeries involved in the transplantation procedure itself and are thus most preventable with prophylactic antimicrobial regimens.^{523–525,527} The frequency of these infections varies from 10% to 55% despite antimicrobial prophylaxis.^{523–525,527,532} It is difficult to assess the efficacy of prophylactic regimens in reducing the rate of infection because prophylaxis has been routinely used in light of the complexity of the surgical procedure; therefore, reliable rates of infection in the absence of prophylaxis are not available. No controlled studies have compared prophylaxis with no prophylaxis.

Choice. Antimicrobial prophylaxis should be directed against the pathogens most commonly isolated from early infections (i.e., gram-negative aerobic bacilli, staphylococci, enterococci). Traditional prophylactic regimens have thus consisted of a third-generation cephalosporin (usually cefotaxime because of relatively greater staphylococcal activity) plus ampicillin.^{525,526,528–530,532} The use of ceftioxin and of ampicillin–sulbactam has also been reported; the efficacy of these regimens compared with that of cefotaxime plus ampicillin cannot be assessed because of different definitions of infection used in the various studies. No randomized, controlled studies have been conducted to compare the efficacy of other antimicrobial prophylactic regimens in the prevention of early postoperative infections.

At least one study used mechanical bowel preparation in conjunction with oral erythromycin base and neomycin sulfate, followed by systemic administration of cefotaxime plus ampicillin.⁵²⁶ Infection rates in that study did not appear to be different from those in studies that did not use preoperative gut sterilization.

Several studies have examined the use of selective bowel decontamination in order to eliminate aerobic gram-negative bacilli and yeast from the bowel before surgery.^{525,530–534} These studies used combinations of nonabsorbable antibacterials (aminoglycosides, polymyxin E) and antifungals (nystatin or amphotericin B) administered orally and applied to the oropharyngeal cavity, in combination with systemically administered antimicrobials. The results of these studies are conflicting and do not currently support the routine use of selective bowel decontamination in patients undergoing liver transplantation.⁵²³

Duration. No studies have assessed the optimal duration of antimicrobial prophylaxis in liver transplantation. Although antimicrobials were administered for five days in older studies,^{526,529} more recent studies have limited the duration of prophylaxis to 48 hours, with no apparent difference in early infection rates.^{525,527,530,532}

Pediatric Efficacy. There are few data specifically concerning antimicrobial prophylaxis in liver transplantation in pediatric patients. The combination of cefotaxime plus ampicillin has been reportedly used in children undergoing living-related-donor liver transplantation; the efficacy of this regimen appeared to be favorable.⁵²⁸

Recommendation. All patients undergoing liver transplantation should receive antimicrobial prophylaxis because of the

high risk of infectious morbidity and mortality associated with these procedures. Cefotaxime 1 g (as the sodium) plus ampicillin 1 g (as the sodium) should be administered intravenously at induction of anesthesia, repeated every 6 hours during the procedure, and given every 6 hours for 48 hours beyond final surgical closure. Other antimicrobial regimens that provide adequate coverage against gram-negative aerobic bacilli, staphylococci, and enterococci may be appropriate, but no randomized, comparative clinical trials have been conducted. (Strength of evidence for prophylaxis = B.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing liver transplantation is cefotaxime 50 mg/kg (as the sodium) plus ampicillin 50 mg/kg (as the sodium) intravenously at induction of anesthesia and repeated every 6 hours for 48 hours beyond final surgical closure. Other antimicrobial regimens that provide adequate coverage against gram-negative aerobic bacilli, staphylococci, and enterococci may be appropriate, but no randomized, comparative clinical trials have been conducted.

Pancreas and Pancreas–Kidney Transplantation

Background. Pancreas transplantation is an accepted therapeutic intervention for type 1 diabetes mellitus; it is the only therapy that consistently achieves euglycemia without dependence on exogenous insulin. Simultaneous pancreas–kidney transplantation is an accepted procedure for patients with type 1 diabetes and severe diabetic nephropathy. Infectious complications are a major source of morbidity and mortality in patients undergoing pancreas or pancreas–kidney transplantation; the frequency of wound infection is reportedly 7% to 50%.^{535–539} These patients may be at increased risk of wound and other infections because of the combined immunosuppressive effects of diabetes and the immunosuppressive drugs used to prevent graft rejection.⁵³⁷ Other factors associated with increased wound infection rates include prolonged (more than four hours) operating time, organ donor of >55 years of age, and enteric rather than bladder drainage of pancreatic duct secretions.⁵³⁷

Organisms. A majority of superficial wound infections after pancreas or pancreas–kidney transplantation are caused by staphylococci (both coagulase-positive and coagulase-negative) and gram-negative aerobic bacilli (particularly *E. coli* and *Klebsiella* species). Deep wound infections also are frequently associated with gram-positive and gram-negative aerobes, as well as *Candida* species.^{535–541}

Efficacy. Although no placebo-controlled studies have been conducted, several open-label, noncomparative studies have suggested that antimicrobial prophylaxis substantially decreases the rate of superficial and deep wound infections after pancreas or pancreas–kidney transplantation. Wound infection rates were 2.4% to 5% with various prophylactic regimens, compared with 7% to 50% for historical controls in the absence of prophylaxis.^{507,540} However, even with antimicrobial prophylaxis, wound infection rates as high as 33% have been reported⁵³⁷; the reason for the wide disparity in infection rates observed with prophylaxis is not readily apparent.

Choice. Because of the broad range of potential pathogens, several studies have used multidrug prophylactic regimens, including imipenem–cilastatin plus vancomycin⁵³⁷;

tobramycin, vancomycin, and fluconazole⁵⁴⁰; and cefotaxime, metronidazole, and vancomycin.⁵⁴² These three regimens resulted in overall wound infection rates of 33%, 2.4%, and 30%, respectively. A recent study evaluated wound infection rates in pancreas–kidney transplantation after single-agent, single-dose prophylaxis with cefazolin.⁵⁰⁷ Only two patients (5%) developed superficial wound infections, defined as the presence of erythema and purulent drainage. Although four additional patients (11%) developed deep wound infections, all infections were associated with bladder anastomotic leaks or transplant pancreatitis. On the basis of limited studies, it appears that multidrug regimens offer no distinct advantage over cefazolin.

Duration. Recent studies have evaluated the use of prophylactic regimens ranging from a single preoperative dose of cefazolin to multidrug regimens of two to five days' duration.^{507,537,540,542} Although longer durations of antimicrobial prophylaxis have been recommended,⁵⁴³ these appear to offer no clear advantages over the single-dose regimen.

Pediatric Efficacy. There are no data concerning antimicrobial prophylaxis for pancreas or pancreas–kidney transplantation in pediatric patients.

Recommendation. The recommended regimen for patients undergoing pancreas or pancreas–kidney transplantation is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia. (Strength of evidence for prophylaxis = B.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing pancreas or pancreas–kidney transplantation is cefazolin 20 mg/kg (as the sodium) intravenously administered at induction of anesthesia.

Kidney Transplantation

Background. Approximately 10,000 kidney transplants are performed in the United States each year.⁵⁴⁴ The rate of postoperative infection after this procedure has been reported to range from 10% to 56%.^{545–552} Graft loss due to infection occurs in up to 33% of cases.⁵⁴⁸ Mortality associated with postoperative infections is substantial and ranges from approximately 5% to 30%.^{546,548,550,553,554}

Well-defined risk factors for wound infection after renal transplantation include contamination of organ perfusate; factors related to the procedure, such as ureteral leakage and hematoma formation; immunosuppressive therapy; and obesity.⁵⁵⁴ In one study, the frequency of wound infection was 12% in patients receiving immunosuppression with azathioprine plus prednisone but only 1.7% in patients receiving cyclosporine plus prednisone.⁵⁵⁵

Organisms. Postoperative wound infections are typically caused by flora of the skin (particularly *S. aureus* and *S. epidermidis*) and of the urinary tract (most frequently *E. coli*). Enterococci and other gram-negative aerobic pathogens are less frequent causes of postoperative infections after kidney transplantation.^{545–552,555,556}

Efficacy. A number of studies have clearly demonstrated that antimicrobial prophylaxis significantly decreases postoperative infection rates in patients undergoing kidney transplantation. These have included at least one randomized controlled trial⁵⁴⁵ and many prospective and retrospective studies comparing

infection rates with prophylaxis and historical infection rates at specific transplant centers.^{546-549,552,555-557} A recent study evaluated wound infection rates in the absence of systemic prophylaxis and found only a 2% rate among 102 patients undergoing renal transplantation.⁵⁵⁸ Possible explanations given for the very low infection rate included local wound irrigation with cefazolin, improved organ procurement techniques, and careful surgical technique employed by a single, very experienced surgical team. This study emphasizes the importance of good surgical technique during the transplant procedure as an effective means of reducing infectious complications. However, on the basis of available literature, the routine use of systemic antimicrobial prophylaxis is justified in patients undergoing renal transplantation.

Three studies using a triple-drug regimen consisting of an aminoglycoside, an antistaphylococcal penicillin, and ampicillin demonstrated infection rates of less than 2%, compared with 10% to 25% with no antimicrobial prophylaxis.^{549,552} Piperacillin plus cefuroxime was also shown to be efficacious; infection rates were 3.7%, compared with 19% in patients not receiving prophylaxis.⁵⁴⁵ Several studies have shown that single-agent prophylaxis with an antistaphylococcal penicillin,⁵⁵⁶ a first-generation cephalosporin,^{547,548} a second-generation cephalosporin,⁵⁵⁷ or a third-generation cephalosporin such as cefoperazone or ceftriaxone^{555,559} can reduce postoperative infection rates to between 0% and 8.4%. Antimicrobial prophylaxis with agents providing good coverage against gram-positive cocci and gram-negative enteric pathogens is very effective in reducing infection rates in patients undergoing kidney transplantation.

Choice. The data do not indicate a significant difference between single-agent regimens and regimens using two or more drugs.^{545,549,552} Also, there appear to be no significant differences between single-agent regimens employing antistaphylococcal penicillins or first-, second-, or third-generation cephalosporins.^{547,548,555-557,559} Studies have directly compared antimicrobial regimens in a prospective, controlled fashion. Single-agent prophylaxis with both cefazolin and ceftriaxone has been reported to result in infection rates of 0%.^{547,559}

Duration. Studies have used various prophylactic regimens ranging from a single preoperative dose of cefazolin or ceftriaxone to multidrug regimens of two to five days' duration.^{545-549,552,555-557} There appear to be no significant differences in wound infection rates between single-dose and multidose regimens.

Pediatric Efficacy. Although pediatric patients were included in studies demonstrating the efficacy of antimicrobial prophylaxis, there are few data specific to pediatric patients.

Recommendation. The recommended regimen for patients undergoing kidney transplantation is cefazolin 1 g (as the sodium) intravenously at induction of anesthesia. (Strength of evidence for prophylaxis = A.)

Pediatric Dosage. The recommended regimen for pediatric patients undergoing kidney transplantation is cefazolin 20 mg/kg (as the sodium) intravenously at induction of anesthesia.

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Developed through the ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on April 21, 1999. Supersedes an earlier version dated April 22, 1992.

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The recommendations in this document do not indicate an exclusive course of treatment to be followed. Variations, taking into account individual circumstances, may be appropriate.

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The bibliographic citation for this document is as follows: American Society of Health-System Pharmacists. ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm.* 1999; 56:1839–88.