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ANTIMICROBIAL PROPHYLAXIS IN SURGERY

Antimicrobial prophylaxis can decrease the incidence of infection, particularly wound infection, after certain operations, but this benefit must be weighed against the risks of toxic and allergic reactions, emergence of resistant bacteria, drug interactions, superinfection and cost (RL Nichols, Emerg Infect Dis 2001; 7:220). Medical Letter consultants generally recommend antimicrobial prophylaxis only for procedures with high infection rates, those involving implantation of prosthetic material and those in which the consequences of infection are especially serious. Recommendations for prevention of surgical site infection and sepsis in surgical patients are listed in the table that begins on page 96. Recommendations for antimicrobial prophylaxis to prevent bacterial endocarditis when patients with prosthetic heart valves, rheumatic heart disease or other cardiac abnormalities undergo dental or surgical procedures are listed on page 98.

CHOICE OF A PROPHYLACTIC AGENT — An effective prophylactic regimen should be directed against the most likely infecting organisms, but need not eradicate every potential pathogen. For most procedures, cefazolin (*Ancef*, and others), which has a moderately long plasma half-life and is active against staphylococci and streptococci, has been effective. For colorectal surgery and appendectomy, cefoxitin *(Mefoxin)* or cefotetan *(Cefotan)* is preferred because they are more active than cefazolin against bowel anaerobes, including *Bacteroides fragilis*. In institutions where methicillin-resistant *Staphylococcus aureus* or methicillin-resistant, coagulase-negative staphylococci are important post-operative pathogens, vancomycin (*Vancocin*, and others) can be used, but routine use of vancomycin for prophylaxis should be discouraged because it may promote emergence of vancomycin-resistant organisms. Long preoperative hospitalizations are associated with increased risk of infection with an antibiotic-resistant organism; local resistance patterns should be taken into account.

Third-generation cephalosporins, such as cefotaxime *(Claforan)*, ceftriaxone *(Rocephin)*, cefoperazone *(Cefobid)*, ceftazidime *(Fortaz*, and others), or ceftizoxime *(Cefizox)*, and fourth-generation cephalosporins such as cefepime *(Maxipime)* should not be used for routine surgical prophylaxis because they are expensive, some are less active than cefazolin against staphylococci, their spectrum of activity includes organisms rarely encountered in elective surgery, and their widespread use for prophylaxis may promote emergence of resistance.

NUMBER OF DOSES — In most instances, a single intravenous dose of an antimicrobial completed 30 minutes or less before the skin incision provides adequate tissue concentrations

throughout the operation. If surgery is prolonged (more than four hours), major blood loss occurs or an antimicrobial with a short half-life (such as cefoxitin) is used, administration of one or more additional doses is advisable during the procedure. Published studies of antimicrobial prophylaxis often use one or two doses postoperatively in addition to one dose just before surgery. Most Medical Letter consultants believe, however, that postoperative doses are usually unnecessary.

CARDIAC — Prophylactic antibiotics can decrease the incidence of infection after cardiac surgery (I Kriaras et al, Eur J Cardiothorac Surg 2000; 18:440). A meta-analysis of seven placebo-controlled randomized studies of antimicrobial prophylaxis for implantation of permanent pacemakers showed a statistically significant reduction in the incidence of infection (A DaCosta et al, Circulation 1998; 97:1796).

GASTROINTESTINAL — Antibiotic prophylaxis is recommended for esophageal surgery in the presence of obstruction, which increases the risk of infection. The risk of infection after gastroduodenal surgery is high when gastric acidity and gastrointestinal motility are diminished by obstruction, hemorrhage, gastric ulcer or malignancy, or by therapy with an H_2-blocker such as ranitidine (*Zantac*, and others) or a proton pump inhibitor such as omeprazole *(Prilosec)*, and is also high in patients with morbid obesity. A dose of cefazolin or cefoxitin given 30 minutes before surgery can decrease the incidence of postoperative infection in these circumstances. Prophylactic antibiotics are not indicated for routine gastroesophageal endoscopy, but some clinicians use them for high-risk patients undergoing esophageal dilatation or sclerotherapy of varices, and most use them before placement of a percutaneous gastrostomy (D Külling et al, Gastrointest Endosc 2000; 51:152; VK Sharma et al, Am J Gastroenterol 2000; 95:3133).

Antimicrobials are recommended before biliary tract surgery for patients with a high risk of infection — those more than 70 years old and those with acute cholecystitis, a nonfunctioning gallbladder, obstructive jaundice or common duct stones. Many clinicians follow similar guidelines for antibiotic prophylaxis of endoscopic retrograde cholangiopancreatography (ERCP). Prophylactic antibiotics are not necessary for low-risk patients undergoing elective laparoscopic cholecystectomy (KJ Dobay et al, Ann Surg 1999; 65:226; A Higgins et al, Arch Surg 1999; 134:611).

Preoperative antibiotics can decrease the incidence of infection after colorectal surgery; for elective operations, an oral regimen of neomycin and erythromycin appears to be as effective as parenteral drugs. Many surgeons in North America use a combination of oral and parenteral agents, but it is unclear if this is more effective than either alone. Preoperative antimicrobials can decrease the incidence of infection after surgery for acute appendicitis. If perforation has occurred, antibiotics should be considered therapeutic and continued as long as clinically indicated.

GYNECOLOGY AND OBSTETRICS — Antimicrobial prophylaxis decreases the incidence of infection after vaginal and abdominal hysterectomy (V Tanos and N Rojansky, J Am Coll Surg 1994; 179:593; AA Kamat et al, Infect Dis Obstet Gynecol 2000; 8:230). Peri- or preoperative antimicrobials can prevent infection when given after cord clamping in emergency cesarean section, in high-risk situations such as active labor or premature rupture of membranes, after first-trimester abortion in high-risk women, and after mid-trimester abortions (D Chelmow et al, Am J Obstet Gynecol 2001; 184:656). One meta-analysis found a protective effect of perioperative antibacterials in all women undergoing therapeutic abortion (GF Sawaya et al, Obstet Gynecol 1996; 87:884).

HEAD AND NECK — Prophylaxis with antimicrobials has decreased the incidence of surgical site infection after head and neck operations that involve an incision through the oral or pharyngeal mucosa (RS Weber, Ear Nose Throat J 1997; 76:790; JP Rodrigo et al, Head Neck 1997; 19:188).

NEUROSURGERY — Studies of antimicrobial prophylaxis for implantation of permanent cerebrospinal fluid shunts have produced conflicting results (EM Brown et al, Lancet 1994; 344:1547). An antistaphylococcal antibiotic can decrease the incidence of infection after craniotomy. In spinal surgery, the post-operative infection rate after conventional lumbar discectomy is low, and antibiotics have generally not been shown to be effective; infection rates are higher after spinal procedures involving fusion, prolonged spinal surgery or insertion of foreign material, and prophylactic antibiotics are often used, but controlled trials demonstrating their effectiveness are lacking (JB Dimick et al, Spine 2000; 25:2544). Despite the low risk of infection, the serious consequences of surgical site infection have led many neurosurgeons to use perioperative antibiotics.

OPHTHALMIC — Data are limited on the effectiveness of antimicrobial prophylaxis for ophthalmic surgery, but postoperative endophthalmitis can be devastating. Most ophthalmologists use antimicrobial eye drops for prophylaxis, and some also give a subconjunctival injection. There is no consensus supporting a particular choice, route or duration of antimicrobial prophylaxis (TJ Liesegang, Cornea 1999; 18:383). There is no evidence that prophylactic antibiotics are needed for procedures that do not invade the globe.

ORTHOPEDIC — Prophylactic antistaphylococcal drugs administered preoperatively can decrease the incidence of both early and late infection following joint replacement. They also decrease the rate of infection in compound or open fractures and when hip and other fractures are treated with internal fixation by nails, plates, screws or wires. One large randomized trial found a single dose of a cephalosporin more effective than placebo in preventing wound infection after surgical repair of closed fractures (H Boxma et al, Lancet 1996; 347:1133). A prospective randomized study in patients undergoing diagnostic and operative arthroscopic surgery concluded that antibiotic prophylaxis is not indicated (JA Wieck et al, Orthopedics 1997; 20:133).

THORACIC (NON-CARDIAC) — Antibiotic prophylaxis is given routinely in pulmonary surgery, but supporting data are sparse. In one study, a single preoperative dose of cefazolin after pulmonary resection led to a decrease in the incidence of surgical site infection, but not of pneumonia or empyema. Other trials have found that multiple doses of a cephalosporin can prevent infection after closed-tube thoracostomy for chest trauma (RP Gonzalez and MR Holevar, Am Surg 1998; 64:617). Insertion of chest tubes for other indications, such as spontaneous pneumothorax, does not require antimicrobial prophylaxis.

UROLOGY —Infectious disease experts do not recommend antimicrobials before most urological operations in patients with sterile urine. When the urine culture is positive or unavailable, or the patient has a preoperative urinary catheter, patients should be treated to sterilize the urine before surgery or receive a single preoperative dose of an appropriate agent (CM Kunin, *Urinary Tract Infections: Detection, Prevention and Management*, 5th ed, Baltimore:Williams & Wilkins, 1997, p 363). Prophylaxis is recommended before transrectal prostatic biopsies because urosepsis has occurred (HM Taylor and JB Bingham, J Antimicrob Chemother 1997; 39:115).

VASCULAR — Preoperative administration of a cephalosporin decreases the incidence of postoperative surgical site infection after arterial reconstructive surgery on the abdominal aorta, vascular operations on the leg that include a groin incision, and amputation of the lower extremity for ischemia (Swedish-Norwegian Consensus Group, Scand J Infect Dis 1998; 30:547). Many experts also recommend prophylaxis for implantation of any vascular prosthetic material, such as grafts for vascular access in hemodialysis. Prophylaxis is not indicated for carotid endarterectomy or brachial artery repair without prosthetic material.

OTHER PROCEDURES —The small number of surgical site infections that would be prevented by antimicrobial prophylaxis make it unwarranted for cardiac catheterization, varicose vein surgery, most dermatologic and plastic surgery, arterial puncture, thoracentesis, paracentesis, repair of simple lacerations, outpatient treatment of burns, dental extractions or root canal therapy. The need for prophylaxis in breast surgery, herniorraphy and other "clean" surgical procedures has been controversial (SL Gorbach, Infect Dis Clin Pract 1999; 8:1; R Gupta et al, Eur J Surg Oncol 2000; 26:363). Medical Letter consultants generally do not recommend it because of the low rate of infection without prophylaxis in many hospitals, the low morbidity of these infections and the potential adverse effects of using prophylaxis in such a large number of patients.

CONTAMINATED ("DIRTY") SURGERY — "Dirty" surgery, such as that for a perforated abdominal viscus, a compound fracture or a laceration due to an animal or human bite, is often followed by infection. Use of antimicrobial drugs for these operations is considered therapy rather than prophylaxis and should be continued postoperatively for several days.

PATIENTS WITH PROSTHETIC JOINTS — Patients with prosthetic joints generally do not require antimicrobial prophylaxis when undergoing dental, gastrointestinal or genitourinary procedures (J Segreti, Infect Dis Clin North Am 1999; 13:871). For long procedures, surgery in an infected area (including periodontal disease) or other procedures with a high risk of bacteremia, and possibly for selected patients at high risk for infection, prophylaxis may be advisable (American Dental Association and American Academy of Orthopaedic Surgeons, J Am Dent Assoc 1997; 128:1).

PATIENTS WITH PENICILLIN ALLERGY — Cefazolin is often used for prophylaxis in penicillin-allergic patients, but such patients may also have allergic reactions to cephalosporins. When allergy prevents the use of a cephalosporin, vancomycin or clindamycin can be used but neither is effective against gram-negative bacteria; in such patients, some Medical Letter consultants would add another agent such as ciprofloxacin to cover gram-negative bacteria depending on the site of surgery and the procedure.

Nature of operation	Likely pathogens	Recommended drugs	Adult dosage before surgery[1]
Cardiac			
Prosthetic valve, coronary artery bypass, other open-heart surgery, pacemaker or defibrillator implant	*Staphylococcus aureus, S. epidermidis, Corynebacterium*, enteric gram-negative bacilli	cefazolin or cefuroxime *OR* vancomycin[3]	1-2 grams IV[2] 1.5 grams IV[2] 1 gram IV
Gastrointestinal			
Esophageal, gastroduodenal	Enteric gram-negative bacilli, gram-positive cocci	*High risk*[4] only: cefazolin[5]	1-2 grams IV
Biliary tract	Enteric gram-negative bacilli, enterococci, clostridia	*High risk*[6] *only:* cefazolin[5]	1-2 grams IV
Colorectal	Enteric gram-negative bacilli, anaerobes, enterococci	*Oral:* neomycin + erythromycin base[7]	
		Parenteral: cefoxitin or	1-2 grams IV
		cefotetan	1-2 grams IV
		OR cefazolin	1-2 grams IV
		+ metronidazole	0.5 grams IV
Appendectomy, non-perforated	Enteric gram-negative bacilli, anaerobes, enterococci	cefoxitin or cefotetan	1-2 grams IV 1-2 grams IV
Genitourinary	Enteric gram-negative bacilli, enterococci	*High risk*[8] *only:* ciprofloxacin	500 mg PO or 400 mg IV
Gynecologic and Obstetric			
Vaginal or abdominal hysterectomy	Enteric gram-negatives, anaerobes, Gp B strep, enterococci	cefazolin or cefotetan or cefoxitin	1-2 grams IV 1-2 grams IV 1 gram IV
Cesarean section	same as for hysterectomy	*High risk*[9] *only:* cefazolin	1 gram IV after cord clamping
Abortion	same as for hysterectomy	*First trimester, high risk*[10]:	
		aqueous penicillin G	2 mill units IV
		OR doxycycline	300 mg PO[11]
		Second trimester: cefazolin	1 gram IV
Head and Neck Surgery			
Incisions through oral or pharyngeal mucosa	Anaerobes, enteric gram-negative bacilli, *S. aureus*	clindamycin + gentamicin OR cefazolin	600-900 mg IV 1.5 mg/kg IV 1-2 grams IV
Neurosurgery			
Craniotomy	*S. aureus, S. epidermidis*	cefazolin *OR* vancomycin[3]	1-2 grams IV 1 gram IV
Ophthalmic	*S. epidermidis*, *S. aureus,* streptococci, enteric gram-negative bacilli, *Pseudomonas*	gentamicin, tobramycin, ciprofloxacin, ofloxacin or neomycin-gramicidin-polymyxin B	multiple drops topically over 2 to 24 hours
		cefazolin	100 mg subconjunctivally
Orthopedic			
Total joint replacement, internal fixation of fractures	*S. aureus, S. epidermidis*	cefazolin *OR* vancomycin[3]	1-2 grams IV 1 gram IV
Thoracic (Non-Cardiac)	*S. aureus, S. epidermidis*, streptococci, enteric gram-negative bacilli	cefazolin or cefuroxime *OR* vancomycin[3]	1-2 grams IV 1.5 grams IV 1 gram IV

(continued)

Nature of operation	Likely pathogens	Recommended drugs	Adult dosage before surgery[1]
Vascular			
Arterial surgery involving a prosthesis, the abdominal aorta, or a groin incision	*S. aureus, S. epidermidis,* enteric gram-negative bacilli	cefazolin *OR* vancomycin[3]	1-2 grams IV 1 gram IV
Lower extremity amputation for ischemia	*S. aureus, S. epidermidis,* enteric gram-negative bacilli, clostridia	cefazolin[5] *OR* vancomycin[3]	1-2 grams IV 1 gram IV
CONTAMINATED SURGERY[12]			
Ruptured viscus	Enteric gram-negative bacilli, anaerobes, enterococci	cefoxitin or cefotetan ± gentamicin *OR* clindamycin + gentamicin	1-2 g IV q6h 1-2 g IV q12h 1.5 mg/kg IV q8h 600 mg IV q6h 1.5 mg/kg IV q8h
Traumatic wound	*S. aureus,* Gp A strep, clostridia	cefazolin[13]	1-2 grams IV q8h

1. Parenteral prophylactic antimicrobials can be given as a single intravenous dose completed 30 minutes or less before the operation. For prolonged operations, additional intraoperative doses should be given q4-8h for the duration of the procedure.
2. Some consultants recommend an additional dose when patients are removed from bypass during open-heart surgery.
3. For hospitals in which methicillin-resistant *S. aureus* and *S. epidermidis* are a frequent cause of postoperative wound infection, or for patients allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even if the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine (*Benadryl*, and others) and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are likely pathogens, such as vascular surgery involving a groin incision, cefazolin or cefuroxime should be included in the prophylaxis regimen for patients not allergic to cephalosporins.
4. Morbid obesity, esophageal obstruction, decreased gastric acidity or gastrointestinal motility.
5. Some Medical Letter consultants favor cefoxitin for better anaerobic coverage in this setting.
6. Age >70 years, acute cholecystitis, non-functioning gall bladder, obstructive jaundice or common duct stones.
7. After appropriate diet and catharsis, one gram of each at 1 PM, 2 PM and 11 PM the day before an 8 AM operation.
8. Urine culture positive or unavailable, preoperative catheter, transrectal prostatic biopsy.
9. Active labor or premature rupture of membranes.
10. Patients with previous pelvic inflammatory disease, previous gonorrhea or multiple sex partners.
11. Divided into 100 mg one hour before the abortion and 200 mg one half hour after.
12. For contaminated or "dirty" surgery, therapy should usually be continued for about five days. Ruptured viscus in postoperative setting (dehiscence) requires antibacterials to include coverage of nosocomial pathogens.
13. For bite wounds, in which likely pathogens may also include oral anaerobes, *Eikenella corrodens* (human), or *Pasteurella multocida* (dog and cat), some Medical Letter consultants recommend use of amoxicillin/clavulanic acid *(Augmentin)* or ampicillin/sulbactam *(Unasyn)* (PF Smith et al, J Clin Pharm Ther 2000; 25:85). For penetrating intracranial wounds, including gunshot injuries, a broad-spectrum antimicrobial such as ampicillin/sulbactam is recommended (R Bayston et al, Lancet 2000; 355:1813).

PREVENTION OF BACTERIAL ENDOCARDITIS

Many physicians believe that antimicrobial prophylaxis before procedures that may cause transient bacteremia can prevent endocarditis in patients with valvular heart disease, prosthetic heart valves or other structural cardiac abnormalities. The effectiveness of this common practice has never been established by controlled trials in humans (G Hall et al, Clin Infect Dis 1999; 29:1). The drugs and dosages in the table are based on those recommended by the American Heart Association (AS Dajani et al, JAMA 1997; 277:1794).

ENDOCARDITIS PROPHYLAXIS[1]

	Dosage for Adults	Dosage for Children*
DENTAL AND UPPER RESPIRATORY PROCEDURES[2]		
Oral		
Amoxicillin[3] (*Amoxil*, and others)	2 grams 1 hour before procedure	50 mg/kg 1 hour before procedure
Penicillin allergy:		
Clindamycin (*Cleocin*, and others)	600 mg 1 hour before procedure	20 mg/kg 1 hour before procedure
OR		
Cephalexin** (*Keflex*, and others) or Cefadroxil** (*Duricef*, and others)	2 grams 1 hour before procedure	50 mg/kg 1 hour before procedure
OR		
Azithromycin *(Zithromax)* or Clarithromycin *(Biaxin)*	500 mg 1 hour before procedure	15 mg/kg 1 hour before procedure
Parenteral (for patients unable to take oral drugs)		
Ampicillin (*Omnipen*, and others)	2 grams IM or IV within 30 minutes before procedure	50 mg/kg IM or IV within 30 minutes before procedure
Penicillin allergy:		
Clindamycin	600 mg IV within 30 minutes before procedure	20 mg/kg IV within 30 minutes before procedure
OR		
Cefazolin** (*Ancef*, and others)	1 gram IM or IV within 30 minutes before procedure	25 mg/kg IM or IV within 30 minutes before procedure
GASTROINTESTINAL AND GENITOURINARY PROCEDURES[2]		
Oral		
Amoxicillin[3]	2 grams 1 hour before procedure	50 mg/kg 1 hour before procedure
Parenteral		
Ampicillin[4]	2 grams IM or IV within 30 minutes before procedure	50 mg/kg IM or IV within 30 minutes before procedure
± Gentamicin[5] (*Garamycin*, and others)	1.5 mg/kg (120 mg max.) IM or IV within 30 minutes before procedure	1.5 mg/kg IM or IV within 30 minutes before procedure
Penicillin allergy:		
Vancomycin (*Vancocin*, and others)	1 gram IV infused *slowly over 1 hour* beginning 1 hour before procedure	20 mg/kg IV infused *slowly over 1 hour* beginning 1 hour before procedure
± Gentamicin[5]	1.5 mg/kg (120 mg max.) IM or IV within 30 minutes before procedure	1.5 mg/kg IM or IV within 30 minutes before procedure

* Should not exceed adult dosage

** Not recommended for patients with history of recent, severe or immediate-type (urticaria, angioedema, anaphylaxis) allergy to penicillin.

1. The risk of endocarditis is considered high in patients with previous endocarditis, prosthetic heart valves, complex cyanotic congenital heart disease such as tetralogy of Fallot, or surgically constructed systemic pulmonary shunts or conduits. The risk is also considered worth treating in patients with other forms of congenital heart disease (but not uncomplicated secundum atrial septal defect), acquired (such as rheumatic) valvular disease, hypertrophic cardiomyopathy, and mitral valve prolapse with regurgitation or thickened leaflets. Viridans streptococci are the most common cause of endocarditis after dental or upper respiratory procedures; enterococci are the most common cause after gastrointestinal or genitourinary procedures.
2. For a review of the risk of bacteremia with various procedures, see AS Dajani et al, JAMA 1997; 277:1794. Among dental procedures, some experts believe that tooth extractions and gingival surgery, including implant placement, have the highest risk of endocarditis (DT Durack, Ann Intern Med 1998; 129:829).
3. Amoxicillin is recommended because of its excellent bioavailability and good activity against streptococci and enterococci.
4. High-risk patients given parenteral ampicillin before the procedure should receive a dose of ampicillin 1 gram IM or IV or a dose of amoxicillin 1 gram orally six hours afterwards.
5. Gentamicin should be added for patients with a high risk of endocarditis (see footnote 1).

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