

The Medical Letter®

On Drugs and Therapeutics

www.medletter.com

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, N.Y. 10801 • A Nonprofit Publication

Vol. 43 (Issue 1116-1117)
October 29, 2001

Also in this issue:
Antimicrobial Prophylaxis
in Surgery..... Page 92
Prevention of Endocarditis ... Page 98

POST-EXPOSURE ANTHRAX PROPHYLAXIS

The Medical Letter article on Drugs and Vaccines against Biological Weapons, published in the previous issue (October 15, 2001, page 87), included a brief discussion of post-exposure prophylaxis of inhalation anthrax. Recent events call for more detail.

ANTIMICROBIAL SUSCEPTIBILITY — Naturally-occurring *Bacillus anthracis* is generally susceptible *in vitro* to many antibiotics, including penicillin G, amoxicillin, doxycycline and other tetracyclines, erythromycin, clarithromycin (*Biaxin*), azithromycin (*Zithromax*), clindamycin, chloramphenicol and the fluoroquinolones. It is not susceptible to aztreonam (*Azactam*), trimethoprim-sulfamethoxazole (*Bactrim*; *Septra*, others) or third-generation cephalosporins (TV Inglesby et al, JAMA 1999; 281:1735). Naturally occurring resistance to penicillin has been reported rarely. The only report of resistance to tetracyclines was in a strain (also resistant to penicillin) altered by genetic engineering for use in a new anthrax vaccine (AV Stepanov et al, J Biotechnol 1996; 44:155). Resistance to fluoroquinolones has not been reported. All recent clinical isolates in the US have been susceptible to ciprofloxacin, tetracyclines, including doxycycline, and penicillins, including amoxicillin. Penicillinase production may be inducible in these organisms; that could lead to development of resistance during treatment of an infection, but should not be a problem in prophylaxis.

POST-EXPOSURE PROPHYLAXIS — Ciprofloxacin was approved by the FDA last year for post-exposure prophylaxis of inhalation anthrax. Penicillin and doxycycline were previously approved for treatment of anthrax. The evidence that these drugs are effective for post-exposure prophylaxis comes mainly from a study in 60 Rhesus monkeys exposed to an inhaled dose of 4×10^5 anthrax spores (about 8 times the LD_{50}), treated for 30 days with an antibiotic, placebo and/or 2 doses of anthrax vaccine, and then observed. Death due to anthrax occurred in 9 of 10 monkeys treated with saline, 8 of 10 given only anthrax vaccine on days 1 and 15, 3 of 10 treated with procaine penicillin G, 1 of 9 treated with ciprofloxacin, 1 of 10 treated with doxycycline, and 0 of 9 given both doxycycline and vaccine. All of the deaths in antibiotic-treated monkeys occurred after discontinuation of the drugs. The last death occurred 58 days after exposure (AM Friedlander et al, J Infect Dis 1993; 167:1239).

DURATION — If exposure to *B. anthracis* is confirmed and anthrax vaccine is available, 3 doses of the vaccine should be given at 0, 2 and 4 weeks, and antibiotics should be continued throughout the 4-week period. If vaccine is not available, antibiotics should be continued for 60 days.

EDITOR: Mark Abramowicz, M.D. DEPUTY EDITOR: Gianna Zuccotti, M.D., M.P.H., Weill Medical College of Cornell University
CONSULTING EDITOR: Martin A. Rizack, M.D., Ph.D., Rockefeller University ASSOCIATE EDITORS: Donna Goodstein, Amy Faucard ASSISTANT EDITOR: Susie Wong
CONTRIBUTING EDITORS: Philip D. Hansten, Pharm. D., University of Washington; Neal H. Steigbigel, M.D., Albert Einstein College of Medicine
ADVISORY BOARD: William T. Beaver, M.D., Georgetown University School of Medicine; Jules Hirsch, M.D., Rockefeller University; James D. Kenney, M.D., Yale University School of Medicine; Gerhard Levy, Pharm.D., State University of N.Y. at Buffalo; Gerald L. Mandell, M.D., University of Virginia School of Medicine; Hans Meinertz, M.D., University Hospital, Copenhagen; Dan M. Roden, M.D., Vanderbilt School of Medicine; F. Estelle R. Simons, M.D., University of Manitoba
EDITORIAL FELLOWS: Elizabeth Stephens, M.D., Oregon Health Sciences University School of Medicine; Arthur M.F. Yee, M.D., Ph.D., Cornell Medical University Medical Center
EDITORIAL ADMINISTRATOR: Marianne Aschenbrenner PUBLISHER: Doris Peter, Ph.D.
Founded 1959 by Arthur Kallet and Harold Aaron, M.D. Copyright © 2001. The Medical Letter, Inc. (ISSN 1523-2859)

POST-EXPOSURE ORAL ANTIBIOTIC PROPHYLAXIS AGAINST *BACILLUS ANTHRACIS*

Drug	Adults	Children
Oral fluoroquinolones		
Ciprofloxacin (<i>Cipro</i>) ¹	500 mg b.i.d.	10-15 mg/kg b.i.d. ²
Oral tetracyclines ³		
Doxycycline (<i>Vibramycin</i> , others) ⁴	100 mg b.i.d.	2.2 mg/kg b.i.d. ²
Oral penicillins ^{3,5}		
Amoxicillin (<i>Amoxil</i> , others) ⁶	500 mg t.i.d.	80 mg/kg/day divided into 3 doses

1. Other fluoroquinolones such as ofloxacin (*Floxin*) 400 mg b.i.d. or levofloxacin (*Levaquin*) 500 mg once daily may also be effective.
2. Should be changed to amoxicillin as soon as susceptibility to penicillin has been confirmed.
3. Susceptible strains.
4. Tetracycline 500 mg q.i.d. should also be effective.
5. Penicillin resistance could emerge during treatment, but should not be a problem in prophylaxis.
6. Penicillin VK 7.5 mg/kg q.i.d. in adults, or 12.5 mg/kg q.i.d. in children, should also be effective for prophylaxis.

ADVERSE EFFECTS — Taken for 30 or 60 days, all of these drugs are likely to cause some adverse effects (*The Medical Letter Handbook of Antimicrobial Therapy* 2000; page 146). The most frequent adverse effects of fluoroquinolones are nausea, vomiting, abdominal pain, dizziness, headache, tremors, restlessness and confusion. Rarely they can cause psychosis and rupture of the Achilles tendon. Tetracyclines, including doxycycline, frequently cause gastrointestinal disturbances. Amoxicillin can cause diarrhea. Penicillin VK would probably be the best tolerated of these drugs for a 30- or 60-day course.

Children and Pregnancy — Doxycycline and other tetracyclines can cause staining and deformity of teeth in children up to 8 years old, and in the newborn when given to pregnant women after the fourth month of pregnancy. Ciprofloxacin and other fluoroquinolones have caused permanent cartilage damage and arthropathy in immature animals. Ciprofloxacin-associated arthropathy has been infrequent when the drug was used in children with cystic fibrosis (RW Warren, *Pediatr Infect Dis* 1997; 16:118).

PRE-EXPOSURE VACCINATION — In several studies, a total of 52 of 55 monkeys previously given 2 doses of anthrax vaccine survived a lethal aerosol challenge without antibiotics (AM Friedlander et al, *JAMA* 1999; 282:2104).

CONCLUSION — If the organism is susceptible, there is no evidence that ciprofloxacin is more effective than doxycycline or a penicillin for post-exposure prophylaxis of anthrax. Vaccination, if the vaccine were available, plus an antibiotic might be the most effective regimen.

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, ceftioxin (*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 ceftioxin) 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 H₂-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 ceftioxin 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 non-functioning 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, herniorrhaphy 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 or anaerobes depending on the site of surgery and the procedure.

PREVENTION OF WOUND INFECTION AND SEPSIS IN SURGICAL PATIENTS

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	<i>Staphylococcus aureus</i> , <i>S. epidermidis</i> , <i>Corynebacterium</i> , 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	<i>High risk</i> ⁴ only: cefazolin ⁵	1-2 grams IV
Biliary tract	Enteric gram-negative bacilli, enterococci, clostridia	<i>High risk</i> ⁶ only: cefazolin ⁵	1-2 grams IV
Colorectal	Enteric gram-negative bacilli, anaerobes, enterococci	<i>Oral</i> : neomycin + erythromycin base ⁷ <i>Parenteral</i> : cefoxitin or cefotetan OR cefazolin + metronidazole	1-2 grams IV 1-2 grams IV 1-2 grams IV 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	<i>High risk</i> 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	<i>High risk</i> ⁹ only: cefazolin	1 gram IV after cord clamping
Abortion	same as for hysterectomy	<i>First trimester, high risk</i> ¹⁰ : aqueous penicillin G OR doxycycline <i>Second trimester</i> : cefazolin	2 mill units IV 300 mg PO ¹¹ 1 gram IV
Head and Neck Surgery			
Incisions through oral or pharyngeal mucosa	Anaerobes, enteric gram-negative bacilli, <i>S. aureus</i>	clindamycin + gentamicin OR cefazolin	600-900 mg IV 1.5 mg/kg IV 1-2 grams IV
Neurosurgery			
Craniotomy	<i>S. aureus</i> , <i>S. epidermidis</i>	cefazolin OR vancomycin ³	1-2 grams IV 1 gram IV

Nature of operation	Likely pathogens	Recommended drugs	Adult dosage before surgery ¹
Ophthalmic	<i>S. epidermidis</i> , <i>S. aureus</i> , streptococci, enteric gram-negative bacilli, <i>Pseudomonas</i>	gentamicin, tobramycin, ciprofloxacin, ofloxacin or neomycin-gramicidin-polymyxin B cefazolin	multiple drops topically over 2 to 24 hours 100 mg subconjunctivally
Orthopedic Total joint replacement, internal fixation of fractures	<i>S. aureus</i> , <i>S. epidermidis</i>	cefazolin OR vancomycin ³	1-2 grams IV 1 gram IV
Thoracic (Non-Cardiac)	<i>S. aureus</i> , <i>S. epidermidis</i> , streptococci, enteric gram-negative bacilli	cefazolin or cefuroxime OR vancomycin ³	1-2 grams IV 1.5 grams IV 1 gram IV
Vascular Arterial surgery involving a prosthesis, the abdominal aorta, or a groin incision	<i>S. aureus</i> , <i>S. epidermidis</i> , enteric gram-negative bacilli	cefazolin OR vancomycin ³	1-2 grams IV 1 gram IV
Lower extremity amputation for ischemia	<i>S. aureus</i> , <i>S. epidermidis</i> , enteric gram-negative bacilli, clostridia	cefazolin ⁵ OR vancomycin ³	1-2 grams IV 1 gram IV
CONTAMINATED SURGERY¹²			
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	<i>S. aureus</i> , 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 PROPHYLAXIS¹

	Dosage for Adults	Dosage for Children*
DENTAL AND UPPER RESPIRATORY PROCEDURES²		
Oral		
Amoxicillin ³ (<i>Amoxil</i> , and others)	2 grams 1 hour before procedure	50 mg/kg 1 hour before procedure
Penicillin allergy:		
Clindamycin (<i>Cleocin</i> , and others)	600 mg 1 hour before procedure	20 mg/kg 1 hour before procedure
OR		
Cephalexin** (<i>Keflex</i> , and others) or Cefadroxil** (<i>Duricef</i> , and others)	2 grams 1 hour before procedure	50 mg/kg 1 hour before procedure
OR		
Azithromycin (<i>Zithromax</i>) or Clarithromycin (<i>Biaxin</i>)	500 mg 1 hour before procedure	15 mg/kg 1 hour before procedure
Parenteral (for patients unable to take oral drugs)		
Ampicillin (<i>Omnipen</i> , 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** (<i>Ancef</i> , 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 PROCEDURES²		
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 (<i>Garamycin</i> , 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 (<i>Vancocin</i> , and others)	1 gram IV infused <i>slowly over 1 hour</i> beginning 1 hour before procedure	20 mg/kg IV infused <i>slowly over 1 hour</i> 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.

- 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.
- 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).
- Amoxicillin is recommended because of its excellent bioavailability and good activity against streptococci and enterococci.
- 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.
- Gentamicin should be added for patients with a high risk of endocarditis (see footnote 1).

THE MEDICAL LETTER® (ISSN 1523-2859) is published and printed in the USA bi-weekly by The Medical Letter, Inc., a non-profit corporation. Second-class postage paid at New Rochelle, NY, and at additional mailing offices. POSTMASTER: Send address changes to THE MEDICAL LETTER at 1000 Main Street, New Rochelle, NY 10801-7537. Subscription fees: 1 year, \$55.00; 2 years, \$94.00; 3 years, \$132.00 (\$27.50—U.S. Funds—per year for individual subscriptions to students, interns, residents, and fellows in the USA and Canada; special fees for bulk orders). Major credit cards accepted. Copyright and Disclaimer: Subscriptions are accepted with the understanding that no part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The editors and publisher do not warrant that all the material in this publication is accurate and complete in every respect. The editors and publisher shall not be held responsible for any damage resulting from any error, inaccuracy or omission.

Phone: 1-800-211-2769 Fax: 1-914-632-1733 WEB SITE: <http://www.medletter.com>