Chapter 28B - Prophylactic Antibiotics

Prophylactic antibiotics are defined as **antibiotics used to prevent infection.** Approximately one-third of hospitalized patients receive antibiotics and, of these, one-half

receive prophylactic antibiotics, primarily for surgical procedures. Although early studies in the 1950s and 1960s concluded that prophylaxis was not helpful, many of these studies were poorly done, and the basic principles of appropriate prophylactic antibiotic use were not understood. In reality, patients often were given therapeutic antibiotics; that is, the infection had already occurred. Since these early studies, **data have shown clearly that prophylactic antibiotics are useful in certain circumstances.**

Wound infections are the second or third most common nosocomial infections among all hospitalized patients. In many settings, appropriate prophylactic use of antimicrobial agents often can reduce the incidence of postoperative wound infections [1] . For some procedures, prophylaxis is not suggested and, in several situations, further studies will be needed to determine their usefulness clearly [1] [2] [3] [4] [5] [6] [7] [8] .

I. **Basic principles of surgical prophylaxis.** Animal model studies as well as clinical studies have established some basic guidelines for surgical antibiotic prophylaxis.
   A. **Timing of antibiotic administration**
      1. **Theory and animal studies.** Animal studies by Burke [9] and others [5] in the late 1950s and early 1960s showed that administration of antibiotics just before, during, and up to 3 hours after surgery effectively prevented infections in wounds experimentally inoculated with bacteria. This was called the **effective period of preventive antibiotic action or the "decisive period"** [5] [9] . The use of antibiotics for a brief period after this effective time period did not prevent wound infection [9] . These experimental studies provided the data on which the timing of prophylactic antibiotics is based. Many clinical studies have been performed that support this principle [1] [2] [3] [4] [5] [6] [7] [8] . A large, recent clinical study of patients receiving prophylactic antibiotics confirms that prophylactic antibiotics are most effective when given 0-2 hours before surgery. Beginning an antibiotic regimen 2-24 hours before surgery is not required or useful. In addition, if antibiotic administration begins more than 3

hours after the surgical incision, the prophylactic regimen is not effective [10] .

2. **Clinical application.** For surgical antibiotic prophylaxis to be successful, the **antibiotic must be given so that good tissue levels are present at the time of the procedure and for the first 3-4 hours after the surgical incision** [1] [2] [5] [9] [10] [11] [12] . There is neither need nor reason to start prophylactic antibiotics days in advance.
3. **Recommended timing.** Recent reviews [1] [4] [6A] suggest administering the parenteral antibiotic **30-60 minutes before the surgical incision is made** (i.e., with the induction of anesthesia). **For cesarean section,** antimicrobial prophylaxis should be delayed until the umbilical cord is clamped and then should be initiated immediately [1] .

B. **Duration of prophylaxis.** This **remains a controversial** issue and an important one in terms of the cost of prophylaxis [1] [2] [3] [4] [5] [6A] . **The optimal duration of perioperative antimicrobial prophylaxis is not known** [1] . Burke [11] has emphasized that since "the effective period lasts no longer than three hours after bacterial contamination of tissue and since bacterial contamination in most surgical procedures ends when the wound is closed, **there is little evidence to support prophylactic administration of antibiotics past the period of operation and recovery of normal physiology following anesthesia.**" Clinical studies by Stone and colleagues [12] and others [4] [6A] [12] [13] also support this approach.

1. **Practical approach. For many surgical procedures, a single dose of antibiotic given just before the procedure provides adequate tissue levels** [4] [13] , especially in **biliary tract** surgery, **hysterectomies,** and **gastric** operations. Some authors suggest that, in addition, two postoperative doses are reasonable [2] . Most experts recommend that antimicrobial prophylaxis should certainly be discontinued within 24 hours of the operative procedure [1] .
   In prophylaxis for nonperforated appendectomy and colorectal surgery, up to 24 hours of prophylaxis often is recommended [2] [13] . In addition, when a prosthetic device is inserted, prophylaxis often is continued beyond one dose [14] . The optimal duration of prophylaxis in open heart surgery [1] and neurosurgery awaits further study [2] [3] . Many experts believe the continuation of prophylaxis until all catheters and drains have been removed is not appropriate [1] . Data are not available to resolve this issue clearly, and largescale studies are needed [2] .
2. **Prolonged procedures.** If a procedure lasts for several hours, repeat doses of the antibiotic may be necessary intraoperatively to maintain adequate and

constant blood and tissue levels [1] . This is particularly important as the period of highest risk for bacterial contamination is most likely the close, not the beginning, of surgery [2] . In prolonged procedures, cefoxitin (with a short half-life) should be readministered every 2 hours until the wound is closed. Whether a similar cephalosporin, cefotetan, which has a longer half-life, is a better agent to use in colorectal surgery awaits further clinical experience with this agent (see Chap. 28F) . When an agent with a longer half-life is used (e.g., **cefazolin), readministration is suggested every 4 hours** [1] . Common regimens are described in sec. **V.B.** See Table 28B-1 (Table Not Available) .

3. **Prosthetic devices.** When a prosthetic device is inserted, prophylaxis often is given for 24-48 hours [3] , although whether these patients need prolonged therapy is unclear. Some sources suggest single doses for prosthetic device surgery or an additional dose when patients are removed from bypass during open heart surgery [4] . Norden and coworkers [14] do not favor single-dose prophylaxis in prosthetic joint surgery, but short courses--regimens spanning 24 hours or less--are favored. Others also favor a three-dose regimen [2] [6] , which is generally what we prefer.

II. **Which procedures benefit from prophylaxis?** In general, when a prosthesis is not involved, prophylaxis is not indicated for low-risk "clean" procedures.

A. **Agents are used when the inoculum of bacteria is high,** as in colonic surgery, surgery of the vagina, or infected biliary procedures **or** where the **insertion of an artificial device** (e.g., heart valve, total hip) reduces the inoculum required to cause infection, and when an infection may be catastrophic or may require repeat surgery.

B. **Clinical studies now support the use of prophylactic agents** in many settings and are reviewed in detail elsewhere [1] [2] [3] [4] [5] [6] [7] [8] [13] [15] . Some examples include the following:

1. **Biliary tract surgery.** Clinical studies suggest that **surgical antibiotic prophylaxis is indicated for the high-risk group** but not for uncomplicated cholecystectomies in patients younger than 60 years. The biliary tract is normally sterile, with only a low rate of colonization when elective operations for stone-related disease are undertaken in young patients [1] . **High-risk** patients include those (1) older than 60 years of age [1] , (2) with obstructive jaundice, (3) with acute cholecystitis or cholangitis, (4) with common duct stones [1] [4] , (5) a nonfunctioning gallbladder [4] , and (6) those who have undergone previous biliary surgery [1] . Prophylactic antibiotics decreased the infection rate from approximately 25% in controls to 5%. The role of prophylactic antibiotics in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) is discussed in sec. **VI.P.**
2. **Gynecologic surgery.** Local antibiotic irrigation has been used in some settings (e.g., prophylaxis of cesarean section [2]) but is not recommended [1] [3] [4] [16] . The role of prophylactic antibiotics in gynecologic and obstetric surgery has been summarized [16] .

a. **Hysterectomy.** Prophylaxis is beneficial in vaginal and possibly in abdominal hysterectomies [3] [4] [8] [16] . Antibiotics selected do not have to be

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active against all pelvic or vaginal organisms. First-generation cephalosporins (e.g., cefazolin) appear to be as effective as second- and third-generation cephalosporins [3] . In the cephalosporin-allergic patients, doxycycline, 200 mg IV (one dose) preoperatively, has been suggested [2] . Some authors favor oral doxycycline use in the cephalosporin-allergic patient: doxycycline, 100 mg PO at bedtime, and another identical dose orally 3-4 hours before the scheduled procedure. Clindamycin, 900 mg IV preoperatively, has also been proposed [16] .

b. **Cesarean sections.** Sections carried out in high-risk patients (e.g., those with premature rupture of membranes or emergency surgery) are associated with a lower rate of postoperative infection when prophylactic antibiotics are used. In this setting, an early infection may already have been established. A first-generation cephalosporin (cefazolin) can be given after the cord is clamped to avoid exposing the infant to the drug [3] [4] [16] . Alternative regimens in the patient truly allergic to cephalosporins have not been studied [16] . One source suggests that metronidazole, 500 mg IV, after clamping the cord is effective [2] .

c. **Therapeutic abortion.** Preoperative antibiotics can prevent infections after first-trimester abortion in women with previous pelvic inflammatory disease and after mid-trimester abortion [4] [16] .

3. **Orthopedics** [4] [6] [15] [17] [18]

a. **Open fractures**

(1) For **simple open fractures,** a first-generation cephalosporin (e.g., cefazolin) is recommended for 18-24 hours [2] [17] [18] .

(2) For more complex open fractures requiring extensive debridement of environmental contaminants or insertion of a prosthetic device, therapeutic courses of antibiotics are recommended (e.g., for 10 days) [2] . (Although cefazolin is suggested in this setting [2] , we have sometimes used ceftriaxone to ensure adequate activity against community-acquired gram-negative bacilli, which can be contaminants of the wound.)

b. **Closed fracture.** The role of antibiotics in this setting is unclear and awaits further clinical study. Norden and colleagues [17] recommended that prophylaxis started

immediately before surgery and lasting 12-18 hours should be offered to all patients with closed fractures undergoing operative fixation [17] while awaiting definitive studies.

c. **Total joint replacement.** Antibiotic prophylaxis reduces the frequency of deep wound infection following total joint replacement [18] . Systemic antibiotic **prophylaxis is recommended** because the consequences of infection are so serious and prophylaxis is beneficial (e.g., short courses of cefazolin). In his review, Norden concluded that antibiotic-impregnated cement alone is effective in the prophylaxis of deep infection after joint replacement. In a recent report of a 10-year follow-up of more than 1,500 consecutive total hip arthroplasties, the incidence of deep infections in those patients who received systemic antibiotics versus gentamicin bone cement was not significantly different (1.6% versus 1.1%). The authors conclude that it would be beneficial to combine the use of systemic antibiotics and antibiotic-containing bone cement to decrease further the rate of deep infections, especially in those departments without an ultraclean-air environment [19] . However, the value of using both techniques over either alone has not been established.
The role of ultraclean-air systems is controversial and has been reviewed by Norden and associates [14] . In summary, he emphasizes that ultraclean-air systems do offer protection against infection in total joint replacement, but that the benefit probably is small when antibiotic prophylaxis also is used [15] .
Operating rooms with ultraclean air help reduce wound infections, but these systems are expensive.

d. **Other orthopedic procedures**
(1) Antibiotic prophylaxis decreases postoperative wound infection when hip and other fractures are treated with **internal fixation by nails, plates, screws, or wires** [4] [20] .
(2) Whether antibiotic prophylaxis should be used for other orthopedic procedures (i.e., with no prosthetic device insertion) is unclear. However,

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there are data suggesting prophylaxis significantly reduced the frequency of infections in those **operations lasting longer than 2 hours** [20] .

e. **Prophylaxis against hematogenous infection after total joint replacement.** Whether patients with indwelling prosthetic joints need antibiotic prophylaxis when undergoing dental, gastrointestinal, or genitourinary

procedures is controversial [6] [14] . However, recent reviews of the data suggest antibiotics usually add little except expense [4] [6A] [20A] [20B] .

Some experimental evidence indicates a high risk of infection of joint implants during bacteremia in a rabbit model, especially in the postoperative period [20] . We emphasize the following:

(1) Proper antibiotic therapy of focal infections is important (to prevent bacteremia), especially urinary tract and skin infections [15] [20] .

(2) Prosthetic joint infections can occur after systemic bacteremias with gram-negative bacilli (e.g., *E. coli*) or staphylococci (e.g., *S. aureus*) especially early in the postoperative period [14] , but there are few data to support joint seeding and subsequent prosthetic joint infection after dental procedures [20A] [20B] . See sec. **(3).** If a surgical procedure with a significant risk of bacteremia (see sec. **VI.C.2**) is indicated, in general, we do not use prophylactic antibiotics unless the prosthesis has only recently been inserted (e.g., within the preceding 8-12 weeks) or dental work has been performed as described in sec. **(3).**

(3) Dental work. Some orthopedic surgeons will use prophylaxis for dental procedures in patients with major joint arthroplasties even though there is no proof that antibiotics are needed in this setting [14] [21] . However, prosthetic joint infection with the type of organism (e.g., viridans streptococci) that commonly causes subacute bacterial endocarditis is a rare event, implying the absence of risk [20A] [20B] .

Norden and colleagues [14] argue, as have others, that using available data and reasonable assumptions, routine dental prophylaxis may be unnecessary and may be associated with an unacceptable level of antibiotic-induced adverse effects if penicillins are used. Modeling indicates cost-effectiveness of administration of erythromycin or cephalexin for higher-risk patients, but there is a paucity of data to confirm these predictions. In the presence of overt or imminent dental sepsis or in immunocompromised patients, prophylaxis is strongly recommended by some against the probable or proven oral pathogen [14] until more data become available.

In their review, Hass and Kaiser [6] agree with the Working Party of the British Society for Antimicrobial Chemotherapy that more information is needed before the routine use of prophylactic antibiotics can be recommended for all patients with prosthetic joints who undergo procedures known to produce transient bacteremia [22] . Providing antibiotic prophylaxis for selected patients with prosthetic joints and particularly

severe periodontal disease, however, may be reasonable, pending more data [6] .

(4) Therefore, recent reviewers emphasize that most patients with indwelling prosthetic joints generally do not require antimicrobial prophylaxis when undergoing dental, gastrointestinal, or genitourinary procedures [4] [6A] [20A] [20B] . For long procedures, surgery in an infected area (including periodontal disease), or other procedures with a high risk of bacteremia, prophylaxis may be advisable [4] .

4. **Gastrointestinal surgery**
   a. **Elective colorectal surgery.** Preoperative antibiotics have been shown to reduce the incidence of postoperative infections [1] [2] [4] [6A] [23] . **Oral antibiotics,** which are poorly absorbed, have been given to reduce colony counts of resident colonic flora. **Parenteral antibiotics** have also been used perioperatively with success. In emergent bowel surgery, parenteral antibiotics are used alone, as time does not allow the use of the oral regimen. Whether oral and parenteral regimens together are better than oral alone remains to be determined [1] [4] . The most common practice in the United States is oral antibiotic administration along with mechanical bowel cleansing the evening before the operation and parenteral antibiotic administration in the operating room just before incision [1] .

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(1) Oral. A common oral regimen consists of an initial mechanical bowel preparation *and* neomycin sulfate (1 g) and erythromycin base (1 g) orally at 1 PM, 2 PM, and 11 PM, on the day prior to abdominal surgery [4] . The details of this oral regimen and the mechanical bowel preparation used with it are reviewed by Nichols [23] .

(2) Parenteral. Data support the use of antimicrobial agents that are effective against both anaerobic and aerobic bowel organisms [4] [24] . **Cefoxitin** is an **appealing** agent in this setting, compared with the first-generation cephalosporins, because cefoxitin has greater activity against bowel anaerobes, including *Bacteroides fragilis* [2] [4] . A limited study suggested that cefoxitin (2 g q6h for 24 hours) was superior to cefazolin (1 g q8h for 24 hours) [15] , although prior data had not shown any clear advantages of cefoxitin in this setting [25] . It is hoped that further studies will clarify this issue. Cefotetan, which has similar activity to cefoxitin but a longer half-life than cefoxitin or cefmetazole, has been used effectively in colorectal surgery and is another option [4] . See sec.

V.B.4. Cefmetazole is another possible agent. (See Chap. 28F.) For other abdominal and pelvic procedures, including obstetric and gynecologic operations, cefazolin has been equally effective [4] and is less expensive compared to cefoxitin or cefotetan.
A combination of metronidazole and ceftriaxone has been shown to be effective in colorectal surgery [26] . Although metronidazole has been used extensively in the United Kingdom for prophylaxis, because of its potential carcinogenic risk (see Chap. 28P) , it is not commonly recommended for prophylaxis in the United States [4] except as an alternate agent--for example, in a patient allergic to cephalosporins [2] . Furthermore, **the third-generation cephalosporins are not recommended for prophylaxis**: They are expensive, their activity against staphylococci often is less than cefazolin, their spectrum of activity against facultative gram-negative bacilli includes organisms rarely encountered in elective surgery, and their widespread use for prophylaxis promotes emergence of resistance to these potentially valuable drugs [4] .

b. **Nonelective colorectal surgery.** In emergency surgery (e.g., for intestinal obstruction), there is no time to use the oral antibiotics plus mechanical bowel preparations. Therefore, a parenteral cephalosporin is advised. Cefoxitin and cefotetan have been commonly used (see sec. **4.a.(2)** and Chap. 28F). Cefmetazole is another option (see Chap. 28F) , but it has a relatively short half-life, as does cefoxitin.
The third-generation cephalosporins are not recommended in this setting, as discussed in sec. **a.** If the operation reveals a bowel perforation, a full therapeutic course of antibiotics will be necessary.

c. **Gastroduodenal surgery.** Compared with lower GI surgery, upper GI surgery has a lower rate of infection because of the lower titer of bacterial flora in the upper GI tract. Ordinarily, patients undergoing surgery for uncomplicated duodenal ulcer require no prophylaxis [8] ; in this situation, the highly acidic environment results in a very low endogenous bacterial density and, thus, rates of postoperative infection are low [1] . However **patients at high risk for infection may benefit from prophylaxis** [1] [3] [4] [8] . Included in this group are patients with diminished gastric motility or acidity (secondary to bleeding or obstructing duodenal ulcer, gastric ulcer, or gastric malignancy), or patients who have received effective acidreducing therapy, whether medical (H_2 -blockers such as ranitidine, or proton-pump inhibitors such as omeprazole [Prilosec]) or surgical. The risk of infection is

also high in patients with morbid obesity [4] . In general, cefazolin is used in this setting [4] . Prophylactic cefazolin can also decrease infectious complications after gastric bypass surgery for obesity or percutaneous endoscopic gastrostomy [4] .

d. **Appendectomy.** Preoperative antibiotics can decrease the incidence of infection following appendectomy [4] . Cefoxitin for one [4] to three doses [2] is commonly used. Cefotetan is another possibility. A perforated or gangrenous appendix requires full therapeutic regimens (see Chap. 11) .

5. **Urologic procedures**

a. **If the urine is infected,** it is preferable to sterilize it before beginning an

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elective procedure on the genitourinary tract. If that is not possible, then antimicrobial therapy targeting the responsible pathogens should be initiated before the procedure and continued until the urinary tract infection has resolved [1] [4] .

b. **If the urine is sterile,** the role of antibiotics remains controversial.
(1) Infectious disease experts do not recommend antimicrobials before urologic operations in patients with sterile urine [2] [4] . If the urine is sterile and the urologic procedure does not involve entry into the intestine, this is considered a clean procedure [1] .
(2) A wide majority of urologists in the United States believe that there is a role for prophylactic antibiotics in transurethral surgery even if the preoperative urine culture is sterile [27] . This belief is based on data indicating that postsurgical bacteriuria develops in many patients who had sterile urines preoperatively. Perhaps the prostate tissue itself may harbor urinary pathogens [28] [29] . See additional related discussion in Chap. 28S .
(3) In general, we discourage the use of prophylactic antibiotics if the urine is sterile. At most, a single preoperative dose is suggested. Because of the lack of agreement about the value of prophylactic antibiotics for transurethral procedures, adhering to local practice may be reasonable in this setting [1] .

6. **Head and neck operations**

a. **Prophylaxis decreases the incidence of wound infection after head and neck operations that involve an incision through the oral or pharyngeal mucosa** [2] [3] [4] [30] **, especially for cancer of the head and neck** [30] .

Various regimens have been used typically for 24 hours: cefazolin, clindamycin, and gentamicin or ampicillin-sulbactam [2] . Even with antibiotic prophylaxis, when cancer patients undergo major head and neck surgery, significant postoperative wound infections may occur, in part due to the extensive excision and reconstruction in these debilitated patients [31] .

b. Infection rates in uncontaminated head and neck surgery (i.e., surgery in which there is no contamination with saliva--parotidectomy, thyroidectomy, rhinoplasty, myringoplasty, or tonsillectomy) are too low to justify prophylaxis [2] [3] . The role of antibiotic prophylaxis in surgery of the chronically draining ear and tonsillectomy awaits further study [30] . Gentamicin eardrops may decrease the incidence of purulent otorrhea after placement of a tympanostomy tube [4] . Prophylaxis for cochlear implant surgery has not been studied in controlled trials. Because of the devastating effect of cochlear implant infection, workers in the field recommend the use of strict aseptic techniques and prophylaxis with antibiotics active against staphylococci [3] .

7. **Neurosurgery.** The **role** of prophylactic antibiotics in neurosurgery remains **unsettled.** In a recent review, Brown [32] emphasized that based on clinical studies, there are no unequivocal indications for the use of prophylactic antibiotics in neurosurgery.

   a. The effectiveness of prophylaxis in decreasing the incidence of infection has not been clearly established in cerebrospinal fluid **(CSF) shunt implantation,** with studies showing conflicting results [4] [30] [32] . This is in part because large enough studies have not been conducted [30] . While awaiting these data, it is reasonable to use prophylaxis in shunt surgery when the endemic rate of infection is higher than 3% [30] . Other reviews suggest prophylaxis if endemic rates of infection exceed 5% [33] . Some authors [3] suggest that no antibiotic prophylaxis is needed in institutions with low shunt infection rates (< 10%). Consideration should be given to intravenous trimethoprim-sulfamethoxazole (TMP-SMX) perioperatively in institutions with high shunt infection rates (> 20%) [2] .

   b. The role of antibiotic prophylaxis in other types of neurosurgery is likewise unclear [30] .
   (1) Antistaphylococcal antibiotics may decrease the incidence of wound infections after craniotomies [4] and are reasonable in this setting [33A] .
   (2) Some reviewers believe the data may favor use of prophylaxis in clean and clean-contaminated neurosurgery and favor antibiotic prophylaxis [30] .

(3) The literature does not support the use of antibiotic prophylaxis in patients with a closed skull fracture, with or without CSF leakage [3] . There are no controlled trials of antibiotic use in patients with open skull fractures. Because these types of injuries are culture-positive at the time of presentation, antibiotic use should be considered to be therapeutic rather than prophylactic. The optimal antibiotic regimen for these patients is undefined [3] .
(4) In conventional lumbar diskectomy, the infection rate is so low that antibiotics are not justified. However, infection rates are higher after spinal procedures involving fusion, prolonged spinal surgery, or insertion of foreign material, and the use of prophylactic antibiotics is common, but controlled trials of such use are lacking [4] .

8. **Cardiovascular surgery.** Prophylactic antibiotics can decrease the incidence of infection after cardiac surgery, including valvular procedures and coronary artery bypass grafting [4] . Single doses appear to be as effective as multiple doses, provided that high concentrations are maintained in the blood throughout the procedure [4] . In contrast, they are not indicated for cardiac catheterization [4] .
9. **Peripheral vascular surgery.** Data support the use of prophylactic antibiotics for arterial reconstructive surgery of the abdominal aorta, vascular operations on the leg that include a groin incision, and amputation of the lower extremity for ischemia [4] . The *Medical Letter* indicates that many clinicians also recommend prophylaxis for implantation of any vascular prosthetic material, including grafts for vascular access in hemodialysis [4] . The utility of antibiotic prophylaxis in carotid artery surgery has not been established but, when infection rates are high, cefazolin for 24 hours has been used [2] . Routine use of prophylaxis is not recommended for carotid endarterectomy or brachial artery repair without prosthetic material [4] .
10. **Thoracic surgery**
    a. **Pulmonary resection.** In patients undergoing this procedure a single preoperative dose of cefazolin caused a decrease in wound infection but no decrease in pneumonia or empyema [4] . Cefuroxime continued for 48 hours after pulmonary resection was more effective in preventing infection, particularly empyema, than one dose at induction and a second dose 2 hours later [33B] .
    b. Other trials have found that multiple doses of a cephalosporin can prevent empyema after closed-tube thoracostomy for chest trauma [4] .
11. **Ocular surgery.** The role of antibiotic prophylaxis for ocular surgery is unclear, but postoperative endophthalmitis can be

devastating. Most ophthalmologists use antimicrobial eye drops for prophylaxis; many also give a subconjunctival injection at the end of the procedure, but controlled studies supporting a particular choice, route, or duration of antimicrobial prophylaxis are lacking [4] .

12. **Trauma**
    a. **Abdominal.** The use of perioperative antibiotics as prophylaxis against infection in the patient with abdominal trauma and suspected ruptured hollow viscus is widely accepted [18] . If at surgery there is no injury to a hollow viscus, reducing the duration (e.g., with cefoxitin) to 12 hours is indicated [7] . For patients found to have intestinal perforation, then a short course of antibiotics (very early therapy for bacterial spillage) for 2-5 days with cefoxitin or a similar agent is advised [2] .
    b. **Chest.** In penetrating thoracic trauma and in the placement of chest tubes in trauma management, prophylactic antibiotics have not been effective according to some reviews [2] , but this is an unsettled area. See related discussion in sec. **10.b.**
13. **Low-risk or "clean" procedures.** Whether the benefits outweigh the risks of antibiotic prophylaxis for these procedures (e.g., hernia repair, breast operations, skin surgery) has been questioned. Some experts suggest prophylaxis [1] may be useful if the patient was at increased risk for infection (e.g., debilitated, diabetic, poor hygiene). Other experts emphasize that routine prophylaxis for these patients is not indicated [2] .
    a. **Breast surgery.** Preliminary studies suggest perioperative cephalosporin therapy in excision of a breast mass, mastectomy, reduction mammoplasty, and axillary node dissection reduced the incidence of postoperative

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infections [34] , especially in patients at higher risk for infection. In a recent review, although controversial, the authors conclude prophylactic antibiotics are useful in this setting [35] . However, most *Medical Letter* consultants do not recommend prophylaxis routinely for breast procedures [4] .

    b. **Herniorrhaphy.** Similarly, preliminary data suggest patients undergoing herniorrhaphy benefited from perioperative cephalosporin prophylaxis [34] . In a patient with additional risk factors for infection, single-dose prophylaxis is reasonable.
14. **Other procedures.** Antibiotic **prophylaxis is not routinely recommended for** cardiac catheterization, GI endoscopy, repair

of simple lacerations, outpatient treatment of burns, arterial puncture, paracentesis, or thoracentesis [1] [2] [3] [4] .

C. **"Dirty" surgery.** In such cases (e.g., bowel perforation, complex fracture), **antibiotics are used therapeutically for full courses.** These antibiotics are therapeutic, not prophylactic, because an early infection already is present. **Animal or human bites also deserve therapeutic courses** [4] **and are discussed in detail** in Chap. 4 .

D. **Laparoscopic surgery.** Few data are available on the role of prophylactic antibiotics in this setting. The *Medical Letter* recently suggested that "until more data become available, the same standards should be applied to laparoscopic surgery as for operations through a traditional incision" [4] . For example, if a patient is in the high-risk group for an open (traditional) cholecystectomy (see sec. **B.1**), he or she should also receive prophylactic antibiotics for a laparoscopic cholecystectomy.

III. **Organisms involved.** An effective prophylactic regimen should be directed against the most likely infecting organisms but need not include drugs active against every potential pathogen. Regimens that only decrease the total number of pathogens permit host defenses to resist clinical infection [4] . Most surgical wound infections are acquired in the operating room from the patients' own microbial flora. The remainder are acquired mainly from the staff in the operating room during surgery. The inanimate environment (e.g., walls, floors, and surgical equipment) has little relevance to the spread of infection [36] .

A. ***Staphylococcus aureus.*** **In wound infections after clean surgery, the major pathogen of concern is *S. aureus,*** which commonly colonizes the nose and the skin. The majority of these are penicillin-resistant. Therefore, any prophylactic agent would need to be effective against these organisms.

B. **Gram-negative bacteria** cause wound infections especially when surgery of the colon, genitourinary tract, or gynecologic organs is undertaken.

C. **Potential for resistant organisms.** In a given hospital, the prevalence of a specific organism may affect antibiotic selection. For example, if methicillin-resistant *S. epidermidis* is a problem in prosthetic device surgery, antibiotic choice is influenced by this fact (see Ayliffe [36]). If a patient has been on protracted antibiotic therapy, his or her flora may be different and a different, broader agent may be indicated.

D. It is unnecessary to use antibiotics active against all the organisms potentially involved in wound infections.

IV. **Potential disadvantages of prophylaxis**

A. **Superinfection with a resistant organism** is a concern. However, this risk is minimal if antibiotics are not initiated until just prior to the start of an operation, if their use postoperatively is for less than 24 hours, and if cephalosporins are used (see **V.B.4**). If antibiotics are used for less than 48 hours, normal flora usually will persist in sites such as the oropharynx.

B. **Toxic or allergic** reactions can occur whenever antibiotics are used. These can be minimized by using safe agents for short periods of time.

C. **Cost.** Antibiotics are expensive and should not be used unnecessarily. However, in patients clearly at risk of wound infections that have been shown to be decreased by antibiotic prophylaxis, the cost of the

antibiotics is negligible compared with the hospitalization cost of a prolonged stay caused by a wound infection [2] [12] . When antibiotic prophylaxis is used, the least expensive effective agent for a brief period is chosen.

D. **A false sense of security** may be created by the use of antibiotics. **Meticulous surgery and careful preoperative and postoperative care are essential** in minimizing wound infections.

V. **Antibiotic agents used in surgical prophylaxis.** These agents must cover *S. aureus*. For distal ileum, appendix, or colon procedures, agents with activity against aerobic and anaerobic bacteria are preferred.

A. **Semisynthetic penicillin** (nafcillin or oxacillin) is, in clean surgery, active against *S. aureus* and is a potential agent. However, although the rationale could be debated, the cephalosporins are used more frequently for surgical prophylaxis.

B. **Cephalosporins are widely favored** in surgical prophylaxis. The cited reasons for preference of the cephalosporins include the following:

1. **Broad spectrum of activity.** These agents are active against most penicillin-susceptible and penicillin-resistant *S. aureus* as well as many *S. epidermidis* and many gram-negative strains, such as *Escherichia coli* and *Klebsiella* spp., which may cause wound infections (see sec. **6**). Cefoxitin and cefotetan are also active against most bowel-related anaerobes.
2. **Few side effects.** Side effects seen with these agents are few, and this is a crucial point for prophylactic antibiotics.
3. **Low incidence of allergic reactions.** With short duration of use, these agents rarely cause rashes or other allergic problems. They can be used in patients with delayed penicillin reactions.
4. **Which cephalosporin?** With the availability of first-, second-, and third-generation agents, the question arises as to which agent is preferable in routine surgical prophylaxis. **Because the first-generation agents are more active against *S. aureus,* are less expensive than the newer agents, and have a narrower spectrum of in vitro activity** (and therefore are less likely to select out resistant bacteria), **these agents are preferred for most surgical procedures.** Furthermore, of the first-generation agents, **cefazolin** has the added advantage of a moderately long serum half-life, making it a **preferred agent for prophylaxis** [1] [4] . In reviews [1] [4] , **for colorectal surgery and appendectomy, cefoxitin or cefotetan is preferred** because these agents are more active against bowel anaerobes, including *B. fragilis* (see sec. **II.B.4**). For the other abdominal and pelvic procedures, including obstetric and gynecologic operations, cefazolin has been equally effective and is less expensive [4] . Single-dose cefotetan may be a more cost-effective agent than multiple doses of cefoxitin in colorectal surgery lasting for more than 2-3 hours. (See sec. **I.B.2** and Chap. 28F , sec. **II.F** under Individual Agents,

for a discussion of cefotetan.)
The *Medical Letter* emphasizes that the **third-generation cephalosporins should not be used** because they are more expensive, have less antistaphylococcal activity than cefazolin, and their spectrum of activity against gramnegative bacilli includes organisms rarely encountered in elective surgery. Their unnecessary and potential widespread use for prophylaxis may promote emergence of resistance to these potentially valuable therapeutic agents [4] . The optimal cephalosporin to use in cardiovascular surgery has been debated, with second-generation cephalosporins (e.g., cefamandole, cefuroxime) purported to have a broader spectrum of activity than the first-generation cephalosporins (e.g., cefazolin) and therefore presumed to be more effective [37] . However, recent studies do not reveal significant differences between the first- and second-generation agents in this setting [37] [38] . Therefore, the more cost-effective agent (cefazolin) seems rational.

5. **Prophylactic dosage.** Few reports have focused on the appropriate dose for prophylaxis [1] .
   a. **Initial dose.** As discussed in sec. **I.A.3,** it is important to have good (i.e., therapeutic) antibiotic levels at the time of surgery. Ideally, perioperative antibiotics are given in the operating room just at the time of anesthesia (i.e., 30-60 minutes before the incision).
   (1) Cefazolin, a first-generation cephalosporin, is used commonly for many procedures, typically at a dose of 1-2 g. Although many regimes use 1 g of cefazolin per dose [4] , others at times suggest 2 g per dose [1] [2] , as in knee replacement when a tourniquet is used and in cholecystectomy [2] .
   (2) Cefoxitin or cefotetan. Both 1-g [1] [4] or 2-g [1] [2] doses have been suggested. For colon surgery, we tend to use the 2-g dose. If cephalosporins are contraindicated, an aminoglycoside (1.7 mg/kg per dose of gentamicin or tobramycin) can be combined with clindamycin (600 mg per dose in adults) or metronidazole or aztreonam and clindamycin [1] .
   (3) In children, 30-40 mg/kg per dose of the cephalosporin has been suggested [1] .
   (4) Vancomycin can be given instead of cefazolin to patients who are allergic to cephalosporins or in institutions where methicillin-resistant

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S. aureus (or coagulase-negative staphylococci) have become important pathogens; routine use of vancomycin for prophylaxis should be discouraged because it promotes emergence of vancomycin-resistant enterococci

[4] . See Chap. 28O .
Because vancomycin provides no activity against facultative gram-negative bacilli, which may be involved in settings such as GI surgery, lower-extremity vascular surgery, or hysterectomy, another agent with gram-negative activity should be added to the regimen under these circumstances. If allergy to cephalosporins is the concern, aztreonam or an aminoglycoside can be used [1] (see sec. **d** for doses, and Chap. 28O).
(5) Cefuroxime has also been studied in noncardiac thoracic surgery. See sec. **II.B.10.**

b. **Intraoperative dosage for prolonged procedures.** It is desirable to maintain high tissue levels of the prophylactic agent throughout the surgical procedure. Therefore, repeat doses may be necessary intraoperatively in procedures lasting longer than 2 hours. When agents with a long biologic half-life are used (e.g., cefazolin), the dose can be repeated every 4 hours intraoperatively. When agents with a shorter half-life are used (e.g., cefoxitin), it is necessary to repeat doses every 2-3 hours intraoperatively. Usually, only one dose of cefotetan (1-2 g) is given preoperatively for a procedure lasting up to 5-6 hours. See sec. **I.B.** and Table 28B-1. (Table Not Available)

c. **Postoperative dosage.** Postoperative administration of prophylactic antibiotics usually is unnecessary and, because of the frequent use of such agents, is expensive to the patient and hospital. Exceptions to this rule are discussed in sec. **I.B.**

d. **For hospitals in which methicillin-resistant *S. aureus* or *S. epidermidis* frequently cause wound infections or for patients with cephalosporin allergies, vancomycin is an alternative agent** for patients undergoing prosthetic device surgery--for example, heart valve replacement, vascular procedures, and total hip replacement. Often 1 g of vancomycin is infused slowly intravenously over 120 minutes [4] . Vancomycin, 15 mg/kg, has also been used [2] . See detailed discussion of vancomycin dosing in Chap. 28O .

6. **Failures** of surgical prophylaxis with postoperative methicillin-susceptible *S. aureus* have been described despite the use of cefazolin [2] [39] [40] . The biologic explanation is very interesting, but the exact clinical application awaits further study.
Presumably, failures occur because cefazolin is more susceptible to inactivation by some beta-lactamase-producing strains of *S. aureus* than other cephalosporins (e.g., cephalothin, cefuroxime, cefamandole) [39] . This in vitro observation has been known for years, but its clinical relevance in the past has been debated and is unclear. **While awaiting additional studies in this area,**

cefazolin still remains the agent of choice for most clinical situations [1] [4] .
However, if methicillin-susceptible *S. aureus* infections continue to occur despite cefazolin (e.g., in cardiovascular or orthopedic procedures), infectious disease consultation is advised to help determine the optimal prophylactic agent to use in an institution if failures are seen with standard regimens.

C. **Ampicillin-sulbactam** (Unasyn) has been used for prophylaxis in head and neck cancer surgery because this agent will cover *S. aureus* and many gram-negative bacilli [41] .

D. **Vancomycin** is indicated when prosthetic device infections due to methicillin-resistant staphylococci are a special problem and at times in the allergic patient.

E. **Topical antibiotic prophylaxis.** Early studies suggest that topical use of antibiotics may be effective in the prevention of surgical wound infections. However, the precise clinical implications of the use of topical agents await further well-controlled, comparative clinical studies. Therefore, unless topical agents are being used as part of a carefully designed clinical study, we do not advocate their use at this time.

VI. **Nonsurgical antibiotic prophylaxis.** There are a few indications for prophylactic antibiotics in the nonsurgical setting.

A. **Prevention of rheumatic fever.** The recommendations that follow are for most of the United States, where the incidence of rheumatic fever remains low. This has been reviewed elsewhere [42] .

1. **Prevention of initial attacks (i.e., "primary" prevention)** of rheumatic fever

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involves the proper therapy of group A beta-hemolytic streptococcal infections of the upper respiratory tract. Studies have indicated that during epidemics, approximately 3% of acute streptococcal group A sore throats are followed by rheumatic fever; in endemic infections, attacks of rheumatic fever may be fewer [42] .

a. **Penicillin is the drug of choice** except in patients who are allergic to this drug. (See Chap. 7 for a detailed discussion of streptococcal pharyngitis and the role of cephalosporins in therapy.) It effectively prevents rheumatic fever even when therapy is started several days after the onset of the acute illness. A single dose of intramuscular benzathine penicillin G (600,000 units for patients weighing 60 lb [27 kg] or less, and 1.2 million units for patients weighing more than 60 lb) ensures treatment for an adequate time because this agent provides adequate blood levels for more than 10 days. **When oral therapy is used, a full 10-day course is necessary.** Penicillin V (in children, 250 mg bid or tid,

and adults, 500 mg bid or tid) for 10 days often is advised [42] ; 250 mg bid in children and 500 mg bid in adults is adequate [43] .

b. **In the penicillin-allergic patient,** erythromycin estolate (20-40 mg/kg/day to a maximum of 1 g/day) in two to four divided doses or erythromycin ethylsuccinate (40 mg/kg/day up to a maximum of 1 g) in two to four divided doses for 10 days has been advised [42] . In adults, 250 mg bid-qid commonly is used. The new macrolide, azithromycin, can be administered once daily and produces high tonsillar tissue concentrations. A 5-day course of azithromycin is approved by the Food and Drug Administration as a second-line therapy for patients 2 years of age or older with streptococcal A pharyngitis [42] . See Chap. 7 and See Chap. 28M . This may be a useful alternative in the penicillin-allergic patient in whom compliance may be improved with this regimen (e.g., a college student).
Oral cephalosporins (e.g., cephalexin or cephradine) for 10 days also are acceptable alternatives and usually are better tolerated [43] [44] . (See Chap. 7.) Tetracycline and sulfonamides should not be used.

2. **Prevention of recurrent attacks of rheumatic fever (i.e., "secondary" prevention).** Patients with a prior history of rheumatic fever generally are at high risk of a recurrence if they develop a group A streptococcal upper respiratory tract infection. Because asymptomatic as well as symptomatic infection can trigger a recurrence, **continuous prophylaxis is recommended for patients with a well-documented history of rheumatic fever or Sydenham's chorea or those with definite rheumatic heart disease.**

a. **The duration** of this continuous prophylaxis **is uncertain** [6A] [42] . Data suggest that recurrences decline with the advancing age of the patient and as the time interval after the most recent attack increases. Some clinicians argue that, ideally, prophylaxis is lifelong. Others will treat patients at least until they reach their early twenties and 5 years have elapsed since the last rheumatic attack [42] and then continue prophylaxis only in those who are at increased risk of exposure to streptococcal infections--for example, parents of young children, schoolteachers, others exposed to young children, as well as medical personnel and those in military service. Those living in crowded conditions and economically disadvantaged populations may also be at increased risk. Even after prosthetic valve surgery for rheumatic heart disease, prophylaxis should be continued, as these patients are theoretically at risk [42] . See detailed discussion in references [6A] and [42] , which emphasize that the decision to discontinue prophylaxis must be individualized.

b. **Regimens**

(1) Intramuscular benzathine penicillin G, 1,200,000 units every month, is the recommended method [42] . In countries where the incidence of acute rheumatic fever is particularly high, or in certain high-risk patients, use of benzathine penicillin G every 3 weeks may be warranted [42] . This regimen is preferred for high-risk patients (e.g., young patients who have experienced a recent episode of rheumatic fever). However, the advantages of benzathine penicillin G must be weighed against the inconvenience to the patient and pain of injection, which causes some individuals to discontinue prophylaxis [42] .

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(2) Oral regimens assume the compliance of the patient; therefore, careful and repeated patient education is essential. Even with optimal compliance, risk of recurrence is still higher in those on regular oral prophylaxis compared with those receiving intramuscular benzathine penicillin G [42] . **Penicillin V,** 250 mg bid, is recommended. **Sulfadiazine,** 1 g once daily for patients weighing more than 60 lb and 500 mg once daily for patients weighing less than 60 lb, also is suggested. These regimens are about equally effective, and one of these regimens is preferred. For the exceptional patient who may be allergic to both penicillin and sulfonamides, erythromycin may be used [42] , and 250 mg bid is suggested [42] .

B. **Prevention of serious infections after splenectomy.** Overwhelming infection due to encapsulated organisms such as *S. pneumoniae*, *Haemophilus influenzae* and, rarely, *Neisseria meningitidis* can occur after splenectomy. Methods of preventing these overwhelming infections, which can occur months or years after splenectomy, remain unclear and controversial [45] [46] [47] [48] [49] . Children may be at particularly high risk, but it can also occur in adults.

An adult, splenectomized after trauma but otherwise healthy, is at risk for overwhelming pneumococcal sepsis, although at a much lower incidence than young children [46] [48] , probably because of the adult's immune status, which supports the rest of the mononuclear-phagocytic system [47] . Recognition that adults as well as children are at increased risk of infection years after splenectomy has led to consideration of spleen-sparing surgical approaches after trauma [46] [47] .

1. **Vaccines.** The **pneumococcal vaccine** usually is given to these patients, but its efficacy in this setting is unclear [46] [47] [48] . If an elective splenectomy is performed, the pneumococcal vaccine should be administered at least 2 weeks before the elective splenectomy [46] . The polysaccharide ***H. influenzae*** **vaccine** is

another useful agent, although efficacy data with this vaccine for this use are not available. The role of **meningococcal vaccine** in this setting has not been established, but it seems a reasonable consideration and has been suggested [48] . (A single-dose vial of the quadrivalent vaccine is available now in the United States.)

2. **Prophylactic antibiotics.** Some experts recommend the use of oral penicillin daily (e.g., penicillin V, 125 mg bid in children and 250 mg bid in adults) in recently splenectomized patients. This is a particularly common practice in children [45] [48] . Whether to use prophylactic penicillin routinely in adults who are not otherwise compromised is a controversial issue [46] [47] [48] . We use prophylactic antibiotics in adults with Hodgkin's disease who have undergone splenectomy, chemotherapy, or radiation therapy. Less frequently, ampicillin is used on a daily basis as it is active against *H. influenzae* as well as *S. pneumoniae*, but it is more likely to cause side effects. Neither the optimal agent nor optimal duration of antibiotics in this setting has been established.
3. **Early therapeutic antibiotics.** Early empiric antibiotic therapy in patients who have undergone a splenectomy is an important consideration. Patients can be given a supply of antibiotic for use if an acute illness develops and medical attention is not immediately available [48] . Oral penicillin and amoxicillin have been used. When these patients present with nonspecific febrile illnesses, often flulike, early antibiotic therapy is rational for unexplained fever or chills. Ideally, appropriate cultures should be obtained, but if facilities for culture analysis are not immediately available, starting antibiotics without cultures is reasonable [46] . In community-acquired bacteremia of unclear primary focus of infection, therapy aimed at the likely pathogens should be instituted early while awaiting cultures. Cefuroxime and ceftriaxone are useful options. See Chap. 2 for a more detailed discussion.
4. **Identification warning.** Because these patients are at risk of fulminant sepsis, we encourage each patient to have some form of personal identification (e.g., medical alert necklace or bracelet, or note in his or her wallet or purse) indicating that he or she has undergone splenectomy. The patients' families should be aware of this potential complication.
5. **Summary.** Because the splenectomized patient is at risk of severe bacterial infections, especially if a remnant is not left behind, it seems prudent that these patients should receive the pneumococcal, *H. influenzae* b, and meningococcal

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vaccines; however, they provide only partial protection against future bacteremias. We routinely use penicillin prophylaxis in children, at least for 2-4 years. In general, we neither routinely

treat adults with prophylactic antibiotics after splenectomy nor use ampicillin in this setting unless the patient has received therapy for Hodgkin's disease. The medical records of these patients should indicate clearly that they have undergone splenectomy and, as stated earlier, we encourage patients to have some form of personal identification indicating that they have undergone splenectomy so that physicians caring for them can be immediately alerted. Early empiric antibiotics are a rational approach.

C. **Prevention of bacterial endocarditis** has been reviewed [50] . Although antimicrobial prophylaxis commonly is used in patients with certain types of valvular heart disease or prosthetic valves, **no adequate, controlled clinical trials of the effectiveness of antibiotic regimens for the prevention of bacterial endocarditis in humans have been done.** Therefore, recommendations are based on in vitro studies, clinical experience, data from animal models, and assessment of both the bacteria most likely to produce bacteremia from a given site and those most likely to result in endocarditis [50] [51] . The American Heart Association (AHA) stresses that its published report "represents recommended guidelines to supplement practitioners in the exercise of their clinical judgment and is not intended as a standard of care for all cases" [50] , as it is impossible to make recommendations for all clinical situations in which endocarditis may develop.

1. **Underlying cardiac disease.** Certain cardiac conditions are more often associated with endocarditis than others. See Table 28B-2 (Table Not Available) . What is meant by "insufficiency" in mitral valve prolapse is not fully clarified in the 1990 recommendations. This is a practical consideration for the clinician because, in patients with mitral valve prolapse, the murmur may vary from one examination to another and because Doppler echocardiography can detect nonaudible (and probably non-endocarditis-predisposing) amounts of valvular insufficiency even in normal valves [52] . In their editorial response, Kaye and Abrutyn [52] suggest that "on the basis of current knowledge, we believe that **prophylaxis is indicated for patients with mitral valve prolapse with a holosystolic murmur;** should be optional in cases of late systolic murmur, either spontaneous or evoked (e.g., standing or the valsalva maneuver); and is not indicated in the absence of a murmur."
   In their 1995 review of this topic, Dickinson and Bisno [6A] emphasize that clinical studies indicate that nearly all cases of infective endocarditis occur in patients with audible systolic murmurs, so prophylaxis is not recommended for patients with isolated systolic clicks. Patients with thickened and redundant valves clearly are at higher risk. They conclude by noting, "more convenient clinical markers are needed, however, to define with precision the subgroup of MVP patients at highest risk [for endocarditis]" [6A] .

2. **Surgical and dental procedures** and instrumentations involving mucosal surfaces or contaminated tissue commonly cause transient (≤15 minutes) bacteremia. Certain procedures are much more likely to initiate the bacteremia that results in endocarditis than are other procedures [50] .
    a. See Table 28B-3. (Table Not Available)
    b. Edentulous patients may develop bacteremia from ulcers caused by illfitting dentures [50] .
3. **Antibiotic regimens.** To reduce the likelihood of microbial resistance, it is important that prophylactic antibiotics be used only during the perioperative period. They should be initiated shortly before the procedure (1-2 hours) and should not be continued for an extended period (no more than 6-8 hours). In the case of delayed healing or of a procedure that involves infected tissue, it may be necessary to provide additional doses of antibiotics [50] (i.e., therapeutic courses).
    a. **For dental, oral, and upper respiratory tract procedures.** Antibiotic prophylaxis is recommended for all dental procedures likely to cause gingival bleeding, including routine professional cleaning. If a series of dental procedures is required, it may be prudent to observe an interval of 7 days between procedures to reduce the potential for the emergence of resistant strains [50] .

        (1) See Table 28B-4 (Table Not Available) . Therapy is aimed at viridans streptococci.

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(2) Amoxicillin now is recommended rather than oral penicillin because amoxicillin is better absorbed from the GI tract and provides higher serum levels [50] .
(3) In penicillin-(or ampicillin- or amoxicillin-) allergic patients, if erythromycin is used, the erythromycin preparations shown in Table 28B-4 (Table Not Available) are recommended because of their more rapid and reliable absorption than other erythromycin formulations, resulting in higher and more sustained blood levels [50] . In patients who have GI side effects with erythromycin (or amoxicillin), clindamycin is preferred.
(4) When the oral regimen cannot be given to a patient, an **alternative parenteral regimen** can be used and is shown in Table 28B-5 (Table Not Available) .
(5) High-risk patients (i.e., individuals with prosthetic heart valves, a previous history of endocarditis, or surgically constructed systemic-pulmonary shunts or conduits) were considered candidates for parenteral regimens in prior endocarditis prophylaxis

recommendations. However, the recommendations [50] recognize that in practice there are substantial logistical and financial barriers to the use of parenteral regimens. In addition, oral regimens used by individuals who have prosthetic valves in other countries have not been associated with prophylaxis failures [50] .
Therefore, the **committee "recommends the use of the standard prophylactic regimen** [see Table 28B-4] (Table Not Available) **in patients who have prosthetic heart valves and in other high-risk groups"** [50] (i.e., the oral regimen). If a practitioner prefers to use parenteral regimens in these high-risk patients, the regimens in Table 28B-5 (Table Not Available) can be used.

b. **For genitourinary and gastrointestinal procedures,** antibiotics are **aimed at enterococci,** for gram-negative bacilli rarely cause endocarditis [50] . **Prophylaxis is no longer recommended for gastrointestinal endoscopic procedures even with biopsy** [50] . These procedures have rarely, if ever, been implicated as the cause of endocarditis [52] .
(1) See Table 28B-6 (Table Not Available) for regimens.

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(2) For high-risk patients (e.g., those with prosthetic heart valves or a previous history of bacterial endocarditis), **the parenteral regimen is still advised** [50] , as in prior endocarditis prophylaxis recommendations (see Table 28B-6) (Table Not Available) .
(3) For low-risk patients, an alternative oral regimen is provided in Table 28B-6 (Table Not Available) .

4. **Miscellaneous**
   a. **Recipients of secondary prevention of rheumatic fever.** Patients who take oral penicillin to prevent recurrent rheumatic fever (see section **A.2**) may have viridans streptococci in their oral cavities that are relatively resistant to penicillin or amoxicillin. In such cases, erythromycin or another of the alternative regimens listed in Table 28B-4 (Table Not Available) and in Table 28B-5 (Table Not Available) should be used rather than amoxicillin (or another penicillin) [50] .

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b. **Renal dysfunction.** In patients who have markedly compromised renal function, it may be necessary to modify or omit the second dose of gentamicin (see Chap. 28H) or vancomycin (see Chap. 28O) .

c. **Concomitant anticoagulation use.** Intramuscular injections should be avoided in patients who receive heparin; warfarin use is a relative contraindication to intramuscular injections. Therefore, intravenous or oral regimens should be used whenever possible [50] .

d. **Cardiac transplantation.** In the 1990 AHA recommendations, it was felt there were insufficient data to support specific recommendations for prevention of bacterial endocarditis in recipients of cardiac transplants [50] .

e. **Open heart surgery.** Patients who undergo surgery for placement of prosthetic heart valves or prosthetic intravascular or intracardial materials are also at risk for the development of bacterial endocarditis, usually caused by *S. aureus*, coagulase-negative staphylococci, or diphtheroids [50] . A first-generation cephalosporin commonly is used, but other considerations affect the antibiotic choice (see sec. **II.B.8**). Prophylactic antibiotics ideally should be continued for no more than 24 hours postoperatively to minimize emergence of resistant microorganisms [50] .

f. **Adjunctive dental care** [50] . **Individuals who are at risk for developing bacterial endocarditis should optimize oral health to reduce the potential of bacterial seeding. Routine dental care and efforts to reduce gingival inflammation** (brushing, flossing, fluoride rinse, and chlorhexidine gluconate mouth rinse) **are important but often not emphasized enough.** Chlorhexidine that is painted on isolated and dried gingiva 3-5 minutes prior to tooth extraction reduces postextraction bacteremia. Other agents such as providone-iodine or iodine and glycerin may also be appropriate. Irrigation of the gingival sulcus with chlorhexidine prior to tooth extraction reduces postextraction bacteremia in adults [50] .

g. **Manipulation of subcutaneous abscesses** can be associated with staphylococcal or streptococcal bacteremias, although if a perineal abscess is manipulated, gram-negative bacilli or enterococci may be a concern (see Table 28B-3) (Table Not Available) . **No formal guidelines are available. Possible approaches include the following:**

(1) For nonperineal abscess drainage

(a) Oral regimen. In adults, dicloxacillin, 500 mg PO or 500-1,000 mg cephalexin (higher dose in high-risk patients) PO 1 hour prior to drainage followed by a similar dose q6h once or twice after the procedure.

(b) Parenteral regimen. In adults, a semisynthetic penicillin (oxacillin or nafcillin) 1-2 g IV or 1 g cefazolin can be given a half hour prior to drainage. An oral dose of dicloxacillin or cephalexin could also be given at 6 and 12 hours after drainage as discussed in sec. **(a).**

(2) For perirectal or perivulvar abscess drainage (which might involve staphylococci, enterococci and, to a lesser extent, gram-negative bacilli), the optimal regimen is not established.

(a) Oral regimen. In the adult, Augmentin (500 mg amoxicillin-125 mg clavulanic acid) 1 hour before the procedure is an appealing agent in the non-penicillin-allergic patient. This could be repeated at 6 and 12 hours after the drainage procedure. In the penicillinallergic patient, a single dose of intravenous vancomycin with an aminoglycoside is an option (see Table 28B-6) (Table Not Available) to ensure enterococcal coverage.

(b) Parenteral. Vancomycin with an aminoglycoside can be used as described in Table 28B-6 (Table Not Available) . Another potential regimen may be ampicillin-sulbactam (Unasyn) or piperacillin-tazobactam (Zosyn) with a single dose before the procedure (see Chap. 28E) .

D. **Oral antibiotics to prevent infections in the leukopenic patient** have been reviewed elsewhere [47] [53] . In general, we do not advocate their routine use unless as part of a special clinical study. See further discussions on TMP-SMX (Chap. 28K) and the fluoroquinolones (Chap. 28S) .

E. **Travelers' diarrhea.** Although this can often be prevented by prophylactic doses of TMP-SMX, TMP, or doxycycline, widespread use of this approach will increase problems of bacterial resistance. Short therapeutic courses therefore are preferred and are discussed in Chap. 21 .

F. **Influenza A** can often be prevented with immunization or amantadine (see Chap. 8) .

G. **Meningitis.** The use of rifampin and other agents to prevent the spread of meningococcal or *H. influenzae* type b meningitis from an index case to close contacts is discussed in Chap. 5 .

H. **Recurrent urinary tract infection.** The use of antibiotics to prevent recurrent episodes of urinary tract infection is reviewed in the individual discussions of these agents in Chap. 28 : TMP-SMX, fluoroquinolones, nitrofurantoin, and mandelamine-ascorbic acid. Also see Chap. 12 .

I. ***Pneumocystis carinii.*** Prevention of recurrent *P. carinii* pneumonia is discussed in Chap. 24 .

J. **Chemoprophylaxis of tuberculosis.** See discussion of isoniazid in Chap. 9 .

K. **Lyme disease.** The use of prophylactic antibiotic treatment of tick bites in endemic areas generally is not indicated. See discussion in Chap. 23 .

L. **Recurrent otitis media in young children.** Although prophylactic regimens are used in this setting, the best regimens are unclear; further clinical studies are needed. This topic is discussed briefly in Chap. 7 and is reviewed elsewhere [54] [55] [56] .

M. **Prevention of infection in renal transplantation recipients.** Prophylaxis with TMP-SMX significantly reduces the incidence of bacterial infection following renal transplantation (especially infection of the urinary tract and bloodstream), can provide protection against *P. carinii* pneumonia, and is cost-beneficial [57] . Patients appear to tolerate this regimen well in this setting [57] .

N. **Prevention of infection in patients with chronic granulomatous disease.** Prophylaxis with TMP-SMX is useful in the prevention of infectious complications and does not appear to be associated with an increase of fungal infections [58] .

O. **Prevention of recurrent cholangitis.** Selected patients with a compromised biliary

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system (e.g., on account of an endoprosthesis in situ, history of choledochojejunostomy or hepaticojejunostomy or sphincteroplasty) who are prone to develop recurrent bouts of cholangitis may benefit from chronic daily prophylactic antibiotics. The aim of suppressive antibiotic therapy is to prevent flare-ups of clinically overt cholangitis. Both TMP-SMX and fluoroquinolones have been used. This topic has been reviewed elsewhere [59] .

P. **Complicated diagnostic or therapeutic endoscopic retrograde cholangiopancreatography.** Although antibiotics have often been given for this procedure because this seems reasonable, data now are supporting prophylactic antibiotic use in this setting [60] [60A] .

Q. For postoperative T-tube cholangiography, routine prophylaxis does not appear to be necessary [61] .

TABLE 28B-1 -- Recommended dose intervals for repeat doses in prolonged procedures

Source: From E.P. Dellinger et al., Quality standard for antimicrobial prophylaxis in surgical procedures. Clin. Infect. Dis. 18:422, 1994.

(Not Available)

TABLE 28B-2 -- Cardiac conditions [a]

Source: From A.S. Dajani, et al., Prevention of bacterial endocarditis: Recommendations by the American Heart Association. J.A.M.A. 264:2919, 1990. Copyright 1990, American Medical Association.

(Not Available)

[a] This table lists selected conditions but is not meant to be all-inclusive.

TABLE 28B-3 -- Dental or surgical procedures[a]

Source: From A.S. Dajani et al., Prevention of bacterial endocarditis: Recommendations by the American Heart Association. J.A.M.A. 264:2919, 1990. Copyright 1990, American Medical Association.

(Not Available)

[a] This table lists selected procedures but is not meant to be all-inclusive.

TABLE 28B-4 -- Recommended standard prophylactic regimen for dental, oral, or upper respiratory tract procedures in patients who are at risk[a]

Source: From A.S. Dajani et al., Prevention of bacterial endocarditis: Recommendations by the American Heart Association. J.A.M.A. 264:2919, 1990. Copyright 1990, American Medical Association.

(Not Available)

[a] Includes those with prosthetic heart valves and other high-risk patients.

TABLE 28B-5 -- Alternative prophylactic regimens for dental, oral, or upper respiratory tract procedures in patients who are at risk

Source: From A.S. Dajani et al., Prevention of bacterial endocarditis: Recommendations by the American Heart Association. J.A.M.A. 264:2919, 1990. Copyright 1990, American Medical Association.

(Not Available)

TABLE 28B-6 -- Prophylactic regimens for genitourinary and gastrointestinal procedures

Source: From A.S. Dajani et al., Prevention of bacterial endocarditis: Recommendations by the American Heart Association. J.A.M.A. 264:2919, 1990. Copyright 1990, American Medical Association.

(Not Available)

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In this recent summary sponsored by the Infectious Disease Society of America, more than 50 experts in infectious diseases and 10 experts in surgical infectious diseases and surgical subspecialties reviewed the recommendations or suggested standards that might be applied without controversy in most hospitals. This is an excellent resource.
For a related report, see T.K. Waddell and O.D. Rotstein, Antimicrobial prophylaxis in surgery: Committee on antimicrobial agents, Canadian Infectious Disease Society. Can. Med. Assoc. J. *151:925, 1994.*

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Review of physiologic factors involved in surgical wound infections. Reviews the timing of effective antibiotic surgical prophylaxis. Includes discussion of bacterial factors, influence of foreign bodies, and so on.

6. Haas, D.W., and Kaiser, A.B. Antimicrobial Prophylaxis of Infections Associated with Foreign Bodies. In A.L. Bisno and F.A. Waldvogel (eds.), *Infections Associated with Medical Devices* (2nd ed.). Washington, DC: American Society for Microbiology, 1994. Pp. 375-388.
See Table 2 on pages 382-383 for suggested regimens for various prosthetic device implants.

6A. Dickinson, G.M., and Bisno, A.L. Antimicrobial prophylaxis of infection. *Infect. Dis. Clin. North Am.* 9:783, 1995.

7. Page, C.P., et al. Antimicrobial prophylaxis for surgical wounds: Guidelines for clinical care. *Arch. Surg.* 128:79, 1993.
Article developed by the Antimicrobial Agents Committee and approved by the Executive Committee of the Surgical Infection Society as a set of guidelines for selection and use of prophylactic antibiotics for surgical wounds.

8. Hirschman, J.V., and Inui, T.S. Antimicrobial prophylaxis: A critique of recent trials. *Rev. Infect. Dis.* 2:1, 1980.
Extensive review of early studies on prophylactic antibiotic use. For a related article, see Veterans Administration Ad Hoc Interdisciplinary Advisory Committee on Antimicrobial Drug Usage, Prophylaxis in surgery. J.A.M.A. *237:1003, 1977, which provides an extensive reference list of early surgical prophylaxis studies.*

9. Burke, J.F. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* 50:161, 1961.
This experimental study helped determine the appropriate timing of prophylactic antibiotic administration. A classic.

10. Classen, D.C., et al. The timing of prophylactic administration of antibiotics and the risk of surgical wound infection. *N. Engl. J. Med.* 326:281, 1992.
Prospective study of 2,847 patients undergoing elective clean or clean-contaminated

surgery. When antibiotics were given 0-2 hours before surgery, wound infections were significantly reduced. See editorial comment by D.R. Wenzel in the same issue, emphasizing the importance of preoperative administration.

11. Burke, J.F. Preventing bacterial infection by coordinating antibiotic and host activity: A time-dependent relationship. *South. Med. J.* 70(Suppl. 1):24, 1977.
Emphasizes the importance of high levels of antibiotics intraoperatively.

12. Stone, H.H., et al. Prophylactic and preventive antibiotic therapy: Timing, duration, and economics. *Ann. Surg.* 189:691, 1979.
When prophylactic antibiotics are started preoperatively in an appropriate way, it is not necessary to continue prophylaxis beyond the time in the recovery room. Further infections are not prevented, but costs rise unnecessarily if prophylactic antibiotics are prolonged.

13. DiPiro, J.T., et al. Single dose systemic antibiotic prophylaxis of surgical wound infections. *Am. J. Surg.* 152:552, 1986.

14. Norden, C., Gillespie, W.J., and Nade, S. Infections in Total Joint Replacements. In *Infections in Bones and Joints*. Boston: Blackwell Scientific, 1994. Pp. 291-319.

15. Maki, D.G., and Mackey, J. Cefazolin, cefoxitin, and cefamandole for prophylaxis in colorectal surgery [abstract no. 466]. Twenty-sixth Interscience Conference of Antimicrobial Agents and Chemotherapy, New Orleans, Sept. 30, 1986.
Concluded that cefoxitin appears to provide greater protection against postoperative surgical infection in colorectal surgery.

16. Hemsell, D.L. Prophylactic antibiotics: In gynecologic and obstetric surgery. *Rev. Infect. Dis.* 13(Suppl. 10):S821, 1991.
Good review with specific guidelines.

17. Norden, C., Gillespie, W.J., and Nade, S. Post-Traumatic and Contiguous Osteomyelitis. In *Infections in Bones and Joints*. Boston: Blackwell Scientific, 1994. Pp. 166-180.

18. Fiore, A.F., Joshi, M., and Caplan, E.S. Approach to Infection in the Multiply Traumatized Patient. In G.L. Mandell, J.E. Bennett, and R. Dolin (eds.), *Principles and Practice of Infectious Diseases* (4th ed.). New York: Churchill Livingstone, 1995. Pp. 2756-2761.

19. Josefsson, G., and Kolmert, L. Prophylaxis with systemic antibiotics versus gentamicin bone cement in total hip arthroplasty: A 10 year survey of 1688 hips. *Clin. Orthoped. Res.* 292:210, 1993.
Follow-up report from this Swedish group who had earlier reported a significant difference at 2 and 5 years in favor of gentamicin bone cement but no difference at 10 years in the infection rate.

20. Norden, C.W. Antibiotic prophylaxis in orthopedic surgery. *Rev. Infect. Dis.* 13(Suppl. 10):S842, 1991.
Good summary by a nationally recognized expert. See related reference [17] and related discussion by J. Segreti and S. Levin, The role of prophylactic antibiotics in the prevention of prosthetic device infections. Infect. Dis. Clin. North Am. *3:357, 1989.*

20A. Wahl, M.J. Myths of dental-induced prosthetic device infections. *Clin. Infect. Dis.* 20:1420, 1995.
Strong argument and review of data to stop the common practice of antibiotic prophylaxis for dental procedures to prevent late prosthetic joint infections as this approach is not based on scientific evidence but rather on "myths."

20B. Steckelberg, J.M., and Osmon, D.R. Prosthetic Joint Infections. In A.L. Bisno and F.A. Waldvogel (eds.), *Infections Associated with Prosthetic Indwelling Medical Devices* (2nd ed.). Washington, D.C.: American Society for Microbiology, 1994. Pp. 259-290.

Data from the Mayo Clinic: in 39,000 large-joint implants with approximately 275,000 joint-years of follow-up, the overall incidence of large-joint implant infections due to dental pathogens (viridans streptococci) was 0.06 per 1000 joint-years--a rate similar to that for endocarditis in the general population. Therefore, routine prophylaxis is not warranted.

21. Nelson, J.P., et al. Prophylactic antimicrobial coverage in arthroplasty patients. *J. Bone Joint Surg. [Am.]*. 72:1, 1990.
See related article by J.W. Little, Managing dental patients with joint prosthesis. J. Am. Dent. Assoc. *125:1374, 1994. Review shows transient dental bacteremias had little or no role in causing late infections of prosthetic joint replacements.*

22. Simmons, N.A., et al. Case against antibiotic prophylaxis for dental treatment of patients with joint prosthesis. *Lancet* 339:301, 1992.

23. Nichols, R.L. Use of prophylactic antibiotics in surgical practice. *Am. J. Med.* 70:686, 1981.

Contains a good discussion of antibiotic prophylaxis in gastrointestinal surgery. For an update of this topic, see S.L. Gorbach, Antimicrobial prophylaxis for appendectomy and colorectal surgery. Rev. Infect. Dis. *13(Suppl. 10):S815, 1991.*

24. Norwegian Study Group for Colorectal Surgery. Should antimicrobial prophylaxis in colorectal surgery include agents effective against both anaerobic and aerobic microorganisms? A double-blind, multicenter study. *Surgery* 97:402, 1985.

25. DiPiro, J.T., et al. Prophylactic parenteral cephalosporins in surgery: Are the newer agents better? *J.A.M.A.* 252:3277, 1984.
Review of 17 published studies. Concludes there is no evidence that administration of second- or third-generation cephalosporins results in lower postoperative infection rates compared with administration of first-generation cephalosporins.

26. Weaver, M., et al. Oral neomycin and erythromycin compared with single-dose systemic metronidazole and ceftriaxone prophylaxis in elective colorectal surgery. *Am. J. Surg.* 151:438, 1986.

27. Mebust, W.K. Prophylactic antibiotics in transurethral surgery. *J. Urol.* 150:1734, 1993.

28. Klimberg, I.W., et al. A multicenter comparison of oral lomefloxacin versus parenteral cefotaxime as prophylactic agents in transurethral surgery. *Am. J. Med.* 92(Suppl. 4A):121S, 1992.
Patients were required to have negative pretreatment urine cultures. Lomefloxacin (400 mg PO once 2-6 hours prior to surgery) or cefotaxime (1 g IV or IM 30-90 minutes before surgery) was given. Lomefloxacin was successful in preventing postoperative infections in 204 of 207 evaluable patients (98%). Cefotaxime was successful in 196 of 206 (95.1%) evaluable patients.
See the two companion, related articles preceding this article in this symposium devoted to lomefloxacin.

29. Vitanen, J., et al. Randomized controlled study of chemoprophylaxis in transurethral prostatectomy. *J. Urol.* 150:1715, 1993.
Concluded that single-dose antibiotic prophylaxis was useful to reduce postoperative infectious complications in this study from Finland of 599 patients who received no antibiotic (22% infections), one double-strength TMP-SMX tablet (12.3% infections), or 2 g ceftriaxone (7.6% infections). Initial urine cultures were sterile.

30. Shapiro, M. Prophylaxis in otolaryngologic surgery and neurosurgery: A critical review. *Rev. Infect. Dis.* 13(Suppl. 10):S858, 1991.

31. Phan, M., et al. Antimicrobial prophylaxis for major head and neck surgery in cancer patients: Sulbactam-ampicillin versus clindamycin-amikacin. *Antimicrob. Agents Chemother.* 36:2014, 1992.

Even with perioperative prophylaxis, wound infections occurred in 20-30% of patients! See reference [41].

32. Brown, E.M. Antimicrobial prophylaxis in neurosurgery. *J. Antimicrob. Chemother.* 31(Suppl. B):49, 1993.
See related article, Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy, Antimicrobial prophylaxis in neurosurgery and after head trauma. Lancet *344:1547, 1994.*

33. Haines, S.J., and Walters, B.C. Antibiotic prophylaxis for cerebrospinal fluid shunts: A meta-analysis. *Neurosurgery* 34:87, 1994.
See the related article, J.M. Langley et al., Efficacy of antimicrobial prophylaxis in placement of cerebrospinal fluid shunts: Meta-analysis. Clin. Infect. Dis. *17:98, 1993.*

33A. Barker, F.G., III. Efficacy of prophylactic antibiotics for craniotomy: A meta-analysis. *Neurosurgery* 35:484, 1994.
Analysis showed an advantage of antibiotics over placebo.

33B. Bernard, A., et al. Antibiotic prophylaxis in pulmonary surgery: A prospective, randomized, double-blind trial of flash cefuroxime versus forty-eight-hour cefuroxime. *J. Thorac. Cardiovasc. Surg.* 107:896, 1994.
The 48 hour-regimen (1.5 g preoperatively and 1.5 g q6h for 48 hours postoperatively) was associated with a 46% infection rate versus a 65% infection rate in the 1.5 g preoperative dose and a similar dose once 2 hours later. The reduction in infection was significant at the p = .005 level.

34. Platt, R., et al. Perioperative antibiotic prophylaxis for herniorrhaphy and breast surgery. *N. Engl. J. Med.* 322:153, 1990.
Although cefonicid was used in this study, presumably similar results would be achieved with more standard regimens (e.g., cefazolin). See related article by R. Platt et al., Prophylaxis against wound infection following herniorrhaphy or breast surgery. J. Infect. Dis. *166:556, 1992. In absence of formal guidelines, surgeons preferentially*

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used prophylaxis in patients at highest risk, e.g., more prolonged procedures, mastectomies, etc.

35. Platt, R., et al. Perioperative antibiotic prophylaxis and wound infection following breast surgery. *J. Antimicrob. Chemother.* 31(Suppl. B):43, 1993.
Meta-analysis of published data of more than 2,587 surgical procedures. Multiauthored and numerous centers involved. Conclusion: Antibiotic prophylaxis (with cephalosporins) reduces the risk of postoperative infections.

36. Ayliffe, G.A.J. Role of the environment of the operating suite in surgical wound infections. *Rev. Infect. Dis.* 13(Suppl. 10):S800, 1991.
See companion article by G.L. Archer, Alteration of cutaneous staphylococcal flora as a consequence of antimicrobial prophylaxis. Rev. Infect. Dis. *13(Suppl. 10):S805, 1991, which discusses how surgical prophylaxis changes the microflora and susceptibility of skin flora and how colonized patients and hospital staff make up a nosocomial reservoir for resistant bacteria.*

37. Curtis, J.J., et al. Randomized, prospective comparison of first- and second-generation cephalosporins as infection prophylaxis for cardiac surgery. *Am. J. Surg.* 166:734, 1993.
Randomized prospective study of 702 patients comparing cefazolin (1 g q8h for 48 hours) with one intraoperative dose at 4 hours versus cefuroxime (1.5 g q12h for 48 hours). There was no difference in the wound infection rates.

38. Townsend, T.R., et al. Clinical trial of cefamandole, cefazolin, and cefuroxime for antibiotic prophylaxis in cardiac operations. *J. Thorac. Cardiovasc. Surg.* 106:664, 1993.

Randomized, double-blind study of 1,641 patients receiving cefazolin, cefamandole or cefuroxime. No differences in effectiveness in preventing operative site infections were demonstrated.

39. Sabath, L. Reappraisal of antistaphylococcal activities of first-generation (narrow-spectrum) and second-generation (expanded-spectrum) cephalosporins. *Antimicrob. Agents Chemother.* 33:407, 1989.
Minireview of this topic, in which there has been a resurgence of interest.

40. Kernodle, D.S., et al. Failure of cephalosporins to prevent *Staphylococcus aureus* surgical wound infections. *J.A.M.A.* 263:961, 1990.

41. Weber, R.S., et al. Ampicillin-sulbactam vs. clindamycin in head and neck oncologic surgery. The need for gram-negative coverage. *Arch. Otolaryngol. Head Neck Surg.* 118:1159, 1992.
Both agents were given preoperatively and for 48 hours postoperatively. Infections occurred in 13% of ampicillin-sulbactam recipients and 27% of clindamycin recipients from whom gram-negative organisms were more commonly isolated. Of greater interest would be a comparison of ampicillin-sulbactam and cefazolin because the latter covers many community-acquired gram-negative organisms.

42. Dajani, A., et al. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: A statement for health professionals. *Pediatrics* 96:758, 1995.
This October 1995 publication from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, the American Heart Association replaces the prior recommendations of this committee published in 1988.
See related articles by A.D. Heggie et al., J. Infect. Dis. 166:1006, 1992, *demonstrating that benzathine penicillin prophylaxis still is effective against group A streptococcal carriage and infection; and H.C. Lue et al., Long-term outcome of patients with rheumatic fever receiving benzathine penicillin G every three weeks versus every four weeks.* J. Pediatr. 125(pt. 1):812, 1994, *which favors the every-3-week schedule.*

43. Bass, J.W. Antibiotic management of Group A streptococcal pharyngotonsillitis. *Pediatr. Infect. Dis. J.* 10:S43, 1991.

44. Klein, J.O. Management of streptococcal pharyngitis. *Pediatr. Infect. Dis. J.* 13:572, 1994.
Group A streptococci remain uniformly susceptible to all penicillins and cephalosporins. Penicillin remains the treatment of choice. Alternative regimens are discussed.

45. Medical Letter. Prevention of serious infections after splenectomy. *Med. Lett. Drugs Ther.* 19:2, 1977.
As of mid-1995, this topic has not been updated in The Medical Letter. *For a related paper, see E.L. Francke and H.C. Neu, Postsplenectomy infection.* Surg. Clin. North Am. 61:135, 1981.

46. Styrt, B. Infection associated with asplenia: Risks, mechanisms, and prevention. *Am. J. Med.* 88(Suppl. 5N):33N, 1990.
A good review.

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47. Schimpff, S.C. Infections in the Cancer Patient: Diagnosis, Prevention, and Treatment. In G.L. Mandell, J.E. Bennett, and R. Dolin (eds.), *Principles and Practice of Infectious Diseases* (4th ed.). New York: Churchill Livingstone, 1995. P. 2666.

48. Buchanan, G.R. Chemoprophylaxis in asplenic adolescents and young adults. *Pediatr. Infect. Dis. J.* 12:892, 1993.
Editorial-like comment. The author typically recommends daily prophylaxis with penicillin for 3 years after splenectomy. He encourages those willing to take prophylaxis beyond that time to do so, but his alternative approach is to give the patient a supply of oral penicillin and, in the event of fever, to take a dose q8h if seeing a physician is delayed. By this method, the author hopes to prevent a fulminant pneumococcal sepsis, though he admits that no scientific evidence supports this approach.

49. Reid, M.M. Splenectomy, sepsis, immunisation and guidelines. *Lancet* 344:970, 1994.
In this October 1994 editorial, the author basically reminds the reader that the best approach for this problem is still unclear and should be studied.

50. Dajani, A.S., et al. Prevention of bacterial endocarditis: Recommendations by the American Heart Association. *J.A.M.A.* 264:2919, 1990.
Most up-to-date summary of SBE prophylaxis. Simpler and less costly regimens are emphasized. Published December 12, 1990. This is a statement from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. These recommendations are being updated in 1996 and will be published in late 1996 or early 1997. For an editorial comment on the 1990 recommendations, see E.A. Petersen, Prevention of bacterial endocarditis. Arch. Intern. Med. 150:2447, 1990.
For a current discussion of the rationale and limitations of SBE prophylaxis, see recent review by D.T. Durack, Prevention of infective endocarditis. N. Engl. J. Med. 332:38, 1995.

51. Wehrmacher, W.H. Myths: Endocarditis. *Arch. Intern. Med.* 154:129, 1994.
Editorial comment on the 1990 American Heart Association (AHA) recommendations of reference [50], again dealing with the issue of the lack of "hard data" for such recommendations and in response to a related article by dentist M.J. Wahl, Myths of dental-induced endocarditis. Arch. Intern. Med. 154:137, 1994, *which also discusses some of the controversial recommendations in reference [50].*
Editorial comment points out that in 1992 the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy updated their recommendations for antibiotic prophylaxis. They are similar to the 1990 AHA guidelines.

52. Kaye, D., and Abrutyn, E. Prevention of bacterial endocarditis: 1991. *Ann. Intern. Med.* 114:803, 1991.
Thoughtful editorial response of AHA recommendations (see reference [50]) pointing out the differences with prior AHA recommendations. Also discusses a rational approach to patients with mitral valve prolapse.
For yet another editorial comment on these guidelines, see P.I. Lerner, Endocarditis prophylaxis: The new guidelines. Cleve. Clin. J. Med. 59:216, 1992. *Concludes by reminding physicians that plaintiff lawyers will "be all too eager to challenge even minor deviations from the guidelines," a conclusion also pointed out in a more recent editorial (reference [51]).*

53. Bodey, G. Antimicrobial prophylaxis for infection in neutropenic patients. *Curr. Clin. Top. Infect. Dis.* 1-43, 1988.

54. Paradise, J.L. Antimicrobial prophylaxis for recurrent acute otitis media. *Ann. Otol. Rhinol. Laryngol.* (Suppl. Jan) 155:33, 1992.
Although questions remain about the choice of drug, optimal dosage schedules and therapy duration, risk of side effects, and the risk of selecting out resistant bacteria, antibiotic prophylaxis is a logical first step in managing recurrent otitis media in a child.

55. Giebink, G.S. Preventing otitis media. *Ann. Otol. Rhinol. Laryngol.* (Suppl. May) 163:20, 1994.

56. Williams, R.L., et al. Use of antibiotics in preventing recurrent acute otitis media and in treating otitis media with effusion. A meta-analytic attempt to resolve the brouhaha. *J.A.M.A.* 270:1344, 1993.
Antibiotics appear to have beneficial but limited effect on recurrent otitis media and short-term resolution of otitis media with effusion. Longer-term benefits for otitis media with effusion have not been shown. See related comments in J.A.M.A. 271:430 *and* 272:203, 1994.

57. Fox, B.C., et al. A prospective, randomized, double-blind study of trimethoprim-sulfamethoxazole for prophylaxis of infection in renal transplantation: Clinical efficacy,

absorption of trimethoprim-sulfamethoxazole, effects on microflora, and the cost-benefit of prophylaxis. *Am. J. Med.* 89:255, 1990.
During the hospitalization after the transplantation surgery, 160 mg TMP and 800 mg SMX bid was given if creatinine clearance was greater than 30 ml/min. After discharge, a single daily dose of 160 mg TMP and 800 mg SMX was used. (If creatinine clearance was < 30 ml/min, one-half the usual dose per day was used.)
For a related article emphasizing the lack of side effects with TMP-SMX prophylaxis and lack of nephrotoxicity in cyclosporine recipients, see D.G. Maki et al., A prospective, randomized, double-blind study of trimethoprim-sulfamethoxazole for prophylaxis of infection in renal transplantation: Side effects of trimethoprim-sulfamethoxazole interaction with cyclosporine. J. Lab. Clin. Med. **119:11, 1992.**

58. Margolis, D.M., et al. Trimethoprim-sulfamethoxazole prophylaxis in the management of chronic granulomatous disease. *J. Infect. Dis.* 162:723, 1990.

59. Van der Hazel, S.J., et al. Role of antibiotics in treatment and prevention of acute and recurrent cholangitis. *Clin. Infect. Dis.* 19:279, 1994.
Good clinical discussion of this topic. Optimal duration of maintenance preventive doses is unclear. Authors suggest treating the patient for 3-4 months and then evaluating whether the antibiotics can be stopped without recurrence of infection. If infection recurs, therapy can be restarted. Lower-than-therapeutic doses may be effective (e.g., one double-strength tablet of TMP-SMX daily rather than bid).

60. Niederau, C., et al. Prophylactic antibiotic treatment in therapeutic or complicated diagnostic ERCP: Results of a randomized controlled clinical study. *Gastrointest. Endosc.* 40:533, 1994.
Prophylactic cefotaxime reduced the incidence of bacteremia.

60A. Byl, B., et al. Antibiotic prophylaxis for infectious complications after therapeutic endoscopic retrograde cholangiopancreatography: A randomized, double-blind, placebo-controlled study. *Clin. Infect. Dis.* 20:1236, 1995.
In this study, uninfected patients were assigned to receive piperacillin (4 g) or placebo tid; prophylaxis was started just before initial ERCP and was continued until biliary drainage was completely unobstructed. Authors concluded that antimicrobial prophylaxis significantly reduces the incidence of septic complications after therapeutic ERCP among patients presenting with cholestasis. No bacteremia was documented in the 30 patients receiving piperacillin. Seven (22%) of 32 patients receiving placebo had bacteremia; pathogens included Pseudomonas *(3),* E. Coli *(3),* Streptococcus sanguis, *and* S. salivarius *(1). All isolates were susceptible to piperacillin.*
Nevertheless, the Medical Letter's *antibiotic of choice for prophylaxis for biliary tract manipulation/surgery is cefazolin, and we also would favor use of cefazolin in most cases of ERCP, unless the patient had a long hospitalization and/or had been treated with protracted antibiotics so that a broader spectrum agent, e.g., piperacillin, aimed at hospital-acquired gram-negatives may be reasonable; in this case we might also give a single dose of an aminoglycoside.*

61. Sheen-Chen, S.M., et al. Postoperative T-tube cholangiography: Is routine antibiotic prophylaxis necessary? A prospective controlled study. *Arch. Surg.* 130:20, 1995.
Study concludes that routine antibiotic prophylaxis to prevent infection following postoperative T-tube cholangiography is not necessary under selected conditions.