

A Guide to Antibiotics for the Interventional Radiologist

Ali Zarrinpar, Ph.D.,¹ and Robert K. Kerlan, Jr., M.D.¹

ABSTRACT

Antibiotics are among the most common pharmaceutical agents used by the interventional radiologist. This article updates some of the practical aspects of the use of antibiotics in interventional radiological practice and provides some general guidelines with respect to indications for and selection of antibiotics. In particular, the objectives of this article are to review the basic pharmacology of the common antibiotic agents, the interventional radiological procedures in which prophylactic antibiotics are usually administered, the specific antimicrobial agents recommended for prophylaxis before common interventional radiological procedures, the appropriate antibiotics for patients allergic to penicillins, and the indications for antibiotic prophylaxis to prevent bacterial endocarditis.

KEYWORDS: Interventional radiology, antibiotics, prophylaxis, review, allergies

Objectives: Upon completion of this article, the reader will understand (1) the specific prophylactic antibiotics recommended for common interventional radiological procedures, (2) which antibiotics are appropriate for patients allergic to penicillin, and (3) which patients and procedures require antibiotic prophylaxis to prevent bacterial endocarditis.

Accreditation: Tufts University School of Medicine (TUSM) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit: TUSM designates this educational activity for a maximum of 1 Category 1 credit toward the AMA Physicians Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Antibiotics are among the most common pharmaceutical agents used by the interventional radiologist. These agents are used prophylactically to prevent infection of an uninfected space as well as to minimize problems associated with septicemia when catheter manipulations are performed within infected fluid collections. Although the administration of antibiotic agents in many interventional radiologic procedures is appropriate and mandated by the standard of care, scientific evidence of the effectiveness of these drugs in specific interventional radiological procedures is limited.¹ This article updates some of the practical aspects

of the use of antibiotics in interventional radiological practice and provides some general guidelines with respect to indications for and selection of antibiotics.

The objectives of this article are to review (1) the basic pharmacology of the common antibiotic agents, (2) the interventional radiological procedures in which prophylactic antibiotics are usually administered, (3) the specific antimicrobial agents recommended for prophylaxis before common interventional radiological procedures, (4) the appropriate antibiotics for patients allergic to penicillins, and (5) the indications for antibiotic prophylaxis to prevent bacterial endocarditis.

Pharmacology in Interventional Radiology; Editors in Chief, Brian Funaki, M.D., Peter R. Mueller, M.D.; Guest Editor, Richard D. Shlansky-Goldberg, M.D. *Seminars in Interventional Radiology*, volume 22, number 2, 2005. Address for correspondence and reprint requests: Robert K. Kerlan, Jr, M.D., Department of Radiology, M-361, University of California, San Francisco, 505 Parnassus, Box 0628, San Francisco, CA 94143.
¹Department of Radiology, University of California, San Francisco. Copyright © 2005 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662. 0739-9529,p;2005,22,02,069,079,ftx,en;sir00296x.

ANTIBIOTIC AGENTS

Antibiotics, as a rule, demonstrate a high degree of "selective toxicity" by being lethal to bacteria and harmless to the patient. To this end, antibiotics take advantage of differences between the bacterial and human cells. There are at least four mechanisms of action that account for this selective toxicity:

1. Inhibition of cell wall synthesis (penicillins, cephalosporins, and vancomycin)
2. Alteration of permeability of the cell membrane (amphotericin, polymyxin, and daptomycin)
3. Alteration or prevention of bacterial protein synthesis (aminoglycosides, macrolides, tetracyclines, and linezolid)
4. Prevention of bacterial nucleic acid synthesis (sulfonamides and quinolones)

Interventional radiologists use a limited number of these agents, with the most common being penicillins, cephalosporins, vancomycin, aminoglycosides, and quinolones.

Penicillins

Penicillins are among the most effective and least toxic antibiotics available. Resistance to these bactericidal antibiotics is generally due to bacterial production of penicillin-binding proteins and β -lactamases or a reduction in the permeability of the bacterial outer membrane. Because they are eliminated largely by the kidneys, dosages must be adjusted in patients with renal insufficiency. Hypersensitivity reactions are the most common side effects of penicillins, and their common immunogenicity precludes persons known to be allergic to one penicillin from being safely administered another. However, in the absence of an alternative, patients can be desensitized.^{2,3}

The use of the natural penicillins, penicillin G and V, for interventional radiological procedures remains infrequent, but they are still used clinically for specific gram-positive bacterial infections (susceptible pneumo-

cocci, streptococci, and meningococci). The aminopenicillins, ampicillin and amoxicillin, are active against most strains of *Proteus mirabilis*, *Listeria*, pneumococci, and non- β -lactamase producing strains of *Haemophilus influenzae*. They are also more active against many community-acquired enterococci. Ticarcillin, a carboxypenicillin, has more activity against *Pseudomonas*, *Serratia*, and *Proteus*. The acylureido-penicillins, mezlocillin and piperacillin, extend the coverage of gram-negative organisms to *Klebsiella*.

There are two solutions to counteract the resistance conferred by β -lactamases. The first is to combine penicillins with β -lactamase inhibitors. Such combinations include amoxicillin-clavulanic acid (Augmentin), ticarcillin-clavulanic acid (Timentin), ampicillin-sulbactam (Unasyn), and piperacillin-tazobactam (Zosyn). With the exception of Augmentin, which is usually reserved for refractory cases of sinusitis and otitis and for animal and human bites, the combination drugs are used to treat polymicrobial infections, such as peritonitis, with Zosyn having the broadest spectrum of activity. The second means to counteract resistance is through β -lactamase-resistant penicillins, methicillin, oxacillin, cloxacillin, dicloxacillin, and nafcillin. The use of these drugs is limited to the treatment of infections with β -lactamase-producing staphylococci.

Cephalosporins

Chemically, cephalosporins are similar to penicillins in that they share a β -lactam ring. The mechanism of action (cell wall inhibition) and mechanisms of bacterial resistance are also similar to those of penicillins. Furthermore, 10% of patients with allergies to one group show cross-reactivity to the other group. Cephalosporins are active against gram-negative and gram-positive bacteria, with the exception of enterococci and methicillin-resistant staphylococci, which are uniformly resistant to all cephalosporins. Cephalosporins are subdivided into four generations by their antibacterial activity (Table 1).

Table 1 Four Generations of Cephalosporins

| Generation | Examples | Activity | Miscellaneous |
|------------|---|---|---|
| First | Cefazolin, cephalexin | Aerobic gram-positive bacteria, some community-acquired gram negative | Least expensive |
| Second | Cefoxitin, cefuroxime, cefotetan, cefaclor | Extended activity against gram negative. Cefoxitin has substantial activity against anaerobes | Decreased activity against gram positives |
| Third | Cefotaxime, ceftazidime, ceftriaxone, ceftizoxime | Most gram-negative bacteria, except <i>Enterobacter</i> and <i>Citrobacter</i> | Ceftriaxone has biliary excretion and is commonly used in biliary prophylaxis |
| Fourth | Cefepime | Like third generation with added stability against plasmid-borne β -lactamases | Does not induce β -lactamase capacity |

Vancomycin

Vancomycin is structurally unrelated to the other antibiotics. Although its mechanism of activity is cell wall inhibition, the precise molecular mechanism differs from that of penicillins and cephalosporins. It is active against gram-positive organisms including enterococci. There is no allergic cross-reactivity with penicillins and cephalosporins. Therefore, it is an alternative agent for patients with serious penicillin allergies. The disadvantages of the use of vancomycin include the need to infuse it slowly over 45 minutes to 1 hour to avoid side effects such as fevers, chills, diffuse erythema (the so-called red-man syndrome, which can also be avoided by pretreating with an antihistamine), and thrombophlebitis. Ototoxicity and nephrotoxicity can also be encountered with vancomycin, especially when administered concomitantly with aminoglycosides. Moreover, indiscriminate use is leading to the emergence of resistant gram-positive bacteria, for which few therapeutic alternatives may be available.^{4,5}

Aminoglycosides

Aminoglycosides inhibit protein synthesis and subsequently lead to altered permeability of cell membranes. This group includes gentamicin, tobramycin, and amikacin. These agents have potent activity against enteric gram-negative organisms. They are also used in combination with other agents to treat selected *Staphylococcus* and *Enterococcus* infections. They have negligible activity against other gram-positive and anaerobic organisms. The major disadvantage of these agents is nephrotoxicity and ototoxicity. Fortunately, these complications are almost never encountered when these agents are used for single-dose prophylaxis. Aminoglycosides are excreted almost entirely by glomerular filtration and thus can accumulate in patients with renal insufficiency. This is also the reason that they are the agent of choice for patients undergoing urinary tract interventions, particularly patients with significant penicillin allergies.

Quinolones

Quinolones, including ciprofloxacin, norfloxacin, and levofloxacin, have a very broad spectrum of activity. Their mechanism of activity is prevention of bacterial nucleic acid synthesis. Quinolones are safe, and although nausea and vomiting are seen in up to 5% of patients, significant toxicity is unusual. Nevertheless, their broad spectrum of activity against both gram-positive and gram-negative organisms makes them suitable for polymicrobial prophylaxis in patients with penicillin allergy. However, quinolones are quite expensive and provide overly broad coverage for routine prophylaxis.

New Drugs

Oxazolidinones comprise a new class of drugs represented by linezolid, the first approved example.^{6,7} Linezolid is primarily active against aerobic gram-positive bacteria. It is approved for use in infections caused by penicillin-resistant pneumococci, methicillin-resistant staphylococci, and vancomycin-resistant enterococci. Its oral bioavailability nearly matches its intravenous (IV) availability, and it is eliminated primarily by nonrenal mechanisms.

Cyclic lipopeptides, the first approved example of which is daptomycin,⁸ bind bacterial membranes and cause a rapid depolarization of membrane potential, leading to cell death. Daptomycin is highly active against aerobic gram-positive bacteria. As an IV agent, it has been approved for the treatment of complicated skin and skin structure infections caused by staphylococci, streptococci, and enterococci. Although its efficacy in the treatment of bacteremia is still under investigation, further clinical experience is likely to expand its role in the treatment of resistant gram-positive organisms.

Although streptogramins are similar in chemical structure and mechanism of antibacterial action to macrolides, the two groups do not share cross-resistance. The combination drug quinupristin and dalbapristin is currently available as an IV agent most useful in the treatment of resistant gram-positive infections, such as those due to streptococci, staphylococci, and enterococci.⁹

ANTIBIOTIC PROPHYLAXIS

Antibiotics are administered either to prevent a clinical infection from developing (antibiotic prophylaxis) or to treat an existing infection (antibiotic therapy). Although interventional radiologists commonly encounter patients undergoing antibiotic therapy, the selection of agents has often been made solely by or in conjunction with the referring clinician. On the other hand, the decision to administer, as well as the selection of, prophylactic antibiotics is usually made by the interventional radiologist.

Spies et al¹⁰ and McDermott et al¹¹ previously published recommendations for the use of prophylactic antibiotics in interventional radiological procedures. These recommendations were based upon the assumption that antibiotic coverage should parallel recommendations for open surgical procedures. Antibiotic prophylaxis for open surgical procedures is usually done in accordance with the recommendations of the National Academy of Sciences/National Research Council (NAS/NRC).¹² The NAS/NRC classified procedures into the following four categories: clean, clean-contaminated, contaminated, and dirty. *Clean* procedures are those in which spaces potentially containing bacteria (gastrointestinal, biliary, genitourinary, and

respiratory tracts as well as inflamed or infected tissue) are not entered. If a noninflamed space containing bacteria is entered, the procedure is considered *clean-contaminated*. A *contaminated* procedure indicates that a space containing inflammation is entered, and the classification *dirty* is applied when pus or free spillage of contaminated material occurs.

On the face of it, using NAS/NRC guidelines appears to be a rational strategy. However, it should be noted that the infectious risks of open surgical procedures differ considerably from those of interventional radiologic procedures. Specifically, surgical prophylaxis is directed at preventing infection of the wound by infected fluid or skin organisms. In contrast, the small incision made during percutaneous drainage procedures seldom serves as a site for a clinically important infection. The risk of percutaneous drainage procedures is that infected fluid under pressure may be entered with a needle or catheter, or both, creating a potential communication with the infected contents and the bloodstream. In these procedures, prophylactic antibiotics are intended to diminish the impact of bacteria that leak into the bloodstream. Therefore, data from studies of surgical wound prophylaxis may not be applicable to interventional radiological procedures performed on the same organ.

Currently, antibiotic prophylaxis is recommended for interventional radiological procedures that are not classified as clean. The selected antibiotic is based on efficacy against likely organisms, toxicity, and cost. The use of prophylactic antibiotics with an extremely broad spectrum of coverage is discouraged as this strategy potentially promotes cultivation of resistant organisms.^{13,14} Moreover, the emergence of drug-resistant enterococci has focused attention on the indiscriminate use of vancomycin as a prophylactic agent.¹⁵

Although the administration of prophylactic antibiotics before the performance of interventional radiological procedures is an extremely common clinical practice, until recently, scientific evaluation was limited. However, as more attention has been focused in this area, some evidence regarding the efficacy of prophylactic antibiotics has accumulated. The following evidence has been presented for the common interventional radiologic procedures.

Nonvascular Interventions

PERCUTANEOUS NEPHROSTOMY

Cronan et al¹⁶ conducted a trial to evaluate the necessity of giving antibiotics before routine nephrostomy tube changes. In this prospective trial, 104 nephrostomy tube changes were performed in 74 patients and an 11% overall incidence of bacteremia was detected. The incidence of bacteremia was nearly identical in the group

receiving preprocedural antibiotics and the group who did not receive any antibiotics. The authors concluded that preprocedural antibiotics were of no benefit for asymptomatic patients undergoing routine nephrostomy tube changes.

A similar evaluation has not been performed for the initial percutaneous nephrostomy procedure, and the majority of interventional radiologists administer IV antibiotics prior to placing a urinary drainage tube.¹ With that in mind, Christiano et al¹⁷ showed that ciprofloxacin is equivalent to cefazolin in preventing postoperative urinary tract infection. As mentioned previously, however, ciprofloxacin is more expensive and potentially provides a broader spectrum than desirable for prophylaxis.

PERCUTANEOUS BILIARY INTERVENTIONS

With regard to the biliary tract, Clark et al¹⁸ reported a retrospective review of 388 interventional biliary tract procedures. In this series, seven patients developed bacteremia. Five of these seven (71%) had received antibiotics; in two cases, the organisms were sensitive to the antibiotics that were given. Brody et al¹⁹ prospectively evaluated the presence of bacteria in the bile of patients undergoing percutaneous drainage for biliary obstruction. These investigators concluded that fever, previous endoscopic or percutaneous biliary instrumentation, and bilioenteric anastomoses were significant predictors of a positive bile culture. Moreover, enterococci were the most commonly isolated organisms. Because of the frequency of enterococcus isolates from obstructed bile, ampicillin and synthetic penicillins (including piperacillin and mezlocillin) with activity against these organisms have theoretical advantages over cephalosporins for biliary prophylaxis. Nevertheless, the only studies evaluating the utility of prophylaxis use cephalosporins as the standard antibiotic, with ciprofloxacin as an equally effective substitute.²⁰⁻²³ Indeed, in one case, antibiotic testing of biliary cultures demonstrated the susceptibility of those organisms to fluoroquinolones.²⁴ The overwhelming majority of interventional radiologists administer IV antibiotics before biliary procedures.¹

RADIOFREQUENCY ABLATION

No scientific evidence is available to guide decision making with regard to prophylactic antibiotics prior to radiofrequency ablation. However, because there is a potentially significant volume of necrotic tissue in potentially contaminated areas (liver, lung, kidney), most investigators consider some type of antibiotic prophylaxis appropriate with coverage of both gram-negative and gram-positive organisms. Either a semisynthetic penicillin derivative or a second- or third-generation cephalosporin would appear most appropriate.²⁵

PERCUTANEOUS GASTROSTOMY

New studies also show the utility of antibiotic prophylaxis in percutaneous gastrostomy placement. These studies show that a single dose of a broad-spectrum antibiotic such as cefazolin is effective in reducing post-operative wound infection.^{26–29}

Antibiotics are also given to the majority of patients undergoing drainage of potentially infected fluid collections. However, in this population of patients, the antibiotics are considered therapeutic rather than prophylactic.

Vascular Interventions

TRANSJUGULAR INTRAHEPATIC

PORTOSYSTEMIC SHUNTS

Deibert et al³⁰ conducted a randomized prospective trial to assess the need for antibiotic prophylaxis before a transjugular intrahepatic portosystemic shunt (TIPS). They found that a single dose of prophylactic cefotiam did not prevent post-TIPS infection. However, this second-generation cephalosporin may not possess the ideal spectrum to cover the organisms normally associated with these infections (staphylococci, enterococci, and *Klebsiella*).

HEPATIC CHEMOEMBOLIZATION

In a retrospective analysis of 494 hepatic chemoembolization procedures, Reed et al³¹ concluded that prophylactic antibiotics decreased the incidence of postprocedural hepatic abscess formation. However, the statistical significance of this conclusion was disputed because only one of nine patients who did not receive prophylactic antibiotics developed an infectious complication. In a small prospective study, Geschwind et al³² compared cephalixin with the combined use of piperacillin-tazobactam and a bowel preparation in high-risk patients with a history of biliary reconstructive surgery. Whereas every patient in the first group developed hepatic abscesses and had to be subsequently treated, none of the patients in the second group developed hepatic abscesses following chemoembolization of the liver.

UTERINE FIBROID EMBOLIZATION

No controlled randomized trials are available to guide the application of antibiotics in uterine fibroid embolization (UFE). Many practitioners use prophylactic antibiotics routinely.^{33,34} In the Ontario Uterine Fibroid Embolization Trial,³⁵ routine antibiotic prophylaxis with cefazolin 1 g IV was used at four hospitals and no prophylaxis at four additional hospitals. One post-UFE infection requiring hysterectomy was noted in each group. Other investigators³⁶ have used a prophylaxis regimen tailored after traditional gynecologic surgical

procedures using either doxycycline or metronidazole and ampicillin. Although no evidence-based recommendations can be made, it would seem that most practitioners use antibiotic prophylaxis in conjunction with UFE.

CENTRAL VENOUS ACCESS

Currently, the Centers for Disease Control and Prevention (CDC) recommend no prophylactic antibiotics for central venous access procedures.³⁷ Controversy dogged this issue partly because of inconsistent reporting, with infectious complications being variously tabulated as the percentage of patients with fevers, frequency of catheter removal for persistent fever, documented catheter colonization, number of tunnel infections, as well as the percentage of exit site infections. Other strategies have been to report infections per access days, life table analysis of catheter dwell time, number of infections within the first month, and duration of time until the first infection. Investigators should be encouraged to perform the prospective series that report the number of infections per catheter days, allowing a more reliable comparison between series. In light of these limitations, it is not surprising that conflicting data exist regarding the usefulness of prophylactic antibiotics in preventing infections in patients undergoing central venous access procedures.

Proponents of antibiotic prophylaxis when placing central venous access catheters or subcutaneous ports are supported by several articles^{38–41} in which the incidence of infection was significantly less in patients who received preprocedural antistaphylococcal agents, especially pediatric patients⁴² (Table 2).

However, opponents of this strategy point to three randomized, prospective, controlled trials^{43–45} in which prophylactic antibiotics did not diminish the incidence of subsequent infections (Table 3).

Data from the interventional radiological literature (Table 4) are limited but do not support conclusively the application of routine antibiotic prophylaxis during placement of central venous catheters. Data from placement of tunneled hemodialysis catheters^{46,47} reveal a similar infection rate despite inconsistent administration

Table 2 Infection Rate during Central Venous Catheter Insertion with and without Antibiotic Prophylaxis at the Time of Insertion

| Series | n | Infections without Prophylaxis | Infections with Prophylaxis |
|--------------------------------------|-----|--------------------------------|-----------------------------|
| Vassilomanolakis et al ³⁸ | 46 | 6/11 (55%) | 4/35 (11%) |
| Lim et al ³⁹ | 44 | 9/21 (43%) | 4/23 (17%) |
| Al-Sibai et al ⁴⁰ | 160 | 50/90 (55%) | 12/70 (17%) |
| Bock et al ⁴¹ | 125 | 8/81 (10%) | 0/44 (0%) |
| Shaul et al ⁴² | 159 | 28/34 (82%) | 25/72 (35%) |

Table 3 Randomized, Prospective Studies of Infection Rate during Central Venous Catheter Insertion with and without Antibiotic Prophylaxis at the Time of Insertion

| Series | n | Infections without Prophylaxis | Infections with Prophylaxis |
|------------------------------|----|--------------------------------|-----------------------------|
| Ranson et al ⁴³ | 72 | 9/36 (25%) | 9/36 (25%) |
| McKee et al ⁴⁴ | 53 | 10/29 (34%) | 7/24 (29%) |
| Ljungman et al ⁴⁵ | 62 | 11/30 (37%) | 15/32 (47%) |

of prophylactic antibiotics. However, a reported series of chest wall ports placed by interventional radiologists⁴⁸ documents a low (5.5%) infection rate when most patients receive prophylactic antistaphylococcal agents. This strategy appears reasonable when a device is implanted, particularly if the patient is immunocompromised.

Another important measure in preventing catheter infections is the use of the antibiotic flush-lock technique to decontaminate the hub and prevent spread of bacteria into the catheter lumen. There is evidence that the use of several agents in the flush including vancomycin, ciprofloxacin, and minocycline⁴⁹⁻⁵² reduces catheter infections. Antibiotic-impregnated catheters also promise to be useful in reducing catheter-related infections.^{53,54} However, the CDC does not recommend routine use of antibiotic lock solutions to prevent infection except in special circumstances, such as patients with a history of multiple infections despite optimal maximal adherence to aseptic technique.³⁷

ARTERIAL STENTS

Although it has been suggested that prophylactic antibiotics should be given during placement of an intra-arterial stent,^{55,56} few cases of stent infection have been reported. These infections have been reported with stents inserted into the iliac, renal, and coronary circulation. Most reported stent infections have occurred with the Palmaz device, probably reflecting the frequency with which this stent is used. A single infection has been reported with a Wallstent used in conjunction with a Palmaz stent. Considering the frequency with which these stents are used, the incidence of infection appears extremely low, making routine administration of antibiotic prophylaxis for arterial stent placement unjustified.

Table 4 Infection Rate during Tunneled Dialysis Catheter Insertion in Interventional Radiology with and without Antibiotic Prophylaxis

| Series | n | Antibiotic | Infection Rate* |
|-------------------------------|-----|------------|-----------------|
| Lund et al ⁴⁶ | 237 | Cefoxitin | 14% |
| Trerotola et al ⁴⁷ | 299 | None | 14% |

*The studies encountered identical infection rates.

ARTERIAL STENT GRAFTS

Because of the presence of prosthetic fabric, it is safe to assume that stent grafts have a greater chance of being infected than bare metal stents. Therefore, prophylactic antibiotics are used routinely prior to placement of an aortic endograft in many centers.⁵⁷ Despite the lack of a controlled trial, the potential mortality of an aortic endograft infection⁵⁸ clearly justifies the administration of prophylactic antibiotics. As the most likely organisms are principally staphylococcal species, cefazolin 1 g IV prior to the procedure would appear to be reasonable.

RECOMMENDATIONS FOR ANTIBIOTIC PROPHYLAXIS

The following recommendations for antibiotic prophylaxis (Table 5) are meant solely as general guidelines. Practitioners should modify these guidelines in accordance with the clinical circumstances of the individual patient and site-specific flora, which differs from hospital to hospital. In many situations, not administering a prophylactic antibiotic or substituting another agent may be more clinically appropriate. First-generation cephalosporins are recommended on the basis of spectrum, toxicity, and cost. Other cephalosporins (second and third generation) should be substituted if indicated by the site-specific flora and have been recommended by McDermott et al.¹¹ All antibiotics should be administered to the patient parenterally, as a single dose, immediately prior to the procedure.

If a patient reports a penicillin allergy, the 5-15% cross-reactivity with cephalosporins should be considered.⁵⁹ If a penicillin allergy is a maculopapular rash, the cephalosporin can usually be administered without significant risk and discontinued if the patient develops an allergic response. If the penicillin allergy suggests an anaphylactoid reaction (urticaria or respiratory compromise), an agent other than a cephalosporin should be given to the patient as described subsequently.

Antibiotic Prophylaxis for Bacterial Endocarditis

The question of which patients to give antibiotic prophylaxis to prevent bacterial endocarditis is also an issue for interventional radiologists. In 1984, the American Heart Association (AHA) presented recommendations for endocarditis prophylaxis, which were updated in 1990⁶⁰ and in 1997.⁶¹ The following is a summary of those recommendations.

Bacterial endocarditis prophylaxis is indicated for all invasive procedures that fall into the clean-contaminated, contaminated, or dirty classification in patients who have the conditions listed in Table 6.

Table 5 Recommendations for Administration of Prophylactic Antibiotics for Routine Interventional Radiologic Procedures

| Procedure | Organisms | Agent | Dose |
|--|--|---|---------------------------|
| Vascular procedures including diagnostic angiography, angioplasty, atherectomy, stent placement, and caval filter placement (clean) | None | None | |
| Arterial stent graft placement (aortic, iliac, superficial femoral) | <i>Staphylococcus</i> | Cefazolin | 1 g IV |
| Chemoembolization of the liver or embolization at other sites intended to produce necrosis (clean, but results in necrotic tissue that may become infected) | <i>Escherichia coli</i> <i>Klebsiella</i> <i>Enterobacter</i> <i>Enterococcus</i> <i>Clostridium</i> | Ampicillin and gentamicin | 2 g IV 1.5 mg/kg IV |
| Uterine artery embolization | <i>E. coli</i> <i>Klebsiella</i> <i>Enterobacter</i> <i>Enterococcus</i> | Cefazolin or ampicillin | 1 g IV 2 g IV |
| Subcutaneous venous access ports, immunocompetent patients (clean, but foreign body inserted in area of subcutaneous dissection) | None | None | |
| Subcutaneous venous access ports, immunocompromised patients (clean, but foreign body inserted in area of subcutaneous dissection) | <i>Staphylococcus</i> | Cefazolin | 1 g IV |
| Transhepatic cholangiography and percutaneous biliary drainage (clean or clean-contaminated), no evidence of biliary infection and no prior surgery or instrumentation | <i>Klebsiella</i> <i>Enterobacter</i> <i>E. coli</i> | Ceftriaxone | 1 g IV |
| Transhepatic cholangiography and percutaneous biliary drainage (clean or clean-contaminated), prior bilioenteric anastomosis or instrumentation | <i>Klebsiella</i> <i>Enterobacter</i> <i>E. coli</i> <i>Enterococcus</i> | Piperacillin-tazobactam or ticarcillin-clavulanic acid or ampicillin-sulbactam | Depends on agent |
| Biliary tube replacement (clean-contaminated) | <i>Klebsiella</i> <i>Enterobacter</i> <i>E. coli</i> <i>Enterococcus</i> | Ceftriaxone or piperacillin-tazobactam or ticarcillin-clavulanic acid or ampicillin-sulbactam | Depends on agent |
| Radiofrequency ablation of liver tumor | <i>Klebsiella</i> <i>Enterobacter</i> <i>E. coli</i> <i>Enterococcus</i> | Ceftriaxone or piperacillin-tazobactam or ticarcillin-clavulanic acid or ampicillin-sulbactam | Depends on agent |
| Percutaneous gastrostomy (clean-contaminated) | None | Cefazolin | 1 g IV |
| Antegrade pyelography and percutaneous nephrostomy (clean or clean-contaminated) | None | Cefazolin | 1 g IV |
| Nephrostomy tube change (clean-contaminated) | <i>E. coli</i> <i>P. mirabilis</i> <i>Enterococcus</i> <i>Pseudomonas</i> | None | |
| Abdominal fluid aspiration of uninfected ascites, lymphocele or simple hepatic or renal cyst (clean) | None | None | |

Bacterial endocarditis prophylaxis is not indicated for invasive procedures in patients with the conditions listed in Table 7.

The recommended regimen for endocarditis prophylaxis for patients undergoing procedures in the genitourinary system, gastrointestinal tract, biliary tract peritoneal cavity, or potentially contaminated

spaces in the retroperitoneum is listed in Table 8. For patients with significant allergy to penicillin, vancomycin, 1 g IV (to be infused over 1 hour), is substituted for ampicillin. In addition, rather than giving the oral dose of amoxicillin 6 hours later, the vancomycin and gentamicin may be repeated 8 hours after the initial dose.

Table 6 Cardiac Conditions Requiring Antibiotic Prophylaxis to Prevent Bacterial Endocarditis when Performing Any "Nonclean" Interventional Radiologic Procedure

| |
|--|
| Prosthetic cardiac valves, including bioprosthetic and homograft valves |
| Previous bacterial endocarditis, even in the absence of heart disease |
| Most congenital cardiac malformations |
| Surgically constructed systemic pulmonary shunts or conduits |
| Rheumatic and other acquired valvular dysfunction, even after valvular surgery |
| Hypertrophic cardiomyopathy |
| Mitral valve prolapse with valvular regurgitation and/or thickened leaflets |

Adapted from Dajani et al.⁶¹

Bacterial endocarditis prophylaxis is not recommended for patients undergoing cardiac catheterization. Although not addressed specifically by the AHA, by inference, prophylaxis would appear unnecessary for diagnostic angiographic procedures. However, if a diagnostic or therapeutic vascular procedure is anticipated to be prolonged, increasing the possibility of breaks in sterile technique, it may be prudent clinically to consider the administration of bacterial endocarditis prophylaxis.

Other situations in which the administration of endocarditis prophylaxis is unclear include tube cholangiography and liver and lung biopsy. Considering the frequency of enterococcal colonization of bile, prophylaxis would appear wise before cholangiography. The necessity of administering prophylaxis before fine-needle biopsy is less clear. However, if there was a concern by either the physician or the patient, the most prudent strategy would be to administer the prophylactic agents before the procedure is performed.

SPECIAL CONSIDERATIONS

Although in most patients the selection of which antibiotic to administer is not difficult, there are several

Table 7 Cardiac Conditions Not Requiring Antibiotic Prophylaxis against Bacterial Endocarditis

| |
|--|
| Isolated secundum atrial septal defect |
| Surgical repair, without residual beyond 6 months, of atrial septal defect, ventricular septal defect, or patent ductus arteriosus |
| Previous coronary artery bypass graft surgery |
| Mitral valve prolapse without valvular regurgitation |
| Physiologic, functional, or innocent heart murmurs |
| Previous Kawasaki disease without valvular dysfunction |
| Previous rheumatic fever without valvular dysfunction |
| Cardiac pacemakers and implanted defibrillators |

Adapted from Dajani et al.⁶¹

clinical situations in which the decision is influenced by specific clinical issues. These clinical issues include the presence of penicillin allergy, acute or chronic renal failure, and hepatic failure.

Penicillin Allergy

Although penicillins are not administered typically as prophylaxis or therapy related to interventional radiological procedures, the 10% cross-reactivity with cephalosporins is commonly of concern. Usually, if a patient claims to have an allergy to penicillins, as up to 10% of patients do,⁶² penicillin or its derivatives are not administered. The decision to administer a cephalosporin in this circumstance generally depends on the nature of the penicillin allergy.⁶³

If a patient describes a true anaphylactic reaction with respiratory or circulatory compromise, cephalosporins should not be administered and an alternative agent should be selected. If coverage of gram-positive cocci is desired, either vancomycin, 500 mg IV over 45 minutes, or clindamycin, 300 mg IV over 15 minutes, should be used. Because of the overuse of vancomycin and the emergence of resistant organisms, clindamycin may be a better choice for gram-positive coverage. If gram-negative coverage is desired, an aminoglycoside should be selected.

If the nature of the penicillin allergy is a rash, cephalosporins generally can be given without adverse reaction.⁶⁴ A more common problem is that patients cannot remember the nature of their allergy.⁶⁵ However, if the reaction was anaphylactic in nature and the patient was an adolescent or an adult, the patient can usually describe the experience.

Renal Failure

Because many antibiotics are excreted by the kidneys and many are also nephrotoxic, questions often emerge as to the appropriate antibiotic for patients in acute or chronic renal failure. Moreover, it is extremely important to investigate which agents have been administered recently to avoid giving additional and potentially toxic agents when adequate blood levels of previously administered agents may be present. Agents removed by dialysis include cephalosporins, most penicillins, aminoglycosides, and metronidazole. Agents not removed by dialysis include vancomycin, mezlocillin, nafcillin, and clindamycin.

If no antibiotic agents have been given previously, it is safe to give a single dose in the normal amount of any antibiotic agent. Despite the nephrotoxicity of many antibiotics, the adverse effect is from an accumulation of the drug. A single dose is virtually always safe to give, including aminoglycosides and vancomycin. If additional doses are required, these doses are given at a

Table 8 Standard Bacterial Endocarditis Prophylactic Regimen

| Situation | Time | Agent | Regimen |
|------------------------------|------------------------------------|----------------|--|
| Standard general prophylaxis | Within 1 hour before the procedure | Amoxicillin | Adult: 2.0 g IV (30-minute infusion) Pediatric: 50 mg/kg IV (30-minute infusion) |
| | then | Gentamicin | Adult: 1.5 mg/kg IV (30-minute infusion) or IM Pediatric: 2 mg/kg (≤ 80 mg) IV (30-minute infusion) |
| | ≤ 6 hours later | Amoxicillin | Adult: 1 g PO Pediatric: 25 mg/kg PO |
| Allergic to penicillin | Within 1 hour before the procedure | Vancomycin | Adult: 1.0 g IV (60-minute infusion) Pediatric: 20 mg/kg IV (60-minute infusion) (≤ 1 g) |
| | then | Gentamicin | Adult: 1.5 mg/kg IV (30-minute infusion) or IM Pediatric: 2 mg/kg (≤ 80 mg) IV (30-minute infusion) |
| | ≤ 6 hours later | No second dose | |

IM, intramuscular; IV, intravenous; PO, by mouth.
Adapted from Dajani et al.⁶¹

more delayed interval depending on the level of renal impairment.

As an alternative strategy, if prolonged antibiotic therapy is anticipated, a reduced dose may be administered at the usual dosing interval. However, in this situation antibiotics are given as a therapeutic strategy for a major infectious disease problem and the administration should be guided by peak and trough blood levels.

Liver Failure

Some antibiotics are excreted by the liver. Therefore, sometimes there are concerns with regard to doses of agents that should be given to patients with hepatic failure. Fortunately, the agents that have predominant hepatic excretion are seldom used by interventional radiologists and include tetracycline, chloramphenicol, and sulfonamides. A reduction in dose would be recommended for these agents depending on the severity of the hepatic compromise. For agents commonly used by interventional radiologists, including cephalosporins, penicillins, vancomycin, and aminoglycosides, no change in dosage is necessary for patients with hepatic failure.

REFERENCES

- Dravid VS, Gupta A, Zegel HG, Morales AV, Rabinowitz B, Freiman DB. Investigation of antibiotic prophylaxis usage for vascular and nonvascular interventional procedures. *J Vasc Interv Radiol* 1998;9:401-406
- Ghosal S, Taylor CJ. Intravenous desensitization to ceftazidime in cystic fibrosis patients. *J Antimicrob Chemother* 1997;39:556-557
- Papakonstantinou G, Bogner JR, Hofmeister F, Hehlmann R. Cefotaxime desensitization. *Clin Investig* 1993;71:165-167
- Recommendations for preventing the spread of vancomycin resistance. Recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 1995;44(RR-12):1-13
- Enright MC. The evolution of a resistant pathogen: the case of MRSA. *Curr Opin Pharmacol* 2003;3:474-479
- Eliopoulos GM. Current and new antimicrobial agents. *Am Heart J* 2004;147:587-592
- Diekema DJ, Jones RN. Oxazolidinone antibiotics. *Lancet* 2001;358:1975-1982
- Streit JM, Jones RN, Sader HS. Daptomycin activity and spectrum: a worldwide sample of 6737 clinical Gram-positive organisms. *J Antimicrob Chemother* 2004;53:669-674
- De Gaudio AR, Di Filippo A. What is the role of streptogramins in intensive care? *J Chemother* 2003;15(suppl 3):17-21
- Spies JB, Rosen RJ, Lebowitz AS. Antibiotic prophylaxis in vascular and interventional radiology: a rational approach. *Radiology* 1988;166:381-387
- McDermott VG, Schuster MG, Smith TP. Antibiotic prophylaxis in vascular and interventional radiology. *AJR Am J Roentgenol* 1997;169:31-38
- Berard F, Gandon J. Postoperative wound infections: the influence of ultraviolet irradiation of the operating room and of various other factors. *Ann Surg* 1964;160(suppl 1):1-192
- Kaye KS, Fraimow HS, Abrutyn E. Pathogens resistant to antimicrobial agents. Epidemiology, molecular mechanisms, and clinical management. *Infect Dis Clin North Am* 2000;14:293-319
- Chavers LS, Moser SA, Funkhouser E, et al. Association between antecedent intravenous antimicrobial exposure and isolation of vancomycin-resistant enterococci. *Microb Drug Resist* 2003;9(suppl 1):S69-S77
- Esposito S, Capuano A, Noviello S, et al. Modification of patients' endogenous bacterial flora during hospitalization in a large teaching hospital in Naples. *J Chemother* 2003;15:568-573
- Cronan JJ, Horn DL, Marcello A, et al. Antibiotics and nephrostomy tube care: preliminary observations. Part II. Bacteremia. *Radiology* 1989;172:1043-1045
- Christiano AP, Hollowell CM, Kim H, et al. Double-blind randomized comparison of single-dose ciprofloxacin versus intravenous cefazolin in patients undergoing outpatient endourologic surgery. *Urology* 2000;55:182-185

18. Clark CD, Picus D, Dunagan WC. Bloodstream infections after interventional procedures in the biliary tract. *Radiology* 1994;191:495-499
19. Brody LA, Brown KT, Getrajdman GI, et al. Clinical factors associated with positive bile cultures during primary percutaneous biliary drainage. *J Vasc Interv Radiol* 1998;9:572-578
20. Davis AJ, Kolios G, Alveyn CG, Robertson DA. Antibiotic prophylaxis for ERCP: a comparison of oral ciprofloxacin with intravenous cephalosporin in the prophylaxis of high-risk patients. *Aliment Pharmacol Ther* 1998;12:207-211
21. Raty S, Sand J, Pulkkinen M, Matikainen M, Nordback I. Post-ERCP pancreatitis: reduction by routine antibiotics. *J Gastrointest Surg* 2001;5:339-345; discussion 45
22. Thompson BF, Arguedas MR, Wilcox CM. Antibiotic prophylaxis prior to endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice: is it worth the cost? *Aliment Pharmacol Ther* 2002;16:727-734
23. Leung JW, Libby ED, Morck DW, et al. Is prophylactic ciprofloxacin effective in delaying biliary stent blockage? *Gastrointest Endosc* 2000;52:175-182
24. Lai EC, Lo CM, Choi TK, Cheng WK, Fan ST, Wong J. Urgent biliary decompression after endoscopic retrograde cholangiopancreatography. *Am J Surg* 1989;157:121-125
25. Ryan JM, Ryan BM, Smith TP. Antibiotic prophylaxis in interventional radiology. *J Vasc Interv Radiol* 2004;15:547-556
26. Dormann AJ, Wiggingshaus B, Risius H, et al. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): results from a prospective randomized multicenter trial. *Z Gastroenterol* 2000;38:229-234
27. Dormann AJ, Wiggingshaus B, Risius H, et al. A single dose of ceftriaxone administered 30 minutes before percutaneous endoscopic gastrostomy significantly reduces local and systemic infective complications. *Am J Gastroenterol* 1999;94:3220-3224
28. Ahmad I, Mouncher A, Abdoolah A, et al. Antibiotic prophylaxis for percutaneous endoscopic gastrostomy: a prospective, randomised, double-blind trial. *Aliment Pharmacol Ther* 2003;18:209-215
29. Sharma VK, Howden CW. Meta-analysis of randomized, controlled trials of antibiotic prophylaxis before percutaneous endoscopic gastrostomy. *Am J Gastroenterol* 2000;95:3133-3136
30. Deibert P, Schwarz S, Olschewski M, Siegerstetter V, Blum HE, Rossle M. Risk factors and prevention of early infection after implantation or revision of transjugular intrahepatic portosystemic shunts: results of a randomized study. *Dig Dis Sci* 1998;43:1708-1713
31. Reed RA, Teitelbaum GP, Daniels JR, Pentecost MJ, Katz MD. Prevalence of infection following hepatic chemoembolization with cross-linked collagen with administration of prophylactic antibiotics. *J Vasc Interv Radiol* 1994;5:367-371
32. Geschwind JF, Kaushik S, Ramsey DE, Choti MA, Fishman EK, Kobeiter H. Influence of a new prophylactic antibiotic therapy on the incidence of liver abscesses after chemoembolization treatment of liver tumors. *J Vasc Interv Radiol* 2002;13:1163-1166
33. Siskin GP, Stainken BF, Dowling K, Meo P, Ahn J, Dolen EG. Outpatient uterine artery embolization for symptomatic uterine fibroids: experience in 49 patients. *J Vasc Interv Radiol* 2000;11:305-311
34. Ryan JM, Gainey M, Glasson J, Doherty J, Smith TP. Simplified pain protocol after uterine artery embolization. *Radiology* 2002;224:610-612
35. Pron G, Bennett J, Common A, et al. Technical results and effects of operator experience on uterine artery embolization for fibroids: the Ontario Uterine Fibroid Embolization Trial. The Ontario UFE Collaborative Group. *J Vasc Interv Radiol* 2003;14:545-554
36. Mehta H, Sandhu C, Matson M, Belli A-M. Review of re-admissions due to complications from uterine fibroid embolization. *Clin Radiol* 2002;57:1122-1124
37. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002;51(RR-10):1-29
38. Vassilomanolakis M, Plataniotis G, Koumakis G, et al. Central venous catheter-related infections after bone marrow transplantation in patients with malignancies: a prospective study with short-course vancomycin prophylaxis. *Bone Marrow Transplant* 1995;15:77-80
39. Lim SH, Smith MP, Machin SJ, Goldstone AH. Prophylactic teicoplanin during insertion of Hickman catheters. *Br J Haematol* 1990;76(suppl 2):27-29
40. Al-Sibai MB, Harder EJ, Faskin RW, Johnson GW, Padmos MA. The value of prophylactic antibiotics during the insertion of long-term indwelling silastic right atrial catheters in cancer patients. *Cancer* 1987;60:1891-1895
41. Bock SN, Lee RE, Fisher B, et al. A prospective randomized trial evaluating prophylactic antibiotics to prevent triple-lumen catheter-related sepsis in patients treated with immunotherapy. *J Clin Oncol* 1990;8:161-169
42. Shaul DB, Scheer B, Rokhsar S, et al. Risk factors for early infection of central venous catheters in pediatric patients. *J Am Coll Surg* 1998;186:654-658
43. Ranson MR, Oppenheim BA, Jackson A, Kamthan AG, Scarffe JH. Double-blind placebo controlled study of vancomycin prophylaxis for central venous catheter insertion in cancer patients. *J Hosp Infect* 1990;15:95-102
44. McKee R, Dunsmuir R, Whitby M, Garden OJ. Does antibiotic prophylaxis at the time of catheter insertion reduce the incidence of catheter-related sepsis in intravenous nutrition? *J Hosp Infect* 1985;6:419-425
45. Ljungman P, Hagglund H, Bjorkstrand B, Lonnqvist B, Ringden O. Perioperative teicoplanin for prevention of gram-positive infections in neutropenic patients with indwelling central venous catheters: a randomized, controlled study. *Support Care Cancer* 1997;5:485-488
46. Lund GB, Trerotola SO, Scheel PF Jr, et al. Outcome of tunneled hemodialysis catheters placed by radiologists. *Radiology* 1996;198:467-472
47. Trerotola SO, Johnson MS, Harris VJ, et al. Outcome of tunneled hemodialysis catheters placed via the right internal jugular vein by interventional radiologists. *Radiology* 1997;203:489-495
48. Simpson KR, Hovsepian DM, Picus D. Interventional radiologic placement of chest wall ports: results and complications in 161 consecutive placements. *J Vasc Interv Radiol* 1997;8:189-195
49. Schwartz C, Henrickson KJ, Roghmann K, Powell K. Prevention of bacteremia attributed to luminal colonization of tunneled central venous catheters with vancomycin-susceptible organisms. *J Clin Oncol* 1990;8:1591-1597

50. Henrickson KJ, Axtell RA, Hoover SM, et al. Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: a randomized, multicenter, double-blind trial. *J Clin Oncol* 2000; 18:1269–1278
51. Carratala J, Niubo J, Fernandez-Sevilla A, et al. Randomized, double-blind trial of an antibiotic-lock technique for prevention of gram-positive central venous catheter-related infection in neutropenic patients with cancer. *Antimicrob Agents Chemother* 1999;43:2200–2204
52. Raad I, Buzaid A, Rhyne J, et al. Minocycline and ethylenediaminetetraacetate for the prevention of recurrent vascular catheter infections. *Clin Infect Dis* 1997;25:149–151
53. Tcholakian RK, Raad II. Durability of anti-infective effect of long-term silicone sheath catheters impregnated with antimicrobial agents. *Antimicrob Agents Chemother* 2001;45: 1990–1993
54. Darouiche RO, Raad II, Heard SO, et al. A comparison of two antimicrobial-impregnated central venous catheters. Catheter Study Group. *N Engl J Med* 1999;340:1–8
55. Bunt TJ, Gill HK, Smith DC, Taylor FC. Infection of a chronically implanted iliac artery stent. *Ann Vasc Surg* 1997; 11:529–532
56. Paget DS, Bukhari RH, Zayyat EJ, Lohr JM, Roberts WH, Welling RE. Infectibility of endovascular stents following antibiotic prophylaxis or after arterial wall incorporation. *Am J Surg* 1999;178:219–224
57. Becker GJ, Kovacs M, Mathison MN, et al. Risk stratification and outcomes of transluminal endografting for abdominal aortic aneurysm: 7-year experience and long-term follow-up. *J Vasc Interv Radiol* 2001;12:1033–1046
58. Heikkinen L, Valtonen M, Lepantalo M, Saimanen E, Jarvinen A. Infrarenal endoluminal bifurcated infected stent with *Listeria monocytogenes*. *J Vasc Surg* 1999;29:554–556
59. Saxon A, Beall GN, Rohr AS, Adelman DC. Immediate hypersensitivity reactions to beta-lactam antibiotics. *Ann Intern Med* 1987;107:204–215
60. Dajani AS, Bisno AL, Chung KJ, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *JAMA* 1990;264:2919–2922
61. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *JAMA* 1997;277:1794–1801
62. Apter AJ, Kinman JL, Bilker WB, et al. Represcription of penicillin after allergic-like events. *J Allergy Clin Immunol* 2004;113:764–770
63. Robinson JL, Hameed T, Carr S. Practical aspects of choosing an antibiotic for patients with a reported allergy to an antibiotic. *Clin Infect Dis* 2002;35:26–31
64. Goodman EJ, Morgan MJ, Johnson PA, Nichols BA, Denk N, Gold BB. Cephalosporins can be given to penicillin-allergic patients who do not exhibit an anaphylactic response. *J Clin Anesth* 2001;13:561–564
65. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. *JAMA* 2001;285:2498–2505