Prevention of Bacterial Endocarditis

Originating Group
American Heart Association

Endorsed by the American Academy of Pediatric Dentistry
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Recommendations by the American Heart Association

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Objective

To update recommendations issued by the American Heart Association last published in 1990 for the prevention of bacterial endocarditis in individuals at risk for this disease.

Participants

An ad hoc writing group appointed by the American Heart Association for their expertise in endocarditis and treatment with liaison members representing the American Dental Association, the Infectious Diseases Society of America, the American Academy of Pediatrics, and the American Society for Gastrointestinal Endoscopy.

Evidence

The recommendations in this article reflect analyses of relevant literature regarding procedure-related endocarditis, in vitro susceptibility data of pathogens causing endocarditis, results of prophylactic studies in animal models of endocarditis, and retrospective analyses of human endocarditis cases in terms of antibiotic prophylaxis usage patterns and apparent prophylaxis failures. MEDLINE database searches from 1936 through 1996 were done using the root words *endocarditis, bacteremia,* and *antibiotic prophylaxis.* Recommendations in this document fall into evidence level III of the US Preventive Services Task Force categories of evidence.

Consensus process

The recommendations were formulated by the writing group after specific therapeutic regimens were discussed. The consensus statement was subsequently reviewed by outside experts not affiliated with the writing group and by the Science Advisory and Coordinating Committee of the American Heart Association. These guidelines are meant to aid practitioners but are not intended as the standard of care or as a substitute for clinical judgment.

Conclusions

Major changes in the updated recommendations include the following: 1) emphasis that most cases of endocarditis are not attributable to an invasive procedure; 2) cardiac conditions are stratified into high-, moderate-, and negligible-risk categories based on potential outcome if endocarditis develops; 3) procedures that may cause bacteremia and for which prophylaxis is recommended are more clearly specified; 4) an algorithm was developed to more clearly define when prophylaxis is recommended for patients with mitral valve prolapse; 5) for oral or dental procedures the initial amoxicillin dose is reduced to 2 g, a follow-up antibiotic dose is no longer recommended, erythromycin is no longer recommended for penicillin-allergic individuals, but clindamycin and other alternatives are offered; and 6) for gastrointestinal or genitourinary procedures, the prophylactic regimens have been simplified. These changes were instituted to more clearly define when prophylaxis is or is not recommended, improve practitioner and patient compliance, reduce cost and potential gastrointestinal adverse effects, and approach more uniform worldwide recommendations.

Introduction

Endocarditis is a life-threatening disease, although it is relatively uncommon. Substantial morbidity and mortality result from this infection, despite improvements in outcome due to advances in antimicrobial therapy and enhanced ability to diagnose and treat complications. Primary prevention of endocarditis whenever possible is therefore very important.

Endocarditis usually develops in individuals with underlying structural cardiac defects who develop bacteremia with organisms likely to cause endocarditis. Bacteremia may occur spontaneously or may complicate a focal infection (e.g., urinary tract infection, pneumonia, or cellulitis). Some surgical and dental procedures and instrumentations involving mucosal surfaces or contaminated tissue cause transient bacteremia that rarely persists for more than 15 minutes. Blood-borne bacteria may lodge on damaged or abnormal heart valves or on the endocardium or the endothelium near anatomic defects, resulting in bacterial endocarditis or endarteritis. Although bacteremia is common following many invasive procedures, only certain bacteria commonly cause endocarditis. It is not always possible to predict which patients will develop this infection or which particular procedure will be responsible.

Table 1. Cardiac Conditions Associated With Endocarditis[2-22]

Endocarditis prophylaxis recommended
High-risk category
Prosthetic cardiac valves, including bioprosthetic and homograft valves
Previous bacterial endocarditis
Complex cyanotic congenital heart disease (eg, single ventricle states, transposition of the great arteries, tetralogy of Fallot)
Surgically constructed systemic pulmonary shunts or conduits
Moderate-risk category
Most other congenital cardiac malformations (other than above and below)
Acquired valvar dysfunction (eg, rheumatic heart disease)
Hypertrophic cardiomyopathy
Mitral valve prolapse with valvar regurgitation and/or thickened leaflets.[1]
Endocarditis prophylaxis not recommended
Negligible-risk category (no greater risk than the general population)
Isolated secundum atrial septal defect
Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus (without residua beyond 6 mo)
Previous coronary artery bypass graft surgery
Mitral valve prolapse without valvar regurgitation[1]
Physiologic, functional, or innocent heart murmurs[1]
Previous Kawasaki disease without valvar dysfunction
Previous rheumatic fever without valvar dysfunction
Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

[1]See text for further details.

This statement provides guidelines for prevention of bacterial endocarditis. It is not intended as the standard of care or as a substitute for clinical judgment. The current recommendations are an update of those made by the committee in 1990[1] and incorporate new data and include opinions voiced by national and international experts at endocarditis meetings around the world.

Cardiac conditions

Certain cardiac conditions are associated with endocarditis more often than others.[2] Furthermore, when endocarditis develops in individuals with underlying cardiac conditions, the severity of the disease and the ensuing morbidity can be variable. Prophylaxis is recommended in individuals who have a higher risk for developing endocarditis than the general population and is particularly important for individuals in whom endocardial infection is associated with high morbidity and mortality.

Table 1[2-22] stratifies cardiac conditions into high- and moderate-risk categories primarily on the basis of potential outcome if endocarditis occurs.

High risk

Individuals at highest risk are those who have prosthetic heart valves, a previous history of endocarditis (even in the absence of other heart disease), complex cyanotic congenital heart disease, or surgically constructed systemic pulmonary shunts or conduits.[2,3] These individuals are at a much higher risk for developing severe endocardial infection that is often associated with high morbidity and mortality.

Moderate risk

Individuals with certain other underlying cardiac defects are at moderate risk for severe infection.[2-4] Congenital cardiac conditions listed in the moderate-risk category include the following uncorrected conditions: patent ductus arteriosus, ventricular septal defect, primum atrial septal defect, coarctation of the aorta, and bicuspid aortic valve. Acquired valvar dysfunction (e.g., due to rheumatic heart disease or collagen vascular disease) and hypertrophic cardiomyopathy are also moderate-risk conditions.

Mitral valve prolapse (MVP) is common, and the need for prophylaxis for this condition is controversial. Only a small percentage of patients with documented MVP develop complications at any age.[5-7] Mitral valve prolapse represents a spectrum of valvular changes and clinical behavior.[5-7] In view of the controversy surrounding the need for prophylaxis of the individual patient with MVP, a detailed description of the spectrum of MVP is warranted.

There are currently no randomized and carefully controlled human trials in patients with underlying structural heart disease to definitively establish that antibiotic prophylaxis provides protection against development of endocarditis during bacteremia-inducing procedures. Further, most cases of endocarditis are not attributable to an invasive procedure. The following recommendations reflect analyses of relevant literature regarding procedure-related endocarditis, including in vitro susceptibility data of pathogens causing endocarditis, results of prophylactic studies in experimental animal models of endocarditis, and retrospective analyses of human endocarditis cases in terms of antibiotic prophylaxis usage patterns and apparent prophylaxis failures.

The incidence of endocarditis following most procedures in patients with underlying cardiac disease is low. A reasonable approach for endocarditis prophylaxis should consider the following: the degree to which the patient's underlying condition creates a risk of endocarditis; the apparent risk of bacteremia with the procedure (as defined in these recommendations); the potential adverse reactions of the prophylactic antimicrobial agent to be used; and the cost-benefit aspects of the recommended prophylactic regimen. Failure to consider all of these factors may lead to overuse of antimicrobial agents, excessive cost, and risk of adverse drug reactions.

Normal mitral valve leaflets close at or below the plane of the mitral annulus. This closure position is controlled by the lengths of the leaflets, their attached chordae and papillary muscles, and the systolic size of the ventricle. The closure position will shift beyond the annular plane toward the left atrium, or prolapse, if the lengths of the valve apparatus, which are constant, become too large for the size of the end-systolic ventricle, which is variable and dynamic. Dehydration and tachycardia are common causes of intermittent MVP.

Abnormal motion of normal mitral valves is found on echocardiographic examination in a small percentage of the adult and adolescent ambulatory population. The high prevalence of such motion abnormalities in young adults underscores that MVP is often an abnormality of volume status, adrenergic state, or growth phase and not of valve structure or function. When normal valves prolapse without leaking, as in patients with one or more systolic clicks but no murmurs and no Doppler-demonstrated mitral regurgitation, the risk of endocarditis is not increased above that of the normal population.[2,6,7] Antibiotic prophylaxis against bacterial endocarditis is therefore not necessary. This is because it is not the abnormal valve motion but the jet of mitral insufficiency that creates the shear forces and flow abnormalities that increase the likelihood of bacterial adherence on the valve during bacteremia.

Normal mitral valves with normal motion often have minimal leaks detectable by Doppler examination. This does not appear to increase the risk of endocarditis. In contrast, the regurgitation that occurs with structurally normal but prolapsing valves originates from larger regurgitant orifices and creates broader areas of turbulent flow. Patients with prolapsing and leaking mitral valves, evidenced by audible clicks and murmurs of mitral regurgitation or by Doppler-demonstrated mitral insufficiency, should receive prophylactic antibiotics.[7-11] This is supported by formal cost-benefit analysis.[12]

Mitral valve prolapse also occurs in the setting of myxomatous degeneration of the mitral valve. This is a progressive disorder that has a spectrum of manifestations.[13,14] The mitral leaflets of these patients appear thickened on the echocardiogram, due to accumulations of proteoglycan deposits.[15] The amount of thickening is variable and may increase with age.[16] There is a range of valve motion in these patients as well: they may prolapse continuously or only with changes in heart rate or volume. Further, when prolapse occurs, it may or may not create valvular insufficiency. In patients of any age, myxomatous mitral valve degeneration with regurgitation is an indication for antibiotic prophylaxis.[11,17,18]

Anterior mitral valve thickening is commonly found in both competent and insufficient myxomatous mitral valves, but its presence increases the likelihood of significant mitral regurgitation.[16] Those with significant regurgitation were older and more likely to be men.[16] Other studies have shown that male sex and age older than 45 years represent increased risk for developing endocarditis.[8,10,11,19] Patients with thickened valves that do not leak on resting examination often develop regurgitation with exercise. These patients with exercise-induced mitral insufficiency have been shown to constitute a higher-risk subset for common complications (syncope, congestive heart failure, progressive regurgitation requiring valve replacement); endocarditis and cerebral embolic events, occurring far less frequently, were not demonstrated to be increased in this small series.[20] Men older than 45 years with MVP, without a consistent systolic murmur, may warrant prophylaxis even in the absence of resting regurgitation.[12,19]

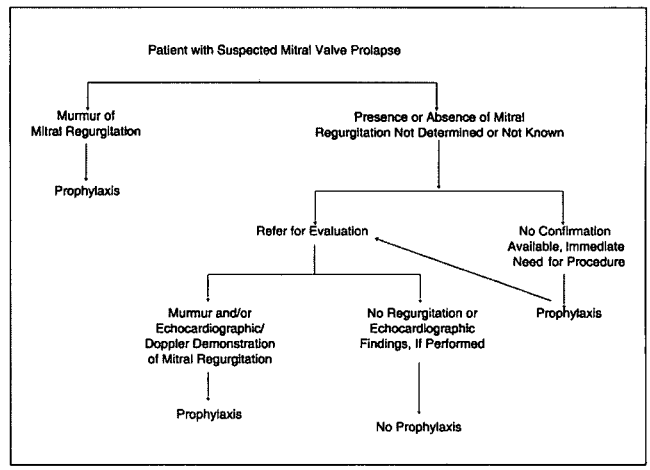

Figure. Clinical approach to determination of the need for prophylaxis in patients with suspected mitral valve prolapse

Some experts feel that an audible nonejection click even without a murmur may identify patients with a potential for intermittent regurgitation and therefore a risk of developing endocarditis. While there are insufficient data on this issue, an isolated click may be an indication for more thorough evaluation of valve morphology and function, including Doppler-echocardiographic imaging or auscultation during maneuvers that elicit or augment mitral regurgitation.

While children and adolescents with MVP may have the same symptoms as adults, such as palpitations or syncope, the development of symptoms in childhood is relatively unusual. The vast majority of children with chest pain or fatigue do not have any form of heart disease, including MVP. Careful evaluation is nevertheless required in children who have isolated clinical findings, such as nonejection systolic click, since this may be the only indicator of important mitral valve abnormality requiring prophylaxis.[21] In the most recent series of reports, MVP has emerged as an important underlying diagnosis associated with endocarditis in the pediatric age group.[3,21]

A clinical approach to determination of the need for prophylaxis in individuals with suspected MVP is given in the Figure.[23]

Table 2. Dental Procedures and Endocarditis Prophylaxis[22,24-26,28-31]

Endocarditis prophylaxis recommended*
Dental extractions
Periodontal procedures including surgery, scaling and root planing, probing, and recall maintenance
Dental implant placement and reimplantation of avulsed teeth
Endodontic (root canal) instrumentation or surgery only beyond the apex
Subgingival placement of antibiotic fibers or strips
Initial placement of orthodontic bands but not brackets
Intraligamentary local anesthetic injections
Prophylactic cleaning of teeth or implants where bleeding is anticipated.
Endocarditis prophylaxis not recommended
Restorative dentistry† (operative and prosthodontic) with or without retraction cord‡
Local anesthetic injections (nonintraligamentary)
Intracanal endodontic treatment; post placement and buildup
Placement of rubber dams
Postoperative suture removal
Placement of removable prosthodontic or orthodontic appliances
Taking of oral impressions
Fluoride treatments
Taking of oral radiographs
Orthodontic appliance adjustment
Shedding of primary teeth.

*Prophylaxis is recommended for patients with high- and moderate-risk cardiac conditions.

†This includes restoration of decayed teeth (filling cavities) and replacement of missing teeth.

‡Clinical judgment may indicate antibiotic use in selected circumstances that may create significant bleeding.

Negligible risk

Although endocarditis may develop in any individual, including persons with no underlying cardiac defect, the negligible-risk category lists cardiac conditions in which the development of endocarditis is not higher than in the general population. Whereas in pediatric patients innocent heart murmurs may be clearly defined on auscultation, in the adult population other studies such as echocardiography may be necessary to confirm that a murmur is innocent. Individuals with innocent heart murmurs have structurally normal hearts and do not require prophylaxis.

Bacteremia-producing procedures

Bacteremias commonly occur during activities of daily living such as routine tooth brushing or chewing. With respect to endocarditis prophylaxis, significant bacteremias are only those caused by organisms commonly associated with endocarditis and attributable to identifiable procedures. The procedures for which prophylaxis is recommended are those known to induce such bacteremias and are discussed below. Invasive procedures performed through surgically scrubbed skin are not likely to produce such bacteremias. Many centers do employ periprocedure prophylaxis for transcatheter insertion of prosthetic devices (septal occluders and vascular coils), however, although there are no data to support the use of antibiotics in the procedures. Routine cardiac catheterization and angioplasty do not require such precautions.

Dental and oral procedures

Poor dental hygiene and periodontal or periapical infections may produce bacteremia even in the absence of dental procedures. The incidence and magnitude of bacteremias of oral origin are directly proportional to the degree of oral inflammation and infection.[24,25] Individuals who are at risk for developing bacterial endocarditis should establish and maintain the best possible oral health to reduce potential sources of bacterial seeding. Optimal oral health is maintained through regular professional care[24,26,27] and the use of appropriate dental products such as manual and powered toothbrushes, dental floss, and other plaque-removal devices. Oral irrigator or air abrasive polishing devices used inappropriately or in patients with poor oral hygiene have been implicated in producing bacteremia, but the relationship to bacterial endocarditis is unknown.[24,28-31] Home-use devices pose far less risk of bacteremia in a healthy mouth than does ongoing oral inflammation.[24,28-31]

Antiseptic mouth rinses applied immediately prior to dental procedures may reduce the incidence or magnitude of bacteremia.[24] Agents include chlorhexidine hydrochloride and povidone-iodine. Fifteen milliliters of chlorhexidine can be given to all at-risk patients via gentle oral rinsing for about 30 seconds prior to dental treatment; gingival irrigation is not recommended. Sustained or repeated frequent interval use is not indicated as this may result in the selection of resistant micro-organisms.[24]

Antibiotic prophylaxis for at-risk patients is recommended for dental and oral procedures likely to cause bacteremia (Table 2).[22,24-26,28-31] In general, prophylaxis is recommended for procedures associated with significant bleeding from hard or soft tissues, periodontal surgery, scaling, and professional teeth cleaning. Similarly, antimicrobial prophylaxis is recommended for tonsillectomy or adenoidectomy. It is recognized that unanticipated bleeding may occur on some occasions. In such an event, data from experimental animal models suggest that antimicrobial prophylaxis

administered within 2 hours following the procedure will provide effective prophylaxis.[32] Antibiotics administered more than 4 hours after the procedure probably have no prophylactic benefit.Procedures for which antimicrobial prophylaxis is not recommended are also listed (Table 2, previous page).

Edentulous patients may develop bacteremia from ulcers caused by ill-fitting dentures. Denture wearers should be encouraged to have periodic examinations or to return to the practitioner if discomfort develops. When new dentures are inserted, it is advisable to have the patient return to the practitioner to correct any problems that could cause mucosal ulceration.

If a series of dental procedures is required, it may be prudent to observe an interval of time between procedures to both reduce the potential for the emergence of resistant organisms and allow repopulation of the mouth with antibiotic susceptible flora. Various studies have suggested an interval of 9 to 14 days.[33,34] If possible, a combination of procedures should be planned within the same period of prophylaxis.

Respiratory, gastrointestinal, and genitourinary tract procedures

Surgical procedures involving the respiratory mucosa may lead to bacteremia; therefore, antimicrobial prophylaxis is recommended (Table 3).[35-58] The use of a rigid bronchoscope may cause mucosal damage, whereas such damage is unlikely with a flexible bronchoscope. Endotraceal intubation per se is not an indication for antibiotic prophylaxis.

The risk of endocarditis as a direct result of an endoscopic procedure is small. Transient bacteremia may occur during or immediately after endoscopy; however, there are few reports of infective endocarditis attributable to endoscopy.[35-43] For most gastrointestinal endoscopic procedures, the rate of bacteremia is 2 to 5%, and the organisms typically identified are unlikely to cause endocarditis.[44,45] The rate of bacteremia does not increase with mucosal biopsy, polypectomy, or sphincterotomy.[46-48] There are no data to indicate that deep biopsy, as may be performed in the rectum or stomach, leads to a higher rate of bacteremia.

Some gastrintestinal procedures are associated with a higher rate of transient bacteremia; for these procedures, antimicrobial prophylaxis is recommended, particularly for patients in the high-risk category (Table 3). Esophageal stricture dilation has been associated with bacteremia rates as high as 45%.[44] However, this number is an average result of several clinical studies in which the rate of bacteremia ranged from 0 to 100%.[49-52] In only one study was the oropharynx the documented source of infection.[52] These studies were performed with differing methods and involved relatively small numbers of patients. Until more data documenting the true rate of bacteremia associated with stricture dilation becomes available, it is prudent to consider this procedure as one potentially associated with an increased risk of transient bacteremia.

Table 3. Other Procedures and Endocarditis Prophylaxis[35-58]

Endocarditis prophylaxis recommended*
Respiratory tract
Tonsillectomy and/or adenoidectomy
Surgical operations that involve respiratory mucosa
Bronchoscopy with a rigid bronchoscope
Gastrointestinal tract*
Sclerotherapy for esophageal varices
Esophageal stricture dilation
Endoscopic retrograde cholangiography with biliary obstruction
Biliary tract surgery
Surgical operations that involve intestinal mucosa
Genitourinary tract
Prostatic surgery
Cystoscopy
Urethral dilation
Endocarditis prophylaxis not recommended
Respiratory tract
Endotracheal intubation
Bronchoscopy with a flexible bronchoscope, with or without biopsy†
Tympanostomy tube insertion
Gastrointestinal tract
Transesophageal echocardiography†
Endoscopy with or without gastrointestinal biopsy†
Genitourinary tract
Vaginal hysterectomy†
Vaginal delivery†
Cesarean section
In uninfected tissue:
Urethral catheterization
Uterine dilatation and curettage
Therapeutic abortion
Sterilization procedures
Insertion or removal of intrauterine devices
Other
Cardiac catheterization, including balloon angioplasty
Implanted cardiac pacemakers,implanted defibrillators, and coronary stents
Incision or biopsy of surgically scrubbed skin
Circumcision

*Prophylaxis is recommended for high-risk patients; it is optional for medium-risk patients.

†Prophylaxis is optional for high-risk patients.

The bacteremia rate associated with sclerotherapy of esophageal varices is approximately 31%.[44] Bacteremia appears to be most associated with increased sclerosant volumes, as can occur with emergency sclerosis for active bleeding, and with relatively longer injection needles. The bacteremia rate is lessened with the use of shorter injection needles and sterile water.[53,54] Endoscopic ligation of varices, or banding, is not associated with increased rates of transient bacteremia.[55]

An obstructed biliary tree, due to benign or malignant disease, may be colonized with a variety of organisms. A prime risk factor for dissemination of infection from an obstructed biliary tree is instrumentation of the obstructed region without provision of adequate drainage. The bacteremia rates for endoscopic retrograde cholangiography in the absence of ductal obstruction are approximately equal to most other endoscopic procedures. Prophylaxis should be considered primarily in cases in which biliary obstruction is known or suspected.

In biliary tract surgery, or in any operative procedure that involves the intestinal mucosa, there is a potential for bacteremia with organisms known to cause endocarditis. It is therefore prudent to provide prophylaxis for patients at high risk to develop endocarditis. Surgery, instrumentation, or diagnostic procedures that involve the genitourinary tract may cause bacteremia. Although the risk that any particular patient will develop endocarditis is low, the genitourinary tract is second only to the oral cavity as a portal of entry for organisms that cause endocarditis. The rate of bacteremia following urinary tract procedures is high in the presence of urinary tract infection (UTI). Sterilization of the urinary tract with antimicrobial therapy in patients with bacteriuria should be attempted prior to elective procedures, including lithotripsy. Results of a preprocedure urine culture will allow the practitioner to choose antibiotics appropriate to the recovered organisms. Procedures for which antimicrobial prophylaxis is or is not recommended are listed in Table 3.

Many procedures involving the urethra and prostatic bed are associated with high rates of bacteremia. The incidence of bacteremia was studied in 300 patients undergoing one of four different urologic procedures: transurethral resection (TUR) of the prostate, cystoscopy, urethral dilation, and urethral catheterization.[56] Bacteremia was most frequent after TUR of the prostate, occurring in 31% of the patients. In the other procedures, bacteremia occurred in 24% following urethral dilatation, in 17% following cystoscopy, and in 8% following urethral catheterization. Bacteremia was significantly associated with both prostatitis on histological examination of resected prostate and prior UTI following TUR and with prior UTI following urethral dilatation and cystoscopy. Preexisting UTI was the major source of organisms causing the bacteremia following TUR but was the source in only about one third of patients following the other procedures. Enterococci and *Klebsiella* were the most frequent organisms. Although bacteremia due to gram-negative bacilli is unlikely to cause endocarditis unless a prosthetic valve is present, it may nevertheless cause life-threatening sepsis. Therefore, an antimicrobial regimen effective against the infective urinary pathogen, eg, enteric gram-negative bacilli, in addition to the enterococcus, should be administered before the invasive genitourinary procedures.

Bacteremia follows uncomplicated vaginal delivery in only 1% to 5% of procedures, usually with various types of streptococci[22]; well-documented cases of endocarditis after normal vaginal delivery are uncommon.[57] Therefore, antibiotic prophylaxis for normal vaginal delivery is not recommended. If an unanticipated bacteremia is suspected during vaginal delivery, intravenous antibiotics can be administered at that time. No bacteremia has been detected in studies following cervical biopsy or manipulation of an intrauterine device (IUD) in the absence of obvious infections.[22] Bacteremia following removal of an infected IUD is unresolved[58] but would seem possible and should warrant prophylaxis, as would other genitourinary procedures in the presence of infection.

Prophylactic regimens

Prophylaxis is most effective when given perioperatively in doses that are sufficient to assure adequate antibiotic concentrations in the serum during and after the procedure. 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 a procedure and should not be continued for an extended period (no more than 6 to 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 for treatment of the established infection.

Practitioners must exercise their own clinical judgment in determining the choice of antibiotics and number of doses that are to be administered in individual cases or special circumstances. Furthermore, because endocarditis may occur in spite of appropriate antibiotic prophylaxis, physicians and dentists should maintain a high index of suspicion regarding any unusual clinical events (such as unexplained fever, night chills, weakness, myalgia, arthralgia, lethargy, or malaise) following dental or other surgical procedures in patients who are at risk for developing bacterial endocarditis.

Regimens for dental, oral, respiratory tract, or esophageal procedures

Streptococcus viridans (a-hemolytic streptococci) is the most common cause of endocarditis following dental or oral procedures, certain upper respiratory tract procedures, bronchoscopy with a rigid bronchoscope, surgical procedures that involve the respiratory mucosa, and esophageal procedures. Prophylaxis should be specifically directed against these organisms. The same regimens are recommended for all these procedures (Table 4[1,22,59-61], next page). The recommended standard prophylactic regimen for all these procedures is a single dose of oral amoxicillin. The antibiotics amoxicillin, ampicillin, and penicillin V are equally effective in vitro against a-hemolytic streptococci; however, amoxicillin is recommended because it is better absorbed from the gastrointestinal tract and provides higher and more sustained serum levels. Previously the recommended dose

Table 4. Prophylactic Regimens for Dental, Oral, Respiratory Tract, or Esophageal Procedures[1,22,59-61]

Situation	Agent*	Regimen†
Standard general prophylaxis	Amoxicillin	Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure
Unable to take oral medications	Ampicillin	Adults: 2.0 g IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure
Allergic to penicillin	Clindamycin	Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure
	or	
	Cephalexin† *or* cefadroxil†	Adults: 2.0 g; children; 50 mg/kg orally 1 h before procedure
	or	
	Azithromycin or clarithromycin	Adults: 500 mg; children: 15 mg/kg orally 1 h before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure
	or	
	Cefazolin†	Adults: 1.0 g; children: 25 mg/kg IM or IV within 30 min before procedure

IM indicates intramuscularly, and IV, intravenously.

*Total children's dose should not exceed adult dose.

†Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins.

Table 5. Prophylactic Regimens for Genitourinary/Gastrointestinal (Excluding Esophageal) Procedures[22]

Situation	Agents*	Regimen†
High-risk patients	Ampicillin plus gentamicin	Adults: ampicillin 2.0 g IM or IV plus gentamicin 1.5 mg/kg (not to exceed 120 mg) within 30 min of starting procedure; 6 h later, ampicillin 1 g IM/IV or amoxicillin 1 g orally
		Children: ampicillin 50 mg/kg IM or IV (not to exceed 2.0 g) plus gentamicin 1.5 mg/kg within 30 min of starting the procedure; 6 h later, ampicillin 25 mg/kg IM/IV or amoxicillin 25 mg/kg, orally
High-risk patients allergic to ampicillin/amoxicillin	Vancomycin plus gentamicin	Adults: vancomycin 1.0 g IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM (not to exceed 120 mg); complete injection/infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM; complete injection/infusion within 30 min of starting procedure
Moderate-risk patients	Amoxicillin or ampicillin	Adults: amoxicillin 2.0 g orally 1 h before procedure, or ampicillin 2.0 g IM/IV within 30 min of starting procedure
		Children: amoxicillin 50 mg/kg orally 1 h before procedure, or ampicillin 50 mg/kg IM/IV within 30 min of starting procedure
Moderate-risk patients allergic to ampicillin/amoxicillin	Vancomycin	Adults: vancomycin 1.0 g IV over 1-2 h complete infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h; complete infusion within 30 min of starting procedure

IM indicates intramuscularly, and IV, intravenously.

*Total children's dose should not exceed adult dose.

†No second dose of vancomycin or gentamicin is recommended.

was 3.0 g 1 hour before a procedure and then 1.5 g 6 hours after the initial dose.[1] Recent comparisons of 2.0-g and 3.0-g dosing indicate that a 2.0-g dose results in adequate serum levels for several hours and causes less gastrointestinal adverse effects.[59] The newly recommended adult dose is 2.0 g of amoxicillin (pediatric dose is 50 mg/kg not to exceed the adult dose) to be administered 1 hour before the anticipated procedure. A second dose is not necessary, both because of the prolonged serum levels above the minimal inhibitory concentration of most oral streptococci[59] and the prolonged serum inhibitory activity induced by amoxicillin against such strains (6 to 14 hours).[60] For individuals who are unable to take or unable to absorb oral medications, a parenteral agent may be necessary. Ampicillin sodium is recommended because parenteral amoxicillin is not available in the United States. Individuals who are allergic to penicillins (such as amoxicillin, ampicillin, or penicillin) should be treated with the provided alternative oral regimens. Clindamycin hydrochloride is one recommended alternative. Individuals who can tolerate first-generation cephalosporins (cephalexin or cefadroxil) may receive these agents, provided they have not had an immediate, local, or systemic IgE-mediated anaphylactic allergic reaction to penicillin. Azithromycin or clarithromycin are also acceptable alternative agents for the penicillin-allergic individual[61] although they are more expensive than the other regimens. When parenteral administration is needed in an individual who is allergic to penicillin, clindamycin phosphate is recommended; cefazolin may be used if the individual does not have an immediate type local or systemic anaphylactic hypersensitivity to penicillin. The previous recommendations from this committee listed erythromycin as an alternate agent for the penicillin-allergic patient. Erythromycin is no longer included because of gastrointestinal upset and complicated pharmacokinetics of the various formulations.[62] Practitioners who have successfully used erythromycin for prophylaxis in individual patients may choose to continue with this antibiotic. The regimen is included in our previous recommendations.[1]

Regimens for genitourinary and nonesophageal gastrointestinal procedures

Bacterial endocarditis that occurs following genitourinary and gastrointestinal tract surgery or instrumentation is most often caused by *Enterococcus faecalis* (enterococci). Although gram-negative bacillary bacteremia may follow these procedures, gram-negative bacilli are only rarely responsible for endocarditis. Thus, antibiotic prophylaxis to prevent endocarditis that occurs following genitourinary or gastrointestinal procedures should be directed primarily against enterococci.

Table 5[1,22] outlines the recommended regimens for prophylaxis for genitourinary or gastrointestinal tract procedures (excluding esophageal procedures). The committee continues to recommend parenteral antibiotics, particularly in high-risk patients. In medium-risk patients requiring prophylaxis, a parenteral (ampicillin) or oral (amoxicillin) regimen is provided. For procedures in which prophylaxis is not routinely recommended, physicians may choose to administer prophylaxis in high-risk patients.

Specific situations and circumstances

Patients already receiving antibiotics

Occasionally, a patient may be taking an antibiotic when coming to the physician or dentist. If the patient is taking an antibiotic normally used for endocarditis prophylaxis, it is prudent to select a drug from a different class rather than to increase the dose of the current antibiotic. In particular, antibiotic regimens used to prevent the recurrence of acute rheumatic fever are inadequate for the prevention of bacterial endocarditis. Individuals who take an oral penicillin for secondary prevention of rheumatic fever or for other purposes may have viridans streptococci in their oral cavities that are relatively resistant to penicillin, amoxicillin, or ampicillin. In such cases, the physician or dentist should select clindamycin, azithromycin, or clarithromycin (Table 4) for endocarditis prophylaxis. Because of possible cross-resistance with the cephalosporins, this class of antibiotics should be avoided. If possible, one could delay the procedure until at least 9 to 14 days after completion of the antibiotic.[33,34] This will allow the usual oral flora to be reestablished.

Procedures involving infected tissues

Incision and drainage or other procedures involving infected tissues may result in bacteremia with the same organism causing the infection. In individuals at risk for endocarditis (the high-and moderate-risk categories in Table 1), it is advisable to administer antimicrobial prophylaxis before the procedure. Prophylaxis should be directed at the most likely pathogen causing the infection. For nonoral soft tissue infections (cellulitis), or bone and joint infections (osteomyelitis and pyogenic arthritis), an antistaphylococcal penicillin or first-generation cephalosporin is an appropriate choice. For patients who are allergic to penicillins, clindamycin is an acceptable alternative. For those unable to take oral antibiotics or who are known to have methicillin sodium-resistant *Staphylococcus aureus* bacteremia, vancomycin is the regimen of choice. For UTI, agents active against enteric gram-negative bacilli (such as aminoglycosides or third-generation cephalosporins) are advisable.

Patients who receive anticoagulants

Intramuscular injections for endocarditis prophylaxis should be avoided in patients who receive heparin. The use of warfarin sodium is a relative contraindication to intramuscular injections. Intravenous or oral regimens should be used whenever possible.

Patients who undergo cardiac surgery

A careful preoperative dental evaluation is recommended so that required dental treatment can be completed before cardiac surgery whenever possible. Such measures may decrease the incidence of late postoperative endocarditis.

Patients who have cardiac conditions that predispose them to endocarditis are at risk for developing bacterial endocarditis when undergoing open heart surgery. Similarly, patients who undergo surgery for placement of prosthetic heart valves or prosthetic intravascular or intracardiac materials are also at risk for the development of bacterial endocarditis. Because the morbidity and mortality of endocarditis in such patients are high, perioperative prophylactic antibiotics are recommended. Endocarditis associated with open heart surgery is most often caused by *S aureus*, coagulase-negative staphylococci, or diphtheroids. Streptococci, gram-negative bacteria, and fungi are less common. No single antibiotic regimen is effective against all these organisms. Furthermore, prolonged use of broad-spectrum antibiotics may predispose to superinfection with unusual or resistant micro-organisms. Prophylaxis at the time of cardiac surgery should be directed primarily against staphylococci and should be of short duration. First-generation cephalosporins are most often used, but the choice of an antibiotic should be influenced by the antibiotic susceptibility patterns at each hospital. For example, high prevalence of infection by methicillin-resistant *S aureus* in a particular inpatient unit should prompt consideration of vancomycin for perioperative prophylaxis. It should be noted, however, that although the majority of nosocomial coagulase-negative staphylococci exhibit the methicillin-resistance phenotype in vitro, endocarditis prophylaxis with first-generation cephalosporins is effective for most patients undergoing cardiac valve surgery.[63] Prophylaxis with the chosen antibiotic should be started immediately before the operative procedure, repeated during prolonged procedures to maintain levels intraoperatively, and continued for no more than 24 hours postoperatively to minimize emergence of resistant micro-organisms. The effects of cardiopulmonary bypass and compromised postoperative renal function on antibiotic levels in the serum should be considered and doses timed appropriately before and during the procedure

Status following cardiovascular procedures

Many reparative cardiac procedures do not modify the patient's long-term risk for infective endocarditis, which continues indefinitely (Table 1). In the case of prosthetic valve replacement, the risk of endocarditis increases postoperatively. In other conditions, such as closure of ventricular septal defect or patent ductus arteriosus without residual leak, the risk of endocarditis diminishes to the level of the general population after a 6-month healing period. Data are insufficient to make recommendations for prophylactic therapy after closure of these lesions by transcatheter devices. There is no evidence that coronary artery bypass graft surgery introduces a risk for endocarditis. Therefore, antibiotic prophylaxis is not needed for individuals who have previously undergone this procedure. Noncoronary vascular grafts may merit antibiotic prophylaxis for the first 6 months after implantation.

There are insufficient data to support recommendations for patients who have had heart transplants. However, such patients are at risk of acquired valvular dysfunction, especially during episodes of rejection. Because of this, and the continuous use of immunosuppression in such patients, most transplant physicians administer prophylaxis according to regimens for the moderate-risk category.

Other considerations

A case of endocarditis, perceived as result of failure to administer a recommended prophylactic regimen, requires careful analysis. It is important to consider the following factors: 1) the time period between the putatively responsible invasive procedure and the onset of clinical symptoms compatible with endocarditis; 2) the etiologic organism causing endocarditis; 3) the likelihood that the putative invasive procedure resulted in bacteremia; and 4) knowledge by the patient of the presence or severity of the underlying lesion and communication of this information to the treating physician or dentist prior to the procedure. Most cases of procedure-related endocarditis occur with a short incubation period of approximately 2 weeks or less following the procedure.[64] A longer incubation period between the invasive procedure and the onset of symptoms significantly lessens the likelihood that the procedure was the proximate cause of the endocarditis. A national registry established by the American Heart Association in the early 1980s analyzed 52 cases of apparent failures of endocarditis prophylaxis.[65] Only 6 (12%) of the 52 cases had received prophylactic regimens that were currently recommended by the American Heart Association. The vast majority of endocarditis due to oral organisms is not related to dental treatment procedures.[24,27] One recent large-scale, population-based, case-control study, done in 54 Philadelphia area hospitals from 1988 to 1990, was unable to demonstrate any independent risk for endocarditis attributable to prior dental treatment.[66] In addition, it is unlikely that cases of viridans streptococcal endocarditis would complicate invasive nonesophageal gastrointestinal or genitourinary procedures. Similarly, enterococcal endocarditis would be a very unusual consequence of dental procedures.

The use of prophylactic antibiotics to prevent infection of joint prostheses during potentially bacteremia-inducing procedures is not within the scope of issues addressed by this committee.

The Council on Scientific Affairs of the American Dental Association has approved the statement as it relates to dentistry. The American Society for Gastrointestinal Endoscopy has approved the statement as it relates to gastroenterology. The authors thank Jeanette Allison for her superb secretarial skills.

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