Chapter 37: Endocarditis

INTRODUCTION

- *Endocarditis* is an inflammation of the endocardium, the membrane lining the chambers of the heart and covering the cusps of the heart valves. *Infective endocarditis* (IE) refers to infection of the heart valves by microorganisms, primarily bacteria.
- Endocarditis is often referred to as either acute or subacute depending on the clinical presentation. Acute bacterial endocarditis is a fulminating infection associated with high fevers, systemic toxicity, and death within days to weeks if untreated. Subacute infectious endocarditis is a more indolent infection, usually occurring in a setting of prior valvular heart disease.

ETIOLOGY

- Most patients with IE have risk factors, such as preexisting cardiac valve abnormalities. Many types of structural heart disease resulting in turbulence of blood flow will increase the risk for IE. Some of the most important risk factors include the following:

  ✔ Highest risk: presence of a prosthetic valve or previous IE

  ✔ Congenital heart disease (CHD), chronic intravenous (IV) access, diabetes mellitus, acquired valvular dysfunction (eg, rheumatic heart disease), cardiac implantable device, chronic heart failure, mitral valve prolapse with regurgitation, IV drug abuse (IVDA), HIV infection, and poor dentition and/or oral hygiene.

- Three groups of organisms cause most cases of IE: staphylococci, streptococci, and enterococci (**Table 37-1**). Staphylococci (*S. aureus* and coagulase-negative staphylococci) are the most common cause of prosthetic valve endocarditis (PVE) within the first year after valve surgery, and *S. aureus* is common in those with a history of IVDA.

TABLE 37-1

Etiologic Organisms in Infective Endocarditis[a]

Agent	Percentage of Cases
Staphylococci	30–70
Coagulase positive *S. aureus*	20–68
Coagulase negative	3–26
Streptococci	9–38
Viridans streptococci	10–28
Other streptococci	3–14
Enterococci	5–18
Gram-negative aerobic bacilli	1.5–13
Fungi	1–9
Miscellaneous bacteria	<5
Polymicrobial infections	1–2
Culture negative	<5–17

[a]Values encompass community-acquired, healthcare-associated, native valve, and prosthetic valve infective endocarditis.

CLINICAL PRESENTATION

- The clinical presentation of patients with IE is highly variable and nonspecific. Fever is the most common finding (more than 90% of patients). The mitral and aortic valves are most often affected.
- IE usually begins insidiously and worsens gradually. Patients may present with nonspecific findings such as fever, chills, weakness, dyspnea, cough, night sweats, weight loss, or malaise.
- Important clinical signs, especially prevalent in subacute illness, may include the following peripheral manifestations (“stigmata”) of endocarditis: Osler nodes, Janeway lesions, splinter hemorrhages, petechiae, clubbing of the fingers, Roth spots, and emboli. The patient may also have a heart murmur (sometimes new or changing), congestive heart failure, cardiac conduction abnormalities, cerebral manifestations, embolic phenomenon, and splenomegaly.
- Without appropriate antimicrobial therapy and surgery, IE is usually fatal. With proper management, recovery can be expected in most patients.
- Factors associated with increased mortality include: congestive heart failure, culture-negative endocarditis, endocarditis caused by resistant organisms such as fungi and gram-negative bacteria, left-sided endocarditis caused by *Staphylococcus aureus*, PVE.
- Ninety to 95% of patients with IE have a positive blood culture. The hallmark laboratory finding is continuous bacteremia; three sets of blood

cultures should be collected over 24 hours. The patient's white blood cell count may be normal or only slightly elevated. Anemia, leukocytosis, and thrombocytopenia may be present. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may be elevated in approximately 60% of patients. Urinalysis may reveal proteinuria and microscopic hematuria.

- Transesophageal echocardiography is important in identifying and localizing valvular lesions in patients suspected of having IE. It is more sensitive for detecting vegetations (90%–100%), compared with transthoracic echocardiography (40%–65%).
- The Modified Duke criteria, encompassing major findings of persistent bacteremia and echocardiographic findings and other minor findings, are used to categorize patients as "definite IE" or "possible IE."

TREATMENT

- Goals of Treatment: relieve the signs and symptoms of disease. Decrease morbidity and mortality associated with infection. Eradicate the causative organism with minimal drug exposure. Provide cost-effective antimicrobial therapy. Prevent IE in high-risk patients with appropriate prophylactic antimicrobials.
- The most important approach to treatment of IE is isolation of the infecting pathogen and determination of antimicrobial susceptibilities, followed by high-dose, bactericidal antibiotics for an extended period.
- Treatment usually is started in the hospital, but in select patients, it may be completed in the outpatient setting as long as defervescence has occurred and follow-up blood cultures show no growth.
- Large doses of parenteral antimicrobials as opposed to oral antimicrobials are currently recommended to achieve bactericidal concentrations within vegetations. An extended duration of therapy is required, even for susceptible pathogens, because microorganisms are enclosed within valvular vegetations and fibrin deposits.
- Outpatient antimicrobial therapy should be considered early in the treatment of IE, after the patient is stable clinically and responds favorably to initial antibiotics.
- Drug dosing for treatment of IE is given in **Table 37-2**. β-Lactam antibiotics, such as penicillin G (or ceftriaxone), nafcillin (or oxacillin), and ampicillin, remain the drugs of choice for streptococcal, staphylococcal, and enterococcal endocarditis, respectively.

TABLE 37-2

Drug Dosing Table for Treatment of Infective Endocarditis[a]

Drug	Brand Name	Recommended Dose	Pediatric (Ped) Dose[b]	Additional Information
Ampicillin	NA	2 g IV every 4 hours	50 mg/kg every 4 hours or 75 mg/kg every 6 hours	24-hour total dose may be administered as a continuous infusion: 12 g IV every 24 hours
Ampicillin–sulbactam	Unasyn®	3 g IV every 6 hours	50 mg/kg every 4 hours or 75 mg/kg every 6 hours	
Aqueous crystalline penicillin G sodium	NA			

• MIC <0.12 mcg/mL (mg/L) (native valve only)		3 million units IV every 4 hours or every 6 hours	50,000 units/kg IV every 6 hours	24-hour total dose may be administered as a continuous infusion: 12–18 million units IV every 24 hours (Ped: 200,000 units/kg IV/24 hours)
• All other indications		4 million units IV every 4 hours or 6 million units IV every 6 hours	50,000 units/kg IV every 4 hours or 75,000 units/kg IV every 6 hours	24 million units IV every 24 hours (Ped: 300,000 units/kg IV every 24 hours)
Cefazolin	N/A	2 g IV every 8 hours	33 mg/kg IV every 8 hours	
Cefepime	Maxipime®	2 g IV every 8 hours	50 mg/kg IV every 8 hours	
Ceftriaxone sodium	N/A	2 g IV or IM every 24 hours	100 mg/kg IV or IM every 24 hours	
		2 g IV or IM every 12 hours (*E. faecalis only*)		
Ciprofloxacin	Cipro®	400 mg IV every 12 hours or 500 mg orally every 12 hours	20–30 mg/kg IV or orally every 12 hours	Avoid use if possible in patients <18 years of age
Daptomycin	Cubicin®	≥8 mg/kg IV every 24 hours	6 mg/kg IV every 24 hours	Doses as high as 10–12 mg/kg IV every 24 hours have been used in adults with enterococcus resistant to penicillin, aminoglycosides, and vancomycin; doses should be calculated using actual body weight
Doxycycline	Vibramycin®	100 mg IV or orally every 12 hours	1–2 mg/kg IV or orally every 12 hours	
Gentamicin sulfate	NA	3 mg/kg IV or IM every 24 hours or 1 mg/kg IV or IM every 8 hours[c]	1 mg/kg IV or IM every 8 hours	Once-daily dosing is only recommended for treatment of streptococcal infections
Linezolid	Zyvox®	600 mg IV or orally every 12 hours	10 mg/kg IV every 8 hours	
Nafcillin or oxacillin	NA	2 g IV every 4 hours	50 mg/kg IV every 6 hours	24-hour total dose may be administered as a continuous infusion: 12 g IV every 24 hours
Rifampin	Rifadin®	300 mg IV or orally every 8 hours	5–7 mg/kg IV or orally every 8 hours	

Streptomycin	NA	7.5 mg/kg IV or IM every 12 hours		
Vancomycin	Vancocin®	15–20 mg/kg IV every 8 hours or every 12 hours	15 mg/kg IV every 6 hours	A loading dose of 25–30 mg/kg may be administered in adults; doses should be calculated using actual body weight; single doses should not exceed 2 g

[a]All doses assume normal renal function.

[b]Should not exceed adult dosage.

[c]Actual body weight should be used when the full aminoglycoside dose is administered once daily; when administered in three divided doses, use ideal body weight or adjusted body weight when actual body weight is >120% ideal body weight.

Nonpharmacologic Therapy

- Surgical intervention to remove the infectious foci and repair valves and/or valvular structures is an important adjunct in the management of both NVE and PVE In most cases, valvectomy and valve replacement are performed to remove infected tissues and restore hemodynamic function. Indications for surgery include heart failure, persistent bacteremia, persistent vegetation, an increase in vegetation size, or recurrent emboli despite prolonged antibiotic treatment, valve dysfunction, paravalvular extension (eg, abscess), or endocarditis caused by resistant organisms.

Streptococcal Endocarditis

- Streptococci are a common cause of IE, with most isolates being viridans group streptococci.
- Most viridans group streptococci are highly sensitive to penicillin G with minimum inhibitory concentrations (MICs) of 0.12 mcg/mL (mg/L) or less. The MIC should be determined for all viridans streptococci and the results used to guide therapy. Approximately 10%–20% are moderately susceptible (MIC 0.12–0.5 mcg/mL [mg/L]).
- Recommended therapy in the uncomplicated case caused by fully susceptible strains in native valves is 4 weeks of either high-dose **penicillin G** or **ceftriaxone**, or 2 weeks of combined penicillin G or ceftriaxone therapy plus **gentamicin** (**Table 37-3**).
- Shorter-course antimicrobial regimens are advocated when possible. With susceptible streptococcal endocarditis (MICs ≤0.12 mcg/mL [mg/L]), a 2-week regimen of high-dose parenteral penicillin G or ceftriaxone in combination with an aminoglycoside is as effective as 4 weeks of penicillin alone.
- When a patient has a history of an immediate-type hypersensitivity to penicillin, vancomycin should be chosen for IE caused by viridans group streptococci. When vancomycin is used, the addition of gentamicin is not recommended.
- For patients with complicated infection (eg, extracardiac foci) or when the organism is relatively resistant (MIC = 0.12–0.5 mcg/mL [mg/L]), combination therapy with an aminoglycoside and penicillin (higher dose) or ceftriaxone for the first 2 weeks is recommended followed by penicillin or ceftriaxone alone for an additional 2 weeks.
- In patients with endocarditis of prosthetic valves or other prosthetic material caused by viridans streptococci and *Streptococcus bovis*, treatment courses are extended to 6 weeks (**Table 37-4**).

TABLE 37-3

Treatment Options for Native Valve Endocarditis by Causative Organism

Agent[a]	Duration	Strength of Recommendation	Comments
Highly Penicillin-Susceptible (MIC ≤ 0.12 mcg/mL [mg/L]) Viridans Group Streptococci and *S. gallolyticus*			
Aqueous crystalline penicillin G sodium[b]	4 weeks	IIaB	2-week regimens are not intended for the following patients: • Most patients >65 years of age • Children • Impairment of the eighth cranial nerve function • Renal function with a creatinine clearance <20 mL/min (0.33 mL/sec) • Known cardiac or extracardiac abscess • Infection with *Abiotrophia, Granulicatella*, or *Gemalla* species
Ceftriaxone	4 weeks	IIaB	
Aqueous crystalline penicillin G sodium[b] plus gentamicin	2 weeks	IIaB	
Ceftriaxone plus gentamicin	2 weeks	IIaB	
Vancomycin	4 weeks	IIaB	Recommended only for patients unable to tolerate penicillin or ceftriaxone
Viridans Group Streptococci and *S. Gallolyticus* Relatively Resistant to Penicillin (MIC >0.12 to ≤0.5 mcg/mL [mg/L])			
Aqueous crystalline penicillin G sodium[b] plus gentamicin	4 weeks	IIaB	
	2 weeks		
Ceftriaxone plus gentamicin	4 weeks	IIbC	
	2 weeks		
Vancomycin	4 weeks	IIaB	Recommended only for patients unable to tolerate penicillin or ceftriaxone
Oxacillin-Susceptible Staphylococci[c]			
Nafcillin or oxacillin	6 weeks	IC	
Cefazolin	6 weeks	IB	For use in patients with nonanaphylactoid-type penicillin allergies; patients with an unclear history of immediate-type hypersensitivity to penicillin should be considered for skin testing
Vancomycin	6 weeks	IB	For use in patients with anaphylactoid-type hypersensitivity to penicillin and/or cephalosporins
Daptomycin	6 weeks	IIaB	For use in patients with immediate-type hypersensitivity reactions to penicillin
Oxacillin-Resistant Staphylococci			
Vancomycin	6 weeks	IB	
Daptomycin	6 weeks	IIbB	

[a]See Table 37-2 for appropriate dosing, administration, and monitoring information.

[b]May use ampicillin in the event of a penicillin shortage.

[c]Regimens indicate treatment for left-sided endocarditis or complicated right-sided endocarditis; uncomplicated right-sided endocarditis may be treated for shorter durations and is described in the text.

Please refer to Table 37-5 for treatment of NVE caused by enterococci.

TABLE 37-4

Treatment Options for Prosthetic Valve Endocarditis (PVE) by Causative Organism

Agent[a]	Duration	Strength of Recommendation	Comments
Highly Penicillin-Susceptible (MIC ≤ 0.12 mcg/mL [mg/L]) Viridans Group Streptococci and *S. gallolyticus*			
Aqueous crystalline penicillin G sodium[b] with or without gentamicin	6 weeks	IIaB	Combination therapy with gentamicin has not demonstrated superior cure rates compared with monotherapy with a penicillin or cephalosporin and should be avoided in patients with CrCl <30 mL/min (0.50 mL/sec)
	2 weeks		
Ceftriaxone with or without gentamicin	6 weeks	IIaB	
	2 weeks		
Vancomycin	6 weeks	IIaB	Recommended only for patients unable to tolerate penicillin or ceftriaxone
Relatively Resistant or Fully Resistant (MIC >0.12 mcg/mL [mg/L]) Viridans Group Streptococci and *S. gallolyticus*			
Aqueous crystalline penicillin G sodium[b] plus gentamicin	6 weeks	IIaB	
Ceftriaxone plus gentamicin	6 weeks	IIaB	
Vancomycin[c]	6 weeks	IIaB	Recommended only for patients unable to tolerate penicillin or ceftriaxone
Oxacillin-Susceptible Staphylococci			
Nafcillin or oxacillin	≥6 weeks	IB	Cefazolin may be substituted for nafcillin or oxacillin in patients with nonimmediate-type hypersensitivity
plus rifampin	≥6 weeks		
plus gentamicin	2 weeks		
Vancomycin	≥6 weeks	IB	Recommended only for patients with anaphylactoid-type hypersensitivity to penicillin and/or cephalosporins
plus rifampin	≥6 weeks		
plus gentamicin	2 weeks		
Oxacillin-Resistant Staphylococci			
Vancomycin	≥6 weeks	IB	
plus rifampin	≥6 weeks		
plus gentamicin	2 weeks		

[a]See Table 37-2 for appropriate dosing, administration, and monitoring information.

[b]May use ampicillin in the event of a penicillin shortage.

[c]The ESC 2015 guidelines recommend gentamicin (3 mg/kg/day) be administered with vancomycin for the initial 2 weeks of therapy in patients with relatively resistant strains to penicillin.

Please refer to Table 37-5 for treatment of PVE caused by enterococci.

Staphylococcal Endocarditis

- Endocarditis is most commonly caused by staphylococci, in particular *S. aureus*, mainly because of increased IVDA, more frequent use of peripheral and central venous catheters, and increased frequency of valve replacement surgery. Coagulase-negative staphylococci (usually *S. epidermidis*) are prominent causes of PVE.
- The recommended therapy for patients with left-sided IE caused by methicillin-susceptible *S. aureus* (MSSA) is 6 weeks of **nafcillin** or **oxacillin** (see **Table 37-3**).
- If a patient has a mild, delayed allergy to penicillin, first-generation cephalosporins (such as **cefazolin**) are effective alternatives but should be avoided in patients with an immediate-type hypersensitivity reaction.
- In a patient with a positive penicillin skin test or a history of immediate hypersensitivity to penicillin, **vancomycin** is an option. Vancomycin, however, kills *S. aureus* slowly and is generally regarded as inferior to penicillinase-resistant penicillins for MSSA. Penicillin-allergic patients who fail on vancomycin therapy should be considered for penicillin desensitization. **Daptomycin** (at a dose of 6 mg/kg/day) is a recommended alternative.
- **Vancomycin** is the drug of choice for methicillin-resistant staphylococci because most methicillin-resistant *S. aureus* (MRSA) and most coagulase-negative staphylococci are susceptible. Reports of *S. aureus* strains resistant to vancomycin are increasing. Daptomycin (at a dose of 6 mg/kg/day) is now a recommended alternative.

Treatment of *Staphylococcus* Endocarditis in IV Drug Abusers

- IE in IV drug abusers is most frequently (60%–70%) caused by *S. aureus*, although other organisms may be more common in certain geographic locations.
- A 2-week course of **nafcillin, oxacillin**, or **daptomycin** without an aminoglycoside is recommended. If vancomycin is selected, the standard 6-week regimen should therefore be used.

Treatment of Staphylococcal Prosthetic Valve Endocarditis

- PVE that occurs within 2 months of cardiac surgery is usually caused by staphylococci implanted at the time of surgery. Methicillin-resistant organisms are common. Vancomycin is the cornerstone of therapy.
- Because of the high morbidity and mortality associated with PVE and refractoriness to therapy, combinations of antimicrobials are usually recommended.
- For methicillin-resistant staphylococci (both MRSA and coagulase-negative staphylococci), **vancomycin** is used with rifampin for 6 weeks or more (see **Table 37-4**). An **aminoglycoside** is added for the first 2 weeks if the organism is susceptible. Due to the risk of developing on therapy resistance, rifampin should not be started until blood cultures have cleared.
- For methicillin-susceptible staphylococci, a **penicillinase-resistant penicillin** is used in place of vancomycin. If an organism is identified other than staphylococci, the treatment regimen should be guided by susceptibilities and should be at least 6 weeks in duration.

Enterococcal Endocarditis

- Enterococci are the third leading cause of endocarditis and are noteworthy for the following reasons: (1) no single antibiotic is bactericidal; (2) MICs to penicillin are relatively high (1–25 mcg/mL [mg/L]); (3) they are intrinsically resistant to all cephalosporins and relatively resistant to

aminoglycosides (ie, “low-level” aminoglycoside resistance); (4) combinations of a cell wall–active agent, such as a penicillin or vancomycin, plus an aminoglycoside are necessary for killing; and (5) resistance to all available drugs is increasing.

- Enterococcal endocarditis ordinarily requires 4–6 weeks of high-dose **penicillin G** or **ampicillin**, plus **gentamicin** for cure (**Table 37-5**). Ampicillin plus ceftriaxone is as effective as ampicillin plus gentamicin and should be considered as a treatment option. A 6-week course is recommended for patients with symptoms lasting longer than 3 months and those with PVE. Relatively low serum concentrations of aminoglycosides appear adequate for successful therapy, such as a gentamicin peak concentration of approximately 3–4 mcg/mL (mg/L; 6.3–8.4 µmol/L).

- In addition to isolates with high-level aminoglycoside resistance, β-lactamase–producing enterococci (especially *Enterococcus faecium*) are increasingly reported. If these organisms are discovered, use of vancomycin or ampicillin–sulbactam in combination with gentamicin should be considered.

TABLE 37-5

Treatment Options for Native or Prosthetic Valve Endocarditis Caused by Enterococci

Agent[a]	Duration[b]	Strength of Recommendation	Comments
Ampicillin-, Penicillin-, and Vancomycin-Susceptible Strains			
Ampicillin plus gentamicin	4–6 weeks	IIaB	Native valve plus symptoms present for <3 months: use 4-week regimen
Aqueous crystalline penicillin G sodium plus gentamicin	4–6 weeks	IIAB	Prosthetic valve or native valve plus symptoms present for >3 months: use 6-week regimen
Ampicillin plus ceftriaxone	6 weeks	IIaB	Recommended regimen if creatinine clearance is <50 mL/min (0.83 mL/sec; at baseline or due to therapy with a gentamicin-containing regimen)
Vancomycin plus gentamicin	6 weeks	IIaB	Recommended only for patients unable to tolerate penicillin or ampicillin
Gentamicin-Resistant Strains			
If susceptible, use streptomycin in place of gentamicin in the regimens listed above if creatinine clearance is >50 mL/min (0.83 mL/sec), cranial nerve VIII function is intact and there is laboratory capability for rapid streptomycin serum concentrations.			
Penicillin-Resistant Strains			
Ampicillin–sulbactam plus gentamicin (β-lactamase–producing strain)	6 weeks	IIbC	
Vancomycin plus gentamicin (intrinsic penicillin resistance[c])	6 weeks	IIbC	May also use in patients with β-lactamase–producing strains who have known intolerance to ampicillin–sulbactam
***Enterococcus faecium* Strains Resistant to Penicillin, Aminoglycosides, and Vancomycin[d]**			
Linezolid	>6 weeks	IIbC	Antimicrobial cure rates may be <50%; bacteriologic cure may only be achieved with cardiac valve replacement
Daptomycin	>6 weeks	IIbC	

[a]See Table 37-2 for appropriate dosing, administration, and monitoring information.

[b]All patients with prosthetic valves should be treated for at least 6 weeks.

[c]Infectious diseases consult highly recommended.

[d]Patients should be managed by a multidisciplinary team that includes specialists in cardiology, cardiovascular surgery, infectious diseases, and clinical pharmacy.

EVALUATION OF THERAPEUTIC OUTCOMES

- The evaluation of patients treated for IE includes assessment of signs and symptoms, blood cultures, microbiologic tests (eg, MIC, minimum bactericidal concentration [MBC], or serum bactericidal titers), serum drug concentrations, and other tests to evaluate organ function.
- Persistence of fever beyond 1 week may indicate ineffective antimicrobial therapy, emboli, infections of intravascular catheters, or drug reactions. In some patients, fever may persist even with appropriate antimicrobial therapy.
- With effective therapy, blood should sterilize with negative cultures within a few days, although microbiologic response to vancomycin may be unusually slower. After the initiation of therapy, blood cultures should be rechecked until they are negative. During the remainder of the therapy, frequent blood culturing is not necessary.
- If bacteria continue to be isolated from blood beyond the first few days of therapy, it may indicate that the antimicrobials are inactive against the pathogen or that the doses are not producing adequate concentrations at the site of infection.
- For all isolates from blood cultures, MICs (not MBCs) should be determined.

PREVENTION OF ENDOCARDITIS

- Antimicrobial prophylaxis is used to prevent IE in patients believed to be at high risk.
- The use of antimicrobials for this purpose requires consideration of the types of patients who are at risk; the procedures causing bacteremia; the organisms that are likely to cause endocarditis; and the pharmacokinetics, spectrum, cost, and ease of administration of available agents. The objective of prophylaxis is to diminish the likelihood of IE in high-risk individuals who are undergoing procedures that cause transient bacteremia.
- The literature lacks adequate evidence to prove the effectiveness or ineffectiveness of antibiotic prophylaxis, and the common practice of using antimicrobial therapy in this setting remains controversial.
- IE prophylaxis should be recommended only for patients with underlying cardiac conditions associated with the highest risk, which includes presence of a prosthetic heart valve, prosthetic material used for cardiac valve repair, prior diagnosis of IE, cardiac transplantation with subsequent valvulopathy, CHD, for dental procedures involving manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa, invasive respiratory procedures involving an incision or biopsy, or invasive procedures involving infected skin, skin structures, or musculoskeletal tissues.
- Antibiotic regimens for a dental procedure are given in **Table 37-6**.

TABLE 37-6

Prophylaxis of Infective Endocarditis

Highest Risk Cardiac Conditions	Presence of a prosthetic heart valve Prosthetic material used for cardiac valve repair Prior diagnosis of infective endocarditis Cardiac transplantation with subsequent valvulopathy Congenital heart disease (CHD)[a]	
Types of Procedures	Dental procedures that require perforation of the oral mucosa or manipulation of the periapical region of the teeth of gingival tissue Invasive respiratory procedures involving an incision or biopsy Invasive procedures involving infected skin, skin structures, or musculoskeletal tissue	
Antimicrobial Options	**Adult Doses[b]**	**Pediatric Doses[b] (mg/kg)**
Oral amoxicillin	2 g	50
IM or IV ampicillin[c]	2 g	50
IM or IV cefazolin or ceftriaxone[c,d,e]	1 g	50
Oral cephalexin[d,e,f]	2 g	50
Oral clindamycin[e]	600 mg	20
Oral azithromycin or clarithromycin[e]	500 mg	15
IV or IM clindamycin[c,e]	600 mg	20

[a]Includes only the following: unrepaired cyanotic CHD, prophylaxis within the first 6 months of implanting prosthetic material to repair a congenital heart defect, and repaired CHD with residual defects at or adjacent to prosthetic material.

[b]All one-time doses administered 30–60 minutes prior to initiation of the procedure.

[c]For patients unable to tolerate oral medication.

[d]Should be avoided in patients with immediate-type hypersensitivity reaction to penicillin or ampicillin (eg, anaphylaxis, urticaria, or angioedema).

[e]Option for patients with nonimmediate hypersensitivity reaction to penicillin or ampicillin.

[f]May substitute with an alternative first- or second-generation cephalosporin at an equivalent dose.

See Chapter 129, Infective Endocarditis, authored by Daniel B. Chastain and Angie Veverka, for a more detailed discussion of this topic.