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# Infective endocarditis

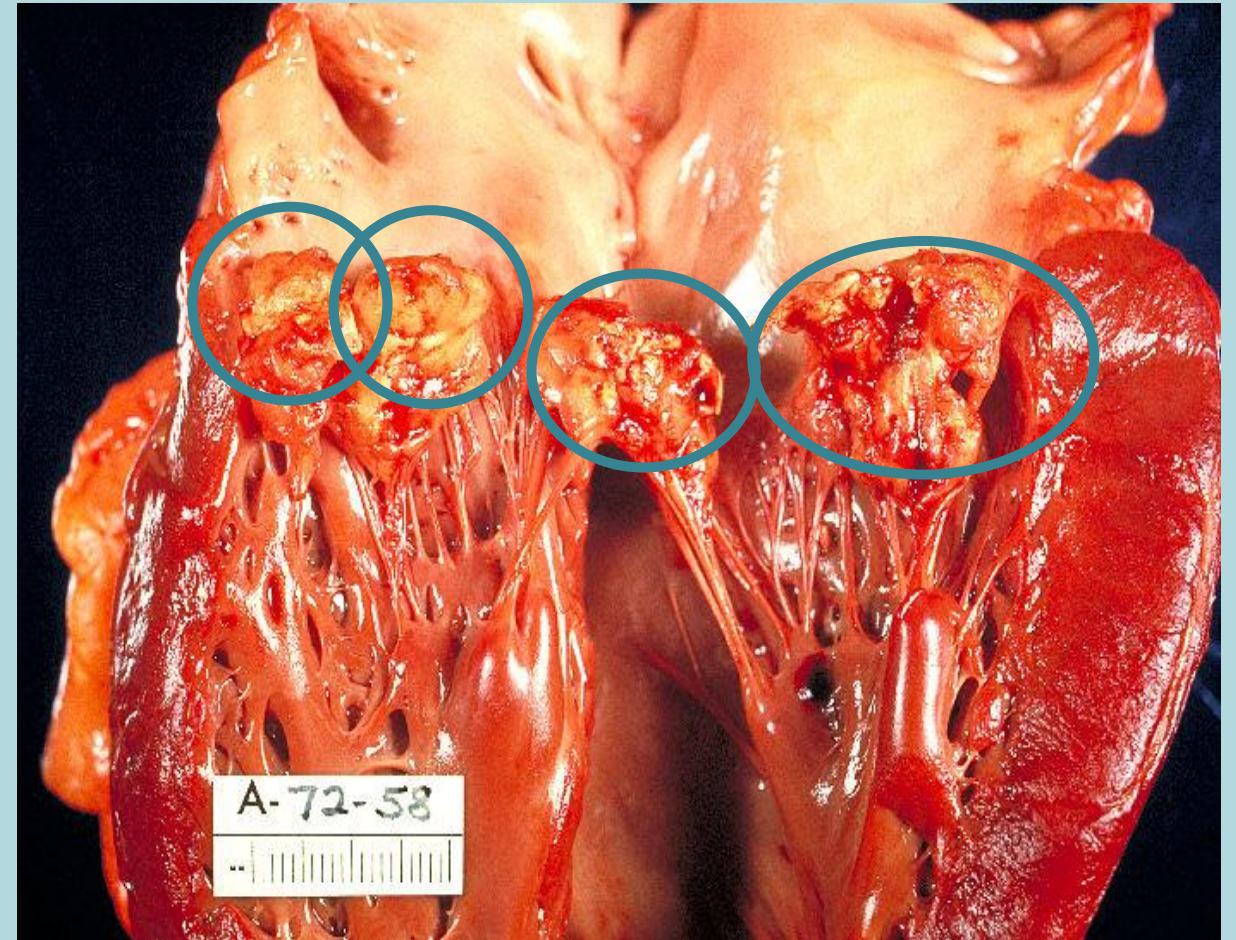
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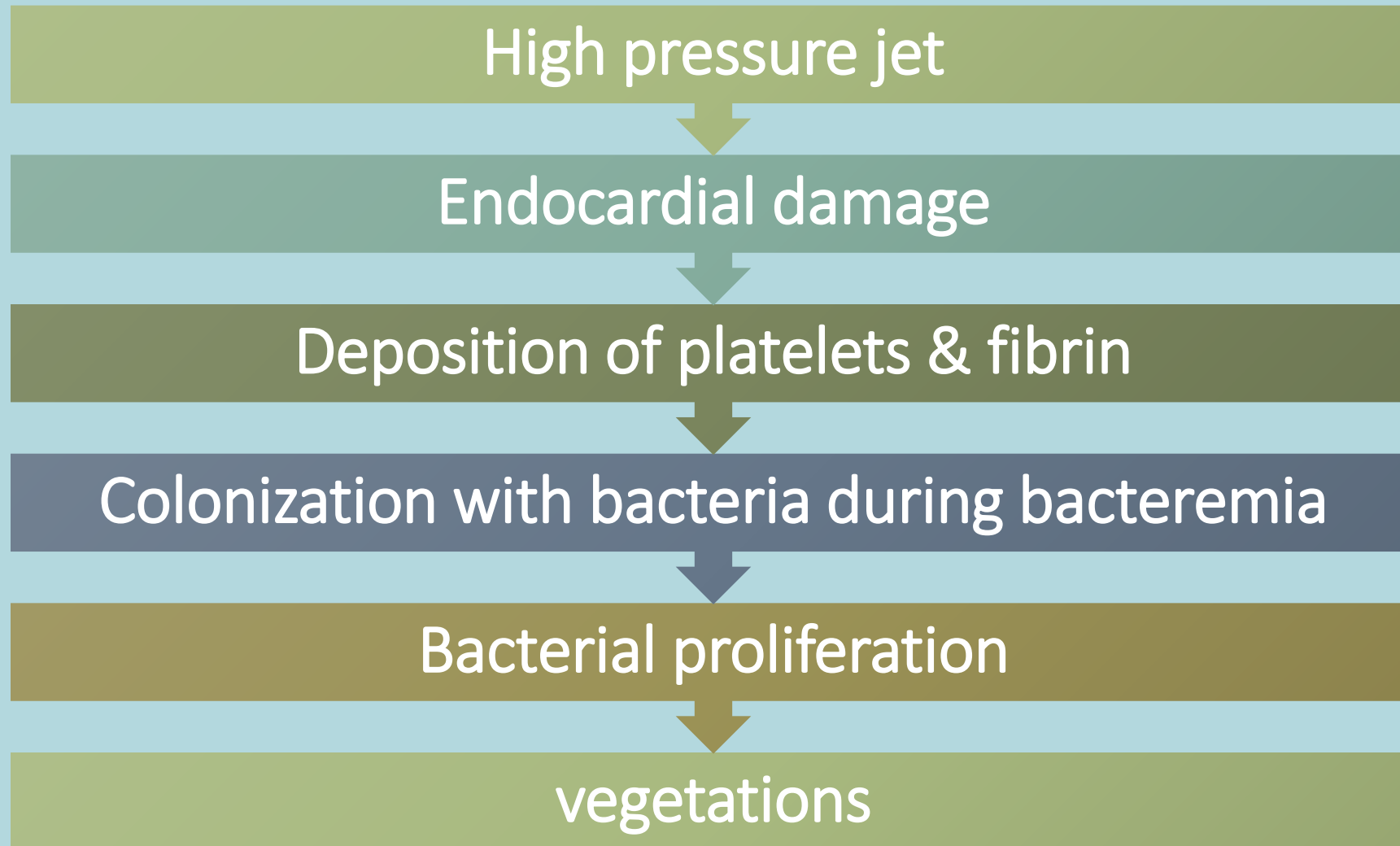
- **Microbial infection of the endothelial surface of the heart**
- **Characteristic lesion: Vegetation**

# Vegetation

- Mass of platelets and fibrin, rich in bacteria, scanty inflammatory cells
- Sites: heart valves, septal defect, chordae tendineae or mural endocardium



# Infective Endocarditis: Pathogenesis



# Pathogens Causing Infective Endocarditis in Children

Bacteria	Fungi
Viridans Streptococcus groups	Candida species
Staphylococcus aureus	<b>Culture Negative</b>
Enterococcus	Fastidious organisms <sup>€</sup>
Coagulase-negative staphylococci	Bartonella sp.
Streptococci: groups A, B, Streptococcus pneumoniae	Tropheryma whipplei
Gram-negative enteric bacilli	Coxiella burnetii (Q fever)
HACEK organisms	
Chlamydochila	
Coxiella burnetii (Q fever)	

Viridans Streptococcus groups: *S. sanguis*, *S. mitis*, *S. mutans*, *S. anginosus*, *S. salivarius*, *S. bovis*

Streptococci: groups A, B (in neonates and elderly), *Streptococcus pneumoniae*

**HACEK organisms: i.e., Haemophilus aphrophilus, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae**

<sup>€</sup> Fastidious organisms: *Abiotrophia* or *Granulicatella* sp.

# Etiology

- **Viridans group streptococci ( S. mutans , S. sanguinis , others)**
  - In children with congenital heart diseases without previous surgery
- **Staphylococcus aureus & coagulase-negative staphylococci (CONS)**
  - Especially following cardiac surgery and in the presence of prosthetic cardiac and endovascular materials
- **Gram-negative endocarditis is rare**
- **Candida species (fungal endocarditis)**
  - Especially in premature infants with central venous catheters and/or receiving parenteral nutrition.

# Epidemiology

- **Rheumatic heart disease used to be a major risk factor for IE but has become much less common.**
- **Patients at highest risk for IE include ...**
  - **those with prosthetic cardiac valves and children who have cyanotic congenital heart disease, either with or without repair.**
  - **The risk in these patients is increased after dental and oral procedures or procedures of the respiratory, genitourinary, or gastrointestinal tracts.**
- **Approximately 8–10% of IE in children occurs without structural heart disease (normal native valve) or other obvious risk factors.**
  - **Use of central vascular catheters is a significant risk factor for native valve endocarditis**
  - **S. aureus is the most likely infective organism in these cases.**



# Clinical Manifestations

# Clinical Manifestations - History

- **Prior congenital or rheumatic heart disease**
- **Preceding dental, urinary tract, or intestinal procedure**
- **Intravenous drug use**
- **Central venous catheter**
- **Prosthetic heart valve**

# Clinical Manifestations - Symptoms

- **Fever, chills**
- **Chest and abdominal pain**
- **Arthralgia, myalgia**
- **Dyspnea**
- **Malaise, weakness**
- **Night sweats**
- **Weight loss**
- **CNS manifestations (stroke, seizures, headache)**

# Clinical Manifestations - Signs

- **Elevated temperature, tachycardia**
- **Cardiac: New or changing murmur, Heart failure, Arrhythmias**
- **Splenomegaly**
- **Clubbing, Arthritis**
- **Embolic phenomena (Roth spots, petechiae, splinter nail bed hemorrhages, Osler nodes, CNS or ocular lesions)**
- **Janeway lesions**
- **Metastatic infection (arthritis, meningitis, mycotic arterial aneurysm, pericarditis, abscesses, septic pulmonary emboli)**

# Local destructive effects of intracardiac infection

- **Destruction of valve leaflets, ruptured chordae**
- **Abscess formation**
- **Perforations or fistulas**
- **Disruption of conductive system**
- **Large vegetations lead to valve obstruction**

# Peripheral manifestations - Vascular phenomena

conjunctival hemorrhage



Janeway lesions



small painless, macular lesions on palms  
and soles of feet

# Peripheral manifestations - Vascular phenomena

splinter haemorrhage



thin linear hemorrhages under nail beds

splinter haemorrhage



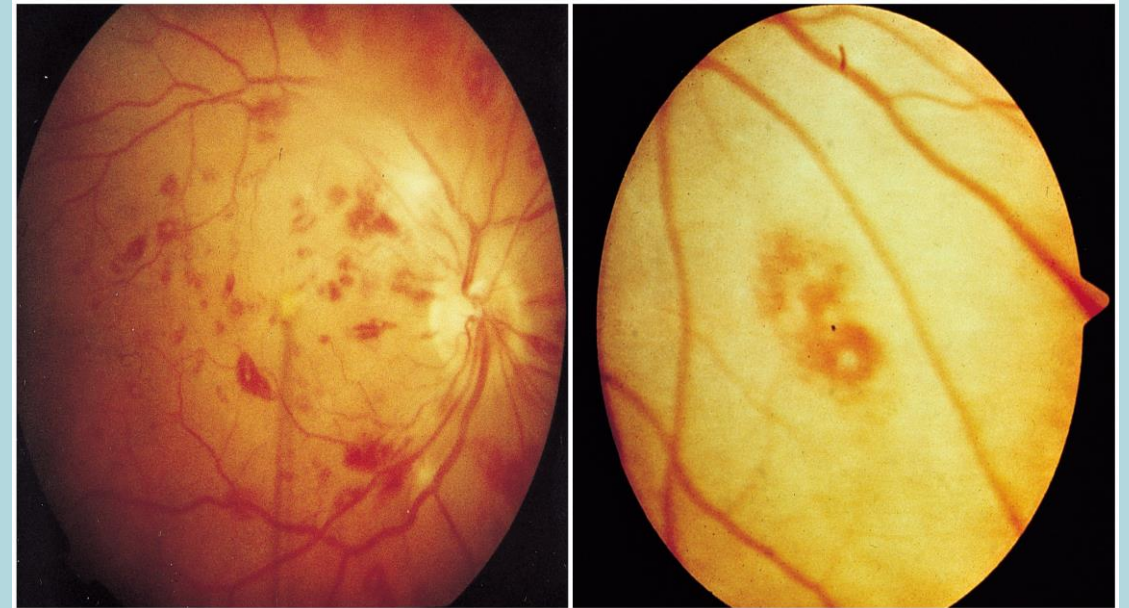
# Peripheral manifestations - Immunologic phenomena

## Osler nodes



small tender red / purple nodules found on distal digits on fingers and toes

## Roth spot



White-centered retinal hemorrhages



# Systemic embolization

- **CNS embolization: focal neurologic deficits, mycotic aneurysm, intracranial hemorrhage**
- **Spleen: pain, splenomegaly**
- **Limbs: ischemia and gangrene**
- **Mesenteric: abdominal pain, hematochezia**
- **septic pulmonary infarcts**

# Specific organ manifestations

- **Neurological manifestations**
  - Headache, confusion, convulsions, long tract signs & focal neurological deficit, meningeal irritation, mycotic aneurysm, intracranial hemorrhage
- **Renal manifestations**
  - Glomerulonephritis, renal failure, focal renal infarcts (hematuria)

# Manifestation in neonates

- **In neonates, the signs and symptoms of IE may be especially subtle and variable, including feeding issues, respiratory distress, and hypotension, in addition to changes in the cardiac exam.**

# Clinical spectrum of disease

- **Acute infective endocarditis**
  - High fever and a sepsis-like picture
  - Petechiae and embolic events common
  - Rapid progression of cardiac and renal failure
- **Subacute infective endocarditis (often)**
  - Caused by infection with low-virulence organisms on top of pre-existing cardiac disease
  - subtle and nonspecific findings i.e. persistent fever, tiredness, weight loss, night sweats

# Clinical spectrum of disease

- **Postoperative IE (following cardiac surgery)**
- **Early postoperative IE:**
  - infection is acquired at the time of surgery
  - High mortality: repeat surgery often required
- **Late postoperative IE:**
  - Community-acquired infection
  - Complication rates lower than early form

# Diagnosis

# Laboratory Studies and Imaging - 1

- The **key to diagnosis** is confirming **continuous bacteremia or fungemia** by culturing the blood.
  - Multiple blood cultures should be obtained before initiating antibiotic therapy
  - At least **three sets** of blood cultures (from different venipuncture sites) are obtained
  - Patients who have recently been treated with antibiotics or who are currently receiving antibiotics should have additional serial cultures performed
  - Despite adequate blood culture techniques, the microbiologic diagnosis is not confirmed in **5–15% of cases, known as culture-negative endocarditis**.
    - The agent in culture-negative endocarditis may be identified by **antibody testing** and examination of the valve tissue (following surgery) by **PCR for bacterial (16 S) or fungal (18 S) ribosomal RNA**.

# Laboratory Studies and Imaging - 2

- **ESR and CRP are often elevated**
- **Leukocytosis, anemia**
- **Hypergammaglobulinemia**
- **Hypocomplementemia**
- **Cryoglobulinemia**
- **Rheumatoid factor**
- **Hematuria**
- **Renal failure: azotemia, high creatinine (glomerulonephritis)**
- **Chest radiograph: bilateral infiltrates, nodules, pleural effusions**



# Laboratory Studies and Imaging - 3

- **Echocardiography should be performed in all cases where IE is suspected**
- **Echocardiographic evidence of valve vegetations, prosthetic valve dysfunction or leak, myocardial abscess, or new-onset valve insufficiency**

# Modified Duke Criteria for Infective Endocarditis

- **Major criteria**
- **Minor criteria**

- **Definite endocarditis**
- **Possible endocarditis**
- **Rejected endocarditis**

# Modified Duke Criteria for Infective Endocarditis

## Major Criteria

### A. Supportive Laboratory Evidence:

Typical microorganism for infective endocarditis from two separate blood cultures: viridans streptococci, *Staphylococcus aureus*, *Streptococcus bovis*, HACEK group (*Haemophilus* spp. *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella* spp., and *Kingella kingae*) or community-acquired enterococci, in the absence of a primary focus

Single positive blood culture for *Coxiella burnetii* or phase I antibody titer >1:800

### B. Evidence of Endocardial Involvement:

Echocardiogram supportive of infective endocarditis.

Definition of positive findings: oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomic explanation or myocardial abscess or new partial dehiscence of prosthetic valve.

New valvular regurgitation (increase or change in pre-existing murmur not sufficient).

# Modified Duke Criteria for Infective Endocarditis

## Minor Criteria

- A. Predisposing heart condition or intravenous drug use
- B. Fever  $\geq 38$  C (100.4°F)
- C. Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions
- D. Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
- E. Positive blood culture not meeting major criterion as noted previously (excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis) or serologic evidence of active infection with organism consistent with infective endocarditis

- **Additional minor criteria to those listed include ...**
  - **newly diagnosed clubbing, splenomegaly, splinter hemorrhages, or petechiae; high ESR or CRP; presence of central nonfeeding or peripheral lines; and microscopic hematuria.**

# Modified Duke Criteria for Infective Endocarditis

- **Definite endocarditis**

- **Pathologic Criteria**

- Microorganisms demonstrated by results of cultures or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathologic lesions; vegetation, or intracardiac abscess confirmed by results of histologic examination showing active endocarditis

# Modified Duke Criteria for Infective Endocarditis

- **Definite endocarditis**
  - **Pathologic Criteria**
  - **Clinical Criteria**
    - 2 major criteria
    - 1 major and  $\geq 3$  minor criteria
    - 5 minor criteria
- **Possible endocarditis**
  - 1 major and 1–2 minor criteria
  - 3–4 minor criteria
- **Rejected endocarditis**
  - 0 major and 1–2 minor criteria
  - 1 major and 0 minor criteria

# Differential Diagnosis

- **Noninfectious causes of endocardial vegetations must be excluded, such as sterile clots or lupus.**
- **Prolonged bacteremia can be caused by infectious endothelial foci outside of the heart, often associated with congenital vascular malformations, vascular trauma, an infected venous thrombosis, or previous vascular surgery.**

# Treatment



# Treatment - Medical

- Severely ill patients must be stabilized with supportive therapies for cardiac failure, pulmonary edema, and low cardiac output.
- Empirical antibiotic therapy may be started for acutely ill patients after blood cultures are obtained.
- With subacute disease, awaiting results of blood cultures to confirm the diagnosis is recommended to direct therapy according to the susceptibility of the isolate.
- Because antibiotics must reach the organisms by **passive diffusion** through the fibrin mesh, **high doses** of **bactericidal antibiotics** are required for an **extended period of treatment** (4–6 weeks).

# Treatment - Surgical

- **Early surgery (during initial hospitalization and before completion of a full course of antibiotics) is indicated in patients with IE ...**
  - **and valve dysfunction resulting in symptoms or signs of heart failure**
  - **caused by fungal or highly resistant organisms (e.g., VRE, multidrug-resistant gram-negative bacilli)**
  - **complicated by heart block, annular or aortic abscess, or destructive penetrating lesions**
  - **and evidence of persistent infection (manifested by persistent bacteremia or fever lasting >5–7 days and provided that other sites of infection and fever have been excluded) after the start of appropriate antimicrobial therapy**
  - **and recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy**
  - **and severe valve regurgitation and mobile vegetations >10 mm**
  - **and mobile vegetations >10 mm, particularly when involving the anterior leaflet of the mitral valve and associated with other relative indications for surgery**

# Complications and Prognosis

- **The major complications of IE are direct damage to cardiac tissue and function and distant complications secondary to septic emboli from vegetations.**
  - **Damage to cardiac valves may cause regurgitation, defects in valve leaflets, abscess of the valve ring, or myocardial abscess. Cardiac function can decline, resulting in heart failure.**
  - **Septic emboli can result in pneumonia, osteomyelitis, and abscesses in the brain, kidneys, and spleen.**

# Prevention

- **Good oral hygiene should be emphasized in all patients at risk for IE.**
- **In certain high-risk patients, prophylactic antibiotics may be considered before certain dental and other invasive procedures of the respiratory tract and/or infected skin or muscle.**

# Underlying cardiac conditions for which Antibiotic prophylaxis is suggested

Prosthetic cardiac valve or material
Presence of cardiac prosthetic valve
Transcatheter implantation of prosthetic valves
Cardiac valve repair with devices, including annuloplasty, rings, or clips
Left ventricular assist devices or implantable heart
Previous, relapse, or recurrent IE
CHD
Unrepaired cyanotic congenital CHD, including palliative shunts and conduits.
Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by transcatheter during the first 6 mo after the procedure
Repaired CHD with residual defects at the site of or adjacent to the site of a prosthetic patch or prosthetic device
Surgical or transcatheter pulmonary artery valve or conduit placement such as Melody valve and Contegra conduit
Cardiac transplant recipients who develop cardiac valvulopathy

# Dental Procedures and Antibiotic prophylaxis

## AP suggested

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa

## AP not suggested

Anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of primary teeth, and bleeding from trauma to the lips or oral mucosa

# Prophylactic Antibiotic Regimens for a Dental Procedure

**Table 464.10** Prophylactic Antibiotic Regimens for a Dental Procedure (2007 AHA Statement)

SITUATION	AGENT	ADULTS	CHILDREN
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin or Cefazolin or ceftriaxone	2 g IM or IV 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin—oral	Cephalexin* <sup>†</sup> or Clindamycin or Azithromycin or clarithromycin	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone <sup>†</sup> or Clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV

IM, Intramuscularly; IV, intravenously.

\*Or other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosage.

<sup>†</sup>Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

From Wilson W, Taubert KA, Gewitz M, et al: Prevention of infective endocarditis: guidelines from the American Heart Association, *Circulation* 116:1736–1754, 2007.

# Pearls for Practitioners

- **Streptococci are the most common cause of native valve endocarditis in children, whereas staphylococci are more common in those with prosthetic material.**
- **If infectious endocarditis is suspected, multiple optimal-volume blood cultures should be obtained prior to starting antimicrobial therapy.**
- **The modified Duke criteria are used to make the diagnosis.**
- **Treatment is typically given entirely parenterally and is guided by the pathogen identified.**