Infective endocarditis

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Objectives

- Define infective endocarditis
- Discuss the pathogenesis, epidemiology and classification of infective endocarditis
- List important risk factors
- Describe the clinical presentation and complications
- Discuss the clinical and laboratory diagnosis
- Discuss the causes and diagnosis of culture negative endocarditis
- Discuss the management and prophylaxis

Definition

- Infectious Endocarditis (IE): an infection of the heart's endocardial surface
- Classified into four groups:
  - Native Valve IE
  - Prosthetic Valve IE
  - Intravenous drug abuse (IVDA) IE
  - Nosocomial IE

Further Classification

- Acute:
  - Affects normal heart valves
  - Rapidly destructive
  - If not treated, usually fatal within 6 weeks
  - Commonly Staph→ Metastatic foci
- Subacute:
  - Often affects damaged heart valves
  - Indolent nature
  - If not treated, usually fatal by one year
  - Commonly viridans

Pathophysiology

1. Turbulent blood flow disrupts the endocardium making it “sticky”
2. Bacteremia delivers the organisms to the endocardial surface
3. Adherence of the organisms to the endocardial surface
4. Eventual invasion of the valvular leaflets

Epidemiology

- Incidence: 1.7— 6.2 / 100 000 person years
- M:F 1.7
- Becoming a disease of the elderly
- Median age
  - PreABx era —35y,
  - Now —58y
- Due to two factors
  - The decline of rheumatic heart disease
  - The increasing proportion of elderly

Prosthetic Valve

- 7 -25 % of cases of infective endocarditis
  - Early ≤12mons
  - Late >12 mons
- 0.94 per 100,000 bioprosthetic
- Initially mechanical valves at greater risk for first 3 mo, then risk same at 5y
  - 1-3.1% risk at 1 yr
  - 2-5.7% at 5 yr

Risk Factors

- **Injection drug use**
  - 100X ↑ risk in young *Staphylococcus aureus*
- **Other risks:**
  1. Poor dental hygiene
  2. Hemodialysis
  3. DM
  4. HIV

- IVDU
  - Rates 150- 2000/ 100 000 person years
  - Higher among patients with known valvular heart disease
- Structural cardiac abnormality
  - 75% of pts will have a preexisting structural cardiac abnormality
  - 10-20% have congenital heart disease

Risk Factors ; Cardiac Abnormality

- High risk
  - Previous IE 4.5(2.5 to 9)%
  - Aortic valve disease12 to 30%
  - Rheumatic valve disease
  - Prosthetic valve
  - Coarctation
  - Complex cyanotic congenital
- Moderate risk
  - MVP w/ MR/thickened leaflets- 5 to 8 times (100/100 000 person years)
  - Mitral Stenosis
  - tricuspid valve
  - Pulmonary Stenosis
  - Hypertrophic Obstructive Cardiomyopathy (HOCM)
  - Low/no risk
    - ASD (secundum)
    - CABG (coronary artery bypass graft)

Risk Factors

- **HIV infection:**
  - A number of cases of IE have been reported in patients with HIV infection
  - It has been suggested that HIV infection is an independent risk factor for IE in IDU
- **Rheumatic valve disease:**
  - Predisposition for young in some countries 37%~76% of cases
  - Mitral 85%, Aortic 50%
  - Degenerative valvular lesions
  - MVProlapse and associated mitral regurgitation ~ 5 to 8 times higher IE risk
  - Aortic valve disease (stenosis or/and regurgitation) is present in 12 to 30 % of cases

Diagnostic approach

- History of prior cardiac lesions
- A recent source of bacteremia

Symptoms

- Acute
  - High grade fever and chills
  - SOB
  - Arthralgias/ myalgias
  - Abdominal pain
  - Pleuritic chest pain
  - Back pain
- Subacute
  - Low grade fever
  - Anorexia
  - Weight loss
  - Fatigue
  - Arthralgias/ myalgias
  - Abdominal pain
  - N/V

The onset of symptoms is usually ~2 weeks or less from the initiating bacteremia

Physical examination

- Look for small and large emboli with special attention to the fundi, conjunctivae, skin, and digits
- Cardiac examination may reveal signs of new regurgitation murmurs and signs of CHF
- Neurologic evaluation may detect evidence of focal neurologic impairment

- Signs
  - Fever
  - Heart murmur
  - Nonspecific signs – petechiae, subungal or "splinter" hemorrhages, clubbing, splenomegaly, neurologic changes
  - More specific signs ~ Osler's Nodes, Janeway lesions, and Roth Spots

Other aspects clinical diagnosis

- WHICH VALVE? R or L heart where would emboli go?
- HEART FUNCTION?
- Pump, acute valve dysfunction conduction
- Look for evidence emboli
- Bleed (intracranial, elsewhere mycotic aneurysm)

Diagnostic approach

1-Positive blood culture results

- A minimum of three blood cultures should be obtained over a time period based upon the severity of the illness

2-Additional laboratory Nonspecific test

- An elevated ESR and/or an elevated level of CRP is usually present
- Most patients quickly develop a normochromic normocytjc anemia
- The WBC count may be normal or elevated

Additional laboratory tests

- ***Abnormal urinalysis***
  - The combination of RBC casts on urinalysis and a low serum complement level may be an indicator of immune-mediated glomerular disease
- ***ECG:***
  - New AV, fascicular, or bundle branch block... .?PERIVALVULAR INVAVSION monitoring, ??pacing

- **Native Valve IE**
  - Staphylococcus aureus (~30%, especially in IV drug users)
  - Strep. (~25%), mostly *S. viridans*
  - Enterococci (5-10%),
  - GNB=HACEK (5%),
  - Fungi
- **Prosthetic Valve IE**

  Early (≤12) 1 - 3.1%
  - Staph aureus
  - Staph epidermidis

  Late (>12 mo) 2 - 5.7%
  - Staph aureus
  - Staph epidermidis
  - Viridans strep
  - Enterococcus
- **IE in IV drug abusers**
  - Staph. aureus(50-60%)

Case Definition: IE

- Duke criteria
- In 1994 investigators from Duke University modified the previous criteria to include
- The role of echocardiography in diagnosis
- They also expanded the category of predisposing heart conditions to include intravenous drug use

Modified Duke criteria

- Proposed: 2000, Addresses TEE, Broad "possible catergorie.
- *S. aureus* risks (13-25% S. aureus bacteremia have IE)
- Definite IE
  - Microorganism (via culture or histology) in a valvular vegetation, embolized vegetation, or intracardiac abscess
  - Histologic evidence of vegetation or intracardiac abscess
- Possible IE
  - 2 major
  - 1 major and 3 minor
  - 5 minor
- Rejected IE
  - Resolution of illness with four days or less of antibiotics

Major criteria

1. MICROBIOLOGY
   - Typical organism from 2 separate cultures OR
   - Microorganism from persistently positive BC OR
   - Single BC + for Coxiella burnetii, or titer >1:800
2. ENDOCARDIAL INVOLVEMEMT
   - New (not changed) murmur of regurgitation
3. POSITIVE ECHO
   - (TEE if prosthetic valve, complicated, or pretest probability possible IE

Minor criteria

Predisposition (heart condition or IV drug use)

1. Fever >/= 38°C
2. Vascular phenomenon (excludes petechiae, splinter hemorrhage)
3. major arterial emboli,
   - Mycotic aneurysm, intracranial or conjunctival hemorrhages. Janeway lesions
4. Immunologic phenomena
   - RF,.Roth's spots glomerulonephritis, Osler's nodes
5. Microbiologic evidence
   - Not meeting major criteria single BC not CNS, serology

Petechiae

1. Nonspecific
2. Often located on extremities or mucous membranes

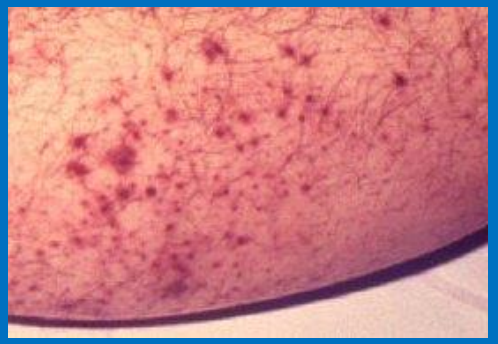
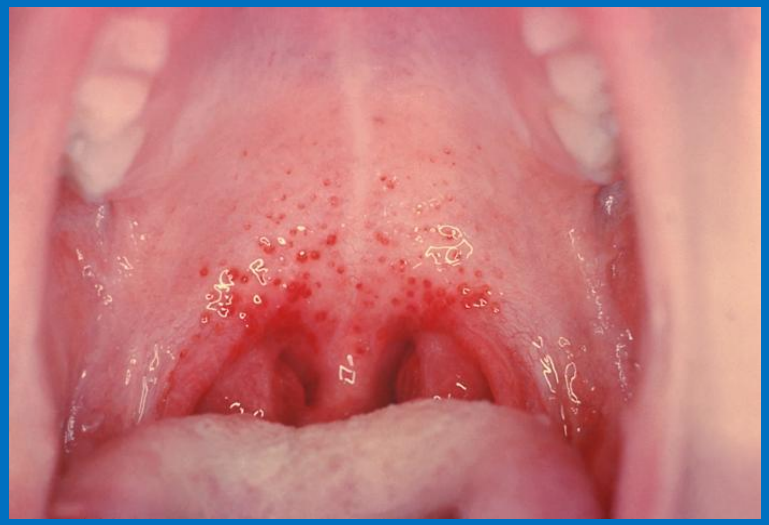


Photo credit, Josh Fierer, M.D.



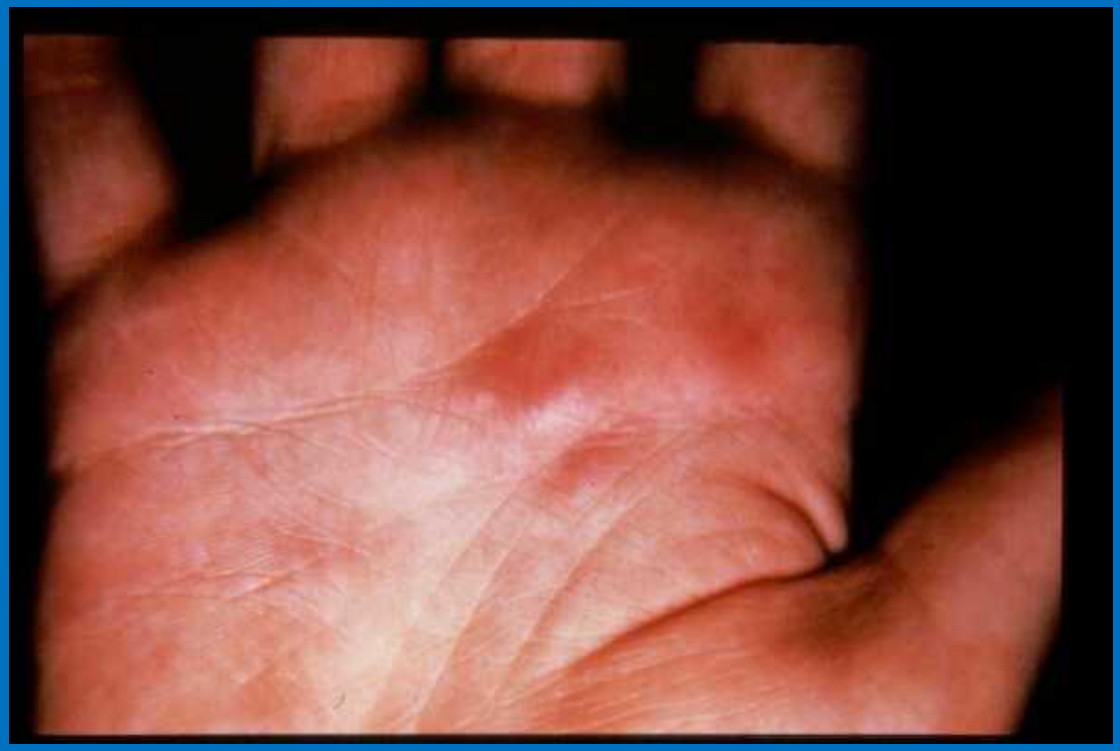
Harden Library for the Health Sciences

Splinter Hemorrhages

1. Nonspecific
2. Nonblanching
3. Linear reddish-brown lesions found under the nail bed
4. Usually do NOT extend the entire length of the nail

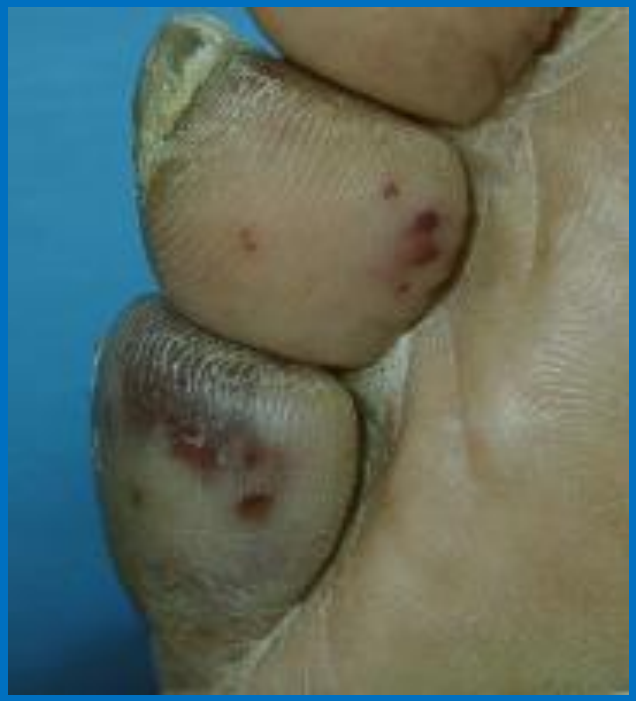
Osler's Nodes

American College of Rheumatology



1. More specific
2. Painful and erythematous nodules
3. Located on pulp of fingers and toes
4. More common in subacute IE

Janeway Lesions



1. More specific
2. Erythematous, blanching macules
3. Nonpainful
4. Located on palms and soles

Complications

- Four etiologies
  - Embolic
  - Local spread of infection
  - Metastatic spread of infection
  - Formation of immune complexes – glomerulonephritis and arthritis

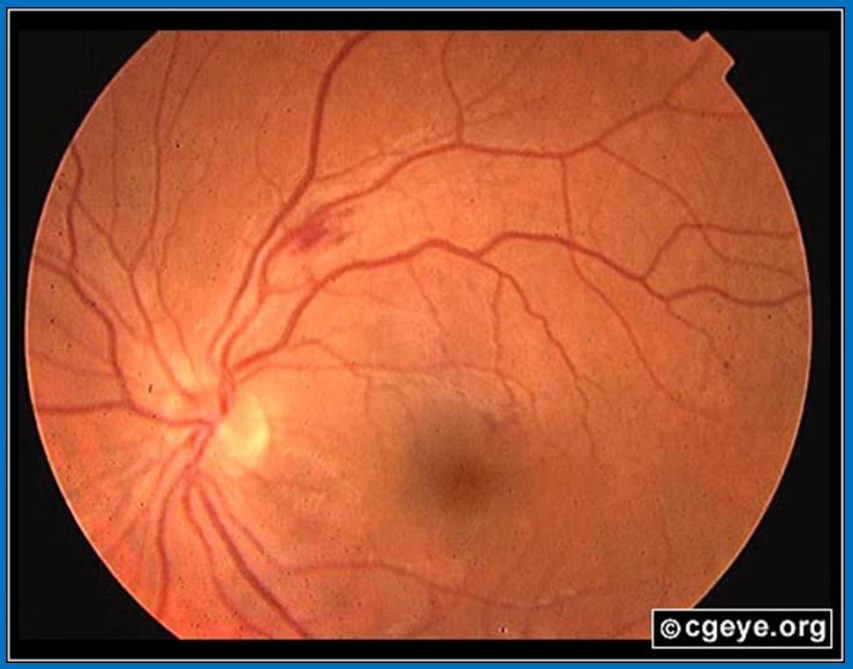
Embolic Complications

- Occur in up to 40% of patients with IE
- Predictors of embolization
  - Size of vegetation
  - Left-sided vegetations
  - Fungal pathogens, S. aureus, and Strep. Bovis
- Incidence decreases significantly after initiation of effective antibiotics

- Stroke
- Myocardial Infarction
  - Fragments of valvular vegetation or vegetation-induced stenosis of coronary ostia
- Ischemic limbs
- Hypoxia from pulmonary emboli
- Abdominal pain (splenic or renal infarction)

Septic Pulmonary Emboli

Septic Retinal embolus

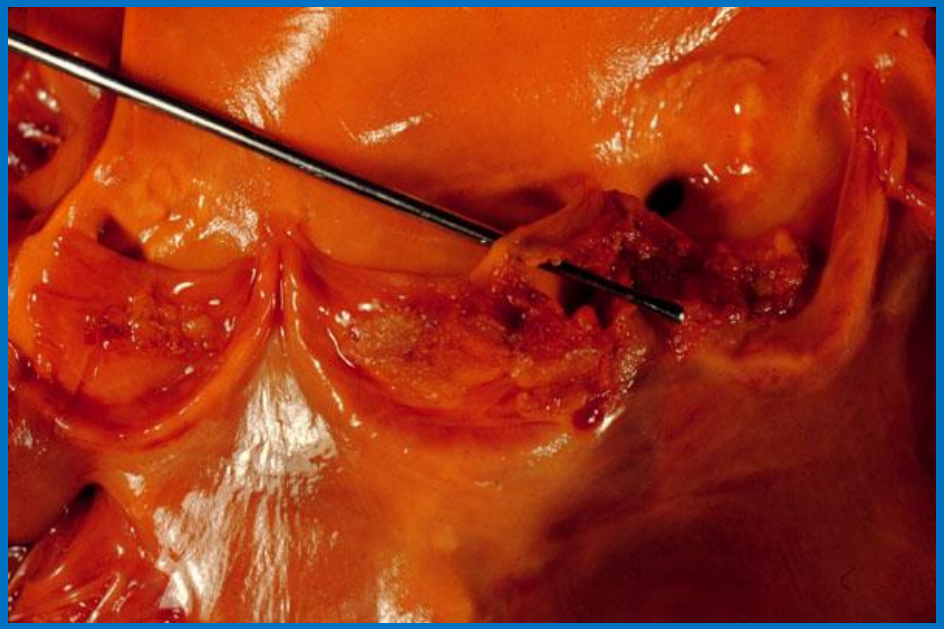


http://www.emedicine.com/emerg/topic164.htm

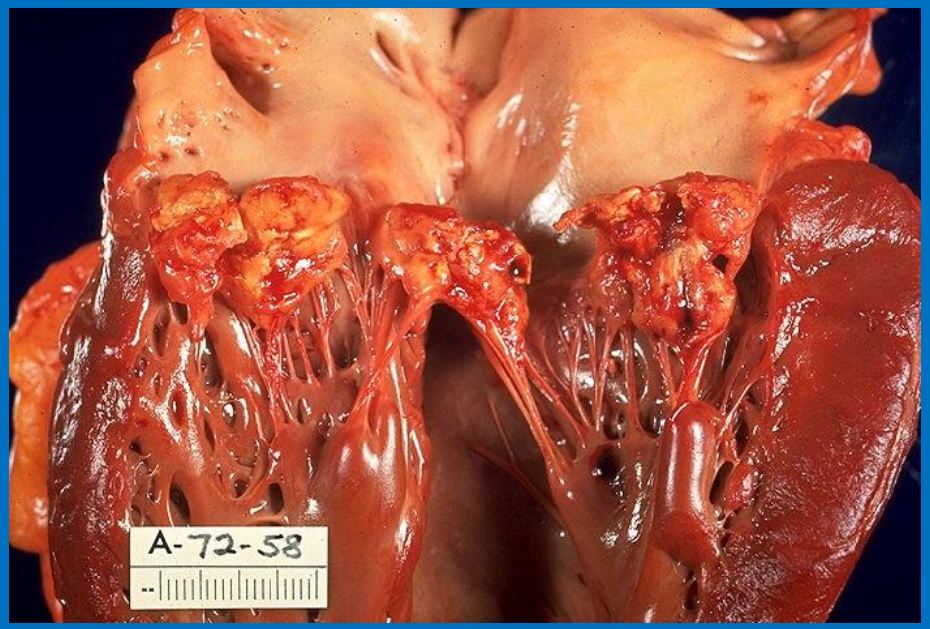
Local Spread of Infection

- Heart failure
  - Extensive valvular damage
- Paravalvular abscess (30~40%)
  - Most common in aortic valve, IVDU, and *S. aureus*
  - May extend into adjacent conduction tissue causing arrythmias
  - Higher rates of embolization and mortality
- Pericarditis
- Fistulous intracardiac connections

Local Spread of Infection



Acute *S. aureus* IE with perforation of the aortic valve and aortic valve vegetations.



Acute *S. aureus* IE with mitral valve ring abscess extending into myocardium.

Metastatic Spread of Infection

- Metastatic abscess
  - Kidneys, spleen, brain, soft tissues
- Meningitis and/or encephalitis
- Vertebral osteomyelitis
- Septic arthritis

Poor Prognostic Factors

- Female
- *S. aureus*
- Vegetation size
- Aortic valve
- Prosthetic valve
- Older age
- Diabetes mellitus
- Low serum albumen
- Apache II score
- Heart failure
- Paravalvular abscess
- Embolic events

Echocardiographic findings

1. Oscillating intracardiac mass
   - On valve or supporting structure,
   - In the path of regurgitation jets,
   - On implanted material, in the absence of an altenate anatomic explanation
2. Abscess
   1. New partial dehiscence of prosthetic valve
   2. New valvular regurgitation (increase or change in pre-existing murmur not sufficient)

Improved diagnostic value of echocardiography in patients with infective endocarditis by transoesophageal approach A prospective study

- Eur Heart J, 1988 Jan;9(i):43.5396 patients were studied consecutively with TEE and TTE
- TEE sensitivity 100 percent for vegetations as compared to 63 percent with TTE
- Both TTE and TEE had specificity of 98%
- 25% of vegetations less than 5 mm,
- 69% of vegetations 6-10 mm, and
- 100% of vegetations greater than 11 mm detected by TEE were also observed with TTE

Culture Negative" IE

- How hard did you look?
- (50% culture neg are d/t previous antibiotics)
- Fastidious bacteria
- Tend to see subacute w/ valve destruction/CHF

Lab Diagnosis! Etiologies"Culture Negative" IE Based on clinical setting

- PCR of vegetation/emboli:
  - *Tropheryma whippelei, Bartonella*
- Histology/stain /culture of vegetation/emboli:
  - Fungus
- Prolonged, cultures:
  - Brucella
- Lysis centrifugation system (Isolator):
  - Bartonella, Legionella (BCYE), fungal
- Serology:
  - Endemic fungi, Bartonella, Q fever, Brucella, Legionella, Chlamydia
- Thioglycolate or cysteine supplemented media.
  - S.aureus satellitism: Abiotrophia (NVS)

Treatment of infective endocarditis

GENERAL CONSIDERATIONS

- Antimicrobial therapy should be administered in a dose designed to give sustained **bactericidal** serum concentrations throughout much or all of the dosing interval.
- In vitro determination of the **minimum inhibitory concentration** of the etiologic cause of the endocarditis should be performed in all patients.

- The **duration** of therapy has to be sufficient to eradicate microorganisms growing within the valvular vegetations.
- The need for prolonged therapy in treating endocarditis has stimulated interest in using **combination** therapy to treat endocarditis.

Indications for surgery in IE

- Combined therapy generally advised with
- Refractory CHF (mortality 56-86% w/o surgery vs 11-35% w/surgery)
- Perivalvular invasive disease
- Uncontrolled infection on maximal medical therapy
- Recurrent systemic emboli, particularly in the presence of large vegetations
- SOME pathogens: Pseudomonas, Brucella, Coxiella, Fungi, Enterococci

Prosthetic same as native valve endocarditis

- Perivalvular infection valve
- Dehiscence
- Excessively mobile prosthesis on echo results in hemodynamic instability

- Prosthetic valve endocarditis that one may attempt medical treatment alone:
  1. >12mo post surgical
  2. VGS or HACEK or Enterococci
  3. No perivalvular extension
- Recurrence after surgery about 7% / 6 years
- Relapse,
  - *S. aureus* usually means surgery
  - *S. aureus*~ RR death 0.18 in surgery plus AB vs ABx alone

VGS, NVS, Sreptococcus MIC (ug/mI)	Native valve	prosthetic valve
<0.1	PenG or Ceph3 4wk	PenG 6wk plus Gent 2wk
>0.1 —0.5	PenG 4wk plus Gent 2wk	PenG 6wk Plus Gent 4wk
>0.5	PenG or Amp plus Gent for 4-6 wk	total 6 wk

MSSA/ MRSA: Most common org	Cloxacillin / Vancomycin 4-6 wk	cloxacillin / vancomycin 6wk, gentamicin 2wk, rifampin 6 wk
HACEK	Ceph 3rd gen (ceftriaxone) for 4wk	6wk
Bartonella	Doxycycline + gentamicin	
Q-fever	Doxycycline +or- hydroxychloroquine 26 months untill the titer below1:400	35% surgical

Prophylaxis

- For High or Mod. cardiac risk conditions (previous list)
- For Dental, rigid bronchoscopy, esophageal procedures, G I mucosal procedures, cystoscopy, prostate surgery
- Antibiotic Prophraxis (American Heart Assoc. JAMA

- **Timing**
- One hour prior to procedure:
  - 2gm Amoxicillin oraly or
  - **600 mg Clindamycin orally or**
  - **2gm Cephalexin orally or**
  - **500mg Clarithromycin orally or**
  - 2 gm Ampicillin intramuscularly

Dental procedures where endocarditic prophylaxis indicated:

1. Extraction
2. Periodontal procedures
3. Implants
4. Root canal
5. Subgingival antibiotics fiber/strips
6. Initial orthodontic bands (not brackets)
7. Intraligamentary local anesthetic
8. Cleaning of teeth/implants if bleeding anticipated

Dental procedures where endocarditic prophylaxis NOT indicated:

1. Filling cavity or local anesthetic
2. Placement of rubber dam
3. Suture removal
4. Orthodontic removal
5. Orthodontic adjustments
6. Dental X-rays
7. Shedding of primary teeth