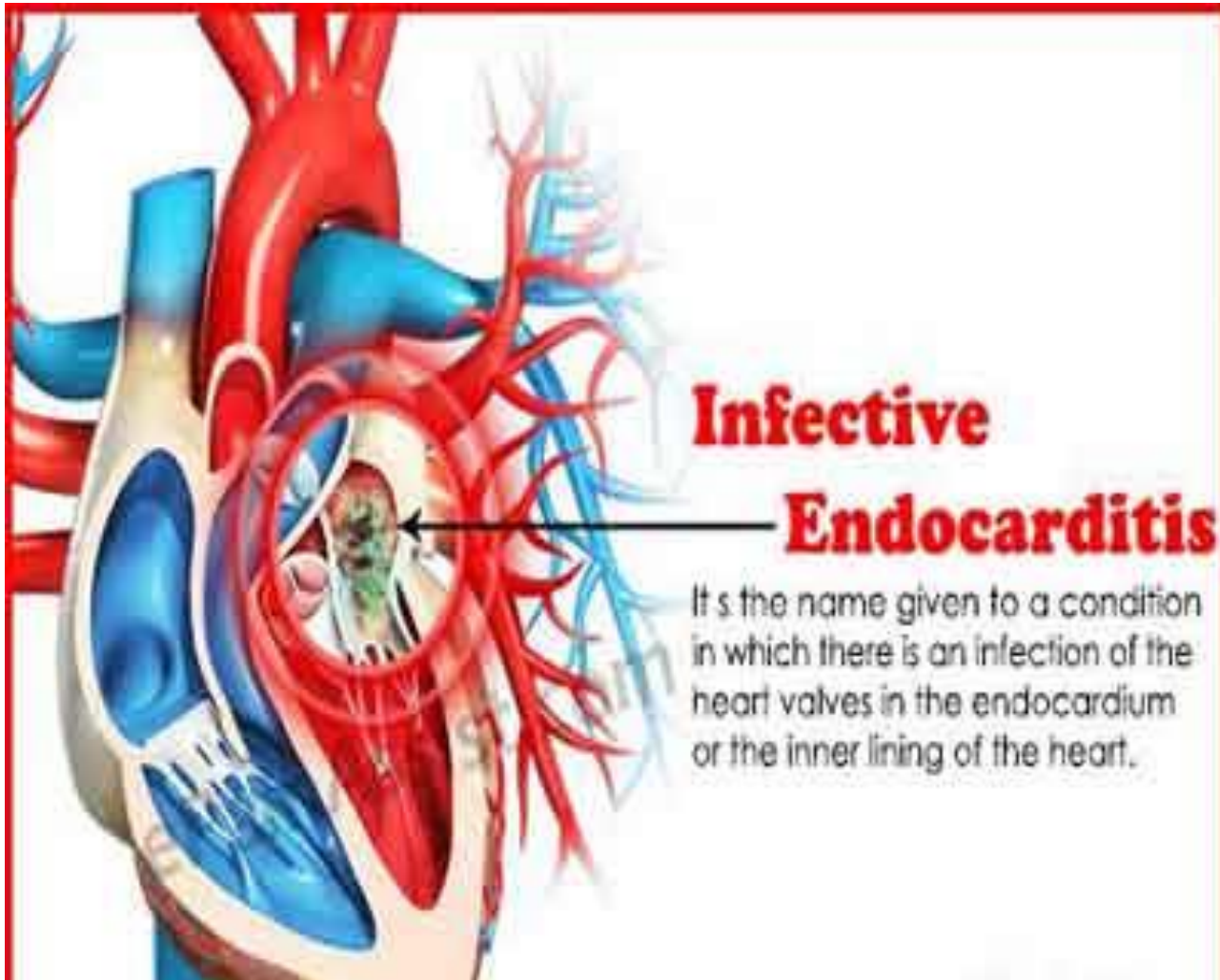
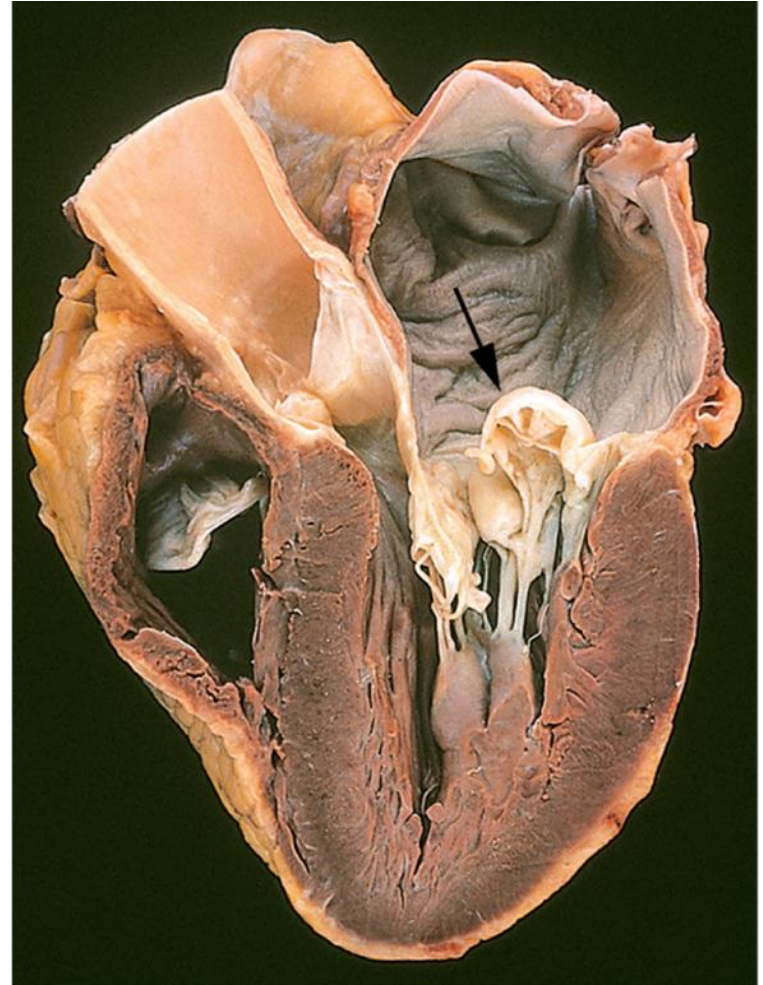


# Infective endocarditis



# Definition

- Infection of the endocardium or vascular endothelium



(Courtesy of William D. Edwards, MD, Mayo Clinic, Rochester, Minn. From Kumar V, Abbas AK, Fausto N. Robbins and Cotran Pathologic Basis of Disease, 7th ed. Philadelphia, Saunders, 2005.)

Fig. 2-2. Prolapse of the posterior mitral valve leaflet into the left atrium.

# Infective Endocarditis

- Febrile illness
- Persistent bacteremia
- Presence of the vegetation: Characteristic lesion in the endothelial surface of the heart



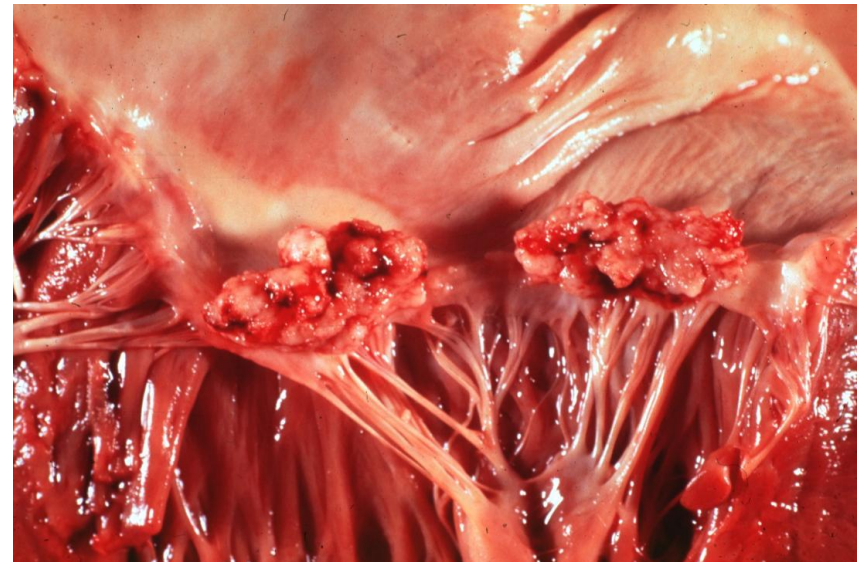
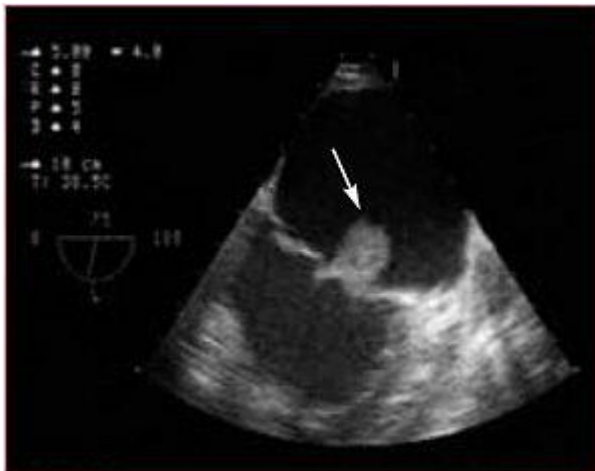
(From Kumar V, Abbas AK, Fausto N, Robbins and Cotran Pathologic Basis of Disease, 7th ed. Philadelphia, Saunders, 2005.)

# Vegetation

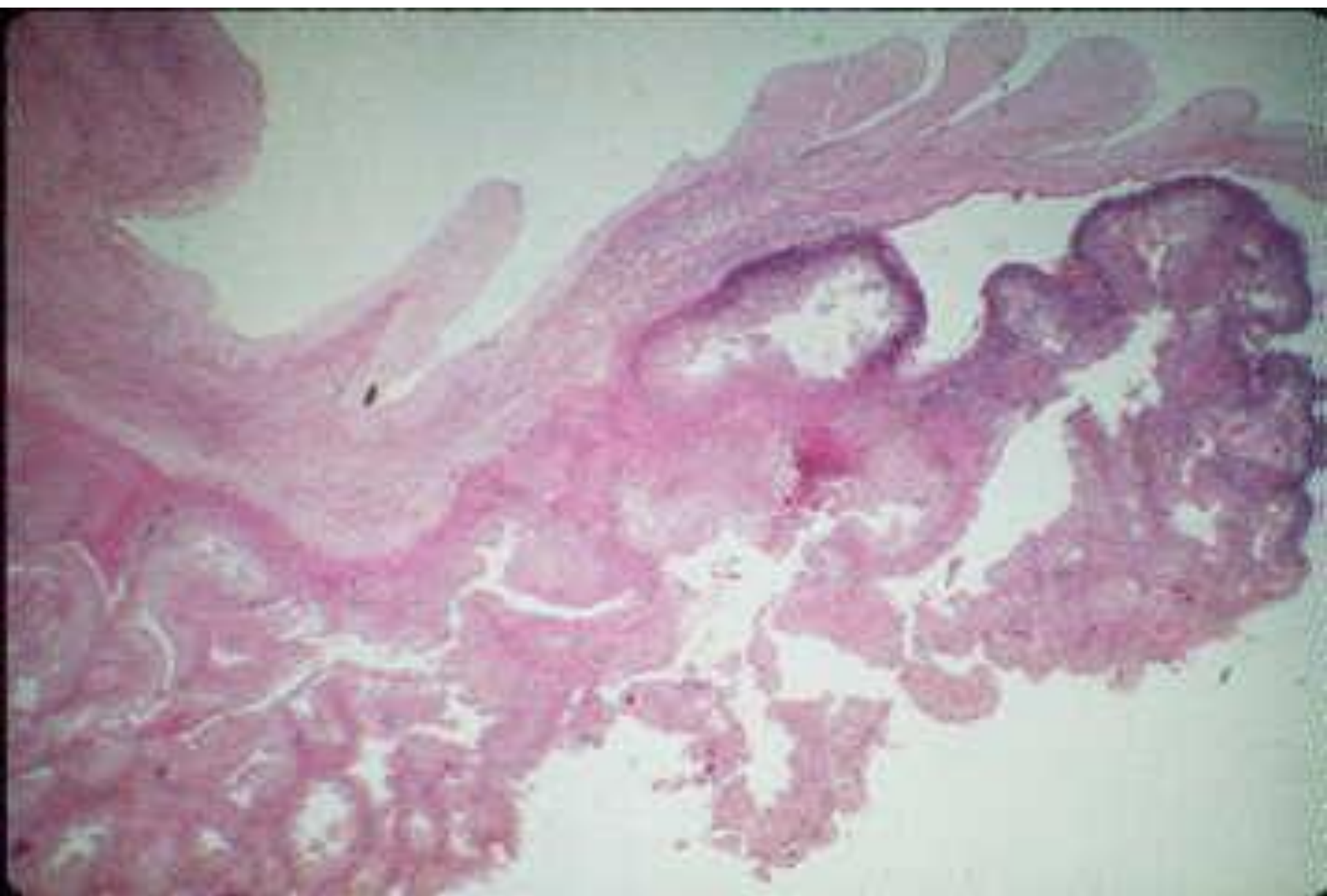
- Characteristic lesion of microbial infection of the endothelial surface of the heart

Variable in size

- Amorphous mass of fibrin & platelets
- Abundant organisms
- Few inflammatory cells





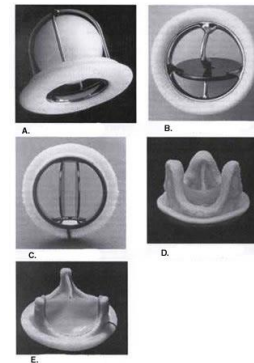


# IE: Four categories

- Native valve endocarditis
- IE in intravenous drug misusers
- Nosocomial IE
- Prosthetic valve endocarditis

# Epidemiology

- Incidence Increases With Age
  - Increase in degenerative cardiac diseases
  - Decreased Immunity
- Prosthetic Heart Valve Infections Are Increasing



- Case rate may vary between 2-3 cases /100,000 to as high as 15-30/100,000 depending on incidence of i.v. drug abuse and age of the population
- 7-25% of cases involve prosthetic valves
- 25-45% of cases predisposing condition can not be identified



# Native Valve Infective endocarditis (NVE)

- Congenital heart disease (with high to low pressure gradients)
  - Acquired heart diseases (rheumatic valvular D)
  - Degenerative heart disease
- 55-75% of patients with NVE have underlying valve abnormalities
- MVP
  - Rheumatic
  - Congenital
  - i.v. drug abuse

# NVE-Congenital heart disease

- Lifelong risk factor
  - 30-40% of childhood IE
  - 10 – 20% of cases in young adults
  - 8% of cases in older adults
- 
- Tetralogy of Fallots > bicuspid aortic valve> coarctation of aorta > VSD
  - In secundum ASD: very rare
  - Surgical correction does not exclude from risk in major CHD

# NVE-Rheumatic heart disease

- 22% in 1933 – 55
- 20 – 25% of cases of IE in 1970's & 80's
- 7 – 18% of cases in recent reported series (Developing countries)
- <1% in 1963 – 72 (in USA)
- AS / AR / MR predisposes commonly
- Rare in MS
- Mitral site more common in women
- Aortic site more common in men

# Mitral valve prolapse

- 2-4% prevalence in the population
- 20% in young women
- Common in ballet dancers ( ~59%; lean body)



# NVE- MVP

- Adult population
  - MVP – prominent predisposing factor
    - 10-100 fold risk compared to general population
    - Accounts for 7 – 30% NVE in cases not related to drug abuse or nosocomial infection
  - Relative risk in MVP ~3.5 – 8.2, largely confined to patients with murmur, but also increased in men and patients >45 years old
    - MVP with murmur – incidence IE 52/100/000 pt. years
    - MVP w/o murmur – incidence IE 4.6/100,000 pt. years



# NVE-Degenerative valve disease

- 25% in > 40 yrs
- 50% in > 60 yrs
- Senile aortic stenosis
- Mitral regurgitation





# IE-Paediatic population



- The vast majority (75-90%) of cases after the neonatal period are associated with an underlying congenital abnormality
  - Aortic valve
  - VSD
  - Tetralogy of Fallot
- Risk of post-op infection in children with IE is 50%
- Microbiology
  - Neonates: *S. aureus*, coagulase negative staph, group B strep
  - Older children: 40% strep, *S. aureus*



# NVE-Intravenous Drug Abuse

- Risk is 2 – 5% per pt./year
- Tendency to involve right-sided valves
  - Distribution in clinical series
    - 46 – 78% tricuspid
    - 24 – 32% mitral
    - 8 – 19% aortic
- Underlying valve normal in 75 – 93%
- *S. aureus* predominant organism (>50%, 60-70% of tricuspid cases)



# NVE-Intravenous Drug Abuse

- Increased frequency of gram negative infection such as *P. aeruginosa* & fungal infections
- High concordance of HIV positivity & IE (27-73%)
  - HIV status does not in itself modify clinical picture
  - Survival is decreased if CD4 count < 200/mm<sup>3</sup>



# NVE-Nosocomial

- In > 60yr
- In > 95% some procedure; intravenous access etc
- Right sided endocarditis is increasingly recognised



# Prosthetic Valve Endocarditis (PVE)

- 10 – 30% of all cases in developed nations
- Cumulative incidence
  - 1.4 – 3.1% at 12 months
  - 3.2 – 5.7% at 5 years
- Early PVE – within 60 days
  - Nosocomial (s. epi predominates)
- Late PVE – after 60 days
  - Community (same organisms as NVE)



# IE- Pathogenesis

- Pathogenesis / pathology / microbiology
- Key issues in pathogenesis in IE
  - Predisposing host factors
  - Characteristics of micro-organisms
  - Role of transient bacteremia
  - Ability of immune system to eradicate micro-organisms once they are located on endocardium

- Predisposing host factors

- Damage to endothelial layer



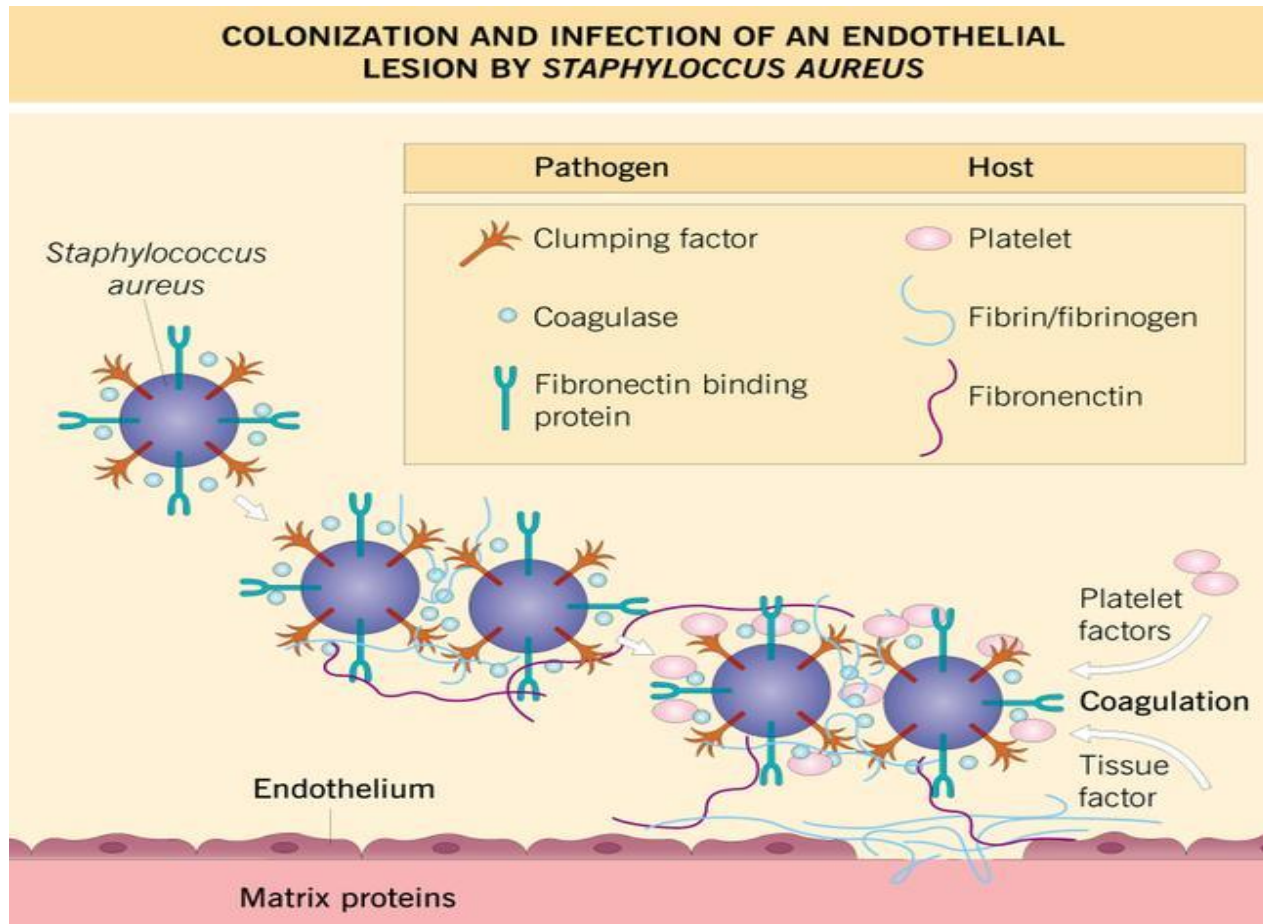
- Platelet – fibrin mesh work



- Nidus for bacterial colonization

- Characters of micro-organism
  - Greatest ability to adhere and colonize damaged valves (*S. aureus* , Strept. Spp, > 80% IE ; greatest ability to adhere)
  - Direct invasion of endothelial cells (coxiella, chlamydia spp, *Staph aureus*)

# Vegetation formation

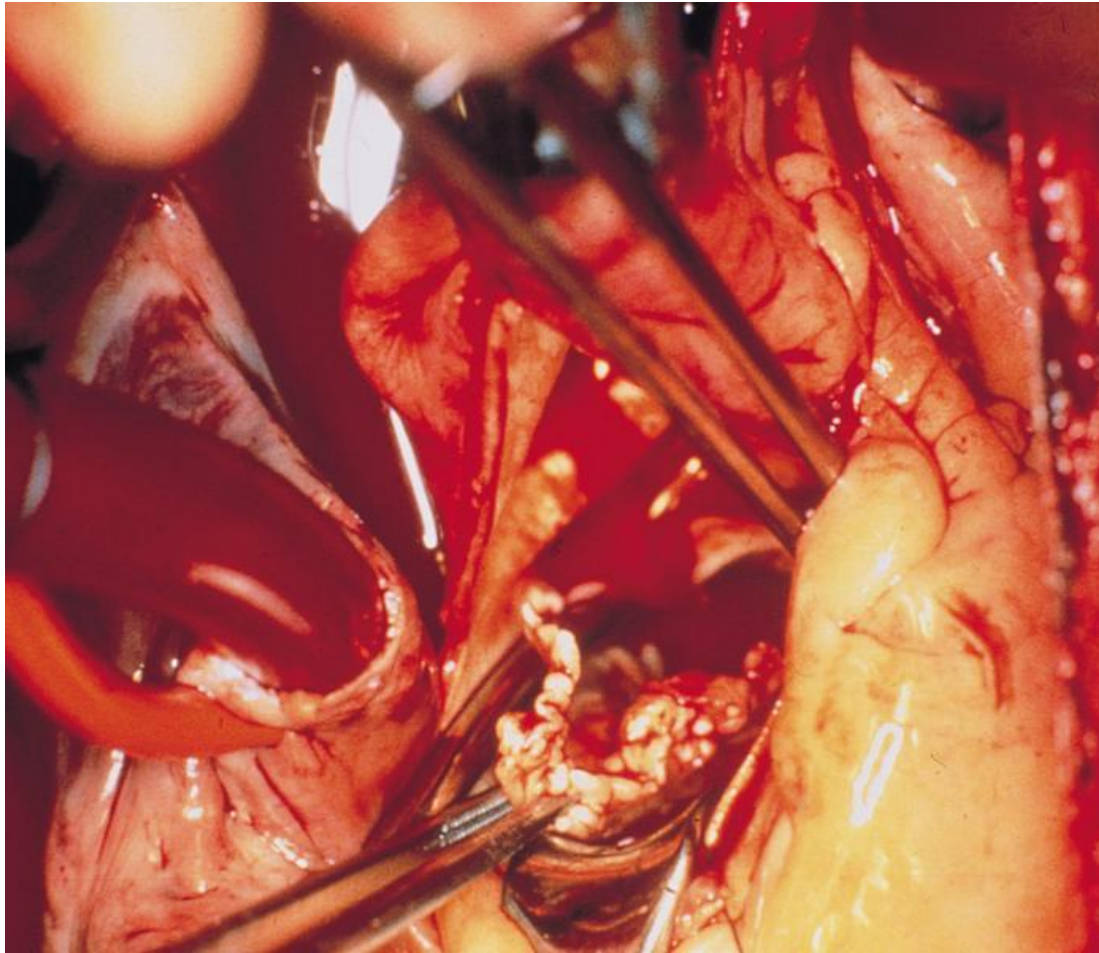




# Vegetation



# Vegetation



# Infective Endocarditis

- Pathology
  - NVE infection is largely confined to leaflets
  - PVE infection commonly extends beyond valve ring into annulus/periannular tissue
    - Ring abscesses
    - Septal abscesses
    - Fistulae
    - Prosthetic dehiscence
  - Invasive infection more common in aortic position and if onset is early

# Microbiology

- Aetiology

- *Streptococcus viridans* (~50% of cases)
  - » Oropharyngeal flora
- *Enterococcus faecalis*
  - » Genito-urinary infections, pelvic surgery
- *Staphylococcus aureus*
  - » IV catheters, parenteral feeding, abscesses
- *Staph. epidermidis*
- *Coxiella burnetii*
- Histoplasma, Candida
  - » IV drug users, alcoholics

# Organisms

- Gram negative organisms
  - *P. aeruginosa*
  - HACEK - slow growing, fastidious organisms that may need 3 weeks to grow out of culture
    - Haemophilus sp.
    - Actinobacillus
    - Cardiobacterium
    - Eikenella
    - Kingella

# Clinical aspects



# Distinction between Acute and Subacute Bacterial Endocarditis

<u>Feature</u>	<u>Acute</u>	<u>Subacute</u>
Underlying Heart Disease	Heart may be normal	RHD, CHD, etc.
Organism	<i>S. aureus</i> , Pneumococcus <i>S. pyogenes</i> , Enterococcus	viridans Streptococci, Enterococcus
Therapy	Prompt, vigorous and initiated on empirical ground	Can often be delayed until culture reports and susceptibilities available



# Clinical presentations

- Acute
  - Toxic presentation
  - Progressive valve destruction & metastatic infection developing in days to weeks
  - Most commonly caused by *S. aureus*
- Subacute
  - Mild toxicity
  - Presentation over weeks to months
  - Rarely leads to metastatic infection
  - Most commonly *S. viridans* or enterococcus

# Infective endocarditis

- Clinical features;
  - Due to infection; septicaemia
  - Due to effects on heart
  - Due to complications

# Infective endocarditis

- Symptoms
  - Fever
  - Rigors
  - Fatigue
  - Malaise
  - Sweats
  - Weight loss

# Infective endocarditis

- Signs
  - Pallor (+icterus)
  - Vasculitic rashes
  - Clubbing, splinter haemorrhages, Janeway lesions, Osler's nodes
  - Roth spots in fundi
  - Firm splenomegaly
  - Changing murmurs

# Clinical Features

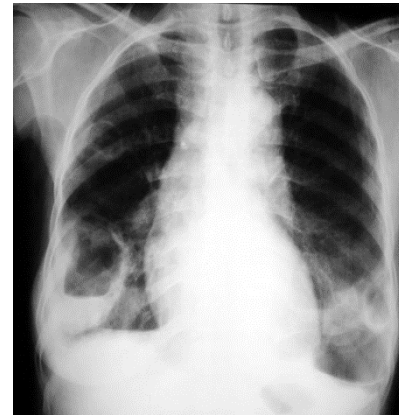
- Interval between index bacteremia & onset of symptoms usually < 2 weeks
  - May be substantially longer in early PVE
- Fever most common sign
  - May be absent in elderly/debilitated pt.
- Murmur present in 80 – 85%
  - Generally indication of underlying lesion
  - Frequently absent in tricuspid IE
- Changing murmur

# Cardiac complications

- Cardiac failure
- Acute valvular dysfunction: regurgitation / obstruction
- Conduction defects
- Intra cardiac abscess formation / septal ruptures

# Complications due to vegetations

- Embolic phenomena; cerebral/ other systemic
- Abscess formation else where (in R/S IE; multiple Pulmonary abscesses)
- Immunological
  - Vasculitis
  - Glomerulonephritis



# Complications due to vegetations

- Embolization

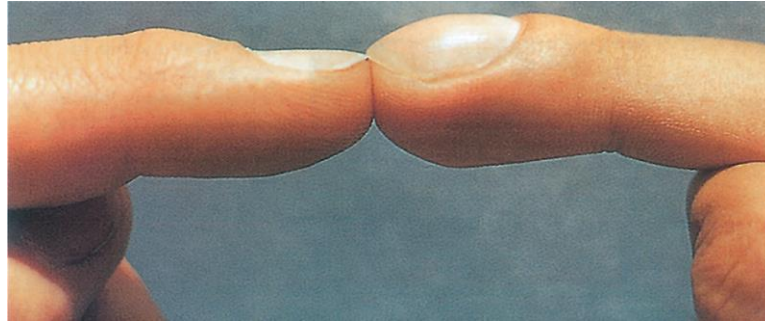
- Clinically evident 11 – 43% of patients
- Pathologically present 45 – 65%
- High risk for embolization
  - » Large > 10 mm vegetation
  - » Hypermobile vegetation
  - » Mitral vegetations (esp. anterior leaflet)
- Pulmonary (septic) – 65 – 75% of i.v. drug abusers with tricuspid IE



# Classical Peripheral Manifestations

- Less common today
- Not seen in tricuspid endocarditis
- Petechiae most common

# Clubbing Of Fingers



# vasculitis



# Osler's nodes



## Osler's Nodes:

Painful  
erythematous  
nodular lesions  
resulting from  
infective  
endocarditis

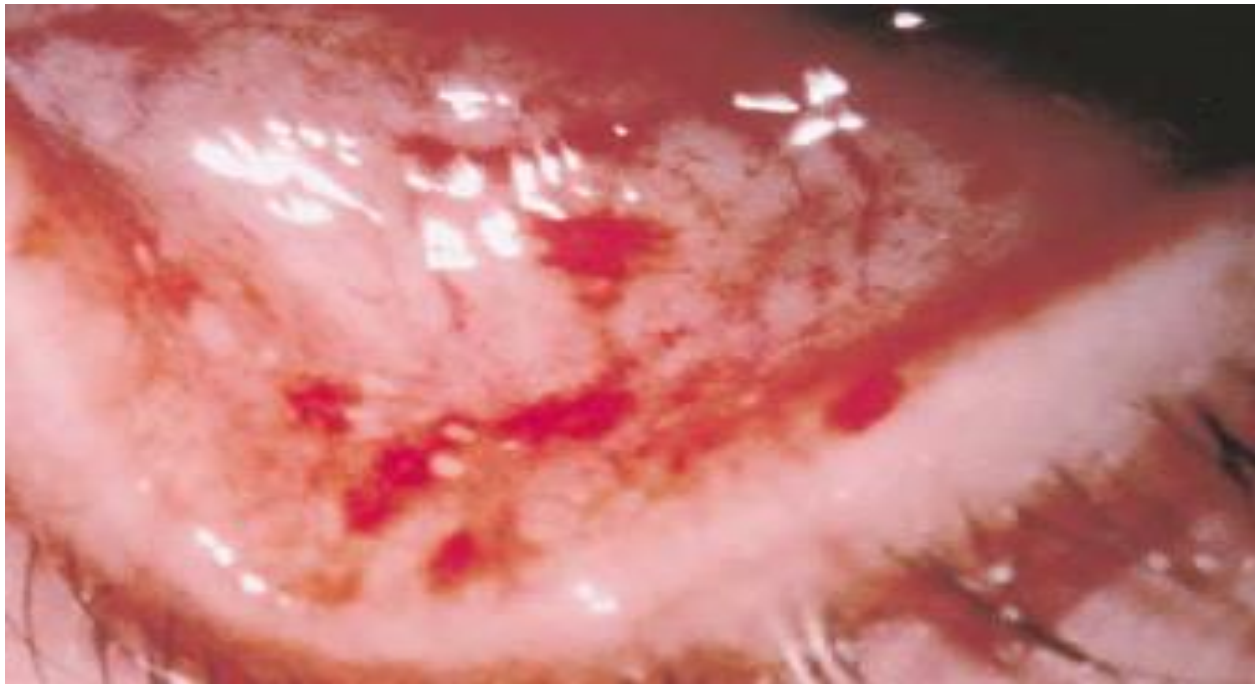




# Splinter haemorrhages



# Sub conjunctival haemorrhages



# Janeway lesions

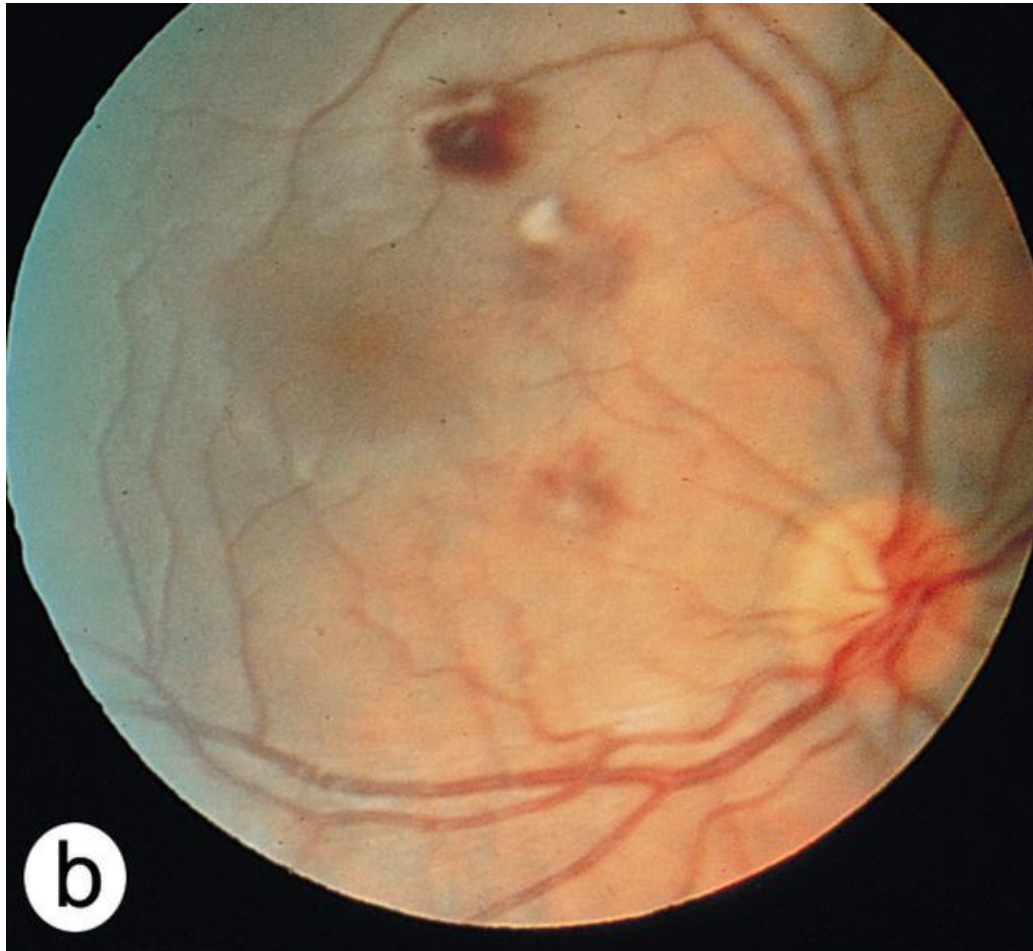




# Vasculitis



# Roth spots



# Lung abscesses



# Infective endocarditis

- Diagnosis;
  - Is a medical emergency.
  - investigations and management should go hand in hand

# Diagnosis

- High index of suspicion in patients with predisposing anatomy or behavior
- Blood cultures
- Echocardiography
  - TTE – 60% sensitivity
  - TEE – 80 – 95% sensitive

# Diagnosis

- Duke diagnostic criteria, developed by Durack and colleagues

# Infective Endocarditis: *Modified Duke Criteria*

MAJOR CRITERIA	minor criteria
<b>1. Blood cultures positive for infective endocarditis</b>	1. Predisposing factor <sup>a</sup>
<b>2. Evidence of endocardial involvement</b>	2. Temperature >38°C
	3. Vascular phenomena <sup>b</sup>
	4. Immunologic phenomena <sup>c</sup>
	5. Microbiologic evidence <sup>d</sup>

<sup>a</sup> Intravenous drug use or a predisposing heart condition.

<sup>b</sup> Vascular phenomena include major arterial emboli, septic emboli, pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhage, and painless skin lesions (i.e., janeway lesions).

<sup>c</sup> Immunologic phenomena include glomerulonephritis, painful nodes (i.e., Osler's nodes), retinal haemorrhages with small, clear centers (i.e., Roth's spots), and positive rheumatoid factor.

<sup>d</sup> Positive blood culture not meeting a major criterion or serologic evidence of an active infection with an organism known to cause infective endocarditis

Two major criteria  
or  
One major and three minor criteria  
or  
Five minor criteria

**Definite  
Diagnosis**

One major and one minor criteria  
or  
Three minor criteria

**Possible  
Diagnosis**

# Major blood culture criteria

- Two blood cultures from two different sites positive for organisms typically found in patients with IE
- Blood cultures persistently positive for one of these organisms, from cultures drawn more than 12 hours apart
- Three or more separate blood cultures drawn at least 1 hour apart



# Major **echocardiographic criteria**

- An oscillating intra-cardiac mass on a valve or on supporting structures, in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomic explanation
- Myocardial abscess
- Development of partial dehiscence of a prosthetic valve
- New-onset valvular regurgitation

# Minor criteria for IE

- Predisposing heart condition or intravenous drug use
- Fever of 38°C (100.4°F) or higher
- Vascular phenomenon, including major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, or Janeway lesions
- Immunologic phenomenon such as glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor
- Positive blood culture results not meeting major criteria or serologic evidence of active infection with an organism consistent with IE
- Echocardiogram results consistent with IE but not meeting major echocardiographic criteria

# A definitive clinical diagnosis

- 2 major criteria or
- 1 major criterion and 3 minor criteria or
- 5 minor criteria

# Basic investigations: IE

- FBC: Neutrophil leucocytosis
- High ESR/ CRP
- UFR : RBC/ Protein / Casts
- LFT; high Alk. PO4 / abn LFT
- High Igs / Low C3 compliment (not indicated routinely)
- ECG / Chest Xray ; for complications

# Goals of Therapy

- Eradicate infection
- Definitively treat sequelae of destructive intra-cardiac and extra-cardiac lesions

# Infective endocarditis

- Management: Principles
  - Start treatment on suspicion
  - Bactericidal antibiotics
  - Intravenous
  - Higher doses
  - Longer periods
  - Manage complications
  - Surgery when indicated

# Infective endocarditis

- Antibiotics;
  - Start with; depends on the suspected organism
  - Change once culture/ ABST is available
- Eg: Strept viridans:
  - Penicillin (4 wks) + Genta (2wks) or
  - Ceftriaxone (4 wks)

# Hickman line for long term IV





# Antibiotic Therapy

- Treatment tailored to etiologic agent
  - Important to note MIC/MBC relationship for each causative organism and the antibiotic used
  - High serum concentration necessary to penetrate avascular vegetation
  - **ID CONSULT EVERY TIME**

Antibiotic used	Adult daily dose	Treatment duration (weeks)	Comments
<i>Penicillin-susceptible (MIC &lt;0.125 mg/l) infe</i>			
Penicillin G <sup>§</sup>	6×2–3 millionU IV	4	Standard treatment. Preferred choice in patients aged >65 years or with impaired renal function
Penicillin G <sup>§</sup> + gentamicin <sup>  </sup>	6×2–3 millionU IV + 1×3 mg/kg IV or IM, respectively	2	Short-term treatment (combination with an aminoglycoside allows a shorter duration of treatment)
Ceftriaxone	1×2g IV or IM	4	Standard treatment. Preferred choice for outpatient therapy, which should be considered in the absence of complications and in patient who are medically stable. Education of patient and staff is essential, as are regular evaluations after discharge (that is, nurse every day and physician in charge once or twice per week)
Ceftriaxone + netilmicin (or gentamicin if netilmicin is not available)	1×2g IV or IM + 1×4mg/kg IV (or 1×3 mg/kg IV or IM for gentamicin), respectively	2	Short-term treatment (combination with an aminoglycoside allows a shorter duration of treatment). Preferred choice for outpatient therapy as above.
Vancomycin <sup>¶</sup>	2×15mg/kg IV	4	For patients allergic to β-lactam
<i>Penicillin resistant (MIC &gt;1mg/l)<sup>*</sup> infection</i>			
Penicillin G <sup>§</sup> + gentamicin <sup>  </sup>	6×2–3 millionU IV + 1×3 mg/kg IV or IM, respectively	4	Gentamicin should be used for only the first 2 weeks of treatment
Vancomycin <sup>¶</sup> + gentamicin <sup>  </sup>	2×15mg/kg IV + 1×3 mg/kg IV or IM, respectively	4	For patients allergic to β-lactam. Gentamicin should be used for only the first 2 weeks of treatment

# Antibiotic Therapy

- Effective antimicrobial treatment should lead to defervescence within 7 – 10 days
  - Persistent fever in:
    - IE due to staph, pseudomonas, culture negative
    - IE with microvascular complications/major emboli
    - Intracardiac/extracardiac septic complications
    - Drug reaction

# Surgical Treatment of Intra-Cardiac Complications

- NYHA Class III/IV CHF due to valve dysfunction
  - Surgical mortality – 20-40%
  - Medical mortality – 50-90%
- Unstable prosthetic valve
  - Surgical mortality – 15-55%
  - Medical mortality – near 100% at 6 months
- Uncontrolled infection

# Surgical Treatment of Intra-Cardiac Complications

- Difficult to cure:
  - Fungal endocarditis
  - Brucella
- *S. aureus* PVE with any intra-cardiac complication
- Relapse of PVE after optimal therapy

# Surgical Treatment of Intra-Cardiac Complications

- Relative indications
  - Perivalvular extension of infection
  - Poorly responsive *S. aureus* NVE
  - Relapse of NVE
  - Culture negative NVE/PVE with persistent fever (> 10 days)
  - Large (> 10mm) or hypermobile vegetation
  - Endocarditis due to highly resistant enterococcus
  - Embolism despite therapy

# Indications for surgery

- Refractory cardiac failure caused by valvular dysfunction
- Persistent sepsis by a surgically removable focus/  
myocardial abscess / prosthesis
- Persistent life threatening embolization

# Mortality

- Overall Rate About 40%
- Death Usually Due To Heart Failure Resulting From Valve Dysfunction
- Highest Death Rate Is In Early Prosthetic Valve Endocarditis



# Antibiotic prophylaxis IE - Dental Management

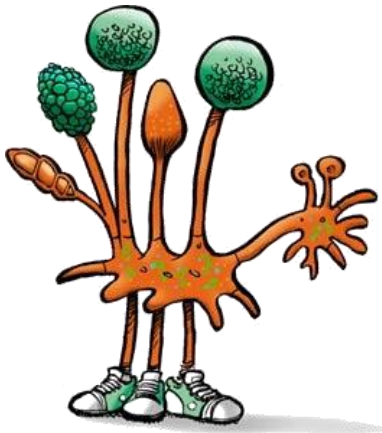
- Prevention In Susceptible Patients: An Academic Issue
- Very Few Cases Related In Time To Dental/Medical Procedures
  - Incidence Has Been Estimated To Be 100-200 Patients Susceptible To BE In A Dental Practice With 2,000 Patients

# Antibiotic Prophylaxis

- Regimen Designed For Alpha-hemolytic Strep (*S. viridans*)
- No Clinical Trials Available To Show This Works! (Actually Prevents BE In Humans)
- 25-50% Hospital Antibiotic Usage Is For Prophylaxis

# Antibiotic Prophylaxis

- Complications: Resistant Bacteria, Toxicity, Allergies, Suprainfections, Costs
- Will Not Prevent All Cases



# Antibiotic Prophylaxis

- Allergy Morbidity Is Higher Than Endocarditis (Allergy To Premed)
  - 400-800 PCN Deaths Per Year

# Infective endocarditis

- Prevention; prophylactic antibiotics
  - Identification of patients at risk
  - Determination of procedures / circumstances resulting in bacteremias
  - Choice of appropriate antibiotic regimen
  - Balancing of known risks against the possible benefits of intervention

# Infective Endocarditis: *Prophylaxis*

INDICATED	NOT INDICATED
✓ Prior history of endocarditis	✗ Previous rheumatic fever or Kawasaki disease without valvular dysfunction
✓ Cardiac valve disease in a transplanted heart	✗ Acquired valvular dysfunction ✗ Bicuspid aortic valve
✓ Unrepaired <b>cyanotic</b> congenital heart disease or incompletely repaired congenital heart disease	✗ Simple atrial septal defect ✗ Mitral valve prolapse with regurgitation ✗ Hypertrophic cardiomyopathy
✓ Congenital heart disease repaired using <b>prosthetic</b> material ✓ A <b>prosthetic</b> heart valve ✓ Valve repair using material <b>prosthetic</b>	✗ Valve repair without prosthetic material

# Infectious Bacterial Endocarditis

## Prophylaxis No Longer Recommended for the Following Conditions

- Ventricular Septal Defect
- Ostium Primum Atrial Septal Defect
- Pulmonary Stenosis
- Aortic Stenosis/Insufficiency
- Mitral Valve Prolapse with Valve Regurgitation
- Patent Ductus Arteriosus
- Coarctation of Aorta
- Rheumatic Heart Disease
- Hypertrophic Cardiomyopathy



Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

## Dental Procedures for which Endocarditis Prophylaxis **IS** Recommended in Patients with the Highest Risk Cardiac Conditions

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



Dajani AS, Taubert KA, Wilson W, et al, JAMA 1997;277:1797  
and Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.



## Dental Procedures for which Endocarditis Prophylaxis **IS NOT** Recommended in Patients with the Highest Risk Cardiac Conditions

- Routine anesthetic injections through non-infected tissue
- Taking dental radiographs
- Placement of removable prosthodontic or orthodontic appliances
- Adjustment of orthodontic appliances
- Placement of orthodontic brackets
- Shedding of deciduous teeth
- Bleeding from trauma to the lips or oral mucosa



Dajani AS, Taubert KA, Wilson W, et al, JAMA 1997;277:1797  
and Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

# Chemoprophylaxis

## Adult Prophylaxis: Dental, Oral, Respiratory, Esophageal Standard Regimen

[Amoxicillin](#) 2g PO 1h before procedure or

[Ampicillin](#) 2g IM/IV 30m before procedure

[Penicillin](#) Allergic

[Clindamycin](#)

600 mg PO 1h before procedure or

600 mg IV 30m before

[Cephalexin](#) OR [Cefadroxil](#) 2g PO 1 hour before

[Cefazolin](#) 1.0g IM/IV 30 min before procedure

[Azithromycin](#) or [Clarithromycin](#) 500mg PO 1h before

# Adult Genitourinary or Gastrointestinal Procedures

## High Risk Patients

### Standard Regimen

Before procedure (30 minutes):

[Ampicillin](#) 2g IV/IM AND

[Gentamicin](#) 1.5 mg/kg (MAX 120 mg) IM/IV

After procedure (6 hours later)

[Ampicillin](#) 1g IM/IV OR

[Amoxicillin](#) 1g PO

[Penicillin](#) Allergic

Complete infusion 30 minutes before procedure

[Vancomycin](#) 1g IV over 1-2h AND

[Gentamicin](#) 1.5 mg/kg IV/IM (MAX 120 mg)

## Moderate Risk Patients

### Standard Regimen

[Amoxicillin](#) 2g PO 1h before OR

[Ampicillin](#) 2g IM/IV 30m before

[Penicillin](#) Allergic

[Vancomycin](#) 1g IV over 1-2h, complete 30m before