INFECTIVE ENDOCARDITIS
INFECTIVE ENDOCARDITIS

• Infection of the endocardial lining is called infective endocarditis.
• Involving the endocardium of valves, mural endocardium and endothelium of arteries-infective end arteritis.
• Earlier known as Bacterial Endocarditis. Term changed to Infective Endocarditis following the realization that infection can occur due to organisms other than bacteria; such as fungi and rickettsiae.
Acute

- Rapid progression of symptoms.
- High grade fever.
- Extensive damage to the heart structures.
- Metastatic lesions.
- Inadequate treatment leads to death within 6 weeks.

Sub acute.

- Pre-existing abnormal valve.
- Indolent course.

CLASSIFICATION

Acute

Sub acute
INFECTIVE ENDOCARDITIS

Classification continue

- Bacterial/ non bacterial
- Native valve endocarditis (8-10%of IE)/ prosthetic valve endocarditis
- Right sided endocarditis – IV drug users( not common in paediatrics), patients on chronic intra vascular catheters.
- Postoperative cases
- Patients on immune suppressive treatment.
INFECTIVE ENDOCARDITIS - IMPORTANCE

1) Associated with significant mortality and morbidity.
   - Pre-antibiotic era- mortality was nearly 100%
   - Antibiotic era- mortality is around 15-25%

2) Clinician’s Dilemma.
   - Presentation is diverse and confusing. E.g.: Fever of unknown origin, anemia, arthritis to stroke of unknown etiology.
INFECTIVE ENDOCARDITIS - IMPORTANCE

3) Changes in the Epidemiology and Microbiology of Infective Endocarditis.
   - Emergence of drug resistant bacteria
   - Taxing therapeutic skills

CHD with IE is more than RHD with IE.

More CHD patients are surviving following intervention/surgery.

Rheumatic fever is on the decline.

4) Advances in Echocardiography and surgery- promoted additional
   prognostic and therapeutic tools.
PATHOGENESIS OF IE

Two factors are important in the pathogenesis of Infective Endocarditis:

• A damaged area of endothelium
• Bacteremia (even if transient)
1) Endothelial damage induced by turbulent blood flow, prosthetic device /valve create substrate for fibrin deposition and platelet leading to formation of NBTE.(non bacterial thrombo embolus)

2) TRANSIENT BACTEREMIA:
- Mucosal surfaces are populated with dense micro-flora. (genitourinary tract, intestine, and oral cavity)
- Damage to the mucosa, releases micro-organisms into the blood stream transiently
PATHOGENESIS OF IE

Damaged endothelial surface of the heart, biofilms on the surface of prosthetic materials and bacterial surface proteins fim A, MSCRAMMS (Microbial surface recognizing adhesive material molecule) facilitates the attachment of micro-organisms which leads to:

- Generation of tissue thromboplastin
- Activation of clotting cascade
- Generation of thrombin
- Formation of vegetation – promotes unrestricted bacterial growth
PATHOGENESIS OF IE

PROLIFERATION OF BACTERIA WITHIN A VEGETATION

• Initially there is a rapid multiplication of bacteria to reach high titers
• Followed by a ‘stationary phase’, less metabolically active, no rapid multiplication makes the organism less susceptible to anti microbial

• Bacteria:
  ▪ Provide continuous stimuli for thrombus formation
  ▪ New layers of fibrin get deposited- vegetation enlarges
  ▪ Micro/macro emboli thrown into arterial circulation
  ▪ Results in peripheral manifestations
  ▪ Continuous seeding of bacteria- kidney involvement/arthritis
Microscopically, the valve in Infective Endocarditis demonstrates friable portions of fibrin and platelets (pink) mixed with inflammatory cells and bacterial colonies (blue).
### PREDISPOSING FACTORS

**CHD**
- VSD (commonest)
- VSD with AR
- TOF
- Tricuspid Atresia
- Valvular Aortic Stenosis
- Bicuspid Aortic valve
- Coarctation of Aorta
- PDA
- Pulmonary stenosis

**RHD**
- Mitral/Aortic valve lesions

**Prosthetic Valves/Pacemakers**
- Post-surgical patients
- Blalock Taussig Shunt

**Host Factors:**
- Drug Addicts- iv/parentral drug abusers
- HIV patients
- PICU/NICU care leading to nosocomial infections
- Burn patients
- BM transplant/heart transplants
MICROBIOLOGY OF IE

• Streptococcus Viridians (VGS)
  - Most common causative organism after dental procedures
• Staph aureus/Staph Epidermidis
  - Secondary to pacemaker/ prosthetic valves; can cause acute endocarditis. And native valve endocarditis
  - CONS-indwelling central venous catheters
• Gram negative bacilli/Pseudomonas
  - Neonates and immuno-compromised patients
  - Enterococci-following lower bowel, genito- urinary manipulations
• Fungal
  - Post- cardiac surgery, I/V drug abusers, immuno compromised patients.
  - Intensive care units (ICU’s)
CLINICAL FEATURES

1) Unexplained fever > 7 days duration in children with known heart disease.
2) Rare below the age of 2 years.
3) Clinical features can be due to:
   1. Presence of infection - bacteremia or fungemia.
   2. Involvement of the Cardiovascular system – valvulitis.
   3. Features of Immunological reaction to infection.
   4. Emboli.
CLINICAL FEATURES

1) Presence of Infection
   • Fever with chills and rigors
   • Generalized weakness and malaise
   • Loss of appetite
   • Loss of weight
   • Myalgia and Arthralgia

2) Involvement of Cardiovascular System
   • CCF.
   • Changing Murmurs.
   • Appearance of new murmurs: Aortic, Mitral or Tricuspid regurgitant murmurs.
   • Valve abscesses cause perforation & rapid deterioration damage to conducting system. Purulent pericarditis.
CLINICAL FEATURES

3) FEATURES OF IMMUNOLOGICAL REACTION TO INFECTION

- Vasculitis leading to petechiae
- Osler’s nodes
- Janeway’s lesions
- Clubbing
- Splenomegaly appear 3 wks after the
- Microscopic hematuria onset of endocarditis
- Splinter hemorrhages
- Roth’s spots- Petechiae in the retina

4) Intracranial involvement

- Stroke, Brain abscess, mycotic aneurysms
- Pulmonary involvement- Lung abscess, Pneumonitis
SPLINTER
HAEMORRHAHAGES

CLUBBING

OSLER’S NODES

ROTH’S SPOTS
CUTANEOUS MANIFESTATION OF IE.
POST OPERATIVE IE

• ACHD repaired without residual defect eliminate the risk of IE 6 months after surgery.
• Central lines, catheters, TPN, prolonged PICU stay increases the risk.
• Incidence of IE less in the first 1 month after surgery except prosthetic valve, persistent hemodynamic changes.
• Trans catheter device before endothelization is having high risk for IE.
NEW BORN IE

• RARE
• 7.3% Of Paediatric IE.1/3 in presence of CHD. Post operative, and prosthetic device
• Most common organism –CONS, staph aureus, gram negative organism and candida.
• Clinical presentation variable septicaemia, CHF, embolic phenomenon osteomyelitis, meningitis, neurological-seizure, hemiparesis, apnoea.
• Immunological manifestations not seen.
Culture-negative Endocarditis (CNE) when a patient has clinical or echocardiographic evidence of IE but persistently negative blood culture

**Most common causes of CNE**
- Current or Recent antibiotic therapy
- Infection caused by a fastidious organism such as Abiotrophia and Granulicatella
- HACEK organism
- Right-sided endocarditis, mar antic endocarditis, Bartonella species
- *Tropheryma whippelii*, *Coxiella burnetii* (Q fever), and *Brucella* species may cause CNE. *Legionella pneumophila*
DUKE CRITERIA FOR IE

MAJOR CRITERIA:

A] Positive blood culture for Infective Endocarditis

1- Typical microorganism consistent with IE from 2 separate blood cultures, as noted below:
   • Viridians streptococci, Streptococcus bovis, or HACEK group, or
   • Community-acquired Staphylococcus aureus or enterococi, in the absence of a primary focus

   OR

2- Microorganisms consistent with IE from persistently positive blood cultures defined as:
   • 2 positive cultures of blood samples drawn > 12 hrs apart
   • All of 3 or majority of 4 separate cultures of blood (with first and last sample drawn 1 hour apart)
DUKE CRITERIA FOR IE

B] Evidence of Endocardial involvement

1- *Positive echocardiogram for IE defined as:*

- Oscillating intra cardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation, or
- Abscess or
- New partial dehiscence of prosthetic valve.

**OR**

2- New valvular regurgitation (worsening or changing of pre-existing murmur not sufficient)
DUKE CRITERIA FOR IE

MINOR CRITERIA

- Predisposition: predisposing heart condition or iv drug abuse
- Fever: temperature > 38°C (100.4°F)
- Vascular phenomenon: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival hemorrhages, and Janeway lesions.
- Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth spots, and Rheumatoid factor.
- Microbiological evidence: positive blood culture, but does not meet a major criterion
- Echocardiographic findings: consistent with IE but do not meet a major criterion serological evidence of active infection with organism consistent with IE.
DUKE CRITERIA FOR IE

Clinical criteria for infective endocarditis requires:

- Two major criteria, or
- One major and three minor criteria, or
- Five minor criteria
DIAGNOSIS

1) Positive blood culture:
   • Gold standard Yield low < 50%
   • To increase positivity to 95%; 3 blood culture samples should be collected; 1-3ml in infants and young children, 5-7 ml older children and adult each; 30 mins apart; preferably during the fever episode.
   • No growth after 48 hours if patient stable withhold antibiotics and take 2-3 repeat blood samples.
   • Acute bacterial endocarditis 3 samples collected within 3 hours

2) Supportive evidence:
   • Anemia-c/c disease, low grade hemolysis caused by prosthetic valve
   • Leucocytosis, thrombo cytopenenia in neonates
   • Raised ESR, Hypergammaglobulinemia
   • Microscopic hematuria
3) **Echocardiography**

- Sensitive diagnostic tool to detect
- Vegetations size > 2mm, Ruptured chordae
- Perforated cusps, Flail cusps
- Sensitivity varies from 70-90%
- If vegetations present- IE present (94%)
- If vegetations absent- IE absent (92%)

**Trans Oesophageal Echocardiography (TEE)**

- Infants and children who had chest wall disruption due to trauma, surgery or congenital anomalies
- Prosthetic valve endocarditis & valve ring abscess.
ECHOCARDIOGRAPHIC IMAGES OF IE

Vegetation on Mitral valve

Vegetation on Tricuspid valve
TREATMENT OF INFECTIVE ENDOCARDITIS

• TREATMENT OF INFECTIVE ENDOCARDITIS

• PREVENTION OF INFECTIVE ENDOCARDITIS
TREATMENT OF IE

Depends on:

• Culture positive IE: choice of antibiotic as per antibiotic sensitivity

• Culture Negative IE: Empiric therapy
ANTIMICROBIAL TREATMENT PRINCIPLES

• A prolonged course of therapy at least 2 weeks and often 4–8 weeks.

• Organisms are embedded within the fibrin-platelet matrix and exist in very high concentrations low rates of bacterial metabolism and cell division, hence decreased susceptibility to β-lactam and other cell wall–active antibiotic drugs.
TREATMENT PRINCIPLES

• Bactericidal rather than bacteriostatic.
• Use intravenous antibiotic drugs rather than intramuscular.
• IV rather oral exception is for ciprofloxacin.
• Staph aureus bacteraemia persist longer than streptococci.
• CVC staph bacteraemia subsides only when catheter is removed.
TREATMENT OF IE

Clinical condition

- CNE
- NATIVE VALVE
- LATE prosthetic valve (>1 year after surgery)

Antibiotics

- Ampicillin/Sulbactam plus Gentamicin
  - With or without Vancomycin
- Alternative Vanco + Genta

Ampicillin 200–300 mg/k q h max 12 grams
Gentamicin 3–mg/kg q8h

Vanco 60mg/kg q6h, max 2 grams
## INFECTIVE ENDOCARDITIS TREATMENT (CONT..)

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Highly susceptible strepto cocci | Penicillin G 2–3 lakh U /kg/day IV q 4h max 12–24 million  
Or Ceftriaxone 100 mg/kg/day q12h  
Other option— Vanco or Cefazolin (100 mg/kg q 8h) or Ceftriaxone |
| Relatively resistant Strepto cocci/enterococci | Penicillin G or Ampicillin plus Gentamicin  
Vanco + Genta for enterococci |
| Treatment | Medication
|-----------|------------------|
| Staphylococci Aureus / CONS | PenicillinG   
Cloxacillin/Naficillin 200MG/kg q 6h max 12 grams  
Cefazolin/vancomycin |
| Penicillin resistant 0.1 micg/ml | Naficillin/Oxacillin+ Genta 5 days or Vanco 40mg/kg qh/ cefazolin |
| MRSA | Vancomycin or Rt sided endocarditis daptomycin 6mg/kg /day |
| Vanco resistant | Daptomycin  
All prosthetic valve anti staph + Rifampicin + genta for 2 weeks |
TREATMENT OF IE

<table>
<thead>
<tr>
<th>Organization</th>
<th>Treatment Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram negative enteric organism</td>
<td>Cefipime, ceftazidime (100-150 mg/kg/day), cefotaxime (200mg/kg/day), ceftriaxone (100mg/kg/day) + genta</td>
</tr>
<tr>
<td>HACEK</td>
<td>Ceftriaxone/ cefotaxime OR AMPI + salbactum ampi+ genta /amikacin</td>
</tr>
<tr>
<td>Candida</td>
<td>AmphotericinB 1mg/kg iv over 3-4 hours Flucytosine 150 mg/kg oral qh</td>
</tr>
</tbody>
</table>
### IE TREATMENT

**Nosocomial endocarditis or “early” prosthetic valve endocarditis**  
(≤1 y after surgery)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin+Gentamicin (Rifampicin if prosthetic material present)</td>
<td>+</td>
</tr>
<tr>
<td>Cefipime /Ceftazidime</td>
<td></td>
</tr>
<tr>
<td>Dose - Rifampicin</td>
<td>20mg/kg/day max 900mg</td>
</tr>
<tr>
<td>Cefipime</td>
<td>100– 150 mg/kg q8 h max 6 grams /day</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>100 – 150 mg/kg q8h max2 –4 grams</td>
</tr>
</tbody>
</table>
COMPLICATIONS

• Cardiac / extra Cardiac complications
• CHF, new or progressive valvular dysfunction as increased regurgitation
  Periannular extension of infection.
• Sinus of Valsalva rupture
• Myocardial dysfunction.
• Obstruction of conduits or shunts,
• Prosthetic valve dysfunction including dehiscence.
• Pericardial effusion
• Septic emboli to the coronary arteries
COMPLICATION OF IE

• Extra cardiac complications and less commonly, immune complex–mediated vasculitis.
• Embolic phenomena from septic vegetation.
• Embolic complications –
  • Cerebral, pulmonary, renal, splenic, coronary, or peripheral arteries.
• Neurological sequelae- stroke, brain abscess, haemorrhage, seizures, diffuse vasculitis, or meningitis,
INDICATION FOR IE PROPHYLAXIS

- A prosthetic heart valve or heart valve repaired with prosthetic material.
- A history of endocarditis.
- A heart transplant with abnormal heart valve function
- Certain congenital heart defects including:
  - CCHD- that has not been fully repaired, including children who have had a surgical shunts and conduits.
  - A CHD defect that's been completely repaired with prosthetic material or a device for the first six months after the repair procedure.
  - Repaired CHD with residual defects, such as persisting leaks or abnormal flow at or adjacent to a prosthetic patch or prosthetic device.
IE PROPHYLAXIS

• Consider prophylaxis in patients before they undergo procedures that may cause transient bacteraemia.
• Manipulation of gingival tissue or the peri-apical region of teeth, or perforation of the oral mucosa
• Incision in the respiratory mucosa.
• Procedures on infected skin or musculoskeletal tissue - incision and drainage of an abscess
ENDOCARDITIS PROPHYLAXIS RECOMMENDED

• High-risk
  – Prosthetic cardiac valves
  – Previous bacterial endocarditis
  – Complex cyanotic heart disease
  – Surgically constructed systemic-pulmonary shunts or conduits

• Moderate-risk
  – Most other congenital heart disease
  – Acquired valvar dysfunction
  – Hypertrophic cardiomyopathy
  – Mitral valve prolapse with regurgitation and/or thickened leaflets
DENTAL PROCEDURES AND IE PROPHYLAXIS: RECOMMENDED

• Dental extractions
• Periodontal procedures
• Dental implants and re-implantation of avulsed teeth
• Endodontic procedures
• Sub gingival placement of antibiotic fibers and strips
• Initial placement of orthodontic bands (not brackets)
• Intra ligamentary local anesthetic injections
• Prophylactic cleaning
OTHER PROCEDURES AND IE PROPHYLAXIS: RECOMMENDED

• **Respiratory**
  – ST&A
  – surgical procedures involving respiratory mucosa
  – Rigid bronchoscopy

• **Gastrointestinal**
  – Sclerotherapy
  – Esophageal stricture dilation
  – ERCP with biliary obstruction
  – Surgery involving biliary tract or intestinal mucosa

• **Genitourinary tract**
  – Prostatic surgery, cystoscopy
  – Urethral dilation
DENTAL PROCEDURES DO NOT REQUIRE ENDOCARDITIS

- Routine anaesthetic 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
ENDOCARDITIS PROPHYLAXIS NOT RECOMMENDED

- Isolated secundum ASD
- Surgically repaired VSD, ASD, or PDA after 6 months (no residue)
- s/p CABG
- MVP without MR
- Previous Kawasaki disease w/o valvular dysfunction
- Previous rheumatic fever w/o valvular dysfunction
- Pacemakers and AICDs
- Flow murmurs
OTHER PROCEDURES AND IE PROPHYLAXIS: NOT RECOMMENDED

• Respiratory
  – Endotracheal intubation
  – PE tubes
  – Flexible bronchoscopy

• Gastrointestinal
  – Trans-esophageal echocardiography
  – Endoscopy (with or without biopsy)
  – Circumcision

• Genitourinary tract
  – Vaginal hysterectomy, and vaginal or Caesarean deliveries
  – In uninfected tissues: urethral catheterization, uterine D&C, therapeutic abortions, sterilization procedures, insertion or removal of IUDs
# PROPHYLACTIC REGIMENS FOR DENTAL, ORAL, RESPIRATORY TRACT, OR ESOPHAGEAL PROCEDURES

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>AGENT</th>
<th>REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard general prophylaxis</td>
<td>Amoxicillin</td>
<td>50 mg/kg orally; 1 hr before the procedure</td>
</tr>
<tr>
<td>Unable to take oral medications</td>
<td>Ampicillin</td>
<td>50 mg/kg IM or IV within 30 mins; before the procedure</td>
</tr>
</tbody>
</table>
| Allergic to penicillin                 | Clindamycin, or Cephalexin, or Azithromycin or Clarithromycin | Clindamycin: 20 mg/kg; 1 hr before the procedure  
Cephalexin/Cefadroxil: 50 mg/kg orally; 1 hr prior to procedure  
Azithromycin: 15mg/kg orally; 1 hr prior to procedure |
| Allergic to penicillin and unable to take oral medication | Clindamycin or Cefazolin   | Clindamycin: 20 mg/kg IV or IM; 30 mins before the procedure  
Cefazolin: 25mg/kg IM or IV ; 30 mins prior to procedure |
# Prophylactic Regimens for Genitourinary & Gastrointestinal (Excluding Esophageal) Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk patients</td>
<td>Ampicillin plus Gentamycin</td>
<td>Ampicillin 50mg/kg IV or IM; + Gentamycin 1.5 mg/kg within 30 mins of the procedure; 6 hrs later Ampicillin 25 mg/kg IM or IV or Amoxicillin 25 mg/kg orally</td>
</tr>
<tr>
<td>High risk patients allergic to Ampicillin or Amoxicillin</td>
<td>Vancomycin plus Gentamycin</td>
<td>Vancomycin 20mg/kg IV over 1-2 hrs; + Gentamycin 1mg/kg IM or IV; complete the infusion within 30 mins of starting the procedure.</td>
</tr>
<tr>
<td>Moderate risk patients</td>
<td>Amoxicillin or Ampicillin</td>
<td>Amoxicillin 50 mg/kg orally 1 hr before procedure or Ampicillin 50 mg/kg IM or IV within 30 mins of starting the procedure.</td>
</tr>
<tr>
<td>Moderate risk pts allergic to Amox./Ampicillin</td>
<td>Vancomycin</td>
<td>complete the infusion within 30 mins of starting the procedure</td>
</tr>
</tbody>
</table>
INDICATIONS FOR SURGERY IN IE

DEFINITE INDICATIONS

• Severe Lt sided CHF unresponsive to medical therapy- Destructive lesions of Aortic/Mitral valve.

• Extension of the Infective Process:

Prosthetic valve Infective endocarditis involving the ring or annulus

OR

Persistent conduction disturbances - AV conduction blocks or Bundle branch blocks.

RELATIVE INDICATIONS:

• Recurrent embolization

• Persistent bacteremia: suspect hidden focus of infection such as perivalvular abscess

• Difficult organisms in PVE such as Pseudomonas/ Fungi/Staph aureus.
INDICATIONS FOR SURGERY IN IE

Embolization chance is more in the following situation

• S.aureus, h influenza, para influenza

• >10mm, increasing size , MV veg, Mobile veg,

• Culture negative - antibiotics fastidious, coxiella, Bartonella

• 3 cultures in 24 hours
THANK YOU