MEDICINE
KING SAUD UNIVERSITY

Lecture :
Infective Endocarditis

important
Extra notes
Doctors notes

وتقال هذه الجملة إذا دهم الإنسان أمر عظيم لا يستطيعه ، أو يصعب عليه القيام به. "لا حول ولا قوة إلا بالله العلي العظيم"

Introduction:

- Endocarditis, irrespective of the underlying cardiac condition,
  is a serious, life-threatening disease that was always fatal in the preantibiotic era.
- Advances in antimicrobial therapy
- Early recognition and management of complications of IE
- Improved surgical technology have reduced the morbidity
- and mortality of IE.
- Numerous comorbid factors, may complicate IE such as
  - older age + young age group (these two categories always at high risk)*
  - diabetes mellitus
  - immunosuppressive conditions or therapy
  - dialysis. غسيل الكلى

* The immune system in elderly become weak while in children not complete developed yet)

Definition:

- Infectious Endocarditis (IE): it is a **serious infection** or colonization of the heart's endocardial surface (**endocardium**) ,**heart valves** (that is associated with low grade bacteremia) **by** (Congenital defects\bacteria\rickettsiae\fungi) , it damages the heart and other organs

Epidemiology:

Incidence: 1.7— 6.2 / 100 000 person years

M:F 1.7

mortality : 30 % - Damage of heart or other organs

Median age: Before antibiotics era 35y but

Now 58y

- Becoming a disease of the elderly
- Due to two factors:
  - ✓The decline of rheumatic heart disease
  - ✓The increasing proportion of elderly

Classified into four groups:

1-Native Valve IE (natural human valve) .

2-Intravenous drug abuse (IVDA) IE(affect the right side –tricuspid valves)

3-Prosthetic Valve IE (Artificial valve).

4-Nosocomial IE (Acquired from hospitals).

Further Classification:

Acute:

- ✓ Affects normal heart valves
- ✓ Highly virulent organisms
- ✓ Rapidly destructive.
- ✓ Metastatic foci
- ✓ If not treated, usually fatal within 6 weeks
- ✓ Commonly Staphylococcus species

Subacute:

- ✓ Often affects damaged heart valves(E.g. as a complication of Rheumatic Fever)
- ✓ Weakly virulent organisms
- ✓ Indolent (lazy) nature.
- ✓ If not treated, usually fatal by one year
- ✓ Commonly Streptococcus viridans (Most common cause of subacute endocarditis)

زمان كان الاندوكاردايتس منتشر اكثر بسبب انتشار الروماتك هارت دزيز لانه يسبب دستركشن او ذا فالف بعدين يجيهم اندوكاردايتس لما يكبروا

ممكن تختلف صياغة التعريف من محاضرة لمحاضرة لكن المعنى واحد

Risk factors: Host factors

General	
Injection drug use: -Increase risk in young to be effected by Staph.aureus	Other risks: -Poor dental hygiene[1] -Hemodialysis[2] -Diabetes.M -HIV(**)
IV drug use : -Higher among patients with known valvular heart disease -IE usually effect the right side of heart in IV drug user because they inject into a vien draining in Rt atrium	Structural cardiac abnormality*: -75% of pts will have a preexisting structural cardiac abnormality -10-20% have congenital heart disease

Cardiac abnormalities or (local)	
Moderate risk : -mitral valve prolapse or regurgitation -Mitral stenosis -Tricuspid valve problems -Pulmonary stenosis -Hypertrophic obstructive cardiomyopathy (HOCM)	Low/no risk: -Atrial septal defect (ASD) -Coronary artery bypass grafting (**CABG**)
High risk: -Previous IE -Aortic valve disease -Rheumatic valve disease (*) -Prosthetic valve -Coarctation -Complex cyanotic congenital + heart surgery	

- **(*)Rheumatic valve disease:**
  -Predisposition for young in some countries 37%-76% of cases
  -effects :Mitral 85%, Aortic 50%
  -Degenerative valvular lesions
  -MV (mitral valve) Prolapse 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

- **(**)HIV infection:**
  -A number of cases of IE have been reported in patients with HIV infection
  -It has been suggested that HIV infection is a independent risk factor for IE in IDU

الأرقام والإحصائيات للفهم وليست للحفظ

There is a lot of abbreviations, try to be familiar ☺ ما راح يسألك عن درجة الخطورة [1]: معدات تنظيف الاسنان [2]: أجهزة تستخدم لتنظيف الدم يستخدمونها للغسيل الكلوي

Risk factors: Host factors (cont.)

Drugs	
Iatrogenic : -Immunosuppressive treatment -cytotoxic agents	self- inflicted: -alcoholism -addiction (injected drugs)
protective factors: -antimicrobial chemotherapy	

Risk factors : bacteria factors

1-virulence	2- number of bacteria in the blood
• virulent bacteria`, staph. aureus and strept. Pneumoniae can infect normal heart	

Predisposing*factors:

A- cardiac lesions	B. systemic factors
• Chronic rheumatic valvular disease • Congenital heart disease and defects • Atherosclerosis • Prosthetic valves : Immediate or Delayed	• Immunosuppressive treatment • Immune defects (disease) • Alcoholism • Iv. Drug abuse

*Predisposing: means “make susceptible”

CAUSATIVE ORGANISMS:

Streptococcus (gram +ve in chains)	**Staphylococcus** (gram +ve in clusters)
✓ Viridans streptococci is the Most common cause of sub- acute bacterial endocarditis (SBE)	✓ Staphylococcus aureus (pyogen) Cause Acute endocarditis
Produce glucagons* → adhere to endocardium E.g : Streptococcus mutans Streptococcus sanguis	✓ Staphylococcus epidermidis Cause Prosthetic heart valves
Others: Streptococcus faecalis Streptococcus faecium Streptococcus pneumoniae	

Others:
Brucella species / Actinobacillus actinomycetes comitans/Rickettisae/Fungi/Coxiella burneti /Candida albicans

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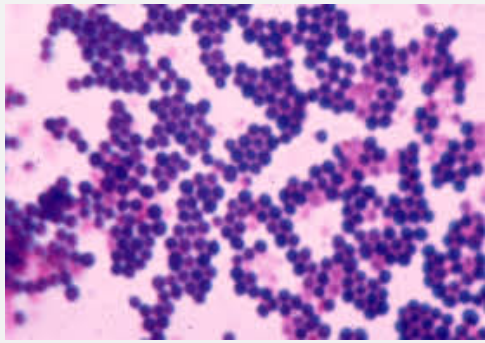
streptococcus



staphylococcus

*Produce polysaccharide layer which help the organism to stick to the valves

Sources of infection:

- Dental extraction* and other dental procedures:
  (Rheumatic heart disease /Congenital heart disease)
- Cardiac surgery (**prosthetic valves**)
- Intravenous medication
- Iv. Drug addiction
- Intracardiac or intravenous catheters
- Obstetric or gynaecologic procedures

Doctor's note:
the cause of endocarditis is disturbance of the blood flow in the heart which will lead to damage of endothelium.
اول شي بيصير دستركشن ..مثل الفلو حق الموية ممكن ينخر الحجر نفس الشي مع الدم
اوف ذا تيشو بعدين الاورنقزم سهل انه يدخل الدم زي لما الواحد يفرش اسنانه راح يصير له
لاكن ما يصير له اندوكردايتس لان قلبه طبيعي (بكتيريما)تلوث في الدم
How the organism get there: The Bacteremia- infection of the lung -direct from pericarditis

Portal of entry:

- Dental extraction bleeding bacteraemia:
  - ✓ Rocking the tooth in the socket pumping effect on the vessels of periodontal ligament , forces bacteria from gingival pockets into blood stream 40 – 80 % bacteraemia
    - Sensitivity of blood culture techniques
    - Severity of gingival infection
- Oral irrigation device.

*Or could be from simple tooth brushing(bleeding during brushing)

Pathophysiology:

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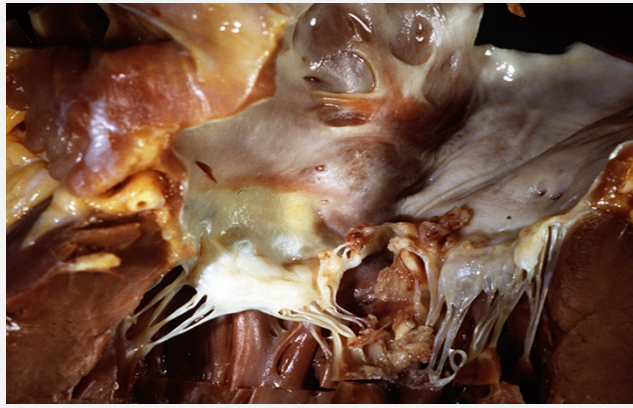
1.Turbulent blood flow disrupts the endocardium making it “sticky”.
2. Bacteremia delivers the organisms to the endocardial surface.
3. Adherence of the organisms to the endocardial surface.
4. Eventual invasion of the valvular leaflets.

Distorted shape causes stasis of blood flow and settee of bacteria on the endocardium

PATHOGENESIS: after 1- settee of bacteria on the endocardium



2- **Formation of vegetations :**

- Fibrin , platelets (thrombi) , bacteria colonies Attached to heart valves
  1. Break off → infected emboli → distant organs (kidney , brain)
  2. Immune complex formation causes glomerular damage → haematuria
  3. Valves infection → destruction → heart failure .
  4. Drug addicts → tricuspid,pulmonary valves of right side of heart → lung emboli → pneumonia

*IE often occurs when there is an underlying cardiac abnormality that creates a high-low pressure gradient.
*The resultant turbulent blood flow disrupts the endocardial surface by peeling away the endothelium.

Sypmtoms

Acute
High grade fever and chills
Shortness of breath (SOB)
Arthralgias[1]/myalgias[2]
Abdominal pain
Pleuritic chest pain
Back pain

Acute
Low grade fever
Anorexia[3]
Arthralgias/ myalgias
Wight loss and fatigue
Abdominal pain
Nausea and vomiting (n/v)

-The onset of symptoms is usually ~2 weeks or less from the initiating bacteremia [4]

Diagnostic approach: The things make you include Infective endocarditis as the diagnosis

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

native valve >acute >most common staph aureus (bad Symptoms)
Prosthetic Valve > Subacute > most common viridans (Flu like Symptoms)
rheumatic heart disease> most common viridans

[1]: Arthralgias (joint pain) [2]:myalgias (muscle pain) [3]: loss of appetite for food [4]:the presence of bacteria in the blood.

Case Definition of Infective Endocarditis:

- Also **Duke criteria**
- In 1994 investigators from Duke University modified the previous criteria to include
- The role of echocardiography in diagnosis
- They 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 bacetremia 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

*It is important to know that duke criteria in general is important in the diagnosis in endocarditis

Duke criteria are a collection of major and minor criteria used to establish a diagnosis of infective endocarditis

Major criteria	Minor criteria
1-microbiology • Typical organism from 2 separate cultures OR Microorganism from persistently positive Blood culture OR Single Blood culture + for Coxiella burnetii, or titer >1:800	1-Predisposition (heart condition or IV drug use)
	2-Fever 38oC or more
2-endocardial involvememt • New (not changed) murmur of regurgitation	3-Vascular phenomenon (excludes petechia, splinter hemorrhage)
	4-major arterial emboli • Mycotic aneurysm, intracranial or conjunctival hemorrhages. Janeway lesions
3-positive echo • (TEE if prosthetic valve, complicated, or pretest probability possible IE	5- Immunologic phenomena • RF,.Roth's spots glomerulonephritis, Osler's nodes
	6-Microbiologic evidence • Not meeting major criteria single BC not CNS serology

Major :Cardiac change > murmur of regurgitation / Microbiology tests

CLINICAL FEATURES:

- **Petechiae:**

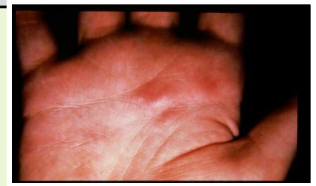
1.Nonspecific
2.Often located on extremities or mucous membranes

- **Splinter haemorrhage**

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

Subungal hemorrhages that extend the entire length of the nail or are primarily located at the proximal end of the nail (near the cuticle) are like due to trauma.

- **Osler's Nodes**

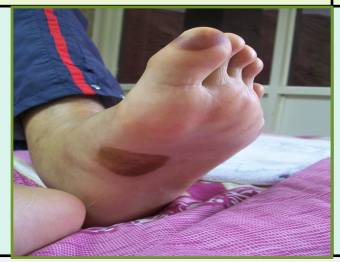


Important symptom in the diagnois
1.More specific 2.Painful and erythematous nodules
3.Located on pulp of fingers and toes 4.More common in subacute IE

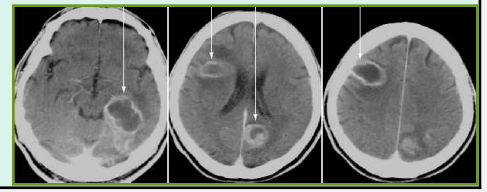
- **Janeway lesions**

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

- **Embolic manifestations**



- **CNS manifestations of endocarditis**



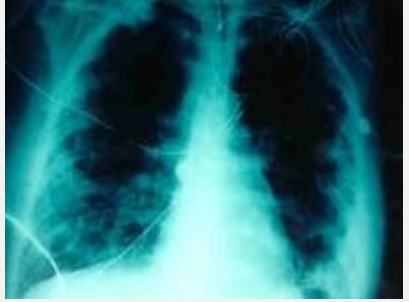
- Onset is insidious (SBE) – 3 weeks after extraction
- Fever (mild and prolonged)
- Malaise , weight loss , weakness and Changing murmurs
- Anaemia , leucocytosis and Hypergammaglobulinaemia
- Microscopic haematuria and Spleenomegaly

Hemotourea → because there is immune response → antigen-antibody complex which will accumulate in the glamour and cause glamournephritis

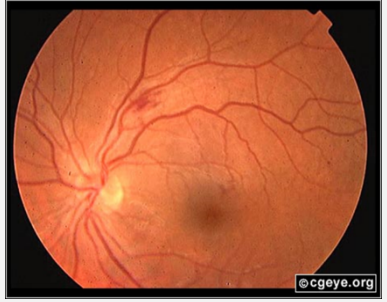
Complications:

Four etiologies:

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



Septic Pulmonary Emboli



Septic Retinal embolus

Embolic complications

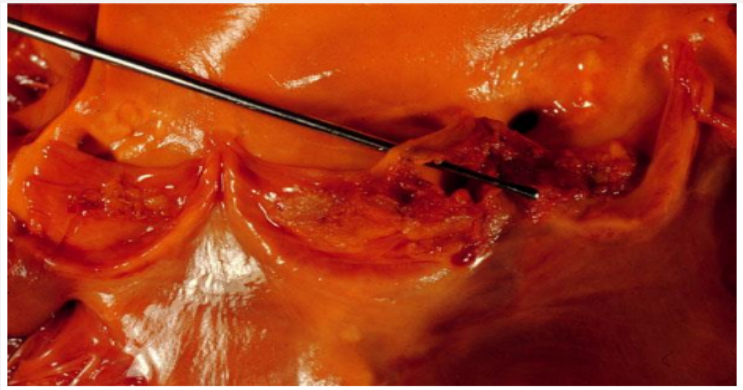
- Occur in up to 40% of patients with IE
- Predictors of embolization
  - ✓ Size of vegetation
  - ✓ Left-sided vegetations
  - ✓ Fungal pathogens, S. aureus, and Strep. Bovis
- Incidence decreases significantly after initiation of effective antibiotics

- 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)

*Systemic emboli are among the most common complications of IE, occurring in up to 40% of patients. Subclinical emboli are often found on autopsy.

Local Spread:

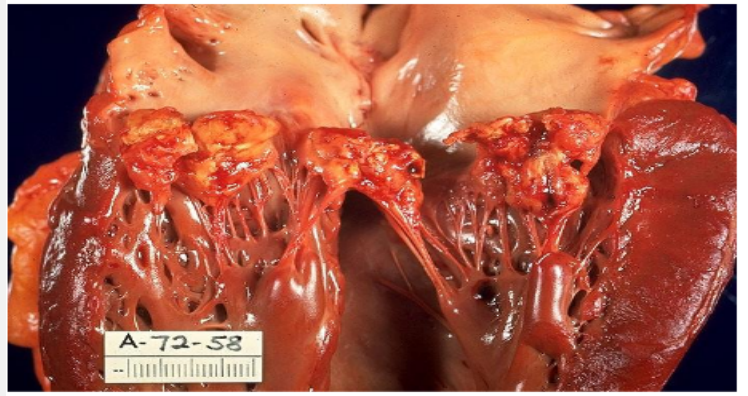
- Heart failure: Extensive valvular damage.
- Paravalvular abscess (30-40%):
  - Most common in aortic valve, IVDU, and S. aureus
  - May extend into adjacent conduction tissue causing arrhythmias
  - Higher rates of embolization and mortality
- Pericarditis
- Fistulous intracardiac connections



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

Metastatic Spread of Infection

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



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

*Abnormal growth made of fibrin, fused platelets, and some microorganisms, all adherent (ملتصقة) to a valve.

Culture Negative IE: الصميلي يقول غالبا ما راح يسال عنها او الاورقانيزم المسبب.د

- How hard did you look?
- (50% culture neg are due to previous antibiotics)

HACEK: 2-3 wk incubation, subculturing

- Tend to see subacute w/ valve destruction/CHF
- If you culture for 3 days and nothing appears, and they were sure it is IE, it is culture negative IE

HACEK is :

- Hemophilus paraphrophilus, aphrophilus.
- Parainfluenzae
- Aggregatibacter(Actinobacillus) actinomycetemcomitans
- Cardiobacterium hominis
- Eikenella corrodens
- Kingella spp.

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, enriched cultures:** HACEK
- **Lysis centrifugation system (Isolator):** Bartonella, legionella (BCYE),fungal
- **Serology:** Endemic fungi, bartonella, Q fever, brucella, legionella, chiamydia
- **Thioglycolate or cysteine supplemented media:** S.aureus satellitism: Abiotrophia (NVS)

اذا جاء للاب المايكرو صمام كان فيه اندوكاردايتيس و يبون يعرفون المسبب و لا طلع في الكلتشر العادي لازم نسوي و ,ايام 5ايام للدم مو 10كلتشر نسوي كلتشر في سبيشال ميديا و نطلب سيرولوجي.

*Some times the organism is culture negative In the culture for endocarditis it has to be kept for 14 days

Laboratory Diagnosis:

1-serial blood culture:

(2-3 sets before antibiotic therapy)

- ✓ Aerobic
- ✓ Anaerobic

2-serological tests:

- ✓ CFT (coxiella burniti)

3-sensitivity test.

4-Additional tests :

- ✓ CBC, ESR and CRP, Complement levels (C3, C4, CH50)
- ✓ RF
- ✓ Urinalysis

5-Imging :

- ✓ Chest x-ray:
  - Look for multiple focal infiltrates and calcification of heart valves
- ✓ ECG:
  - Rarely diagnostic
  - Look for evidence of ischemia, conduction delay, and arrhythmias
- ✓ Echocardiography:
  - looking for vegetation

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.

- Classification of Endocarditis Depending upon where the infection is located:

1- Native Valve IE:
-Strep. (55%), mostly S.viridans
-Staph. (30%), mostly S.aureus
-Enterococci (5-10%),
-HACEK (5%),
-Fungi

2- Prosthetic Valve IE:
-Early (1-2 months) (1 - 3.1%)
50% Staphylococci S.epidermidis > S.aureus, gnb, enterococci
-Late (more than 12 months) 2 - 5.7%

3- IE in IV drug abusers:
-Staph. Aureus (50-60%)

Endocarditiis causes: continuous **Bacteraemia**

There are **three** clinical patterns of **bacteremia**:

- ✓ **Transient:**
  - lasts minutes to hours:
    1-following manipulation of infected tissues(abscess,furuncle,or during a surgical procedure)
    2-instrumentation of contaminated mucosal surfaces (dental procedures,cytoscopy,or sigmoidoscopy)
    3-at the onset of bacterial pneumonia,arthritis,osteomylitis,and meningitis.

- ✓ **Intermittent**:
  - commonly occurs with undrained abscesses.

- ✓ **Contineous**:
  - reflects an endovascular infection such as endocarditis or endarteritis,suppurative thrombophlebitis,or an infected aneurysm.
  - It also occurs in the first two weeks of typhoid fever and brucellosis.

Technique for collection of blood for culture:

- Blood for culture contaminated by normal skin flora e.g.
  - ✓ Staphylococcus epidermidis
  - ✓ Diphtheriods and
  - ✓ Propioniobacteria(anaerobic diphtheroides)
- So first we have to clean the site (mainly anticubital fossa)with alcohol 70%and leave for (1-1.5 minutes) or cholorhexidine or iodine
- Blood culture by automated machines e.g. Bactec or Bactalert-upto 5 days when signal positive, the specimen is gram stained
- reported to clinician then cultured identified and tested for antimicrobial susceptibility

NOTE: *from females slides*

- Bacteraemia may follow scaling , tooth brushing, endodontic therapy .
- Lack of clinical effect of many bacteraemia is due to small number or low virulence
- They are rapidly cleared by normal body defence (leucocytes)
- Strept. Faecalis may cause endocarditis after genitourinary or gut procedures

Staph (arues / epidermis) → drug abusers

TREATMENT:

- Disk diffusion test (not sufficient)
- MIC , MBC.
- Criteria of antibiotic:
  - ✓ Bactericidal
  - ✓ Parenteral
  - ✓ High dose
  - ✓ Prolonged
- Viridans streptococci: *we use bactericidal drugs only
  1. Benzyl penicillin I.V (4 MU الدوز) every 4 hrs for 4 weeks*
  2. (OR) penicillin + gentamicin
- Streptococcus faecalis
  1. ampicillin + gentamicin I.V
- ○ Recurrence after cure is common in:
  (drug addicts / immunodeficient patients)

MORTALITY:

- With antibiotic treatment 30%
- High mortality
  - Virulance of organism or sever infection
  - Presence of underlying disease
  - Elderly
  - Inadequate treatment
- poor prognosis
  - Candidal
  - Staphylococcus
  - Gram-negative

Doctor's notes
1- Duration must be sufficient
2- We have to do MBC test (minimum bacteriocidal Concentration) to determine the lowest concentration of antibacterial agent "antibiotic" required to kill this pathogen.
3- Also we need to do MIC test (minimum inhibitory concentration) to determine the lowest concentration of chemicals needed to stop the growth of pathogen. (bacteriostatic)
4- We need prolonged + combination therapy to treat endocarditis

Notes: doctor's notes

important

S. viridans	Penicillin G + gentamycin
MSSA / MRSA (most common)	Cloxacillin + vancomycin (we can use gentamycin or rifampicin instead of vancomycin لكن باختلاف فترة العلاج)
Q fever (coxiella burant)	Doxycylin (from tetracyclin family)
HACEK	Cephalosporin 3rd generation
Burotonella	Aminoglycoside + flouroquinolones

خذ في عين الاعتبار أن فترة العلاج الزمنية تختلف باختلاف الفالف.
Native valve or prosthetic valve (needs more time or even surgery)

Prophylaxisis :

- In case he has prosthatic valve or abnormal valve he is more susciptable to be infected .
- We give prophylaxis for certain people
  نص ساعة –بساعة (غالبا)يعني مانعطي أي شخص لازم أشخاص معينين بحالات معينة ونعطيهم قبل العملية
- Mainly gram +ve bacteria → clindamycin , amoxicillin , cephalexine (oraly) , ampicillin (IM)
- We give prophylaxis for :
  1- previous history with cardiac disease (previous endocarditis)
  2- dental extraction
  3- bronchoscopy and others..

Notes: doctor's notes

important

- Infective endocarditis has 2 types Native , prosthetic:
1-native Acute: staph aureus (most common) , sub acute: streptococci viridians
2-Prothetic : staph epidermis
- General Risk factors: old age , HIV , Cardiac (valvular Heart diseases) , bad dental hygiene , DM, IV drug uses , congenital heard disease.
- Moderate Risk factors: stenosis , prolapse.
- High Risk factors : Rheumatic valve , prosthetic valve
- There has to be bacteremia in order for endocarditis to occur , YOU MUST do a minimum of 3 blood cultures
- Physical examination signs Fever , Murmur , Positive Blood cultures , thrombus
-Left valves are more serious
- Treatment :
- 1- streptococci viridians; Penicillin , gentamycin
- 2-Staph Areus : Colaxcillin , Vancomycin
- Prophylaxis is used usually for Dental , Rigid Bronchoscopy , Esophageal procedures , GI mucosal procedures , Cystoscopy , Prostate surgery. Antibiotics used for prophylaxis Clindamycin, Cephalexin , clarithromycin.

هنلك بعض السلايدات ما ضفناها لعدم شرح الصميلي لها

متى نحتاج نسوي سيرجيري عشان نأخذ عينة من الفالف؟

1) Heart Failure 2) not Responding to medical treatment
3) Recurrent systemic emboli (we have stop it by the surgrey)
also in case some pathogen ------> pseudomonas , fungi ,coxiella and Entrococci

SAQ:

A 68 year old Patient is presented to you with a Rheumatic valve disease , on examination you find Degenerative valvular lesions , with high grade fever , abdominal pain , Back pain , pleuritic chest pain , arthralgia and heart murmurs , he tells you that symptoms began 2 weeks ago and they were progressing ever since.

1-Based on the information what is the causative bacteria?

ANS: Staph Aureus

2- How would you confirm your diagnosis?

ANS: by obtaining at least 3 Blood cultures , ECG , (elevated ESR or CRP usually present and maybe high WBC)

3- What is the treatment needed?

ANS: cloxcillin , vancomycin

4-if a patient has a prosthetic valve what is the most likely causative bacteria?

ANS: Staph epidermis

5-Name other organisms that could cause Endocarditis:

ANS: streptococci viridians , staph epidermis , HACEK (Haemophilus , Actinobacillus , cardiobacterium , Eikenella ,kingella)

GOOD LUCK!

MICROBIOLOGY TEAM:

- Waleed Aljamal (leader)
- Ibraheem Aldeeri
- Ibrahim Fetyani
- Abdulaziz almohammed
- Abdulmalik alghannam
- Omar albabtain
- Turki maddi
- Mohammad alkahil
- Meshal Eiaidi
- Khalid Alhusainan
- Khalid Alshehri
- Nasir Aldosarie
- Shrooq Alsomali (leader)
- Shatha Alghaihab
- Ruba Barnawi
- Reem Alshathri
- Lama Altamimi
- Aseel Nasser
- Lama Al musallam
- Reema Albarrak

The Editing File

We are waiting for your feedback

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