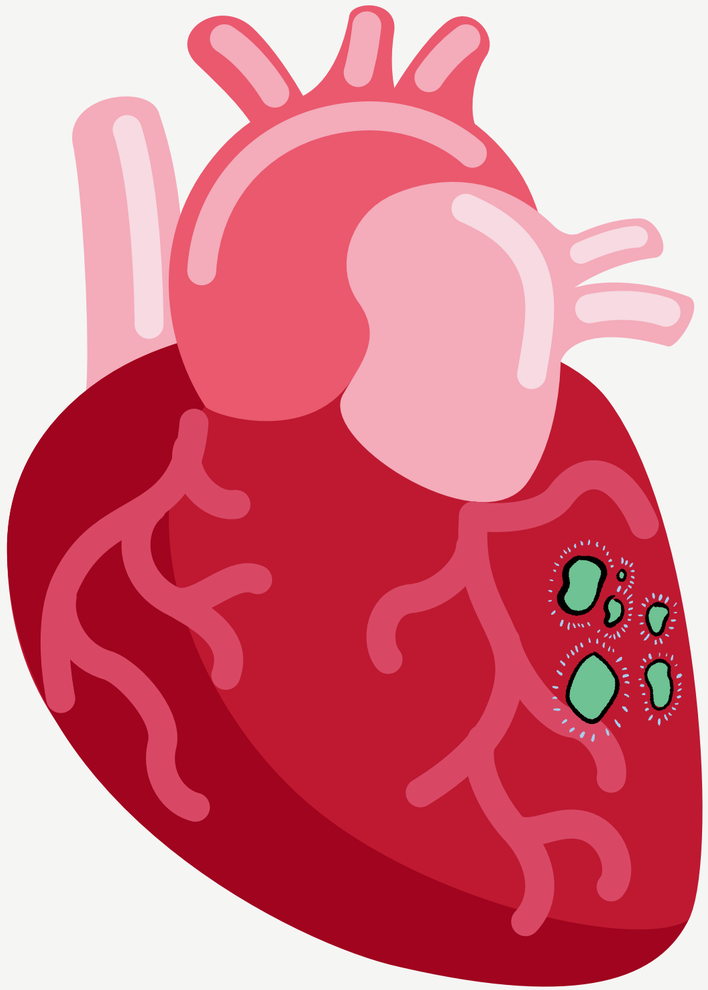
INFECTIVE ENDOCARDITIS

Lecture no.2



Editing File

Color index:

Main text	Girls' slides
Important	Boys' slides
Dr. notes	Extra

(اللَّهُمَّ انْفَعْنِي بِمَا عَلَّمْتَنِي، وَعَلِّمْنِي مَا يَنْفَعُنِي، وَزِدْنِي عِلْمًا)

OBJECTIVES

- DEFINE AND DIFFERENTIATE THE VARIOUS TYPES OF ENDOCARDITIS
- DISCUSS THE EPIDEMIOLOGY, RISK FACTORS AND PATHOGENESIS OF INFECTIVE ENDOCARDITIS
- RECOGNIZE THE CLINICAL PRESENTATION OF INFECTIVE ENDOCARDITIS
- DISCUSS THE CULTURE NEGATIVE ENDOCARDITIS
- DESCRIBE THE LABORATORY DIAGNOSIS AND INVESTIGATION OF INFECTIVE ENDOCARDITIS
- RECALL THE COMMONEST CAUSATIVE ORGANISMS OF INFECTIVE ENDOCARDITIS

Helpful Video

INFECTIOUS ENDOCARDITIS (IE)

Definition

An infection of the heart's endocardial surface. (particularly valves)
(endocardium not myocardium!)

Epidemiology

INCIDENCE	MALE:FEMALE	MEDIAN AGE		IT BECAME MORE COMMON IN ELDERLY PATIENTS DUE TO TWO FACTORS:
1.7— 6.2 / 100,000 person years (not common) no need to memorize the numbers	1:7	PreABx era (pre antibiotics era) 35y Now 58y	Becoming a disease of the **elderly** because of A decreased incidence of rheumatic heart disease	-The decline of rheumatic heart disease - The increasing proportion of elderly

CLASSIFICATION OF IE

<table>
<tr><th colspan="3">Classification into four groups
(organisms are very important)</th></tr>
<tr><td>Native valve IE</td><td colspan="2">Staph.sp , mostly Staphylococcus (30%) Acute most common in native valve
Strep. (25%), mostly Streptococcus .viridans , streptococcus gallolyticus Subacute
Enterococci (-10%), HACEK group (-2%), Culture negative (-10%)
Rare Brucella (common in saudi arabia) , Q-fever chlamydia and bartonella, leigionella, Non-TB and Troperyma whipplei
Fungi Empirical treatment vancomycin + ceftriaxone or gentamicin
Alternative Daptomycin</td></tr>
<tr><td rowspan="3">Prosthetic valve</td><td colspan="2">‣ 7 -25 % of cases of infective endocarditis.
‣ 0.94 per 100,000 bioprosthetic.
‣ Initially mechanical valves at greater risk for first 3 months, then have the same risk at 5 years:
1-3.1% risk at 1 year. 2-5,7% at 5 year.</td></tr>
<tr><td>Early <12 months
(1-3.1%)</td><td>Late <12 months
(2-5,7%)</td></tr>
<tr><td>50% Staphylococci
Staphylococcus . epidermidis more common than S. aureus, diptheroid, Enterobactrales (rare)</td><td>Staph. aureus (50-60%) - Staphylococcus . epidermidis - Viridans strept - Enterococcus
Empirical treatment vancomycin + gentamicin + Rifampin</td></tr>
</table>

CLASSIFICATION OF IE CONT…

Classification into four groups (organisms are very important)	
Intravenous drug abuse IE	**Staph.aureus** (50-60%)
Nosocomial IE	A rare complication of nosocomial bacteraemia; however, it is an infection of great importance because of its high mortality and because in many cases it is potentially preventable

FURTHER CLINICAL CLASSIFICATION

	Acute	subacute
effects	**Normal** heart valves	**Damaged** heart valves
onset	Invasive, damaging, suppurative (Rapidly destructive)	Not invasive, suppurative (Indolent nature) (Not acute symptoms)
fatality	If not treated usually fatal within 6 weeks	if not treated usually fatal by 1 year
causative organsim	Usually by virulence bacteria like **staph.aureus** ,commonly staph: Metastatic foci	Commonly **viridans streptococci,**usually the organism is low virulent or non virulent
symptoms (fever is the most important symptom)	• **High grade fever** and chills • SOB(shortness of breath) • Arthralgias/myalgias • Abdominal pain • Pleuritic chest pain • Back pain • palpitation • Heart failure in severe cases	• **Low grade fever** • Anorexia • Weight loss • Fatigue • Arthralgias/myalgias • Abdominal pain • N/V nausea and vomiting • Weakness , decrease appetite

PATHOPHYSIOLOGY

1

INJURY OF ENDOTHELIUM

TURBULENT (NON STREAM NOT SMOOTH) BLOOD FLOW DISRUPTS THE ENDOCARDIUM MAKING IT “STICKY”.

2

BACTERIA ACCESS TO BLOODSTREAM

BACTEREMIA DELIVERS THE ORGANISMS TO THE ENDOCARDIAL SURFACE.

(BACTEREMIA SHOULD NATURALLY BE RESOLVED, BUT IF SOMEONE HAD PRIORLY INJURED OR ABNORMAL HEART VALVE THIS SIMPLE BACTEREMIA MIGHT LEAD TO DISASTERS (IN THIS CASE IT MIGHT LEADS TO ENDOCARDITIS))

3

ADHERE TO ENDOCARDIUM

ADHERENCE OF THE ORGANISMS TO THE ENDOCARDIAL SURFACE

4

INVASION AND CAUSE OF DISEASE

EVENTUAL INVASION OF THE VALVULAR LEAFLETS (CUSPS)

RISK FACTORS

INJECTION DRUG USE	IVDU (IV DRUG USE)	HIV INFECTION (RHEUMATIC FEVER)	RHEUMATIC VALVE DISEASE	OTHER RISKS
100x ↑ risk in young staphylococcus aureus (in young children)	• Rates 150-2000/100000 person years • Higher among patients with known valvular heart disease	• 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 (injecting drug user)	• Predisposition for young in some countries 37%-76% of cases • (it's more common in developing countries) • Mitral 85%, Aortic 50% Degenerative valvular lesions • MV 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	• Poor dental hygiene • Hemodialysis • DM (Diabetes Mellitus) • HIV • old age—> old people with atherosclerosis will be more susceptible to have IE

RISK FACTORS CONTINUED...

CARDIAC ABNORMALITIES

HIGH RISK

- Previous IE 4.5(2.5to9)%
- Aortic valve disease 12-30%
- Rheumatic valve disease
- Prosthetic valve
- Coarctation
- Complex cyanotic congenital

MODERATE RISK

- mitral valve prolapse
- MR thickened leaflets- 5 to 8 times(100/100000 person years)
- Mitral stenosis
- Tricuspid valve
- Pulmonary stenosis
- Hypertrophic obstructive cardiomyopathy (HOCM)

LOW/NO RISK

- atrial septal defect ASD (secundum)
- CABG (coronary artery bypass grafting)

Structural cardiac abnormality:

➢ 75% of pts will have a pre existing structural cardiac abnormality

➢ 10-20% have congenital heart disease

DIAGNOSTIC APPROACH

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 congestive heart failure

-neurologic evaluation may detect evidence of focal neurologic impairment

-Signs: (fever and heart murmur)
(non specific signs: petechiae,subungual or splinter hemorrhages, clubbing, splenomegaly, neurologic change

-Osler nodes, janeway lesions, and roth spots

OTHER ASPECT CLINICAL DIAGNOSIS

-which valve?
right or left 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 3 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 c reactive protein (crp) is usually present
-most patients quickly develop a normochromic normocytjc anemia
-WBC count normal or elevated

ADDITIONAL LABORATORY TESTS

1- abnormal urinalysis

the combination of RBC casts on urinalysis and a low serum complement may be an indicator of immune mediated glomerular disease

2- ECG

new av, fascicular or bundle branch block.. perivalvular invasion monitoring? pacing?

SIGNS FOR ENDOCARDITIS

Specific signs	
osler nodes	**Janeway lesions**
1- more specific 2- painful and erythematous nodules 3- located on pulp of fingers and toes 4- more common in subacute IE	1- more specific 2- erythematous , blanching macules 3- nonpainful 4- located on palms and soles

SIGNS FOR ENDOCARDITIS CONT...

Non specific signs	
Petechiae	**Splinter hemorrhages**
1- nonspecific 2- often located on extremities or mucous membranes	1- nonspecific 2- nonblanching 3- linear reddish brown lesions found under the nail bed 4- usuaaly do not extend the entire length of the nail

ECHOCARDIOGRAPHIC FINDINGS

Echocardiographic findings

oscillating intracardiac mass:

1- on valve or supporting structure

2- in the path of regurgitation jets

3- on implanted material , in the absence of an altenate anatomic explanation

Abscess:

1- new partial dehiscence of prosthetic valve

2- new valvular regurgitation (increase or change in pre existing murmur not sufficient)

ECHOCARDIOGRAPHIC CULTURE

1- HOW HARD DID YOU LOOK?

2- (50% CULTURE NEG ARE D/T PREVIOUS ANTIBIOTICS)

3- FASTIDIOUS BACTERIA

4- BRUCELLA COMMON IN SAUDI ARABIA (RAW MILK AND MEAT AND AEROSOL)

5- HACEK 2-3 WEEK INCUBATION, SUBCULTURING

6- TEND TO SEE SUBACUTE W/VALVE DESTRUCTION/ CHF

7- HAEMOPHILUS PARAPHROPHILUS

8- AGGREGATIBACTER (HAEMOPHILUS) APHROPHILUS

9- AGGREGATIBACTER (ACTINOBACILLUS) ACTINOMYCETEMCOMITANS

10- CARDIOBACTERIUM HOMINIS

11- BARTONELLA SP (EMPIRICAL TREATMENT CEFTRIAXONE OR CIPROFLOXACIN)

12- EIKENELLA CORRODENS

13- KINGELLA SPP.

ECHOCARDIOGRAPHIC FINDINGS

improved diagnostic value of echocardiography in patients with infective endocarditis by transoesophageal approach a prospective study

we can see thrombus even if it was small

- EUR HEART J, 1988 JAN;9(I);43.5396 PATIENTS WERE STUDIED CONSECUTIVELY WITH TEE AND TEE
- 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
- 100% OF VEGETATIONS GREATER THAN 11 MM DETECTED BY TEE WERE ALSO OBSERVED WITH TTE

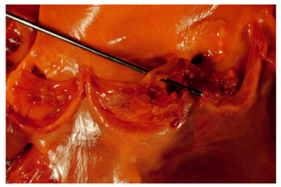
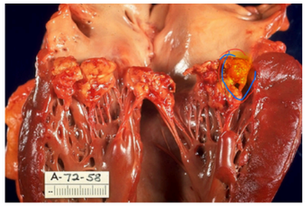
HOW WILL YOU DETECT THE ORGANISM IF CULTURE NEGATIVE

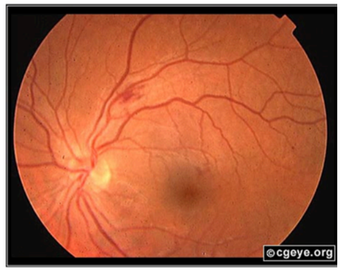
LABORATORY TEST	ETIOLOGY
PCR OF VEGETATION I EMBOLI	TROPHERYMA WHIPPELEI, BARTONELLA
HISTOLOGY / STAIN / CULTURE OF VEGETATION / EMBOLI	FUNGUS
PROLONGED , ENRICHED CULTURES	**BRUCELLA** **most common cause in KSA if the culture negative** , HACEK
LYSIS CENTRIFUGATION SYSTEM (ISOLATOR)	BARTONELLA , LEGIONELLA (BCYE) , FUNGAL
SEROLOGY	ENDEMIC FUNGI , BARTONELLA , Q FEVER , BRUCELLA , LEGIONELLA , CHLAMYDIA
THIOGLYCOLATE OR CYSTEINE SUPPLEMENTED MEDIA	S. AUREUSNATELLITISM: ABIOTROPHIA (NVS)

POOR PROGNOSTIC FACTORS

- FEMALE
- OLDER AGE
- AORTIC VALVE
- PROSTHETIC VALVE
- VEGETATION SIZE
- HERAT FAILURE
- APACHE II SCORE
- LOW SERUM ALBUMEN
- DIABETES MELLITUS
- S AUREUS
- PARAVALVULAR ABSCESS
- EMBOLIC EVENTS

COMPLICATIONS (IMPORTANT) focus in general outline

Embolic antibiotics. complications	❖ Occur in up to 40% of patients with IE ❖ Predictors of embolization : - Size of vegetation. - Left-sided vegetations. - Virulent organisms (Fungal pathogens, S. aureus, and Strep.Bovis). ❖ Incidence decreases significantly after initiation of effective Embolic antibiotics.	Includes: u dont have to memorize it استنتجها 1-Brain: Stroke 2-Heart : Myocardial infarction (Fragments of valvular vegetation or vegetation-induced stenosis of coronary ostia). 3- Lung / Pulmonary circulation: Hypoxia from septic pulmonary emboli. 4-Abdomen: Abdominal pain (splenic or renal infarction) 5-Extremities: Ischemic limbs 6- Eye: septic retinal embolus
Local spread of infection (inside the heart)	1- Heart failure due to extensive valvular damage. 2- 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. percentages not important 3-Pericarditis 4- Fistulous intracardiac connection Abnormal connection between one of the coronary arteries and a heart chamber or another blood vessel.	 Acute *S. aureus* IE with perforation of the aortic valve and aortic valve vegetations. 

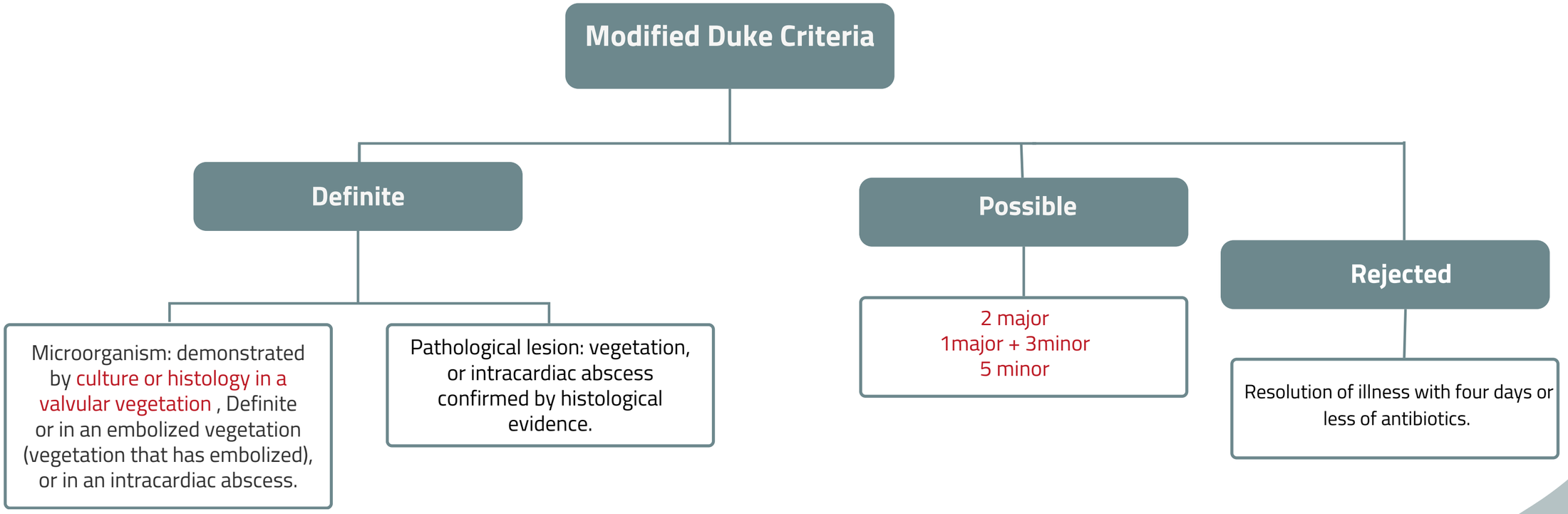


COMPLICATIONS (IMPORTANT)

Metastatic spread of infection	1-Metastatic abscess: Kidneys, spleen, brain, soft tissues Metastatic spread 2-Meningitis and/or encephalitis of infection 3-Vertebral osteomyelitis (especially staph aureus in older people) 4-Septic arthritis
Formation of immune complexes	(glomerulonephritis and arthritis)

MODIFIED 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.
➢ Proposed:2000, Addresses TEE, Broad “Possible categories.
➢ S.Aureus risks (13-25% S,Aureus Bacteremia have IE)



MODIFIED DUKE CRITERIA

Major Criteria	Minor Criteria
1-**Microbiological evidence: Positive blood culture (BC)** ‣ Typical organism from two separate blood cultures. ‣ with organisms that can cause IE (e.g.: s.aureus,s.viridans, Enterococci organisms) ‣ Persistently positive blood cultures. ‣Single positive blood culture for for Coxiella Burnetii, or titer greater than Major 1:800.	1-Predisposition: Predisposing to heart condition or IV drug use. 2- Fever greater than 38C. 3-Microbiological evidence: ‣ Positive blood culture but NOT meeting major criteria ‣ Serology test, single BC not CNS
2-Examination evidence / endocardial Involvement: New (not changed) murmur of Regurgitation.	4- Vascular phenomena: Includes: major arterial emboli (emboli travelling within the arterial circulation) causing: Mycotic aneurysm, Intracranial or conjunctival hemorrhages, Janeway lesions -More specific- Excludes : Petechiae(it's a vascular phenomena) , and Splinter Hemorrhages -Non specific-
3- Positive Echo: (Transesophageal echocardiography if prosthetic valve, complicated, or pretest probability possible IE)	5-Immunologic phenomena: ‣ Rheumatoid factor (RF). ‣ Roth's spots (retinal hemorrhage with pale center). ‣ Glomerulonephritis. ‣ Osler's nodes - Specific and painful-

TREATMENT OF I.E

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 (enough dosage) 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

1. Refractory CHF(mortality 56-86% w/o surgery vs 11-35%w/surgery)
2. Perivalvular invasive disease.
3. Recurrent systemic emboli, particularly in the presence of large vegetations
4. Uncontrolled infection on maximal medical therapy.
5. Some pathogens : Pseudomonas, brucella, coxiella, fungi, enterococci. (these always need surgery especially fungi) Pseudomonas & Brucella loves the Valve
6. Usually advised with combined therapy.

TREATMENT OF I.E

Staph aureus->cloxacillin
Strep-> penicillin

Valve	MSSA/MRSA	VGS,NVS, Streptococcus MIC (ug/ml)	HACEK	Bartonella	Q-fever
Native	Cloxacillin (or vancomycin 4-6 wk in case of MRSA) +/- gentX 3-5d	<0.1: PenicillinG or cephalosporin 4wk >0.1-0.5: PenicillinG 4wk + Gentamicin 2wk >0.5: PenicillinG or Ampicillin + Gentamicin for 4-6wk	Cephalosporin For 4wk	Aminoglycoside and flouroquinolones(or B–Lactam)	Doxycycline +or- Q-hydroxychloroquine 26 months untill the titer below 1:400
Prosthetic	Cloxacillin (or vancomycin 6 wk in case of MRSA) In addition to Gentamicin2wk & Rifampin 6wk	<0.1: PenicillinG 6wk + Gentamicin 2wk >0.1-0.5: PenicillinG 6wk + Gentamicin 4wk >0.5: Total 6wk	Cephalosporin For 6wk	-	35%surgical

TREATMENT CONT.. & PROPHYLAXIS

Prosthetic same as native valve endocarditis	
In case of prosthetic valve endocarditis, When do we need surgery? And when medical therapy alone is enough?	
Surgical intervention needed	❖ Perivalvular infection valve. ❖ Dehiscence, a surgical complication where the edges of a wound no longermeet. ❖ Excessively mobile prosthesis on echo results in is hemodynamic instability. ❖ S. aureus usually means surgery ❖ Relapse and recurrence after surgery about 7% in 6 years. S. aureus risk rate of death is 0.18 in (surgery + antibiotics) vs (antibiotics alone).
Medical treatment may Be sufficient (No surgery)	❖ 12 months or more post surgery. ❖ Viridans group streptococci (VGS) or HACEK or Enterococci. ❖ No perivalvular extension (the valve extend to the adjacent periannular areas and erode into nearby cardiac chambers)

TREATMENT CONT.. & PROPHYLAXIS

Prophylaxis	
Predisposing Cardiac Conditions	‣ Prosthetic cardiac valve or prosthetic material used for cardiac valve repair ‣Previous infective endocarditis (IE) ‣Congenital Heart Disease ‣ Cardiac Transplantation recipients ‣ Any Manipulation of gingival tissue, dental periapical regions, or performationg the oral mucosa.
Timing	One hour prior to procedure
Treatment	Amoxicillin->one gram or clindamycin

Q1:B
Q2:C
Q3:C

MCQs:

Q1/ which one of the following cardiac abnormalities have a high risk of IE?

A	mitral stenosis	B	aortic valve disease	C	atrial septal defect	D	mitral valve prolapse

Q2/ Which of the following signs is more specific for endocarditis?

A	splenomegaly	B	Splinter Hemorrhages	C	Janeway Lesions	D	Petechiae

Q3/ Infective Endocarditis is an infection of?

A	pericardium	B	myocardium	C	endocardium and heart valve	D	endocardium

Q4:A
Q5:D
Q6:A

MCQs:

Q4/ What is the drug of choice for staph.aureus?

A	cloxacillin	B	penicillin	C	gentamicin	D	doxycycline

Q5/ All are true about echocardiographic findings regarding infective endocarditis except:

A	Vegetations are seen on the valve	B	Abscess might be revealed	C	TEE is better than TTE	D	TTE is better than TEE

Q6/ Infective endocarditis is becoming a disease of the elderly, this mainly due to:

A	The decline of rheumatic heart disease	B	The increasing proportion of younger generations	C	The decreasing proportion of elderly	D	The increasing incidence of IV drug use

SAQs:

Q1/ what are the indications of surgery in the treatment of IE?

-significant valvular damage
-valve is prosthetic
-medically failing therapy

Q2/ A 63-year-old gentleman with a history of mitral valve prolapse presents to his internist with a 2-week history of fever, night sweats, and general malaise. Three weeks ago, he underwent periodontal surgery for gingival hyperplasia, for which he did not receive antibiotic prophylaxis. He denies a history of drug abuse. His physical exam is notable for a temperature of 39 deg C and a faint pansystolic murmur loudest at the cardiac apex. Splinter hemorrhages are seen under his nails.

A) Your diagnosis? Subacute endocarditis **B) What is the most likely causative organism in this case?** Strept. viridans **C) What are the specific signs that you will be looking for to confirm your diagnosis?** osler's nodes, janeway lesions, and roth spots **D) Your treatment plan?** depending on the MIC, Penicillin alone, Gentamicin will be added if the bacteria is less sensitive **E) What is the predisposing risk factor in this case?** Mitral valve prolapse **F) Briefly explain the pathogenesis of his condition.** endothelial injury (his mitral valve prolapse) followed by bacteremia, then adherence and finally invasion **G) Beside the physical examination, what are the test that you should ask for to confirm your diagnosis?** Minimum of 3 blood cultures, Echocardiography, Non-specific lab tests such as ESR, urinalysis.

Meet The Team :)

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