HKCC CORE CARDIOLOGY CERTIFICATE COURSE MODULE 3 (7 APRIL 2019)

INFECTIVE ENDOCARDITIS

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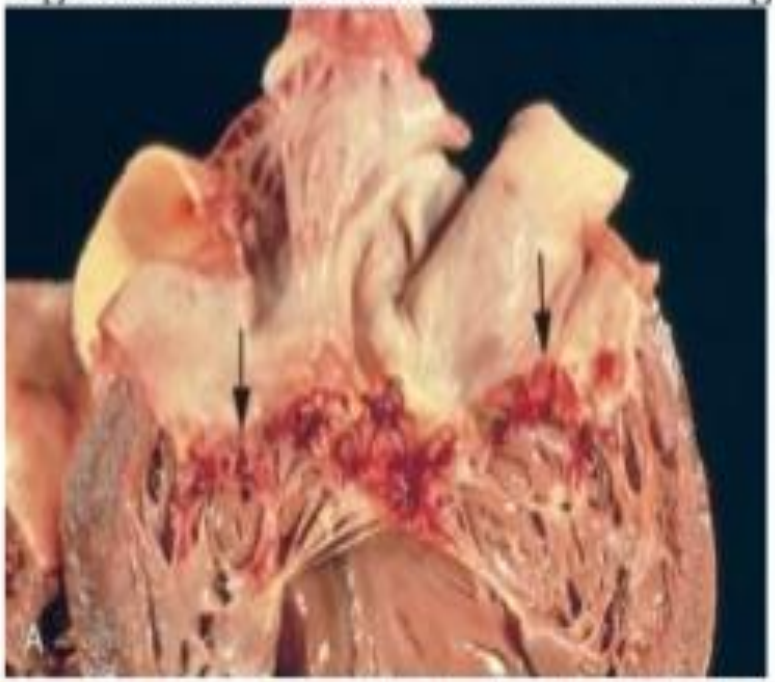
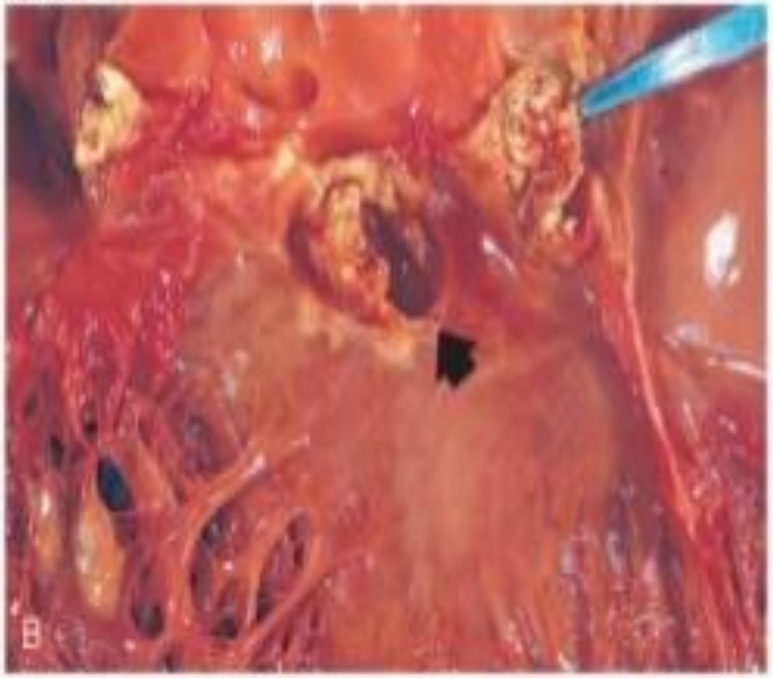
INFECTIVE ENDOCARDITIS

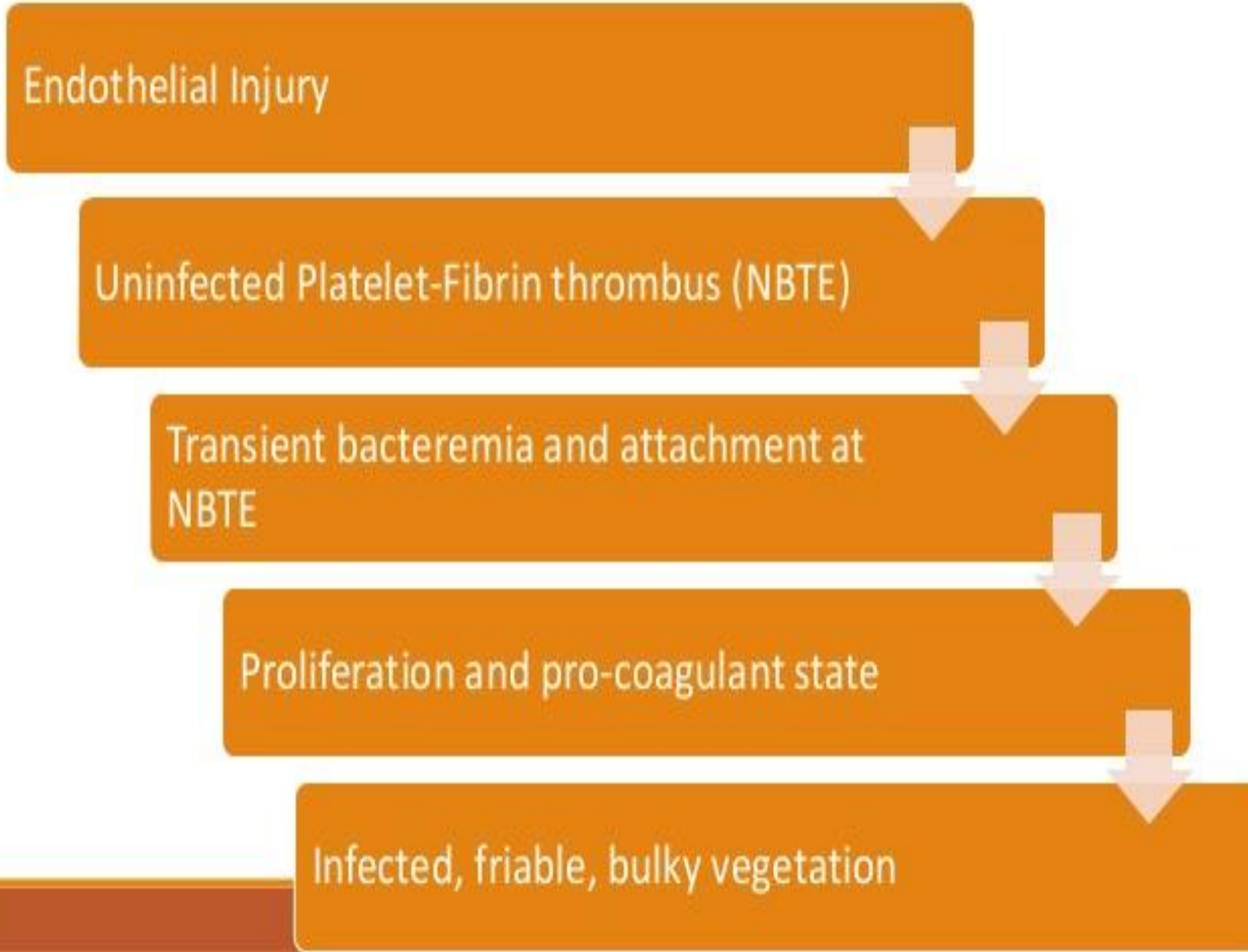
- Clinical Features
- Diagnosis & Common Errors
- Treatment: Choice of Antibiotics, Duration, Interval Assessment & Follow-up
- When is Urgent Surgery Indicated?
- Antibiotic Prophylaxis

Morphology

- Friable, bulky vegetation containing fibrin, inflammatory cells, and microbes
- Aortic and mitral valves involved most commonly.
- Right side valve involvement in iv drug users.






Endothelial Injury
Uninfected Platelet-Fibrin thrombus (NBTE)
Transient bacteremia and attachment at NBTE
Proliferation and pro-coagulant state
Infected, friable, bulky vegetation

NON-BACTERIAL THROMBOTIC ENDOCARDITIS

- Sterile vegetations consisting of fibrin and platelet aggregates on cardiac valves
- Neither bacteraemia nor with destructive changes of the underlying valve
- Associated with CTD, autoimmune disorders, hypercoagulable states, septicaemia, severe burns, tuberculosis, uraemia or AIDS
- A potentially life-threatening source of thromboembolism

CLASSIFICATION

ACUTE ENDOCARDITIS

- Destructive and stormy infection, frequently of a previously normal heart valve, with a highly virulent organism
- Haematogenoulsy seeds
- If untreated, leads to death within weeks

SUBACUTE ENDOCARDITIS

- Organisms of low virulence causing infection in a previously abnormal heart, particularly on deformed valves
- Disease appear insidiously and pursue a protracted course of weeks to month
- Recover after appropriate antibiotic treatment

INFECTION OF THE ENDOCARDIAL SURFACE

- Heart valves
- Septum defect
- Mural endocardium
- Intra-cardiac devices

  - INFECTIVE ENDARTERITIS - analogus

PREDISPOSING FACTORS

CARDIAC AND VASCULAR ABNORMALITIES

+ Rheumatic Heart Disease
+ Myxomatous mitral valve
+ Degenerative calcific valvular stenosis
+ Bicuspid aortic valves
+ Prosthetic valves

HOST FACTORS

+ Neutropenia
+ Immunodeficiency
+ Malignancy
+ Therapeutic immunosuppression
+ Diabetes mellitus
+ Alcohol
+ IV drug abuse

CLINICAL FEATURES

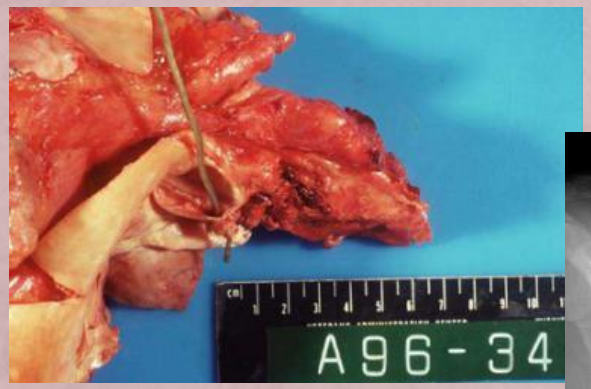
Symptoms

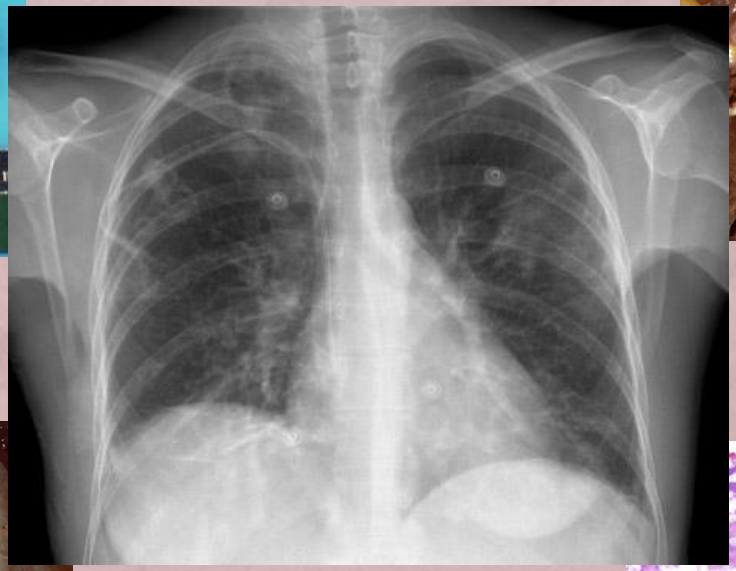
- Damage to intracardiac structures
- Embolization of vegetation fragments
- Haematogenous infection
- Immune complex

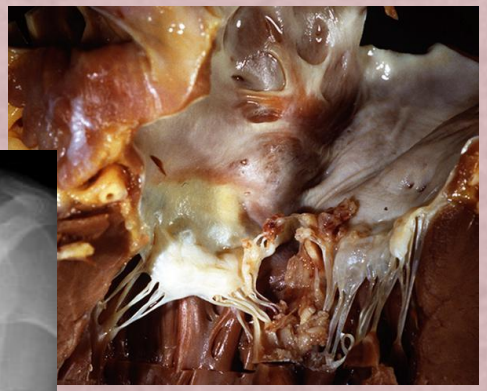
Constitutional symptoms

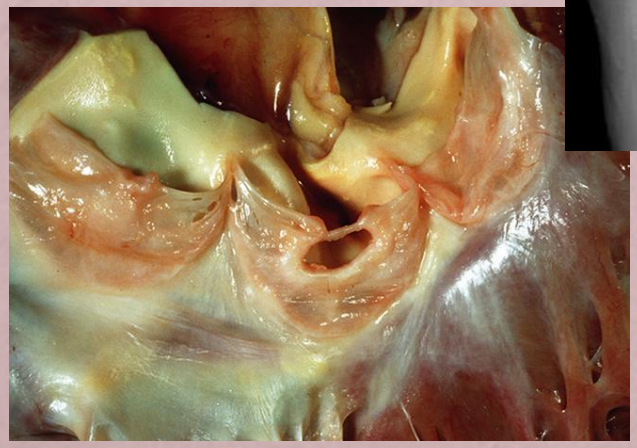
- Cytokine release?

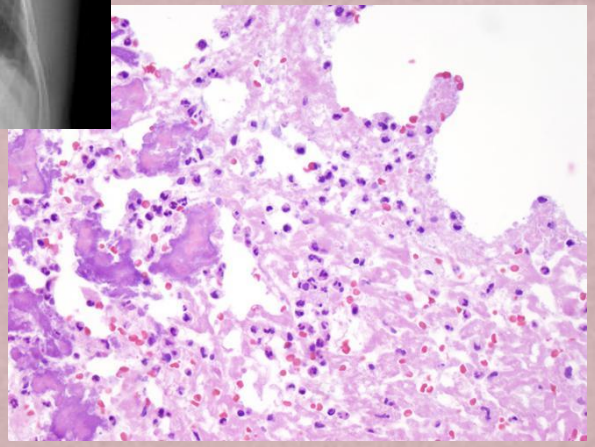
INFECTIVE ENDOCARDITIS

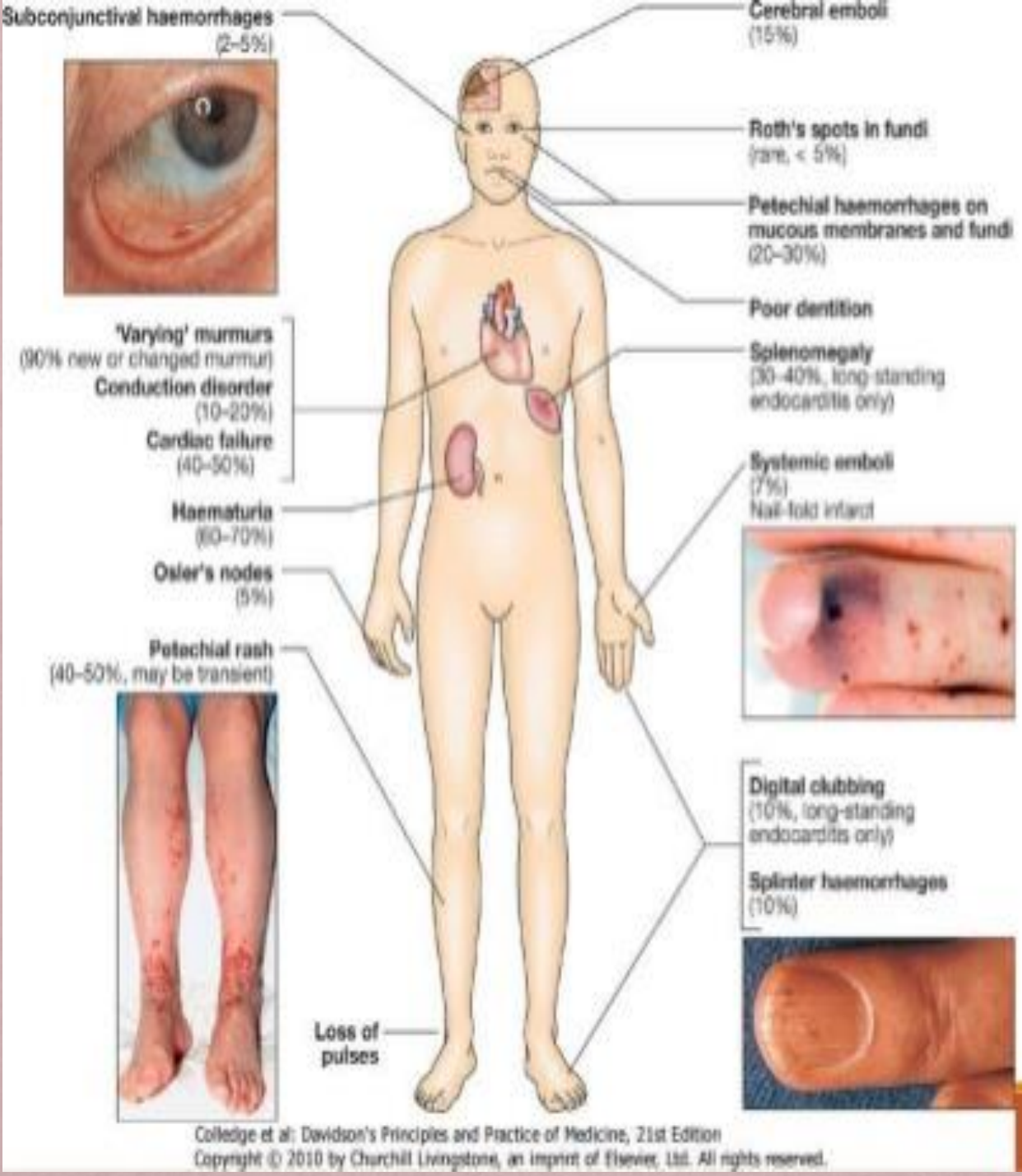










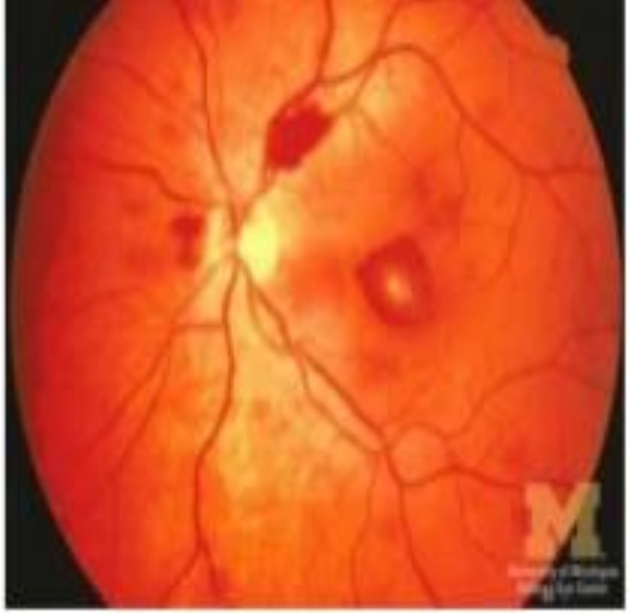


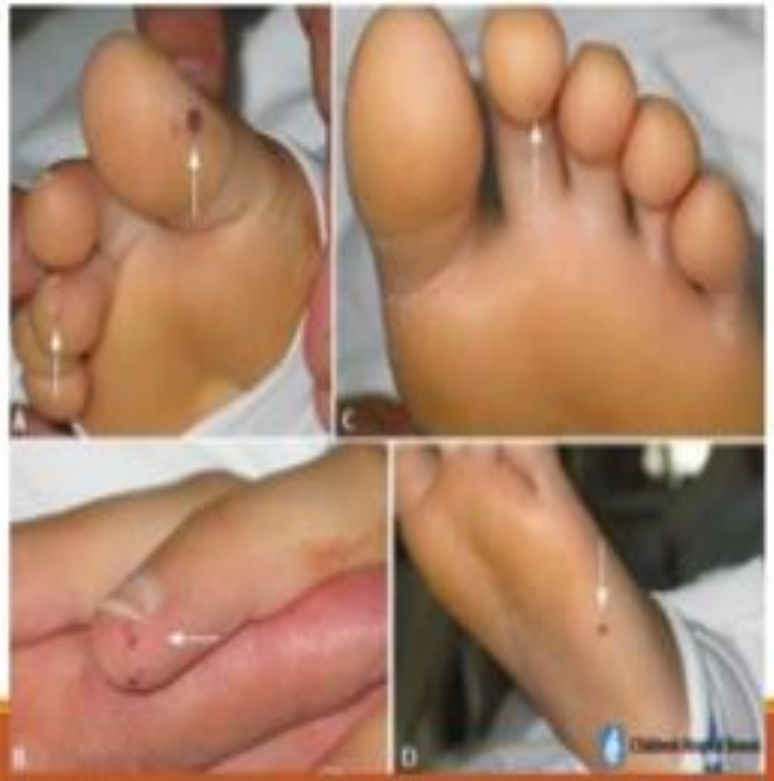
Sub-acute Endocarditis

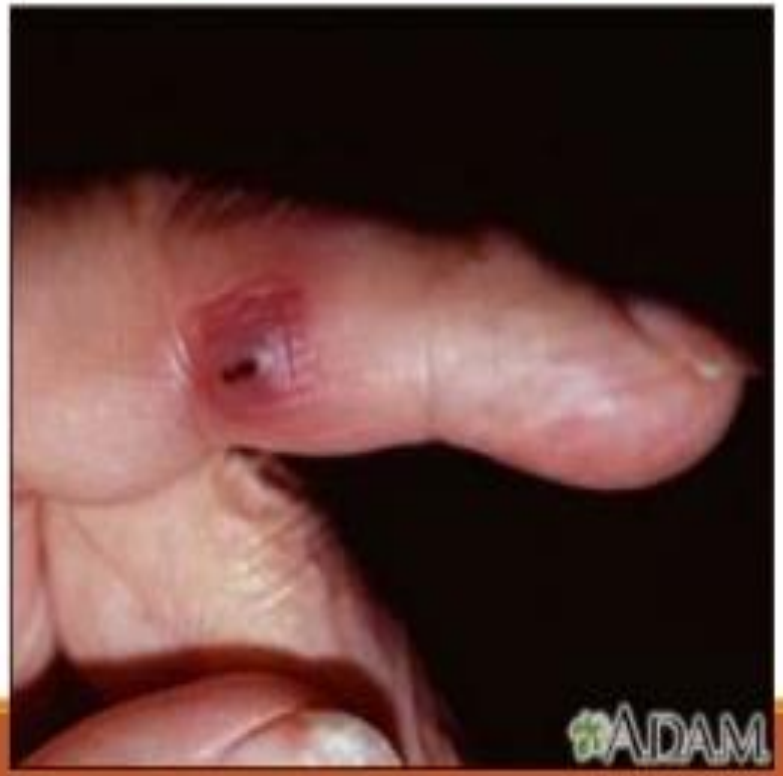
- Persistent fever
- Constitutional symptoms
- New signs of valve dysfunction
- Heart failure

- Embolic Stroke
- Peripheral arterial embolism

- Other features






A.D.A.M.

MODIFIED DUKE CRITERIA FOR DIAGNOSIS OF INFECTIVE ENDOCARDITIS

Definitive Endocarditis if,

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

Possible Endocarditis if,

- One major and one minor or,
- Three minor

MAJOR CRITERIA

Positive blood culture

- Typical organism from two cultures (viridians streptococci, streptococcus bovis, HACEK group, staphylococcus aureus, enterococci)
- Persistent positive blood cultures taken > 12 hours apart
- Three or more positive cultures taken over more than 1 hour
- Single positive blood culture for Coxiella burnetii or antiphase I IgG abtibody titre >1:800

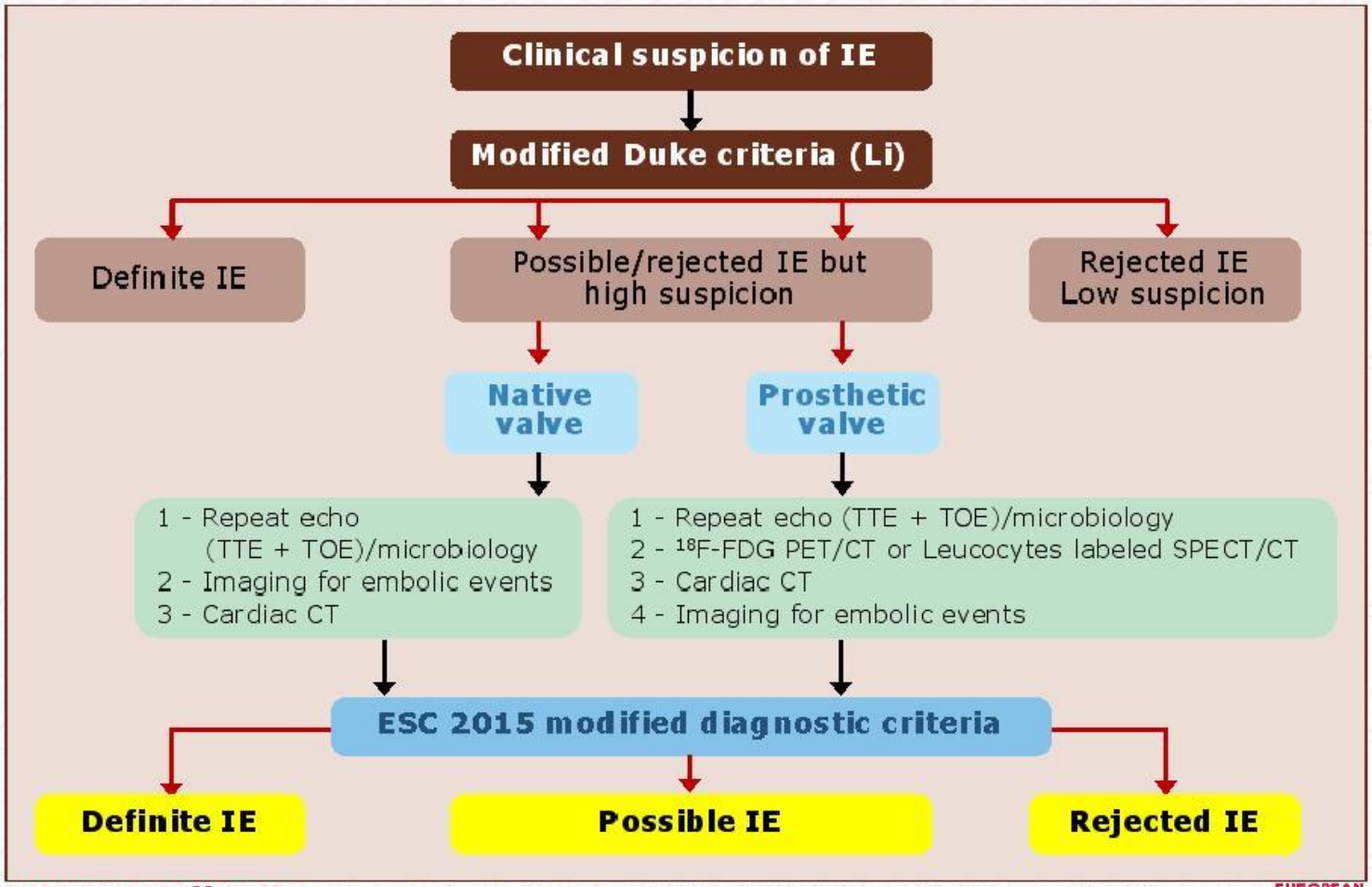
Endocardial involvement

- Positive echocardiographic findings of infective endocarditis: vegetation or abscess or new partial dehiscence of prosthetic valve
- New valvular regurgitation

MINOR CRITERIA

- Predisposition: Predisposing valvular or cardiac abnormality
- Intravenous drug misuse
- Pyrexia ≥ 38 °C (≥ 100.4°F)
- Embolic phenomenon
- Vasculitic (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages & Janeway's lesions) / immunologic phenomenon (glomerulonephritis, Osler's nodes, Roth Spots, and rheumatoid factor)
- Blood cultures suggestive: organism grown but not achieving major criteria or serological evidence of active infection

ESC 2015 algorithm for diagnosis of IE



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INVESTIGATIONS FOR IE

- Complete blood counts
  - May show anaemia and increased WBC counts.
- Urea and Creatinine:
  - May be elevated due to glomerulonephritis
- Liver biochemistry:
  - Serum alkaline phosphatase may be increased
- Inflammatory markers
  - CRP, ESR are increased in infection. CRP also helps in monitoring response to therapy.
- Urine
  - Proteinuria and haematuria occur frequently.

Microbiology

- Blood cultures:
  - Key diagnostic investigation in infective endocarditis.
  - Isolation of microorganism from culture is important for diagnosis and also for treatment.
  - As least 3 sets of samples should be taken from different venepuncture sites over 24 hours.

- Serology
  - Can be sent when the diagnosis is suspected and the cultures are negative
  - They aid in cases where the organisms will not grow in blood cultures (Coxiella, Legionella, Bartonella)
  - ECG

    To detect complications like MI, conduction abnormalities.
  - CHEST X RAY

- **Echocardiography**
  - It can identify the presence and size of vegetations, detect intracardiac complications and assess cardiac function.
  - Transthoracic echocardiography is noninvasive and has high specificity for visualizing vegetations.
  - Transoesophageal echocardiography is more sensitive than TTE. It can detect small vegetations, prosthetic endocarditis and intra cardiac complications.

ECHOCARDIOGRAPHIC PREDICTORS OF SYSTEMIC EMBOLIZATION IN PATIENTS OF IE

- Large valvular vegetations (>10mm in diameter)
- Multiple vegetations
- Mobile but pedunculated vegetations
- Non-calcified vegetations
- Vegetations that are increasing in size
- Prolapsing vegetations

PITFALLS IN DIAGNOSING IE

- Thrombotic nonbacterial endocarditis
- Vasculitis
- Temporal arteritis
- Marantic endocarditis – uninfected vegetations seen in patients with malignancy and chronic diseases
- Connective tissue disease e.g. Libman Sacks endocarditis – bland vegetations in SLE
- Fever of unknown origin (FUO)
- Intra-abdominal infections
- Septic pulmonary infarction
- Tricuspid regurgitation

DIFFERENTIAL DIAGNOSES

- Antiphopholipid Syndromes
- Atrial Myxoma
- Lyme Disease
- Systemic Lupus Erythematosus
- Polymyalgia Rheumatica
- Primary Cardiac Neoplasms
- Reactive Arthritis

COMPLICATIONS OF IE

- Myocardial infarction, pericarditis, cardiac arrhythmia
- Cardiac valvular insufficiency
- Congestive heart failure
- Sinus of Valsalva aneurysm
- Aortic root or myocardial abscesses
- Arterial emboli, infarcts, mycotic aneurysms
- Arthritis, myositis
- Glomerulonephritis, acute renal failure
- Stroke syndromes
- Mesenteric or splenic abscess or infarct

MICROBIOLOOGY

- Over ¾ cases – Streptococci or Staphylococci
- Streptococci
  - *viridans* group (Strep. mitis, Strep. sanguis) and Stept. pneumoniae and Strep. pyogenes
  - Commensal in upper respiratory tract
  - Chewing or teeth brushing, or dental treatment
  - Most common cause of subacute bacterial endcarditis
- Staphylococci – most common cause of acute bacterial endocarditis
  - Skin infection, abscesses or vascular access sites (e.g. iv and central lines)
  - Highly virulent and invasive organism

MICOBIOLOGY

- Enterococcus faecalis, E. faecium and Strep. Bovis – bowel or urinary tract
- Stept. Milleri and Strept. Bovis: large bowel neoplasms
- Staph. Epidermidis – coagulase – negative
  - Most causative agent for artificial valve
  - Normal skin commensal
  - Erroneously contamination
- Staph. Epidermidis & Staph. Lugdenensis – otherwise normal heart

MICROBIOLOGY

- ***Coxiella buretii*** – Q fever endocarditis
  - Farm animals
  - Hepatic complications and purpura
  - Life-long antibiotic therapy may be required
- ***HACEK*** group (*Haemophilus spp., Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenalla spp. & Kingella kingae*) Gram-negative bacteria
- ***Brucella*** – goats or cattle, often affects the aortic valve
- ***Yeasts and fungi (Candida, Aspergillus)***
  - Previously normal or prosthetic valve
  - Particularly in immunocompromised patient

MICROBIOLOGY

- Staphylococcus aureus (35%): Either healthy or deformed valves, IV drug abusers (polymicrobial), device
- Streptococcus viridans (32%): Native but previously damaged/abnormal valves
- Enterococci (8%)
- CoNS (Coagulase Negative Staphylococcus) – S. epidermidis (4%): Prosthetic valve endocarditis, devices
- G negative bacilli of HACEK group (4%)
- Yeast and Fungi (1%)
- Culture negative endocarditis (5%)

PATHOGENESIS

Portal of entry:

+ Dental / Surgical Procedures
+ Contamination by IV drug use
+ Obvious infections (Respiratory system/Skin)
+ Occult source from gut, oral cavity
+ Trivial injuries.
+ Intravascular catheter infection
+ Nosocomial wounds
+ Chronic invasive procedures

TREATMENT

Antimicrobial Therapy

Therapy requires identification of specific pathogen and its susceptibility to antimicrobials.

Empirical therapy should be started as soon as possible targeting most likely pathogens.

Bactericidal drugs should be used.

TREATMENT

Resolution of fever occurs in 5 to 7 days. If fever persists patient should be evaluated for complications like para-valvular abscess and extra-cardiac abscess.

Serologic abnormalities resolve slowly and do not reflect response to treatment.

MICROBIOLOGIC CURE RATE FOR ENDOCARDITIS

Native Valve Endocarditis	Antimicrobial therapy alone	Antimicrobial therapy plus Surgery
Virridan Streptococci, group A strep	98	98
Enterococcus	90	>90
S. aureus (young IVDU)	90	>90
S. aureus (elderly patients with underlying disease)	50	70
Gram negative aerobic bacilli	40	65
Fungus	<5	50

MICROBIOLOGIC CURE RATE FOR ENDOCARDITIS

Prosthetic Valve Endocarditis	Antimicrobial therapy alone		Antimicrobial therapy plus Surgery	
	Early PVE	Late PVE	Early PVE	Late PVE
Viridan streptococci, group A strep	NA	80	NA	90
Enterococcus	NA	60	NA	75
S. aureus	25	40	50	60
Coagulase negative staphylococcus	20	40	60	70
Gram negative aerobic bacilli	<10	20	40	50
Fungus	<1	<1	30	40

Antibiotic treatment
Oral *Streptococci* and *Streptococcus bovis* group

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Strains penicillin-susceptible (MIC ≤0.125 mg/L) oral and digestive streptococci				
Standard treatment: 4-week duration				
Penicillin G	12–18 million U/day i.v. either in 4–6 doses or continuously	4	I	B
	or			
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses	4	I	B
	or			
Ceftriaxone	2 g/day i.v. or i.m. in 1 dose	4	I	B
In beta-lactam allergic patients				
Vancomycin	30 mg/kg/day i.v. in 2 doses	4	I	C

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Antibiotic treatment
Oral *Streptococci* and *Streptococcus bovis* group

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Strains relatively resistant to penicillin (MIC 0.250–2 mg/l)				
Standard treatment				
Penicillin G	24 million U/day i.v. either in 4–6 doses or continuously	4	I	B
	or			
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses	4	I	B
	or			
Ceftriaxone	2 g/day i.v. or i.m. in 1 dose	4	I	B
	with			
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	B
In beta-lactam allergic patients				
Vancomycin	30 mg/kg/day i.v. in 2 doses	4	I	C
	with			
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	C

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Antibiotic treatment
Staphylococcus spp. Native valves

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Native valves				
Methicillin-susceptible staphylococci				
(Flu)cloxacillin or oxacillin	12 g/day i.v. in 4–6 doses	4–6	I	B
Alternative therapy				
Cotrimoxazole WITH Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses) 1800 mg/day IV in 3 doses	1 i.v. + 5 oral intake 1	IIb	C
Penicillin-allergic patients or methicillin-resistant staphylococci				
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses	4–6	I	B
Alternative therapy				
Daptomycin	10 mg/kg/day i.v. once daily	4–6	IIa	C
Alternative therapy				
Cotrimoxazole WITH Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses) 1800 mg/day IV in 3 doses	1 i.v. + 5 oral intake 1	IIb	C

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Antibiotic treatment
Staphylococcus spp. Prosthetic valves

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Prosthetic valves				
Methicillin-susceptible staphylococci				
(Flu) cloxacillin or oxacillin	12 g/day i.v. in 4–6 doses	≥6	I	B
WITH Rifampin	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥6		
AND Gentamicin	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2		
Penicillin-allergic patients and methicillin-resistant staphylococci				
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses	≥6	I	B
WITH Rifampin	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥6		
AND Gentamicin	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2		

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Antibiotic treatment
Enterococcus spp.

Antibiotic	Dosage and route	Duration weeks	Class	Level
Beta-lactam and gentamicin-susceptible strains				
Amoxicillin *with* Gentamicin	200 mg/kg/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 1 dose	4–6 2–6	I	B
	or			
Ampicillin *with* Ceftriaxone	200 mg/kg/day i.v. in 4–6 doses 4 g/day i.v. or i.m. in 2 doses	6 6	I	B
	or			
Vancomycin *with* Gentamicin	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 1 dose	6 6	I	C

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e 19 Antibiotic treatment of blood culture-negative infective endocarditis (adapted from Brouqui et al.[19]

Pathogens	Proposed therapy[a]	Treatment outcome
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600/24 h) for ≥3–6 months[b] orally	Treatment success defined as an antibody titre <1:60. Some authors recommend adding gentamicin for the first 3 weeks.
C. burnetii (agent of Q fever)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:200, and IgA and IgM titres <1:50.
Bartonella spp.[d]	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%.
Legionella spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) i.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown.
Mycoplasma spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 months[e]	Optimal treatment unknown.
T. whipplei (agent of Whipple's disease)[f]	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally for ≥18 months	Long-term treatment, optimal duration unknown.

Antibiotic therapy
Empirical treatment

Antibiotic	Dosage and route	Class	Level
Community-acquired NVE or late PVE (≥12 months post surgery)			
Ampicillin WITH (Flu)cloxacillin or oxacillin WITH Gentamicin	12 g/day i.v. in 4–6 doses 12 g/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 1 dose	IIa	C
Vancomycin WITH Gentamicin	30–60 mg/kg/day i.v. in 2–3 doses 3 mg/kg/day i.v. or i.m. in 1 dose	IIb	C
Early PVE (<12 months post surgery) or nosocomial and non-nosocomial healthcare associated endocarditis			
Vancomycin WITH Gentamicin WITH Rifampin	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 1 dose 900–1200 mg i.v. or orally in 2 or 3 divided doses	IIb	C

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SURGERY - INDICATIONS

- ✓ Patients with direct extension of infection to myocardial structures
- ✓ Prosthetic valve dysfunction
- ✓ Congestive heart failure
- ✓ Badly damaged valves
- ✓ IE caused by fungi or gram -ve or resistant organisms
- ✓ Large vegetations on echocardiography
- ✓ Recurrent embolic attacks

SURGICAL TREATMENT OF INTRA-CARDIAC COMPLICATIONS

- Unavailable effective antimicrobial therapy
  - 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
  - Peri-valvular 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

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

Indications and timing of surgery

Indications for surgery	Timing	Class	Level
1. Heart Failure			
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.	Urgent	I	B
2. Uncontrolled infection			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation).	Urgent	I	B
Infection caused by fungi or multiresistant organisms.	Urgent/elective	I	C
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci.	Urgent	IIa	B
PVE caused by staphylococci or non-HACEK Gram negative bacteria.	Urgent/elective	IIa	C
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episode despite appropriate antibiotic therapy.	Urgent	I	B
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk.	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm).	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery.	Urgent	IIb	C

RELAPSE & REINFECTION

- The actual risk of recurrence among survivors of IE – between 2% and 6%
- Two main types of recurrence are distinguishable: relapse and reinfection.
- ‘relapse’ refers to a repeat episode of IE caused by the same microorganism (molecular methods including strain-typing techniques)
- ‘reinfection’ describes an infection caused by a different microorganism
- the timing of the second episode of IE may also be used to distinguish relapse from reinfection
- Generally speaking, a recurrence caused by the same species within 6 months following the initial infection represents relapse, whereas later events suggest reinfection

FACTORS FOR RELAPSE

- Inadequate antibiotic treatment (agent, dose, duration)
- Resistant microorganisms, i.e. *Brucella spp.*, *Legionella spp.*, *Chlamydia spp.*, *Mycoplasma spp.*, *Mycobacterium spp.*, *Bartonella spp.*, *Coxiella Burnetii*, *fungi*
- Polymicrobial infection in an IVDA
- Empirical antimicrobial therapy for BCNIE
- Periannular extension
- Prosthetic valve IE
- Persistent metastatic foci of infection (abscesses)
- Resistance to conventional antibiotic regimens
- Positive valve culture
- Persistence of fever at the seventh postoperative day
- Chronic dialysis

FOLLOW UP OF IE

- Clinical follow-up should be done by the Endocarditis Team or by a Heart Valve Clinic specialist. Regular clinical and echocardiographic follow-up should be performed during the first year following completion of treatment.
- ESC 2015 Task Force also recommends to take blood samples (i.e. white cell count, CRP, etc.), and blood cultures systematically at the initial follow up visit, and otherwise if there is clinical suspicion.

PREVENTION

- Prophylactic regimen targeted against likely organism
  - Strep. viridans – oral, respiratory, oesophogeal
  - Enterococcus – genitourinary, gastrointestinal
  - S. aureus – infected skin, mucosal surfaces

ANTIBIOTIC PROPHYLAXIS

Prophylaxis

High risk category

- ✓ Prosthetic cardiac valves
- ✓ Previous bacterial endocarditis, even in absence of heart disease
- ✓ Complex cyanotic congenital heart disease (TGA, TOF)
- ✓ Surgically constructed systemic pulmonary shunts

Cardiac conditions at highest risk of IE

Recommendations	Class	Level
Antibiotic prophylaxis should only be considered for patients at highest risk of IE: 1. Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair. 2. Patients with previous IE. 3. Patients with congenital heart disease. a. Any cyanotic congenital heart disease. b. Any type of congenital heart disease repaired with a prosthetic material whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.	IIa	C
Antibiotic prophylaxis is not recommended in other forms of valvular or congenital heart disease.	III	C

European Heart Journal (2015);36:3075-3123 - doi:10.1093/eurheartj/ehv319

ESC 2015 GUIDELINES ON IE

- Antibiotic prophylaxis is not recommended for patients at intermediate risk of IE, i.e. any other form of native valve disease (including the most commonly identified conditions: bicuspid aortic valve, mitral valve prolapse and calcific aortic stenosis)
- Both intermediate- and high- risk patients should be advised of the importance of dental and cutaneous hygiene

PREVENTION – THE PROCEDURE

- Dental procedures known to produce bleeding
- Tonsillectomy
- Surgery involving GI, respiratory mucosa
- Esophageal dilation
- ERCP for obstruction
- Gallbladder surgery
- Cystoscopy, urethral dilation
- Urethral catheter if infection present
- Urinary tract surgery, including prostate
- I&D of infected tissue

Procedures at highest-risk of IE

Recommendations	Class	Level
A. Dental procedures • Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.	IIa	C
• Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces, or following the shedding of deciduous teeth or trauma to the lips and oral mucosa.	III	C
B. Respiratory tract procedures • Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, transnasal or endotracheal intubation.	III	C
C. Gastrointestinal or urogenital procedures or TOE • Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE.	III	C
D. Skin and soft tissues procedures • Antibiotic prophylaxis is not recommended for any procedure.	III	C

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ESC 2015 GUIDELINE ON IE

- Dental procedure – antibiotic prophylaxis recommended for at risk procedures involve manipulation of the gingival or periapical region of the teeth of perforation of the oral mucosa(including scaling and root canal procedures)
- Other at risk procedures – no compelling evidence that bacteraemia resulting from respiratory tract procedures, gastrointesinal or genitourinary procedures, including vaginal and caesarean delivery, or dermatological or musculoskeletal procedures cause IE

Prophylaxis for dental procedures at risk

Situation	Antibiotic	Single-dose 30–60 minutes before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or Ampicillin[a]	2 g orally or i.v.	50 mg/kg orally or i.v.
Allergy to penicillin or ampicillin	Clindamycin	600 mg orally or i.v.	20 mg/kg orally or i.v.

[a]Alternatively, cephalexin 2 g i.v. for adults or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.

"Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin or ampicillin due to cross-sensitivity".

European Heart Journal (2015);36:3075-3123 - doi:10.1093/eurheartj/ehv319

ESC 2015 - PROPHYLAXIS FOR NON-DENTAL PROCEDURES

Systemic antibiotic prophylaxis is not recommended for non-dental procedures, antibiotic therapy is only needed when invasive procedures are performed in the context of infection for high risk patients

A. Respiratory tract procedures – patients undergo an invasive respiratory tract procedure to treat established infection (i.e. drainage of an abscess) should receive antibiotic regimen containing an anti-staphylcoccal drug

B. Gastrointestinal or genitourinary procedures – in the case of an established infection or if antibiotic therapy is indicated to prevent wound infection or sepsis associated with a GI or GU procedures. Regimen should include an agent active vs enterococci (i.e. ampicillin, amoxicillin or vancomycin; only in patients unable to tolerate beta-lactams)

C. Dermatological or musculoskeletal procedures – for high risk patients undergoing surgical procedures involving infected skin(including oral abscesses), skin structure or musculoskeletal tissue, it is reasonable that the therapeutic regimen contains an agent active vs staphylococcal and beta-haemolytic streptococci

2017 AMERICAN HEART ASSOCIATION AND AMERICAN COLLEGE OF CARDIOLOGY FOCUSED UPDATE OF THE 2014 AHA/ADA GUIDELINE FOR MANAGEMENT OF PATIENTS WITH VALVULAR DISEASE

Antibiotic prophylaxis is reasonable for the subset of patients at increased risk of developing IE and at high risk of experiencing adverse outcomes from IE for the following:

1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts
2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords
3. Previous infective endocarditis
4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device
5. Cardiac transplant with valve regurgitation due to a structurally abnormal valve

Main principles of prevention in IE

1. The principle of antibiotic prophylaxis when performing procedures at risk of IE in patients with predisposing cardiac conditions is maintained.
2. Antibiotic prophylaxis must be limited to patients with the highest risk of IE undergoing the highest risk dental procedures.
3. Good oral hygiene and regular dental review are more important than antibiotic prophylaxis to reduce the risk of IE.
4. Aseptic measures are mandatory during venous catheter manipulation and during any invasive procedures in order to reduce the rate of health care-associated IE.
5. Whether the reduced use of antibiotic prophylaxis is really associated with a change in the incidence of IE needs further investigations

European Heart Journal (2015);36:3075-3123 - doi:10.1093/eurheartj/ehv319

The « Endocarditis team »

- **Characteristics of the reference centre**

1. Immediate access to diagnostic procedures should be possible, including TTE, TOE, multislice CT, MRI, and nuclear imaging.
2. Immediate access to cardiac surgery should be possible during the early stage of the disease, particularly in case of complicated IE
3. Several specialists should be present on site (the "Endocarditis Team"), including at least cardiac surgeons, cardiologists, anaesthesiologists, ID specialists, microbiologists and, when available, specialists in valve diseases, CHD, pacemaker extraction, echocardiography and other cardiac imaging techniques, neurologists, and facilities for neurosurgery and interventional neuroradiology.

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The « Endocarditis team »

Recommendations	Class	Level
Patients with complicated IE should be evaluated and managed at an early stage in a reference centre, with immediate surgical facilities and the presence of a multidisciplinary "Endocarditis Team", including an ID specialist, a microbiologist, a cardiologist, imaging specialists, a cardiac surgeon, and, if needed a specialist in CHD.	IIa	B
For patients with non-complicated IE managed in a non-reference centre, early and regular communication with the reference centre and, when needed, with visit to the reference centre, should be made.	IIa	B

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Cardiac device-related infective endocarditis (CDRIE)

Recommendations	Class	Level
A. Diagnosis		
1. Three or more sets of blood cultures are recommended before prompt initiation of antimicrobial therapy for CIED infection.	I	C
2. Lead-tip culture is indicated when the CIED is explanted.	I	C
3. TOE is recommended in patients with suspected CDRIE with positive or negative blood cultures, independent of the results of TTE, to evaluate lead-related endocarditis and heart valve infection	I	C
4. Intracardiac echocardiography may be considered in patients with suspected CDRIE, positive blood cultures and negative TTE and TOE.	IIb	C
5. Radiolabelled leukocyte scintigraphy and ^{18}F-FDG PET/CT scanning may be considered additive tools in patients with suspected CDRIE, positive blood cultures, and negative echocardiography.	IIb	C

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Cardiac device-related infective endocarditis (CDRIE)

Recommendations	Class	Level
B. Principles of treatment		
1. Prolonged (i.e. before and after extraction) antibiotic therapy and complete hardware (device and leads) removal are recommended in definite CDRIE, as well as in presumably isolated pocket infection.	I	C
2. Complete hardware removal should be considered on the basis of occult infection without other apparent source of infection.	IIa	C
3. In patients with NVE or PVE and an intracardiac device with no evidence of associated device infection, complete hardware extraction may be considered.	IIb	C
C. Mode of device removal		
1. Percutaneous extraction is recommended in most patients with CDRIE, even those with vegetations >10 mm.	I	B
2. Surgical extraction should be considered if percutaneous extraction is incomplete or impossible or when there is associated severe destructive tricuspid IE.	IIa	C
3. Surgical extraction may be considered in patients with large vegetations (>20 mm).	IIb	C

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Cardiac device-related infective endocarditis (CDRIE)

Recommendations	Class	Level
D. Reimplantation		
1. After device extraction, reassessment of the need for reimplantation is recommended.	I	C
2. When indicated, definite reimplantation should be postponed if possible to allow a few days or weeks of antibiotic therapy.	IIa	C
3. A "temporary" ipsilateral active fixation strategy may be considered in PM-dependent patients requiring appropriate antibiotic treatment before reimplantation.	IIb	C
4. Temporary pacing is not routinely recommended.	III	C
E. Prophylaxis		
1. Routine antibiotic prophylaxis is recommended before device implantation.	I	B
2. Potential sources of sepsis should be eliminated ≥2 weeks before implantation of a intravascular/cardiac foreign material, except in urgent procedures.	IIa	C

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Right-sided infective endocarditis

Recommendations	Class	Level
Surgical treatment should be considered in the following scenarios: • Microorganisms difficult to eradicate (e.g. persistent *fungi*) or bacteraemia for >7 days (e.g. *Staphylococcus aureus, P. aeruginosa*) despite adequate antimicrobial therapy or • Persistent tricuspid valve vegetations >20 mm after recurrent pulmonary emboli with or without concomitant right heart failure or • Right HF secondary to severe tricuspid regurgitation with poor response to diuretic therapy.	IIa	C

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Anti-thrombotic therapy in IE

Recommendations	Class	Level
Interruption of antiplatelet therapy is recommended in the presence of major bleeding.	I	B
In intracranial haemorrhage, interruption of all anticoagulation is recommended.	I	C
In ischaemic stroke without haemorrhage, replacement of oral anticoagulant (anti-vitamin K) therapy by unfractionated or low-molecular-weight heparin for 1–2 weeks should be considered under close monitoring.	IIa	C
In patients with intracranial haemorrhage and a mechanical valve, unfractionated or low-molecular-weight heparin should be reinitiated as soon as possible following multidisciplinary discussion.	IIa	C
In the absence of stroke, replacement of oral anticoagulant therapy by unfractionated or low-molecular-weight heparin for 1–2 weeks should be considered in case of *Staphylococcus aureus* IE under close monitoring.	IIa	C
Thrombolytic therapy is not recommended in patients with IE.	III	C

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CASE STUDY – CHUNG SY F/44

Lower limb petechial rash x 2/52 Jan 2019

High fever, CBP – Hb 6.6, WCC 8.0

CXR – radio-opacity L peritracheal region

Urine multistix – RBC +++

TTE 1/2019 – vegetation over mitral valve 1x0.7cm

TEE 1/2019 – vegetation on AMVL 1.2x0.9cm, flail PMVL, severe MR

Blood culture – Strep. gordoni, MIC 0.03

Bone marrow – normal

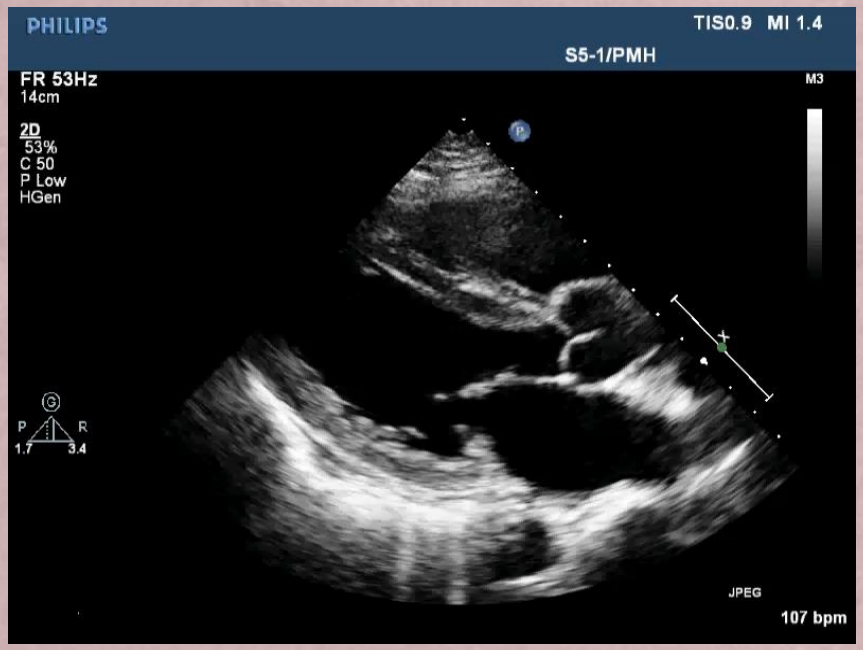
PET-CT hyper-metabolic focus in right buttock but not found by sonography

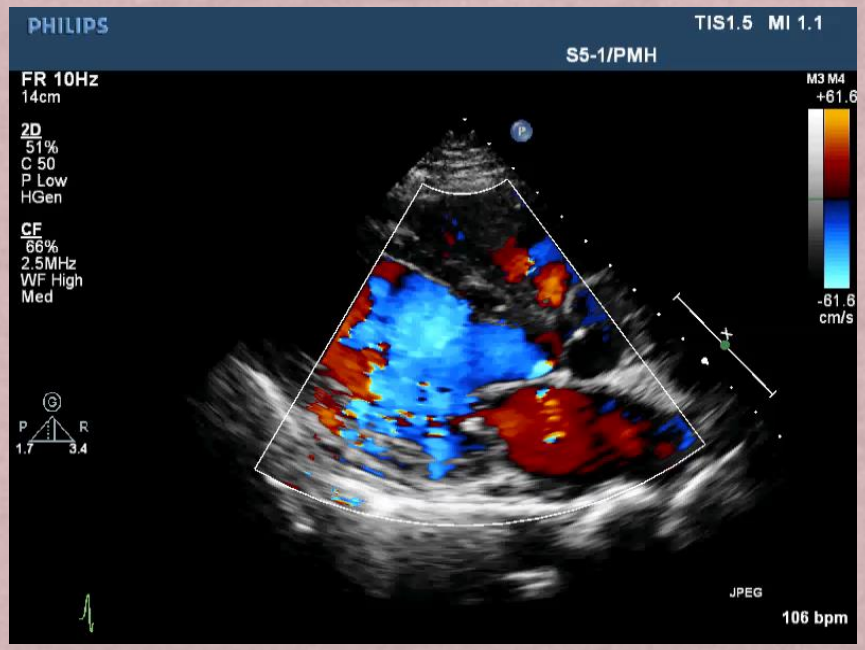
Treated with Penicilln G 4MU Q6H for 4 weeks

Repeat echo 2/2019 and 3/2019 – still severe MR

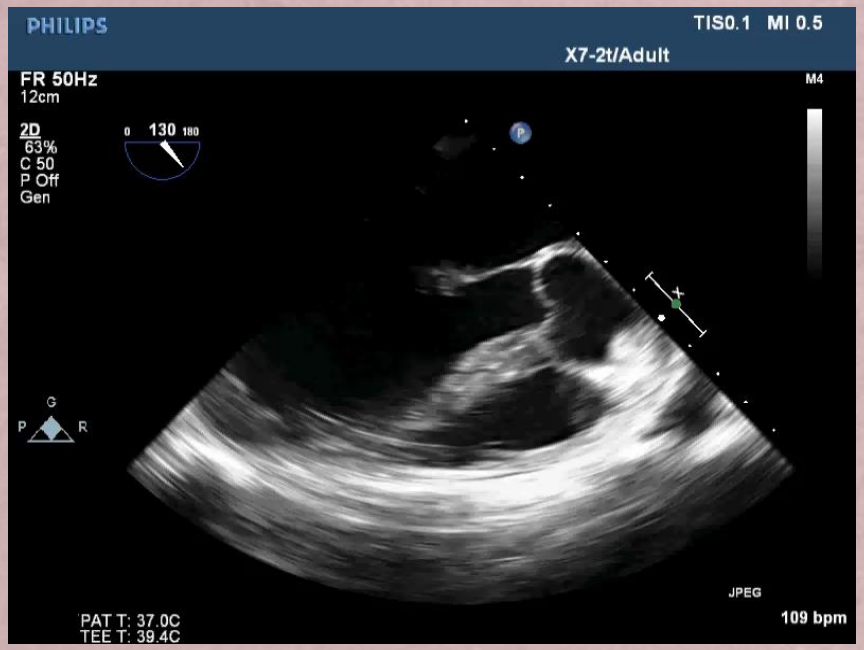
Refer CTS for MVR, coronary angiogram normal

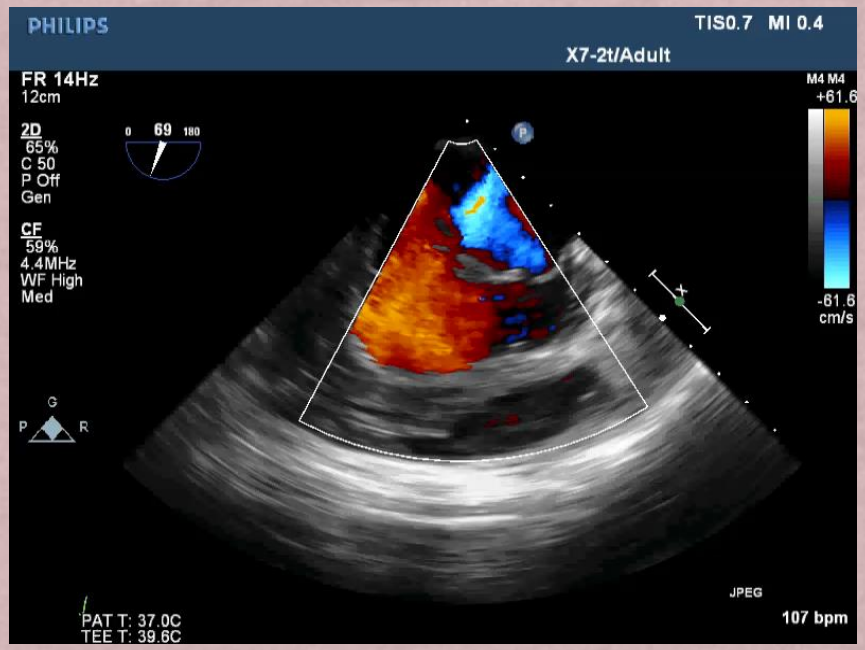
CASE STUDY – CHUNG SY F/44 (TTE)





CASE STUDY – CHUNG SY F/44 (TEE)





CASE STUDY – LAW Y L M/38

IgA nephropathy CRT 2011 and 7/2018 in mainland China with HD in between transplant

Hypertension/hyperlipidaemia

AF on apixaban

cardiac arrest at OPD visit Nov 2018, resuscitated VT and subsequently found to have tricuspid IE complicated by CHB, given tazocin, gentamycin, vancomycin and Valganciclovir,

Echo – huge tricuspid vegetation, refer QEH CTS for valvular replacement x suspected fungal endocarditis

Bradycardia induced Torsade - temporary transvenous pacing in QEH CCU

Renal consulted for immunosuppressant adjustment

Blood x beta-D-Glucan positive and titre > 500pg/ml, CMV pp65 negative

ID team –Ceftaroline and Micafungin

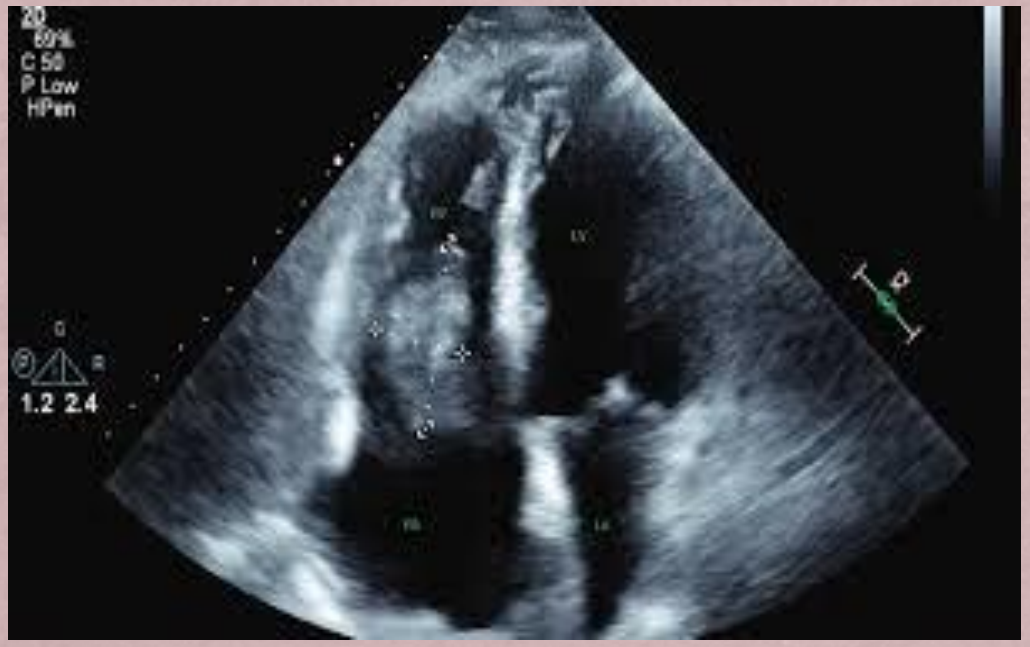
Sudden L parietal ICH with haematoma expansion

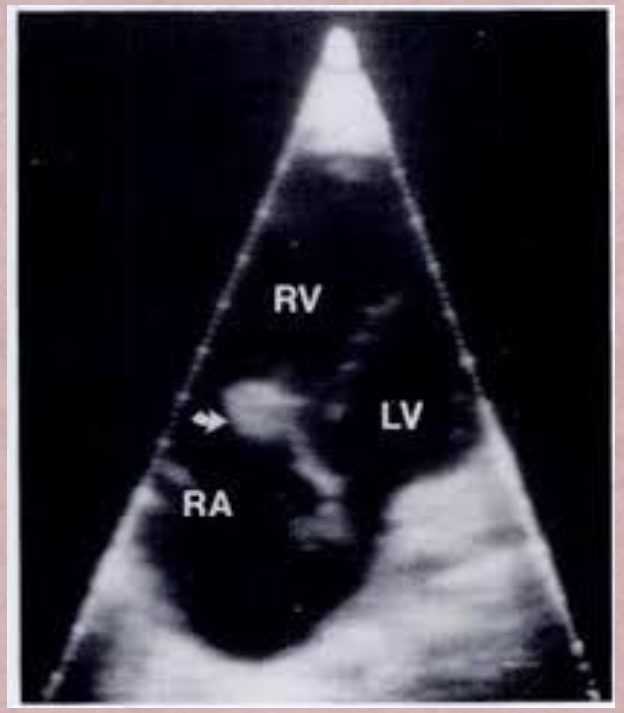
ID team started liposomal amphotericin B

Condition deteriorated with GCS drop and septic shock

Neurosurgical – not for intervention, succumbed early Dec 2018

FUNGAL ENDOCARDITIS



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