INFECTIVE ENDOCARDITIS

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EPIDEMIOLOGY

- IE is a relatively rare but serious disease with high mortality despite the improvement in dg. and th.
- Estimated annual incidence 3-10/100 000
- The profile of patients and pathogens has changed over time (rheumatic fever x PM/ICD)
- Predisposing factors:
  - prosthetic valves
  - elderly patients with degenerated valves
  - i.v. drug users
  - i.v. catheters, pacemaker electrodes

Untreated IE – 100 % fatal!

CLASSIFICATION

- **NVE** - native valve endocarditis
- **PVE** - prosthetic valve endocarditis
- **IVDU** - intravenous drug users
- IE on **PM / ICD** electrodes

CLASSIFICATION

- **Relapse** - repeat IE within 6 months and proven identical pathogen
- **Reinfection, -** new microorganism, or the same species but > 6 months
- **Early PVE** - within 1 year (usually aggressive nosocomial infection of sewing material)
- **Late PVE** - > 1 year after surgery/implantation

Relapse - suggests an incompletely treated primary episode that results in the emergence of the original microorganism from a protected source (such as deep-tissue infection or seeded prosthetic hardware)

"reinfection" is primarily used to describe infection with a new microorganism episode of IE caused by the same species within 6 months after the initial episode represents a **relapse**, whereas IE caused by the same species >6 months after treatment of the initial episode represents **reinfection** (historically referred to as "recurrent IE")

PATHOPHYSIOLOGY

- IE is rare in healthy individuals despite common bacteremia (dental procedures, toothbrushing…)

x

- Any injury to endocardial surface (degenerative changes, impact of catheters, electrodes, prosthetic materials…) → endocardial damage, exposing EC matrix → factor III, platelet activation, fibrin-platelet (sterile) vegetation → increase risk of bacterial seeding

NVE

- **Rheumatic valvular disease** – usually mitral valve followed by the aortic valve
- **Congenital heart disease -** patent ductus arteriosus, ventricular septal defect, tetralogy of Fallot (TOF), *any native or surgical high-flow lesion*
- **Mitral valve prolapse with MR**
- **Degenerative heart disease**
  - aortic stenosis in elderly ,bicuspid valve, Marfan syndrome
  - mitral regurgitation

CLINICAL PRESENTATION

- **Variable!**
- Fever (95%), signs of systemic disease (nausea, weight loss….)
- Heart murmur (85%)
- Septic embolization (20-50%)
  - brain, kidneys, spleen
  - pulmonary
- Peripheral microembolization less common

DIAGNOSTIC TESTING

Blood cultures

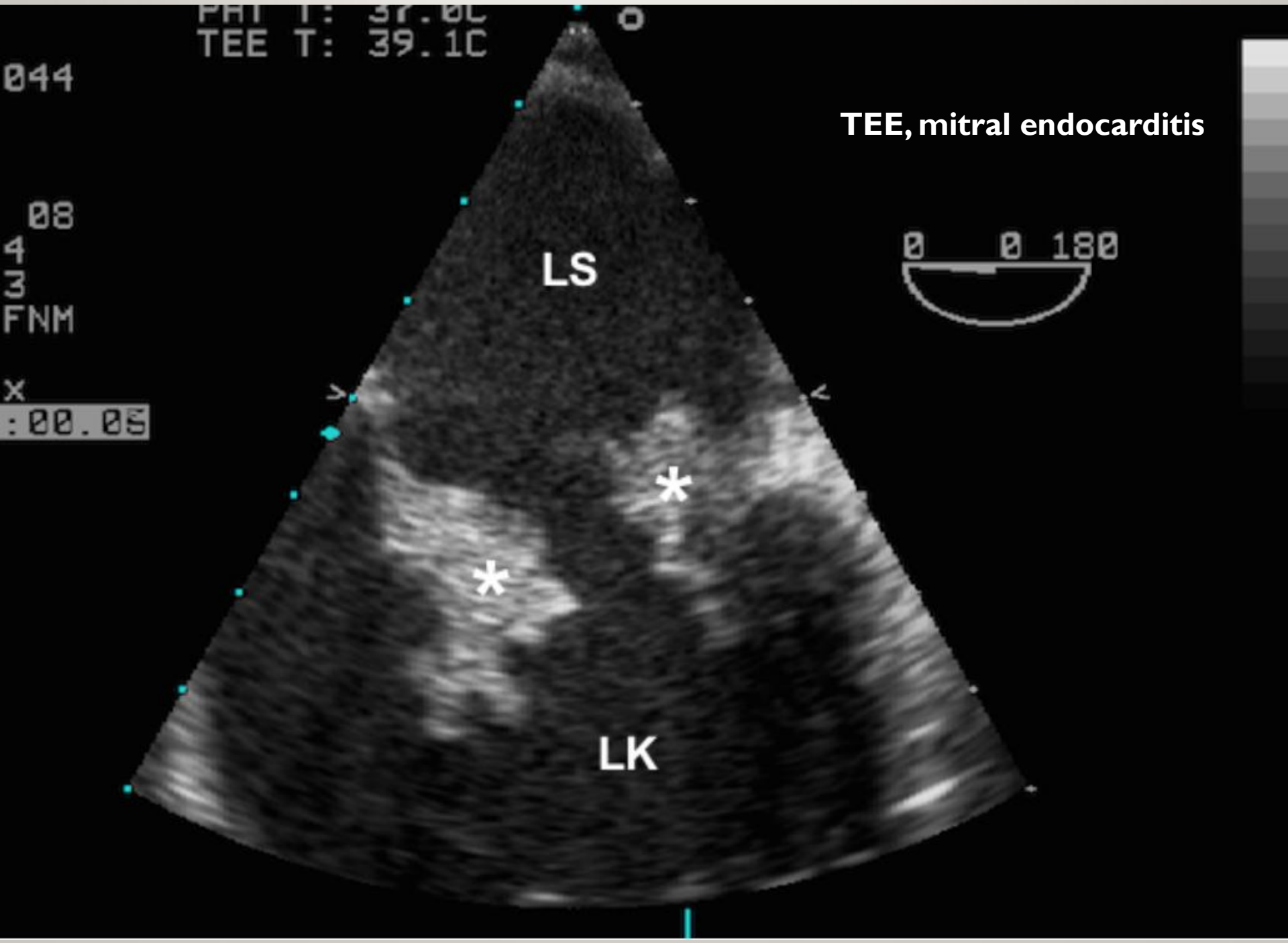
- 3 sets (aero + anaerobe) at different times + from diff. sites
- 85-90% - **streptococci, staphylococci, enterococci**
- 10% culture negative
  - (usually due to previous ATB th.)
  - less commonly HACEK (*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)*
  - Fungi – Candida, Aspergillus
  - Intracellular pathogens: Coxiella, Bartonella

85-90% known from first 2 sets

DIAGNOSTIC TESTING

Echocardiography

- TTE - low sensitivity (40-60%)
- TEE - sensitivity 90 - 100%
- vegetations / abscess / new prosthetic valve dehiscence = specific
- new regurgitation / obstruction


TEE T: 39.1C
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3
FNM
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0 0 180
LS
LK
TEE, mitral endocarditis

DUKE CRITERIA
(IE PROBABILITY)

Definite IE

Pathological criteria

- Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

Clinical criteria

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

Possible IE

- 1 major criterion and 1 minor criterion; or
- 3 minor criteria

Rejected IE

- Firm alternate diagnosis; or
- Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or
- Does not meet criteria for possible IE, as above

DUKE

Major criteria

1. Blood cultues positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
   - *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
   - Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
   - ≥2 positive blood cultures of blood samples drawn >12 h apart; or
   - All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

2. Imaging positive for IE

a. Echocardiogram positive for IE:
   - Vegetation;
   - Abscess, pseudoaneurysm, intracardiac fistula;
   - Valvular perforation or aneurysm;
   - New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

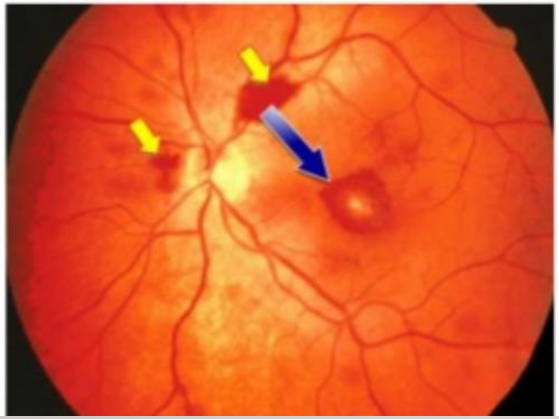
c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Splinter hemorrhage

Osler node



Roth's spot

Janeway lesion

Janeway lesions painless, small erythematous or haemorrhagic macular or nodular microabscess, caused by septic emboli

Osler nodes and Janeway lesions are similar, but **Osler's nodes** present with tenderness and are of immunologic origin

Roth's spots are retinal hemorrhages with white or pale centers, are usually caused by immune complex mediated vasculitis often resulting from bacterial endocarditis.

TREATMENT

- **ATB therapy**

- **Surgery** - performed in high-risk patients
  - Age/comorbidities/PVE/DM
  - Complicated IE (heart failure, shock…)
  - High-risk agents (S.aureus, fungi…), ATB failure
  - TTE/TEE high-risk morphology parameters – risk of embolisation

ANTIBIOTICS

- **beta-lactam** (penicillin, cefalosporin)

- **glycopeptide** (vancomycin)
- **aminoglycosides** (gentamicin)
- **rifampicin** in PVE

Fungi – ATB centre expert consult

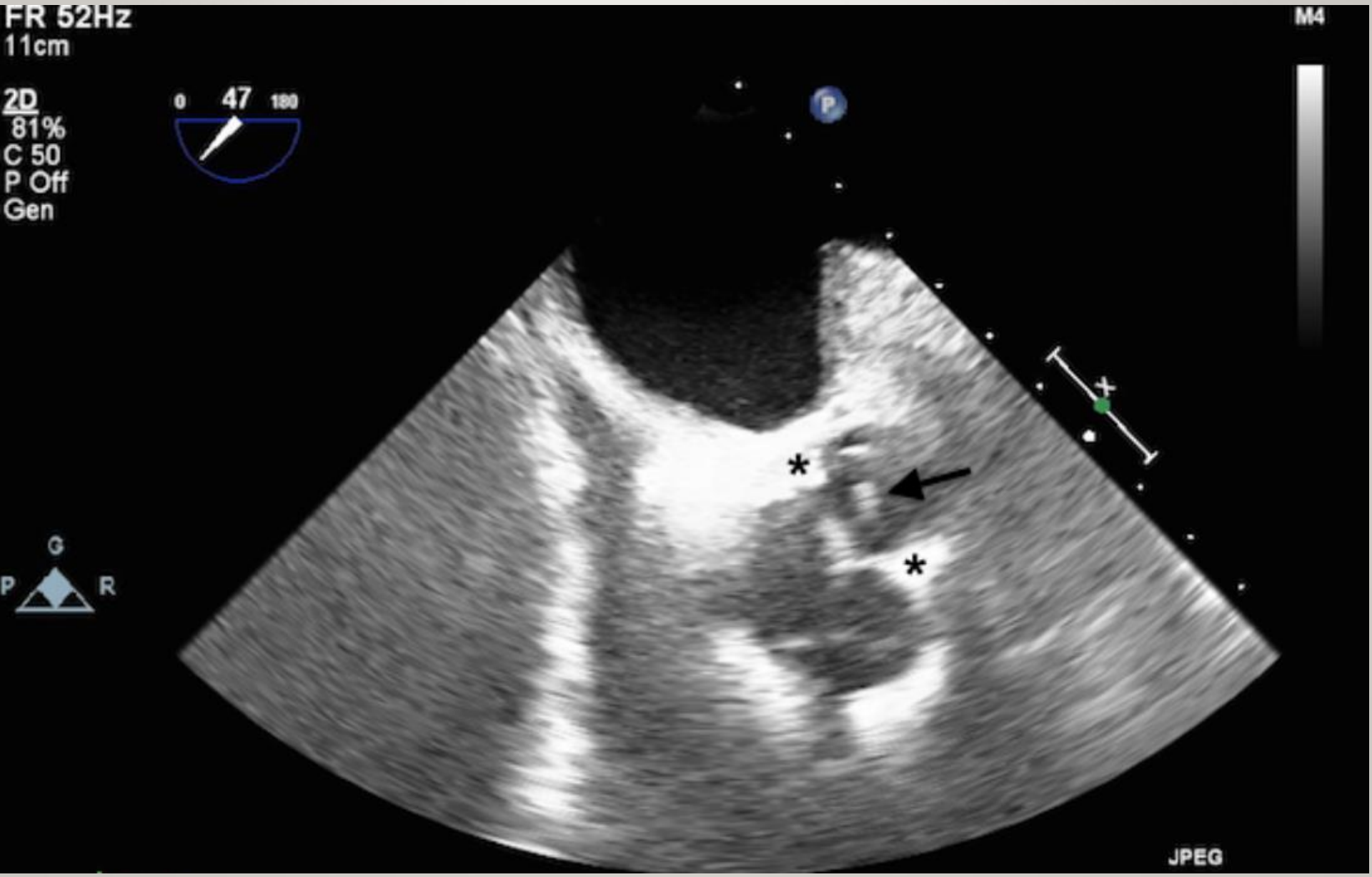
ANTIBIOTICS

- Streptococci: PEN/CEF + GENTA, (VANCO)
- Enterococci: like streptococci, PEN resist. common
- Staphylococci: MET/OXA + GENTA
- **Empiric therapy** - should focus on S. aureus
- HACEK/early PVE/fungi - require expert ATB consult
- PVE - prolonged (min. 6w) + RIFAMPIN

SURGERY

- **progressive heart failure** (emergency in shock)
- **signs of ATB th. failure** - continuous fever, abscess, vegetation, valve dehiscence…
- **embolization potential** (> 10 mm)


FR 50Hz
15cm
2D
63%
C 50
P Low
HGen
M3
P
R
1.7
3.4
JPEG


FR 52Hz
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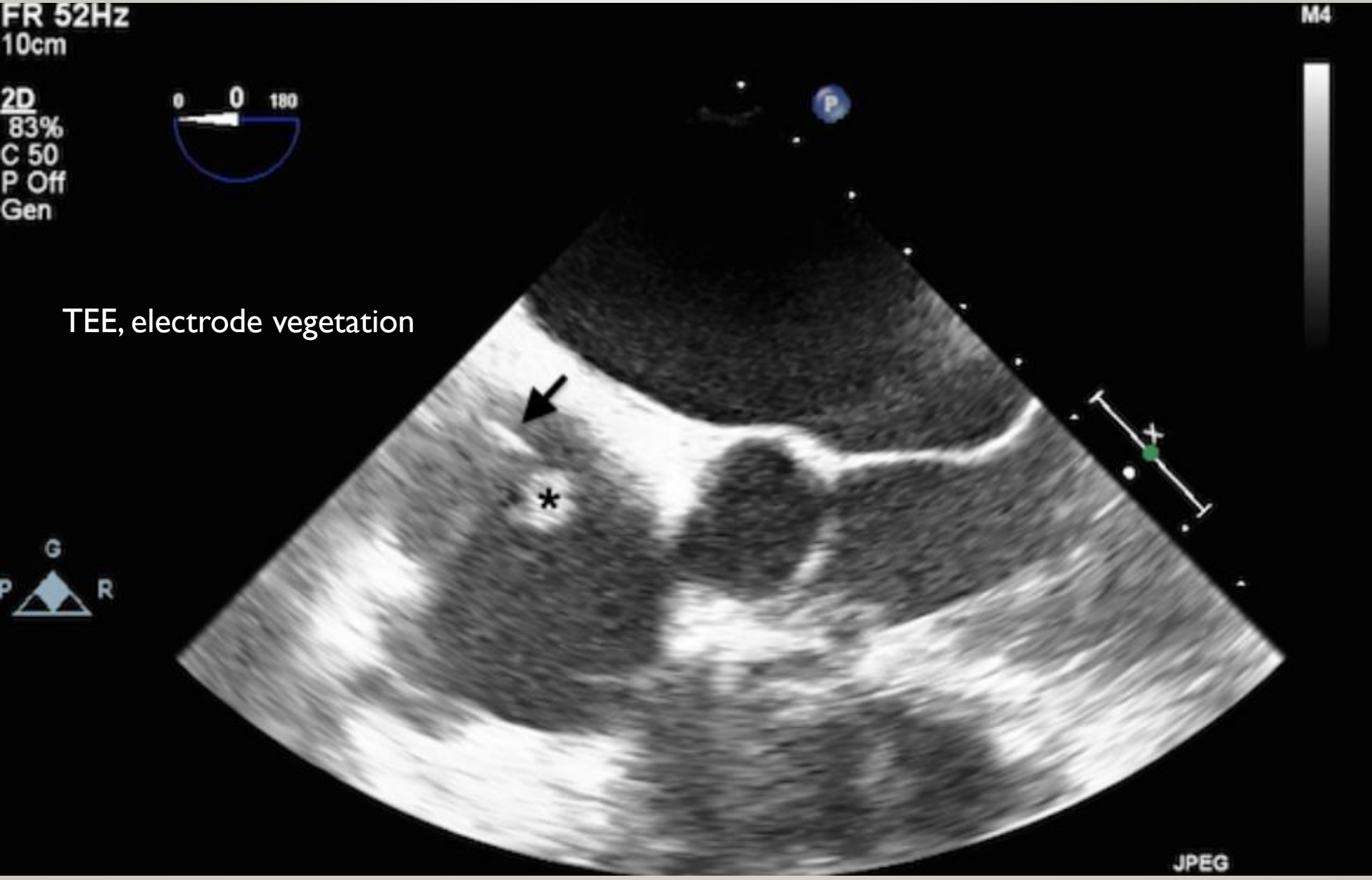
PM/ICD IE

- IE on/close to electrodes
- S. aureus most likely
- Electrode withdrawal necessary (embolisation during withdrawal common, rarely clinically significant)



TEE, electrode vegetation

IVDU

- Most commonly Tricuspid valve
- S. aureus, pseudomonas, G-, fungi, polymicrobial
- Fever, septic pulmonary embolisation (cough, hemoptysis, pulmonary abscesses, …)
- Mortality < 10% , but high likelihood of recurrence, surgery common

PREVENTION

- High risk patients only
  - Prosthetic valve implant
  - Previous IE
  - Congenital Heart Disease patients
- High-risk procedures (dental)

Recommendations	Class[a]	Level[b]
Antibiotic prophylaxis should be considered for patients at highest risk for 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 a previous episode of IE. (3) Patients with CHD: (a) Any type of cyanotic CHD. (b) Any type of CHD 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 CHD.	III	C

Table 6 Recommended prophylaxis for high-risk dental procedures in high-risk patients

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.

Cardiac Conditions for which IE Prophylaxis Recommended for Dental Procedures

- Prosthetic Cardiac Valve
- Previous Infective Endocarditis
- Congenital Heart Disease (CHD)
  - Unrepaired Cyanotic CHD, Including Palliative Shunts and Conduits
  - Completely Repaired CHD with Prosthetic Material or Device, whether by Surgery or by Catheter Intervention, during the first 6 months after the procedure
  - Repaired CHD with Residual Defects at the Site or Adjacent to the Site of a Prosthetic Patch or Prosthetic Device (which Inhibit Endothelialization)
- Cardiac Transplant Recipients who Develop Valvulopathy

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

Infectious Bacterial Endocarditis Prophylaxis No Longer Recommended for the Following Conditions

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

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

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

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

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

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

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

Dajani AS, Taubert KA, Wilson W, et al, JAMA 1997;277:1797
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