

# Infezioni delle protesi valvolari e vascolari

## Aspetti Cardiologici

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## EI: Dimensioni del problema

- In USA da 10.000-15.000 nuovi casi di EI per anno
- EI incrementa con l'età ( > 50% EI >60 aa)
- Trend favorito dall'invecchiamento della popolazione
- Nei giovani ( <40 aa) abuso di droghe è la causa >

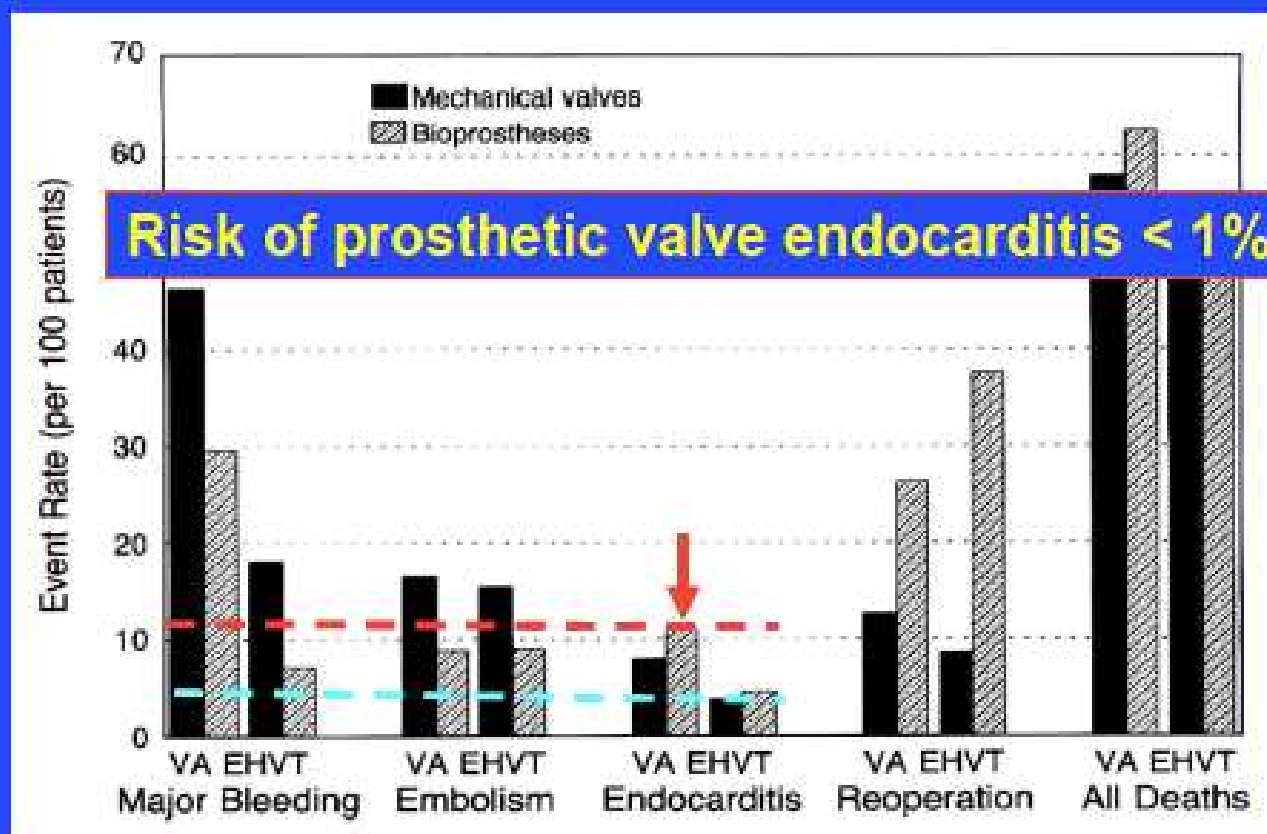
# EIP: Dimensioni del problema



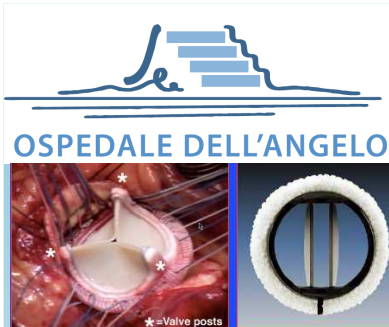
- Endocardite Infettiva Protesica: rappresenta il 20-26% di tutte le endocarditi Infettive / Euro Heart Survey
- In Italia vengono impiantate dalle 10/15.000 protesi valvolari all'anno
- EIP: incidenza da 1% al 6% delle valvole protesiche nel 1° anno dall'impianto e di circa l'1% ( 0,3-1,2%) negli anni successivi, ed ha una prognosi in genere sfavorevole

# PVE Dimensioni del problema

## Risk of Infection



Hammermeister KE et al, NEJM 1993 (12 yr event rates)



# EIP: Dimensioni del problema

- Colpisce indistintamente le protesi valvolari biologiche e meccaniche
- Patogenesi più frequentemente stafilococcica e micotica e più raramente streptococcica nella EIP precoce, mentre la tardiva è sostenuta da Stafil. Streptococchi orali e Gram neg.
- Elevata mortalità intraospedaliera: 15%-40%

# Classification and definitions

## According to location of infection and absence or presence of intracardiac material

### Left-sided native valve IE

### Left sided prosthetic valve IE (PVE)

- Early PVE (< 1 year)
- Late PVE (>1 year)

### Right-sided IE

### Device-related IE

- Permanent pacemaker
- Permanent cardioverter-defibrillator

## According to the mode of acquisition

### Health care associated IE

- Nosocomial (Hospitalisation >48 h before IE)
- Non nosocomial: IE starting <48 h after admission
  - Home based nursing, IV treatment, Haemodialysis, or IV chemotherapy (<30 days before)
  - Hospitalisation in acute care <90 days before IE
  - Resident in a nursing home or long-term facility

### Community-acquired IE

### Intravenous drug-abuse IE



# **Infective Endocarditis**

## **New guidelines ESC 2009**

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- 1. Prevention**
- 2. Diagnosis**
- 3. Prognostic assessment**
- 4. Treatment**
- 5. Specific situations**

# Infective Endocarditis

## New guidelines ESC 2009

- 1. Prevention**
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# IE prevention: main changes

1. The principle of antibiotic prophylaxis when performing procedures at risk of IE in patients with predisposing cardiac conditions is maintained but,
2. Antibiotic prophylaxis must be limited to patients with the highest risk of IE undergoing the highest risk dental procedure.
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 catheterization and during invasive procedures.
5. Prospective epidemiological studies are needed to evaluate if the reduced use of prophylaxis is associated with a change in the incidence of IE.



# Cardiac conditions at highest risk of IE

Recommendations	Class	Level
<b>Antibiotic prophylaxis should only be recommended for patients at highest risk of IE:</b> <ol style="list-style-type: none"> <li>1. Patients with a prosthetic valve or any prosthetic material used for cardiac valve repair,</li> <li>2. Patients with previous IE,</li> <li>3. Patients with congenital heart disease (CHD): <ol style="list-style-type: none"> <li>a. Cyanotic CHD with or without previous interventions,</li> <li>b. CHD with complete repair (surgical or percutaneous) for the next 6 months,</li> <li>c. When a residual defect persists after cardiac surgery or percutaneous technique.</li> </ol> </li> </ol>	<b>IIa</b>	<b>C</b>
<b>Antibiotic prophylaxis is no longer recommended in other forms of valvular or CHD.</b>	<b>III</b>	<b>C</b>

# Procedures at highest risk of IE (1)

## Dental procedures

Recommendations	Class	Level
<b>AB should be considered only</b> for dental procedures with manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.	<b>IIa</b>	<b>C</b>
<b>AB is not recommended</b> for local anaesthetic injections in non infected tissue removal of sutures, dental X-rays. Placement or adjustment of removable prosthodontic or orthodontic appliances or braces. After the shedding of deciduous teeth or trauma to the lips and oral mucosa.	<b>III</b>	<b>C</b>



## Procedures at highest risk of IE (2)

Antibiotic prophylaxis is not recommended for :

Recommendations	Class	Level
1. <b>Respiratory tract procedures</b> (Bronchoscopy, laryngoscopy, transnasal or endotracheal intubation).	III	C
2. <b>Gastrointestinal procedures</b> (Gastroscopy, colonoscopy, cystoscopy, transoesophageal echo).	III	C
3. <b>Skin and soft tissue procedures.</b>	III	C



# Recommended prophylaxis for dental procedures at risk

Single dose 30-60 min before procedure

Situation	Antibiotic	Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or Ampicillin	2 g p.o. or i.v.	50 mg/kg p.o. or i.v.
Allergy to penicillin or ampicillin	Clindamycin	600mg p.o. or i.v.	20 mg/kg p.o. or i.v.

# Infective Endocarditis

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# Diagnosi di EVP

- **Clinica**
- **Strumentale:** eco TT, eco TE, RMN
- **Ematochimica-culturale**



# Clinical presentation

## IE must be suspected in the following situations

- New regurgitant murmur.
- Embolic events of unknown origin.
- Sepsis of unknown origin (especially if associated with IE causative organisms).
- Fever - The most frequent sign of IE:
  - Intracardiac prosthetic material,
  - Previous history of IE,
  - Previous valvular or CHD,
  - Other predispositions for IE predisposition and recent intervention with associated bacteriemia,
  - Evidence of CHF,
  - New conduction disturbance,
  - Positive blood cultures with typical IE causative organisms or positive serology for chronic Q fever,
  - Vascular or immunologic phenomena: embolic event, Roth spots, splinter haemorrhage, Janeway lesions, Osler's node,
  - Focal or non-specific neurological symptoms and signs,
  - Evidence of pulmonary embolism/infiltration (right-sided IE),
  - Peripheral abscesses (renal, splenic, cerebral, vertebral) of unknown causes.



## Diagnosis of Prosthetic Valve Endocarditis

### Clinical Features

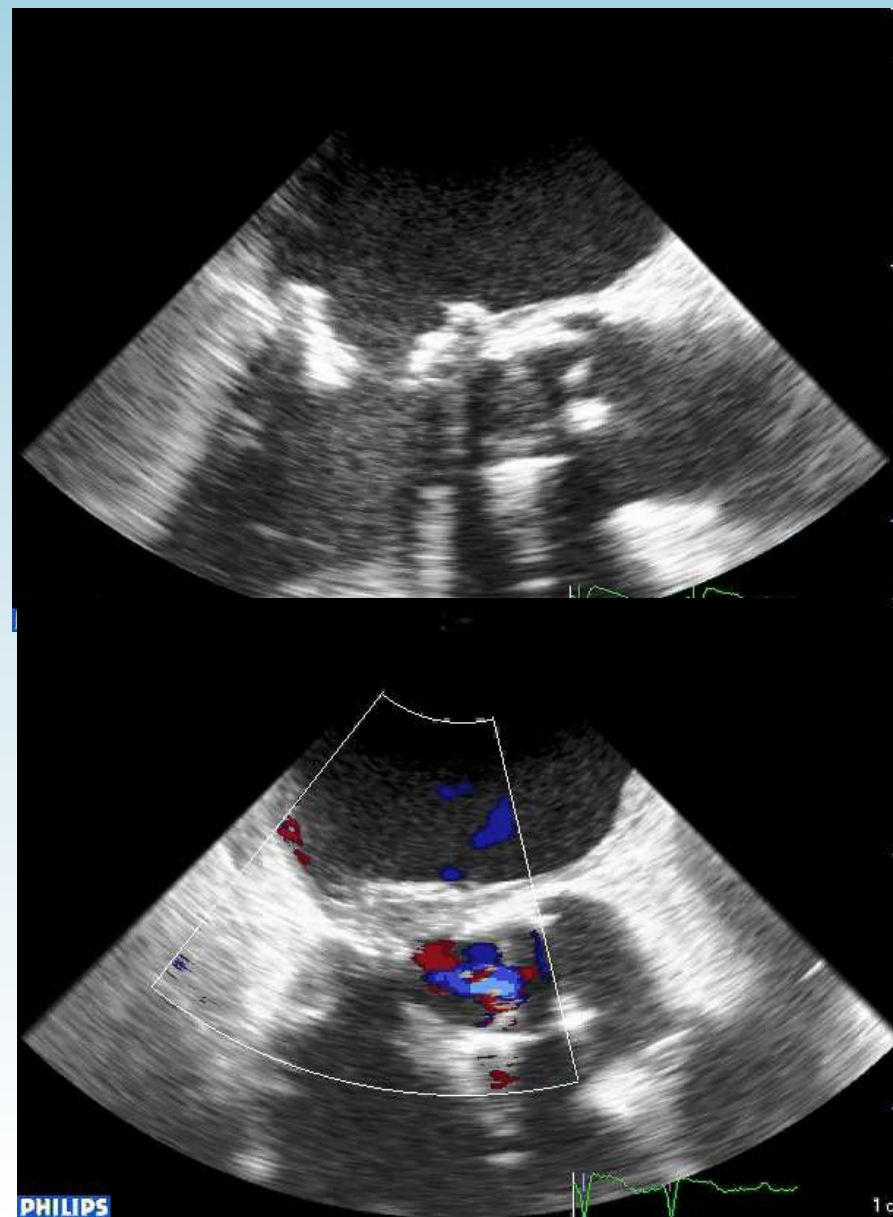
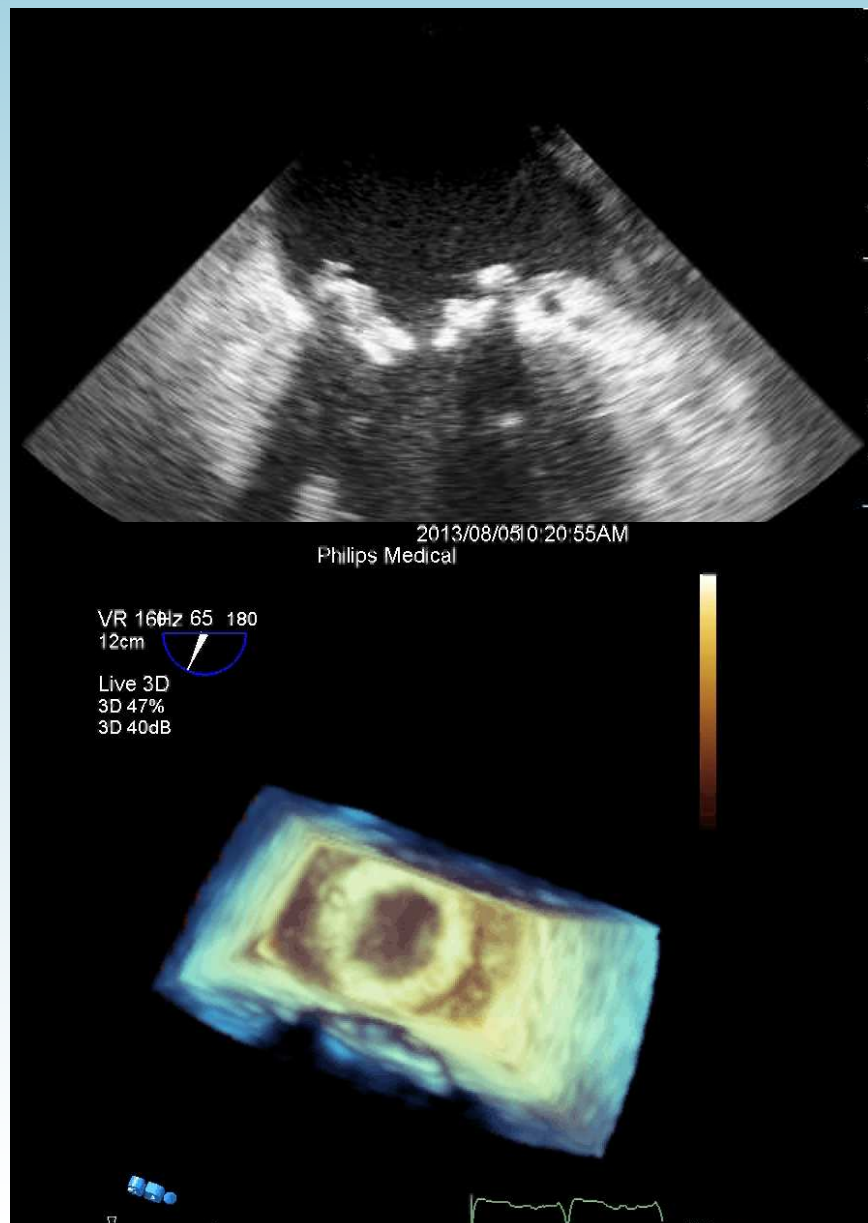
<b>Fever</b>	<b>95%</b>
<b>New murmur or <math>\Delta</math> murmur</b>	<b>10- 25%</b>
<b>Pre-existing murmur</b>	<b>85- 95%</b>
<b>Osler's nodes</b>	<b>10-15%</b>
<b>Janeway lesions</b>	<b>3- 5%</b>
<b>Roth spots</b>	<b>2-10%</b>
<b>Anemia</b>	<b>70-90%</b>
<b>Circulating immune complexes</b>	<b>95%</b>
<b>Elevated CRP, RF</b>	<b>94-97%</b>
<b>Microscopic hematuria</b>	<b>30-60%</b>

# EIP: Ruolo dell'ecocardiografia

- Uomo 72 aa
- 6 anni prima sottoposto SVM e SVA con due bioprotesi (RAA)
- Prostatite in ipertrofia prostatica 1 mese prima comparsa di febbre 38-38,5 da 2 settimane con qualche puntata settica da una settimana (terapia antibiotica inadeguata)
- Dolori toracici da 5 gg e ricovero in Malattie Infettive



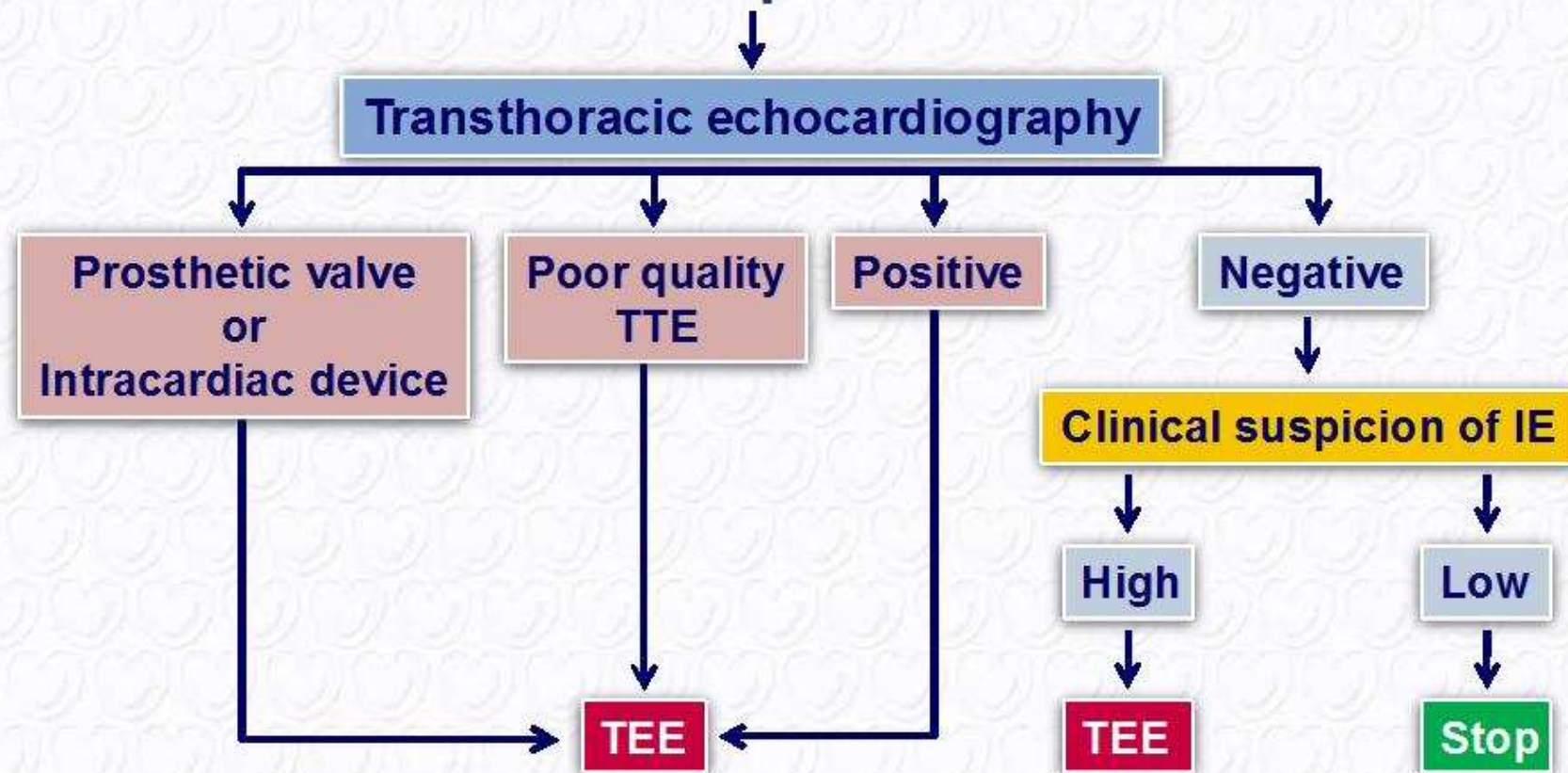
# EIP: Ruolo dell'ecocardiografia





# Indications for echocardiography

## Clinical suspicion of IE



*If initial TEE is negative but persistent suspicion of IE: repeat TEE within 7-10 days*



# Anatomic and echo definitions

	Surgery / Necropsy	Echocardiography
<b>Vegetation</b>	Infected mass attached to an endocardial structure or an implanted intracardiac material	Oscillating or non oscillating intracardiac mass or other endocardial structures or non implanted intracardiac material
<b>Abscess</b>	Perivalvular cavity with necrosis and purulent material not communicating with the cardiovascular lumen	Thickened non-hogeneous perivalvular area with echodense or echolucent appearance
<b>Pseudoaneurysm</b>	Perivalvular cavity communicating with the cardiovascular lumen	Pulsatile perivalvular echo-free space with colour-Doppler flow detected
<b>Perforation</b>	Interruption of endocardial tissue continuity	Interruption of endocardial tissue continuity traversed by colour Doppler flow
<b>Fistula</b>	Communication between 2 neighbouring cavities through a perforation	Colour-Doppler communication between 2 neighbouring cavities through a perforation
<b>Valve aneurysm</b>	Saccular outpouching of valvular tissue	Saccular bulging of valvular tissue
<b>Dehiscence of a prosthetic valve</b>	Dehiscence of the prosthesis	Paravalvular regurgitation identified by TTE/TTE with or without rocking motion of the prosthesis

# Role of echocardiography in IE (1)

## A. Diagnosis

Recommendations	Class	Level
1. <b>TTE</b> is recommended as the first-line imaging in suspected IE.	I	B
2. <b>TEE</b> is recommended in patients with high clinical suspicion of IE and normal TTE.	I	B
3. <b>Repeat TTE/TEE</b> within 7-10 days in case of negative initial examination and if clinical suspicion of IE persists.	I	B
4. <b>TEE</b> should be considered in most of adult patients with suspected IE, even in case of positive TTE.	IIa	C
5. <b>TEE</b> is not indicated in patients with a good quality negative TTE and low suspicion of IE.	III	C



# Role of echocardiography in IE (2)

Recommendations	Class	Level
<b>B. Follow-up under medical therapy:</b>		
1. Repeat TTE and TEE is recommended as soon as a new complication of IE is suspected.	I	B
2. Repeat TTE and TEE should be considered during F.U. of uncomplicated IE: time & mode depend on the initial findings, type of microorganisms and initial response to treatment.	IIa	B
<b>C. Intraoperative echocardiography</b> Recommended in all cases of IE requiring surgery.	I	C
<b>D. Following completion of treatment</b> TTE is recommended at completion of antibiotic treatment for evaluation of cardiac and valve morphology and function.	I	C



## Microbiological diagnosis

### Diagnosis of Prosthetic Valve Endocarditis **Bacteriology**

#### **Early (within 2 months)**

Staph aureus  
Staph epidermidis  
Gram negative bacilli

#### **Late**

Strep viridans  
Staph aureus

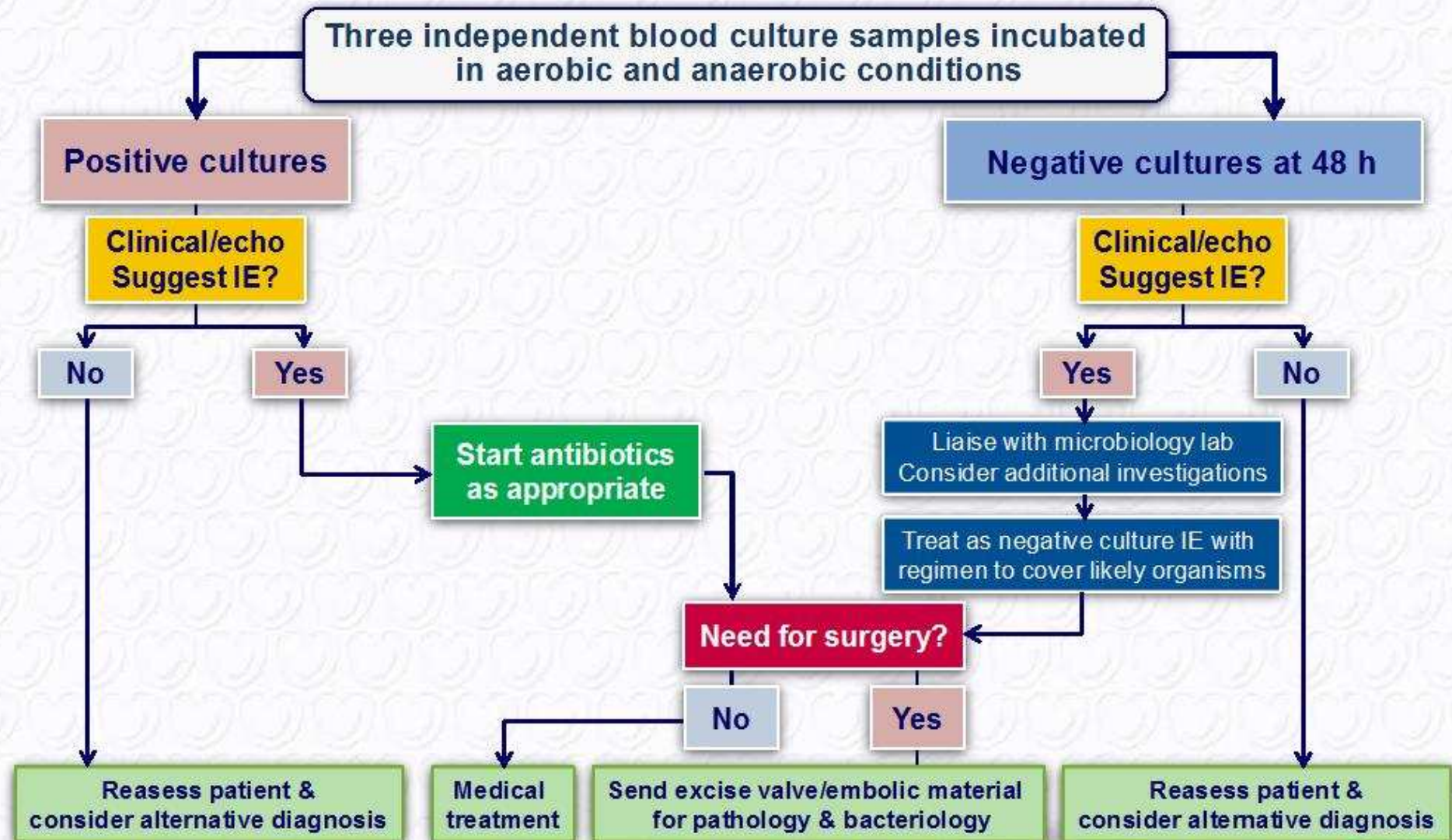
Culture negative in 5%

#### **Other**

HACEK group  
Fungi  
Coxiella (Q-fever)  
Brucella  
Bartonella  
Chlamydia

**Almost any organism  
can cause endocarditis**

# Microbiological diagnosis





# Modified Duke criteria for the diagnosis of IE

(Adapted from Li & al)

## MAJOR CRITERIA

### Blood culture positive for IE

- Typical microorganisms consistent with IE from 2 separate blood cultures:  
*Viridans streptococcus*, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus* or community acquired enterococci in the absence of a primary focus.
- Microorganisms consistent with IE from 2 persistently positive blood cultures:  
*At least 2 positive blood cultures of blood samples drawn > 12 h apart or all of 3 or a majority of  $\geq 4$  separate cultures of blood with first & last sample drawn at least 1 h apart.*
- Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1:800.

### Evidence of endocardial involvement

- Echocardiogram positive for IE. (*Vegetation, Abscess, New partial dehiscence of prosthetic valve*).
- New valvular regurgitation.

## MINOR CRITERIA

- Predisposition: Predisposing heart condition, injection drug use.
- Fever: temperature > 38°C.
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysms.
- Intracranial haemorrhages, conjunctival haemorrhages, Janeway lesions.
- Immunologic phenomena: glomerulonephritis Osler's node, Roth's spot, rheumatoid factor.
- Microbiological evidence: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE.



# Diagnosis of IE

Diagnosis of IE is definite  
in the presence of

**2** Major criteria  
or  
**1** major and **3** minor criteria  
or  
**5** minor criteria

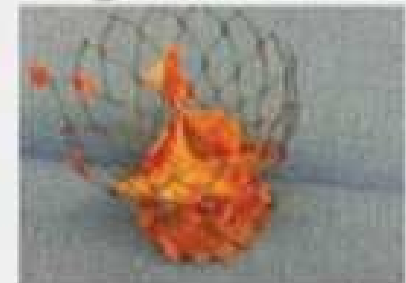
Diagnosis of IE is possible  
in the presence of

**1** Major and **1** minor criteria  
or  
**3** minor criteria

Adapted from LI Js et al., *Clin Infect Dis*. 200;30:633-638

# A Diagnostic Challenge

- The sensitivity of the modified-Duke criteria is **lower** than in native valve IE especially when applied early in the course of the disease  $\approx 70\%$
- Blood cultures are more frequently **negative**
- Echocardiography (TTE + TEE) are **negative or inconclusive** in  $\approx 30\%$  of cases
- Emergence of “TAVI endocarditis”



# **Infective Endocarditis**

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# Crucial role of prognostic assessment

## Patient Characteristics

- Elderly
- Prosthetic valve IE
- Insulin dep. diabetes
- Co-morbidity

## Microorganisms

- S. Aureus
- Fungi
- Gram-negative bacilli

## Complicated IE

- Heart failure
- Renal failure
- Stroke
- Septic shock
- Periannular complications

## Echocardiographic findings

- Periannular complications
- Severe left-sided valve regurgitation
- Low LVEF
- Pulmonary hypertension
- Large vegetations
- Severe prosthetic dysfunction
- Premature valve closure/signs of  $\uparrow$  diastolic Pr.

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# Antibiotics

## *Staphylococcus* spp. Prosthetic valves

Antibiotic	Dosage & route	Duration	Class	Level		
Prosthetic valves						
Methicillin-susceptible Staphylococci						
(Flu)cloxacillin or Oxacillin <i>with</i> Rifampin and Gentamicin	12 g/day i.v. in 4-6 doses  1200 mg/day i.v. or orally in 2 doses  3 mg/kg/day i.v or i.m. in 2 or 3 doses <i>Paediatric doses</i> – Oxacillin and (Flu)cloxacillin as above – Rifampicin 20 mg/kg/day i.v. or orally in 3 equally divided doses	≥ 6 weeks  ≥ 6 weeks  2 weeks	I	B		
Penicillin-allergic patients and Methicillin-resistant Staphylococci						
Vancomycin <i>with</i> Rifampin and Gentamicin	30 mg/kg/day i.v. in 2 doses  1200 mg/day i.v. or orally in 2 doses 3 mg/kg/day i.v or i.m. in 2 or 3 doses  <i>Pediatric doses as above</i>	≥ 6 weeks  ≥ 6 weeks 2 weeks				

# Antibiotics

## *Enterococcus* spp.

Antibiotic	Dosage & route	Duration	Class	Level
<b>Beta-lactam and Gentamicin susceptible strain</b>				
<b>Amoxicillin</b> <i>with</i> <b>Gentamicin</b>	200 mg/kg/day i.v. in 4-6 doses  3 mg/kg/day i.v. in 2 or 3 doses	4-6 weeks	I	B
OR				
<b>Ampicillin</b> <i>with</i> <b>Gentamicin</b>	200 mg/kg/day i.v. in 4-6 doses  3 mg/kg/day i.v. in 2 or 3 doses	4-6 weeks	I	B
OR				
<b>Vancomycin</b> <sup>a</sup> <i>with</i> <b>Gentamicin</b>	30 mg/kg/day i.v. in 2 doses  3 mg/kg/day i.v. or i.m. in 2 or 3 doses	6 weeks	I	C

<sup>a</sup> = for patients unable to tolerate beta-lactams



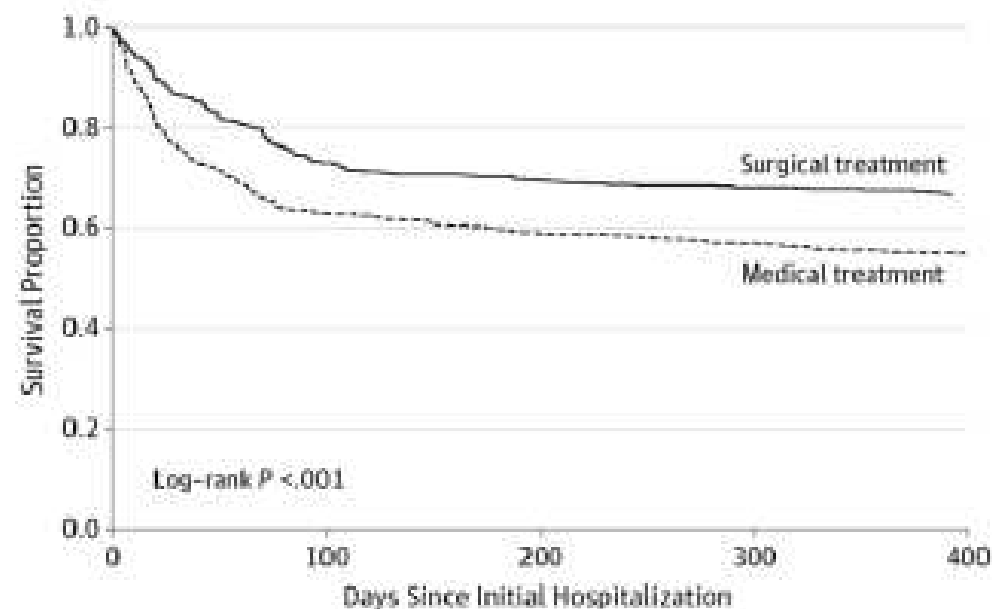
# Antibiotics

## Empirical treatment

Antibiotic	Dosage & route	Duration	Comments	Class	Level
Native valves					
Ampicillin-Sulbactam or Amoxicillin-Clavulanate with Gentamicin	12 g/day i.v. in 4 doses	4-6 weeks	Patients with blood-culture negative should be treated in consultation with an infectious disease specialist	IIb	C
	12 g/day i.v. in 4 doses	4-6 weeks			
	3 mg/kg/day i.v. or i.m. in 2 or 3 doses	4-6 weeks			
Vancomycin with Gentamicin with Ciprofloxacin	30 mg/kg/day i.v. in 2 doses	4-6 weeks	For patients unable to tolerate $\beta$ -lactams	IIb	C
	3 mg/kg/day i.v. or i.m. in 2 or 3 doses	4-6 weeks			
	1000 mg/day orally in 2 doses or 800 mg/day i.v. in 2 doses	4-6 weeks			
Prosthetic valves (early < 12 months post surgery)					
Vancomycin with Gentamicin with Rifampin	30 mg/kg/day i.v. in 2 doses	6 weeks	If no clinical response, surgery and perhaps extension of the antibiotic spectrum to gram-negative pathogens must be considered	IIb	C
	3 mg/kg/day i.v. or i.m. in 2 or 3 doses	2 weeks			
	1200 mg/day i.v. or orally in 2 doses				
Prosthetic valves (late > 12 months post surgery)					
Same as Native valves					

## Is surgery always needed in PVE?

- ◆ PVE is the most serious complication of valve replacement
- ◆ very high (20-50%) mortality
- ◆ best therapeutic strategy debated



Lalani T- JAMA 2013



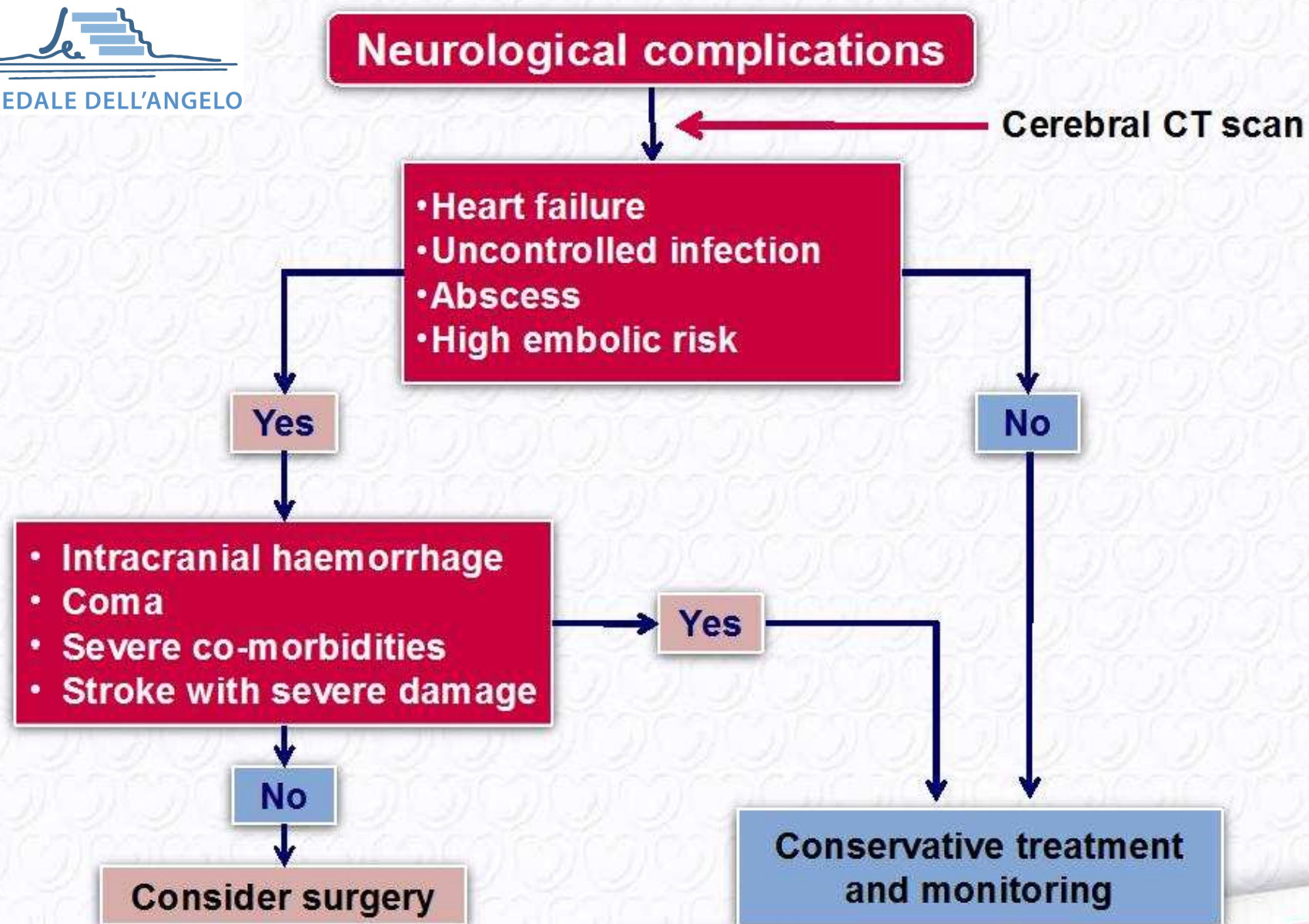
## PVE: is surgery the best option?

Author	Patients (n)	% surgery (%)	mortality (med) (%)	mortality (surg) (%)	surgery better
Wang (2005)	367	42	23	25	NO
Akowuah (2003)	66	57	46	24	YES
Habib (2005)	104	49	25	17	NO
Alonso-Valle (2010)	133	80	42	26	YES
Lopez (2013)	257	61	33	33	NO
Wolff (1995)	122	53	48	25	YES
Lalani (2013)	1025	48	27	22	NO

# Prosthetic valve endocarditis (PVE)

Indications for surgery in PVE	Timing	Class	Level
<b>A. HEART FAILURE</b>			
PVE with severe prosthetic dysfunction (dehiscence or obstruction) causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
PVE with fistula into a cardiac chamber or pericardium causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
PVE with severe prosthetic dysfunction and persisting heart failure.	Urgent	I	B
Severe prosthetic dehiscence without heart failure.	Elective	I	B
<b>B. UNCONTROLLED INFECTION</b>			
Locally uncontrolled infection (abscess, false aneurysm, enlarging vegetation).	Urgent	I	B
PVE caused by fungi or multiresistant organisms.	Urgent/elective	I	B
PVE with persisting fever and positive blood culture > 7-10 days.	Urgent	I	B
PVE caused by <i>staphylococci</i> or gram <i>negative bacteria</i> : (most cases of early PVE).	Urgent/elective	I	C
<b>C. PREVENTION of EMBOLISM</b>			
PVE with recurrent emboli despite appropriate treatment.	Urgent	I	B
PVE with large vegetations (10 mm) and other predictors of complicated course (HF, persistent infection, abscess).	Urgent	I	B
PVE with isolated very large vegetations (> 15 mm).	Urgent	IIb	C





## El su pace maker e ICD

- IE su CD: 1,9 x 1000 dispositivi impiantabile (5%)
- Local device Infection (LDI= tasca)
- Cardiac device related EI (CDRIE):  
coinvolgono device e cateteri
- Prognosi sfavorevole



# Cardiac device related IE

Recommendations	Class	Level
<b>A. PRINCIPLES of TREATMENT</b>		
Prolonged antibiotic therapy and device removal are recommended in definite CDRIE.	I	B
Device removal should be considered when CDRIE is suspected on the basis of occult infection without other apparent source of infection.	IIa	C
In patients with native or prosthetic valve IE and an intracardiac device with no evidence of associated device infection, device extraction must be considered.	IIb	C
<b>B. MODE of DEVICE REMOVAL</b>		
Percutaneous extraction is recommended in most patients with CDRIE even those with large (>10 mm) vegetations.	I	B
Surgical extraction should be considered if percutaneous extraction is incomplete or impossible or when severe destructive tricuspid IE is associated.	IIa	C
Surgical extraction may be considered if in patients with very large (>25 mm) vegetations.	IIb	C
<b>C. REIMPLANTATION</b>		
After device extraction, reassessment of the need for reimplantation is recommended.	I	B
When indicated, reimplantation should be postponed if possible to allow a few days or weeks of antibiotic therapy.	IIa	B
Temporary pacing is not recommended.	III	C
<b>D. PROPHYLAXIS</b>		
Routine antibiotic prophylaxis is recommended before device implantation.	I	B

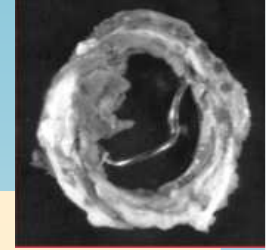


# Antithrombotic therapy

Recommendations: antithrombotic therapy	Class	Level
Interruption of antiplatelet treatment is only recommended in case of major bleeding.	I	B
In haemorrhagic stroke without cerebral haemorrhage, replacement of oral anticoagulation by Unfractionated heparin (UFH) for 2 weeks with a close monitoring of APT or ACT.	I	C
In intracranial haemorrhage (ICH), interruption of all anticoagulation is recommended.	I	C
In patients with ICH and a mechanical valve, UFH should be re-initiated asap with a close monitoring of APT or ACT following multi-disciplinary discussion.	IIb	C
In the absence of stroke, replacement of oral anticoagulation by UFH during 2 weeks may be considered in case of <i>S. aureus</i> IE with a close monitoring of APT or ACT.	IIb	C



## “ Take home message...”



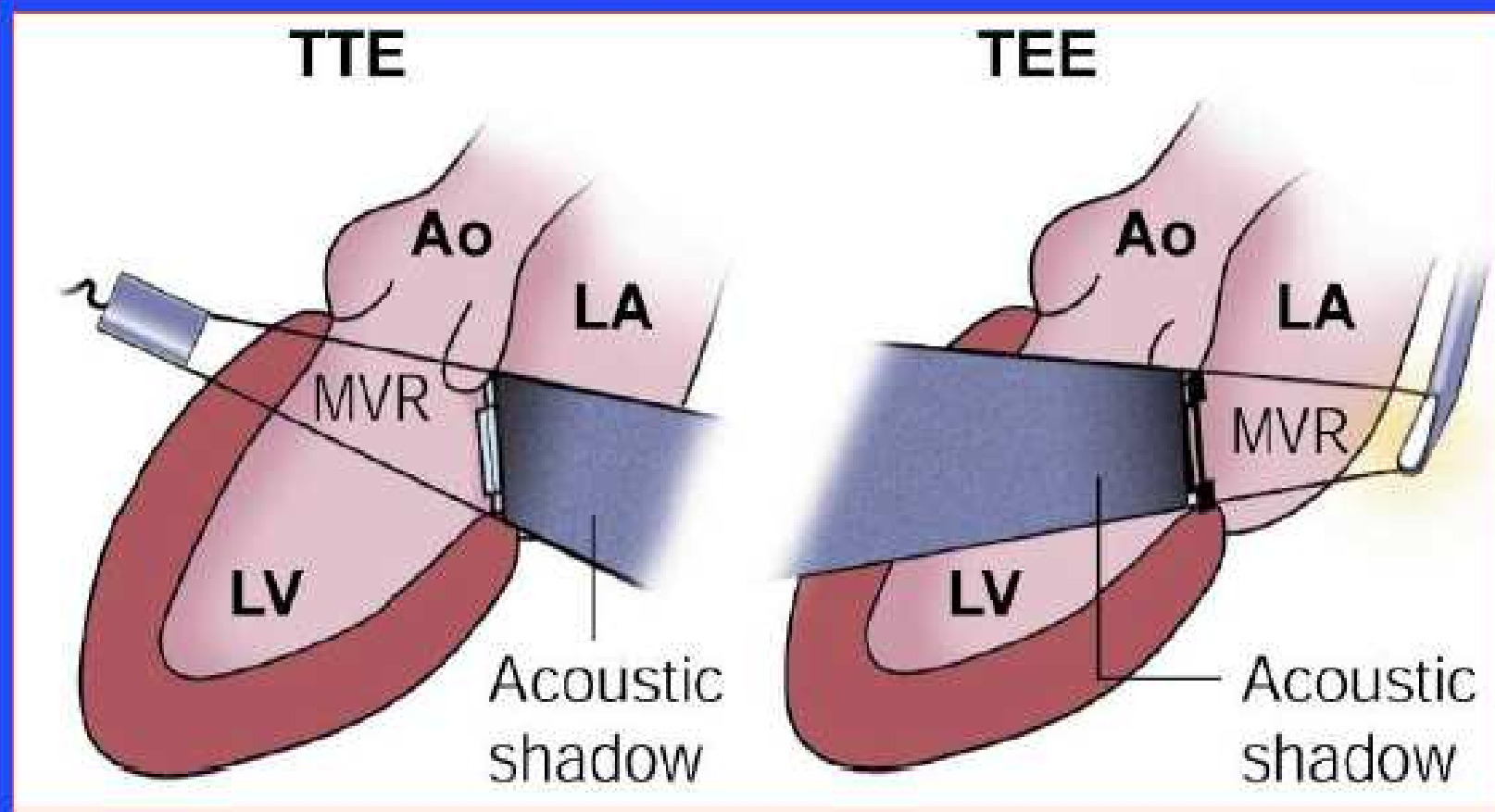
- Stratificare il paziente in base al sospetto clinico, strumentale, laboratoristico
- Gestione in team: cardiologo/infettivologo/cardiochirurgo/neurologo
- Partire sempre da un esame ma
- Approccio diagnostico dei quesiti clinici
- Utilizzare al meglio ogni singolo esame per stratificare al
- Approccio multidisciplinare al paziente sulle strategie più adatte terapeutica



Thank you

## Diagnosis of Prosthetic Valve Endocarditis

# Echocardiography





# Indications for surgery - Native IE

Recommendations: Indications for surgery	Timing	Class	Level
<b>A. HEART FAILURE</b>			
Aortic or mitral IE with severe acute regurgitation or valve obstruction causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
Aortic or mitral IE with fistula into a cardiac chamber or pericardium causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
Aortic or mitral IE with severe acute regurgitation and persisting HF or echo-cardiographic signs of poor hemodynamic tolerance (early mitral closure or pulmonary hypertension).	Urgent	I	B
Aortic or mitral IE with severe acute regurgitation and no HF.	Elective	IIa	B
<b>B. UNCONTROLLED INFECTION</b>			
Locally uncontrolled infection.	Urgent	I	B
Persisting fever and positive blood culture > 7-10 days.	Urgent	I	B
Infection caused by fungi or multiresistant organisms.	Urgent/elective	I	B
<b>C. PREVENTION of EMBOLISM</b>			
Aortic or mitral IE with large vegetations (>10 mm) following one or more embolic episodes, despite appropriate antibiotic treatment.	Urgent	I	B
Aortic or mitral IE with large vegetations (10 mm) and other predictors of complicated course (HF, persistent infection, abscess).	Urgent	I	C
Isolated very large vegetations (>15 mm).	Urgent	IIb	C

# Right sided endocarditis

**Surgical treatment should be considered  
in the following scenarios**

Recommendations	Class	Level
Microorganisms difficult to eradicate (e.g. persistent fungi) or bacteriemia for > 7 days (e.g. <i>S. aureus</i> , <i>P. aeruginosa</i> ) despite adequate antimicrobial therapy.	IIa	C
Persistent tricuspid valve vegetations > 20 mm after recurrent pulmonary emboli with or without concomitant right heart failure.		
Right heart failure secondary to severe tricuspid regurgitation with poor response to diuretic therapy.		



# Infective Endocarditis

## New guidelines ESC 2009

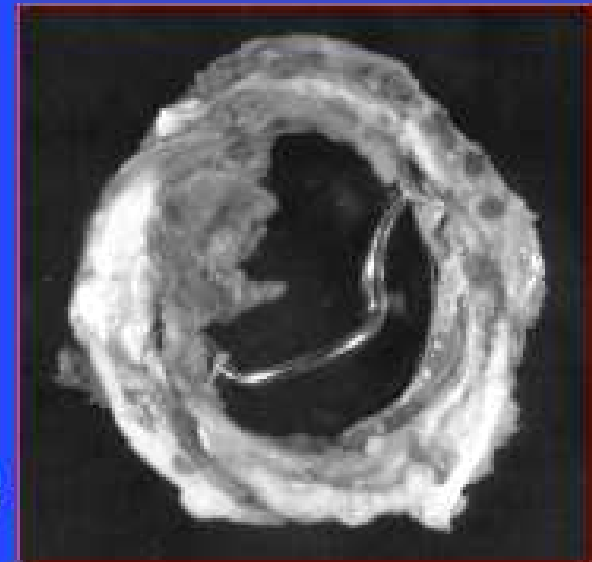
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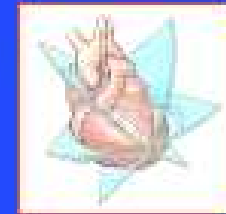
## Conclusions

- High index of suspicion
- Patient education
- Start with Duke criteria
- Hold blood cultures for 4-6 wks
- TEE early in disease course
- Re-evaluate if symptoms persist
- New molecular techniques have promise



# Diagnosis of Prosthetic Valve Endocarditis

## Duke Criteria



### ***Definite Endocarditis***

- 2 major
- 1 major + 3 minor
- 5 minor

### ***Probable Endocarditis***

- 1 major + 1 minor
- 3 minor

**Pt with prosthetic valve  
and history of fever and  
embolic events**

**Already has  
3 minor criteria  
for endocarditis ?**



# Antibiotics

## Oral & group *D Streptococci*

Antibiotic	Dosage & route	Duration	Class	level
<b>Penicilline susceptible (MIC &lt; 0.125 mg/L) oral &amp; group <i>D streptococci</i></b>				
<b>Standard treatment</b>				
Penicilline G or	12-18 millions U/day in IV in 6 doses	4 weeks	I	B
Amoxicilline or	100-200 mg/kg/day in 4-6 doses	4 weeks	I	B
Ceftriaxone	2 g/day i.v or i.m. in 1 dose  <i>Paediatric doses</i> – Penicillin G 200,000 U/kg/day i.v. in 4-6 divided doses – Amoxicilline 300 mg/kg/day i.v. in 4-6 equally divided doses – Ceftriaxone 100 mg/kg/day i.v. or i.m. in one dose	4 weeks	I	B

# Neurological complications

Recommendations	Class	Level
After a silent cerebral embolism or TIA, surgery is recommended without delay if an indication remains.	I	B
Following intracranial haemorrhage, surgery must be postponed for a least one month.	I	C
Neurosurgery or endovascular therapy are indicated for very large, enlarging or ruptured intracranial aneurysm.	I	C
After a stroke, surgery indicated for HF, uncontrolled infection, abscess or persistent high embolic risk should not be delayed. Surgery should be considered as long as coma is absent and cerebral haemorrhage has been excluded by cranial CT.	IIa	B
Intracranial aneurysm should be looked for in any patient with IE and neurological symptoms. CT or MR angiography should be considered for diagnosis.	IIa	B
Conventional angiography should be considered when non-invasive techniques are negative and the suspicion of intracranial aneurysm remains.	IIa	B



# Antibiotics

## Oral & group *D* Streptococci

Antibiotic	Dosage & route	Duration	Class	Level
<b>Penicilline susceptible (MIC &lt; 0.125 mg/L) oral &amp; group <i>D</i> streptococci</b>				
<b>Two-week treatment</b>				
Penicilline G or	12-18 millions U/day i.v. in 6 doses	2 weeks	I	B
Amoxicilline or	100-200 mg/kg/day in 4-6 doses	2 weeks	I	B
Ceftriaxone with	2 g/day i.v. or i.m. in 1 dose	2 weeks		
Gentamycin or Netilmicin	3 mg/kg/day i.v. or i.m. in 1 dose 4-5 mg/day	2 weeks 2 weeks	I	B
	<i>Pediatric doses:</i> – Penicillin, Amoxicillin and Ceftriaxone as above – Gentamycin 3 mg/kg/day i.v. or i.m. in one dose or 3 equally divided doses		I	B
<b>In-beta-lactam allergic patients</b>				
Vancomycin	30 mg/kg/day i.v. in 2 doses <i>Paediatric doses:</i> – 40 mg/kg/day i.v. in 2-3 equally divided doses	4 weeks	I	C

# Antibiotics

## Oral & group *D* Streptococci

Antibiotic	Dosage & route	Duration	Class	Level
<b>Strains relatively resistant to Penicillin (MIC 0.125-2 mg/L)</b>				
<b>Standard treatment</b>				
<b>Penicilline G</b> or	24 million U/day in IV in 6 doses	4 weeks	I	B
<b>Amoxicilline</b> or	200 mg/kg/day in 4-6 doses	4 weeks	I	B
<i>with</i> <b>Gentamycin</b>	3 mg/kg/day i.v. or i.m. in 1 dose	2 weeks	I	B
<b>In-beta-lactam allergic patients</b>				
<b>Vancomycin</b> <i>with</i>	30 mg/kg/day i.v. in 2 doses (same for pediatric doses)	4 weeks	I	C
<b>Gentamycin</b>	3 mg/kg/day i.v. or i.m. in 1 dose	2 weeks	I	C



# Antibiotics

## *Staphylococcus* spp. Native valves

Antibiotic	Dosage & route	Duration	Class	Level
<b>Native valves</b>				
<i>Methicillin susceptible Staphylococci</i>				
(Flu) cloxacillin or	12 g/day i.v. in 4-6 doses	4-6 weeks	I	B
Oxacillin <i>with</i> Gentamicin	3 mg/kg/day i.v. or i.m. in 2 or 3 doses  <i>Pediatric doses</i> – Oxacillin or (Flu)cloxacillin 200 mg/kg/day i.v. in 4-6 equally divided doses – Gentamicin 3mg/kg/day i.v. or i.m. in 3 equally divided doses	4-6 weeks  3-5 days	I	B
<b>Penicillin-allergic patients or Methicillin-resistant <i>Staphylococci</i></b>				
Vancomycin <i>with</i> Gentamicin	30 mg/kg/day i.v. in 2 doses  3 mg/kg/day i.v. or i.m. in 2 or 3 doses	4-6 weeks  3-5 days	I	B