Valvular Heart Disease and Infective Endocarditis

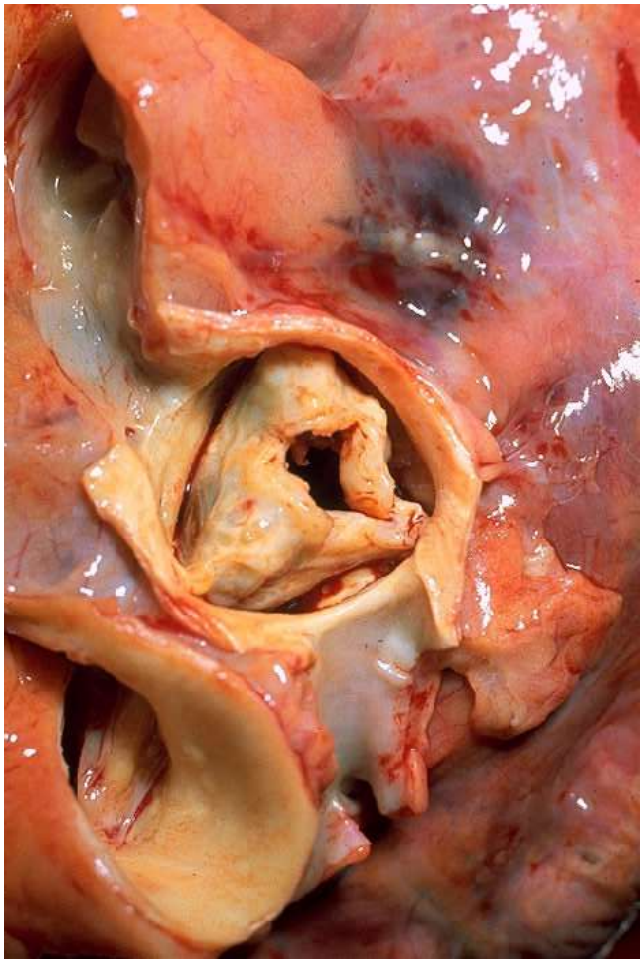
LECTURE IN INTERNAL MEDICINE FOR V COURSE STUDENTS

M. Yabluchansky, L. Bogun, L. Martymianova, O. Bychkova, N. Lysenko, N. Makienko
V.N. Karazin National University Medical School' Internal Medicine Dept.

Valvular Heart Disease

Plan of the Lecture

- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines



https://upload.wikimedia.org/wikipedia/commons/b/b4/Aortic_stenosis_rheumatic,_gross_pathology_20G0014_lores.jpg

Definition

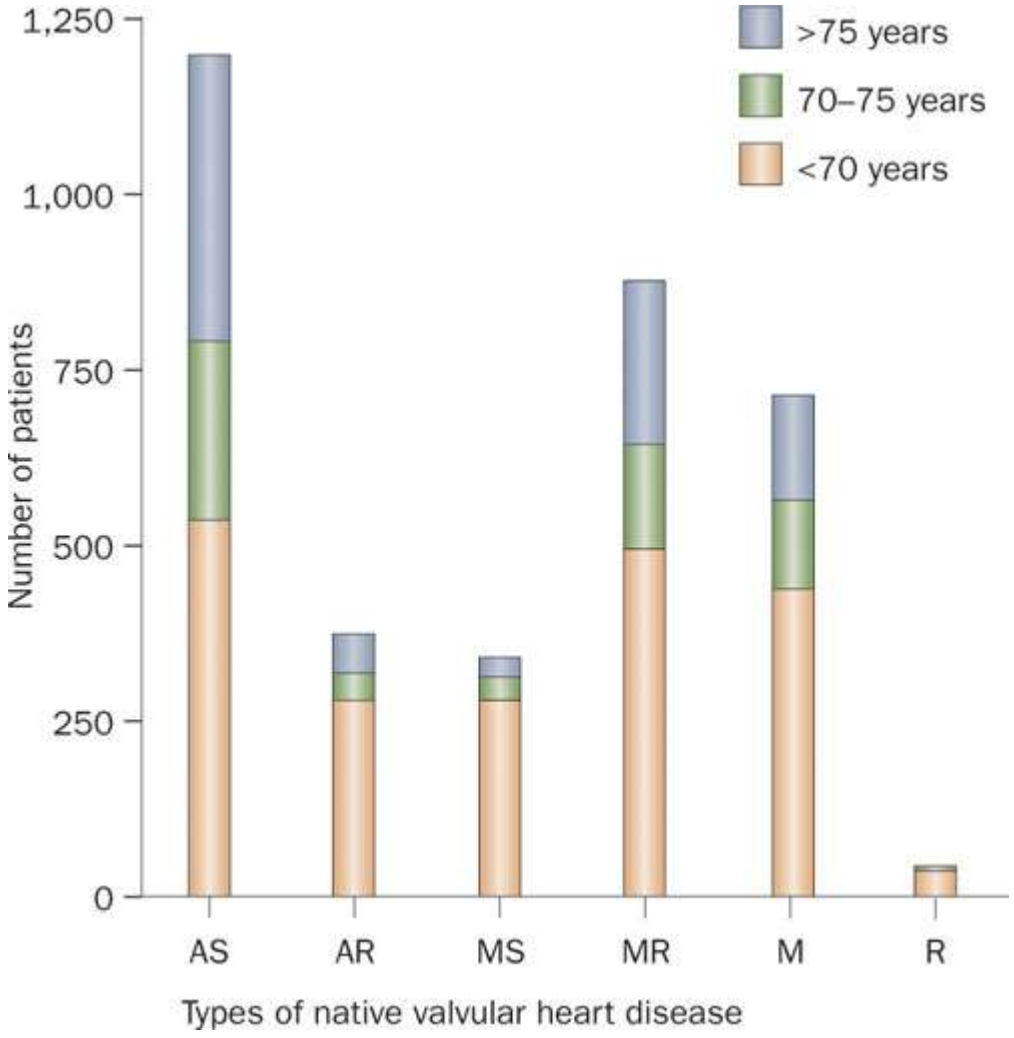
Valvular heart disease (VHD) is any disease process involving one or more of the four valves of the heart (the aortic and mitral valves on the left and the pulmonary and tricuspid valves on the right).

There are two types of heart valve disease:

- Valvular stenosis, that occurs when a heart valve doesn't fully open due to stiff or fused leaflets.
- Valvular insufficiency (regurgitation, incompetence, "leaky valve“), that occurs when a valve does not close tightly

http://www.webmd.com/heart-disease/guide/heart-valve-disease https://en.wikipedia.org/wiki/Valvular_heart_disease

Epidemiology



- Valvular heart disease occur largely as a result of aging.
- Most people are in their late 50s when diagnosed, and more than one in ten people over 75 have it.
- Abbreviation: AR, aortic regurgitation; AS, aortic stenosis; M, multiple valve disease; MR, mitral regurgitation; MS, mitral stenosis; R, right-sided heart disease.

http://www.nature.com/nrcardio/journal/v8/n3/fig_tab/nrcardio.2010.202_ft.html https://en.wikipedia.org/wiki/Valvular_heart_disease

Risk Factors and Etiology

- Aortic stenosis: calcification of tricuspid aortic valve with age, calcification of bicuspid aortic valve, rheumatic fever.
- Aortic regurgitation: 1) acute: infective endocarditis, trauma; 2) chronic: 2a) primary valvular: rheumatic fever, bicuspid aortic valve, Marfan's syndrome, Ehlers–Danlos syndrome, ankylosing spondylitis, systemic lupus erythematosus; 2b) disease of the aortic root: syphilitic aortitis, osteogenesis imperfecta, aortic dissection, Behçet's disease, reactive arthritis, systemic hypertension.
- Mitral stenosis: almost always caused by rheumatic heart disease.
- Mitral regurgitation: 1) acute: endocarditis, mainly *S. aureus,* papillary muscle rupture or dysfunction, including mitral valve prolapse; 2) chronic: rheumatic fever, Marfan's syndrome, cardiomyopathy.
- Tricuspid regurgitation: 1) secondary to right ventricular dilation; 2) Other causes: tricuspid endocarditis, rheumatic fever, Ebstein's anomaly, carcinoid syndrome and myxomatous degeneration.

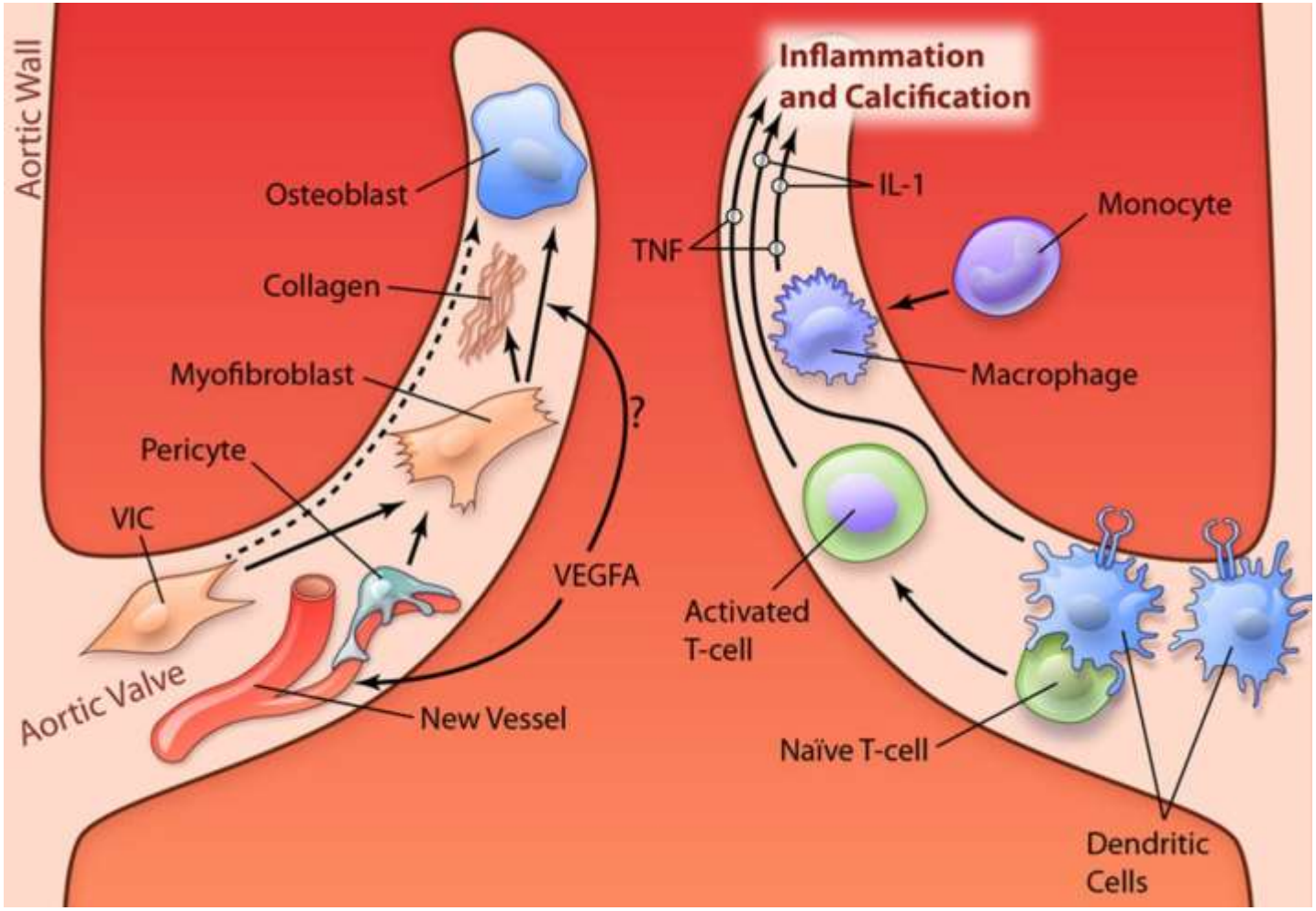
https://en.wikipedia.org/wiki/Valvular_heart_disease

Mechanisms

- Aortic stenosis: obstruction through the aortic ostium causes increased pressure in the LV and impaired flow through the aorta.
- Aortic regurgitation: insufficiency of the aortic valve causes backflow of blood into the LV during diastole.
- Mitral stenosis: progressive obstruction of the mitral ostium causes increased pressure in the left atrium and the pulmonary circulation; congestion may cause thromboembolism, and atrial hypertension may cause atrial fibrillation.
- Mitral regurgitation: insufficiency of the mitral valve causes backflow of blood into the left atrium during systole.
- Tricuspid regurgitation: insufficiency of the tricuspid valve causes backflow of blood into the right atrium during systole.

https://en.wikipedia.org/wiki/Valvular_heart_disease

Mechanisms
(Accents on Inflammation)



http://circresearch.com/gallery/fibrocalcific-aortic-valve-disease-opportunity-to-understand-disease-mechanisms-using-mouse-models/

Classification
(International Classification of Diseases (ICD)

I34 Nonrheumatic mitral valve disorder

I35 Nonrheumatic aortic valve disorders

I36 Nonrheumatic tricuspid valve disorders

I37 Pulmonary valve disorders

I38 Endocarditis, valve unspecified

I39* Endocarditis and heart valve disorders in diseases classified elsewhere

Q22 Congenital malformations of pulmonary and tricuspid valves

Q23 Congenital malformations of aortic and mitral valves

Q24 Other congenital malformations of heart

Q25 Congenital malformations of great arteries

apps.who.int/classifications/icd10/browse/2016/en#/I46

Classification
(Types)

Valve involved	Stenotic disease	Insufficiency/regurgitation disease
Aortic valve	Aortic valve stenosis (AS)	Aortic insufficiency/regurgitation (AR)
Mitral valve	Mitral valve stenosis (MS)	Mitral insufficiency/regurgitation (MR)
Tricuspid valve	Tricuspid valve stenosis	Tricuspid insufficiency/regurgitation
Pulmonary valve	Pulmonary valve stenosis	Pulmonary insufficiency/regurgitation

https://en.wikipedia.org/wiki/Valvular_heart_disease

Classification
(Stages of Progression of VHD)

Stage	Definition	Description
A	At risk	Patients with risk factors for development of VHD
B	Progressive	Patients with progressive VHD (mild-to-moderate severity and asymptomatic)
C	Asymptomatic severe	Asymptomatic patients who have the criteria for severe VHD:
		C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated
		C2: Asymptomatic patients with severe VHD with decompensation of the left or right ventricle
D	Symptomatic severe	Patients who have developed symptoms as a result of VHD

http://content.onlinejacc.org/article.aspx?articleid=1838843

Clinical Investigation

- Aortic stenosis: heart failure symptoms; angina pectoris; syncope, usually exertional.
- Aortic regurgitation: heart failure symptoms; palpitations; angina pectoris; in acute cases: cyanosis and circulatory shock.
- Mitral stenosis: heart failure symptoms.
- Mitral regurgitation: heart failure symptoms; palpitations; pulmonary edema.
- Tricuspid regurgitation: symptoms of right-sided heart failure (ascites, hepatomegaly, edema, jugular venous distension, and atc.).

https://en.wikipedia.org/wiki/Valvular_heart_disease

Diagnosis

- Aortic stenosis: chest X-ray (calcific aortic valve, enlarged LV and atrium); ECG (LV hypertrophy and left atrial abnormality; echocardiography (LV hypertrophy, thickened and immobile aortic valve and dilated aortic root); cardiac chamber catheterization (stenosis in valve area).
- Aortic regurgitation: chest X-ray (LV hypertrophy, dilated aorta); ECG (LV hypertrophy); echocardiogram (dilated left aortic root and reversal of blood flow in the aorta).
- Mitral stenosis: chest X-ray (left atrial enlargement); echocardiography (left atrial enlargement, thick and calcified mitral valve with narrow and "fish-mouth"-shaped orifice and signs of right ventricular failure in advanced disease).
- Mitral regurgitation: chest X-ray (dilated LV); echocardiography (mitral reverse flow, dilated left atrium and LV with decreased LV function).
- Tricuspid regurgitation: echocardiography (tricuspid prolapse or flail), ECG (enlargement of RV and atrium).

https://en.wikipedia.org/wiki/Valvular_heart_disease

Diagnosis

(Echocardiographic Criteria for the Definition of Severe Valve Stenosis)

	Aortic stenosis	Mitral stenosis	Tricuspid stenosis
Valve area (cm^2)	<1.0	<1.0	–
Indexed valve area (cm^2/m^2 BSA)	<0.6	–	–
Mean gradient (mmHg)	>40[a]	>10[b]	≥5
Maximum jet velocity (m/s)	>4.0[a]	–	–
Velocity ratio	<0.25	–	–

https://eurheartj.oxfordjournals.org/content/ehj/33/19/2451.full.pdf

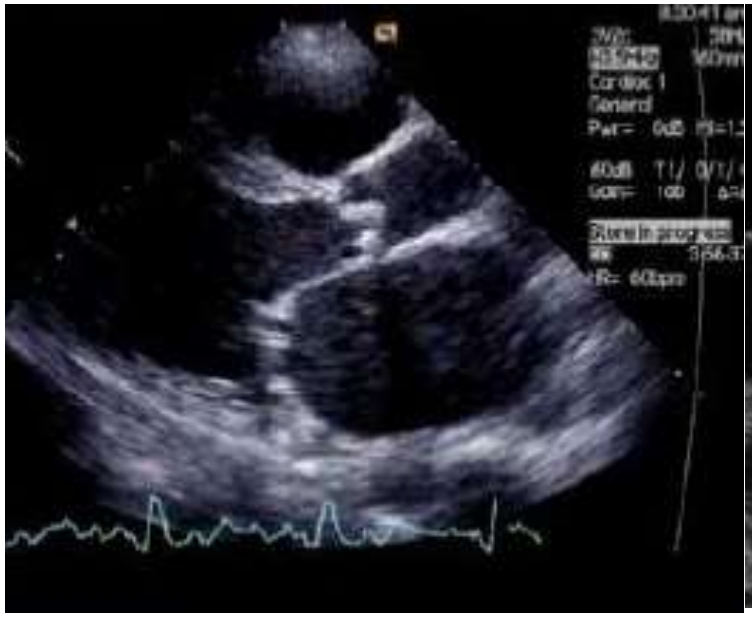
Diagnosis

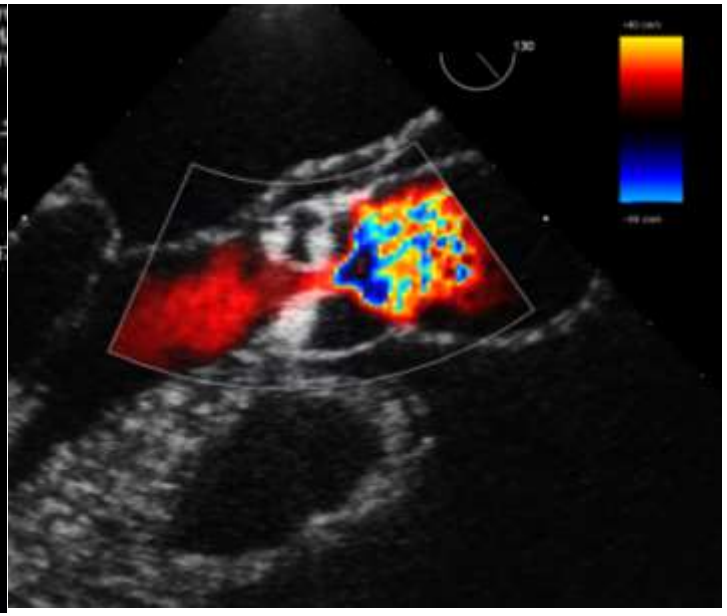
(Echocardiographic Criteria for the Definition of Severe Valve Regurgitation)

	Aortic regurgitation	Mitral regurgitation		Tricuspid regurgitation
Qualitative				
Valve morphology	Abnormal/flail/large coaptation defect	Flail leaflet/ruptured papillary muscle/ large coaptation defect		Abnormal/flail/large coaptation defect
Colour flow regurgitant jet	Large in central jets, variable in eccentric jets[a]	Very large central jet or eccentric jet adhering, swirling, and reaching the posterior wall of the left atrium		Very large central jet or eccentric wall impinging jet[a]
CW signal of regurgitant jet	Dense	Dense/triangular		Dense/triangular with early peaking (peak <2 m/s in massive TR)
Other	Holodiastolic flow reversal in descending aorta (EDV >20 cm/s)	Large flow convergence zone[a]		–
Semiquantitative				
Vena contracta width (mm)	>6	≥7 (>8 for biplane)[b]		≥7[a]
Upstream vein flow[c]	–	Systolic pulmonary vein flow reversal		Systolic hepatic vein flow reversal
Inflow	–	E-wave dominant ≥1.5 m/s[d]		E-wave dominant ≥1 m/s[e]
Other	Pressure half-time <200 ms[f]	TVI mitral/TVI aortic >1.4		PISA radius >9 mm[g]
Quantitative		Primary	Secondary[h]	
EROA (mm^2)	≥30	≥40	≥20	≥40
R Vol (ml/beat)	≥60	≥60	≥30	≥45
+ enlargement of cardiac chambers/vessels	LV	LV, LA		RV, RA, inferior vena cava

https://eurheartj.oxfordjournals.org/content/ehj/33/19/2451.full.pdf

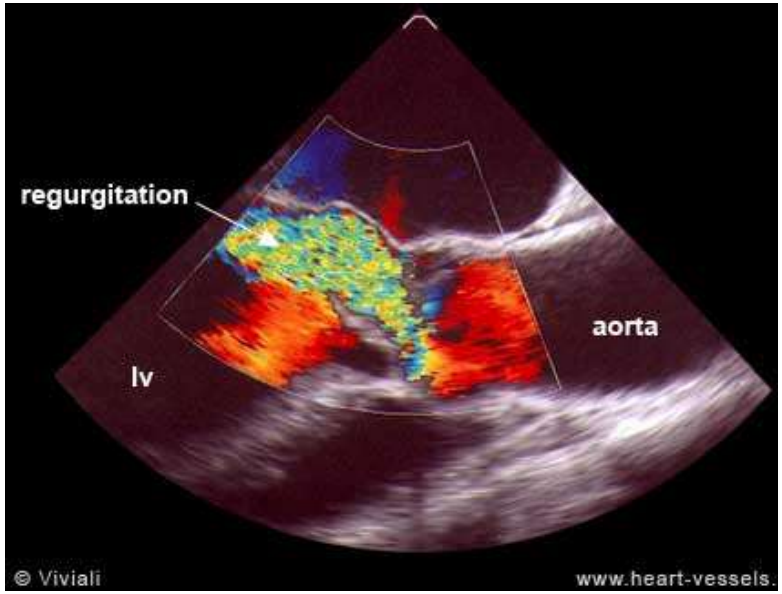
Diagnosis
(Aortic Stenosis)

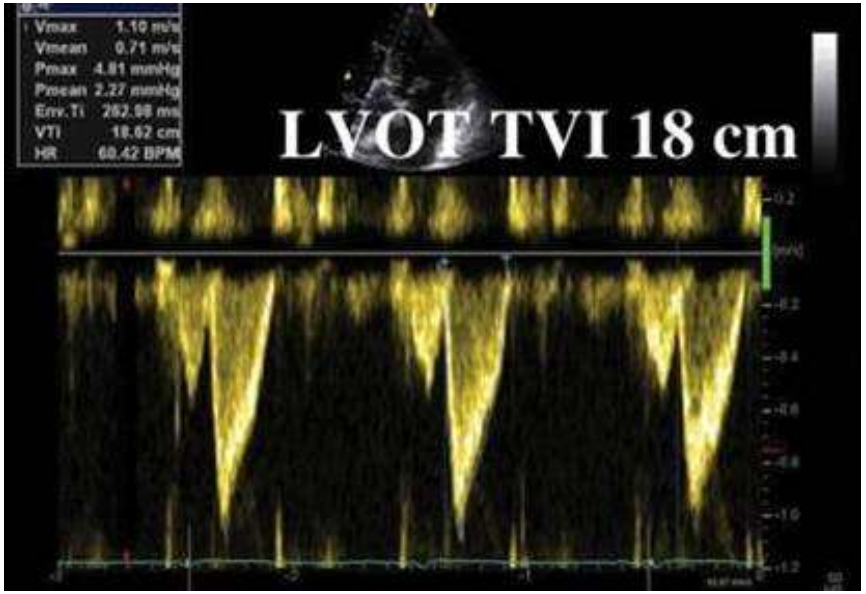




http://www.inventivemedical.com/wp-content/uploads/2014/10/Pathology-4-aortic-stenosis-Doppler-1.png https://en.wikipedia.org/wiki/Valvular_heart_disease

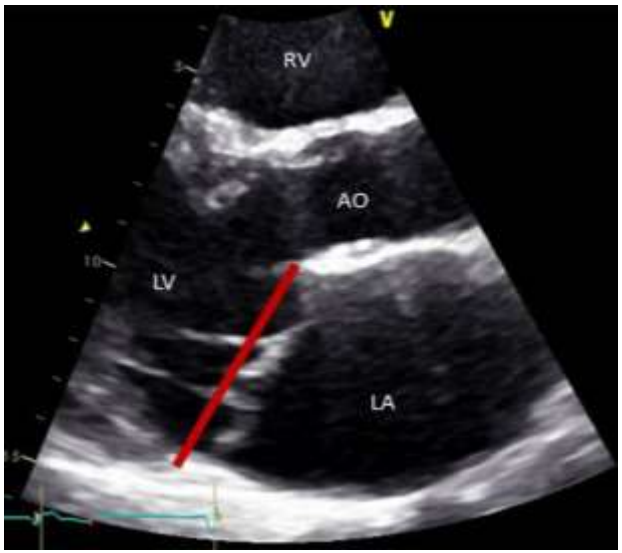
Diagnosis
(Aortic Regurgitation)



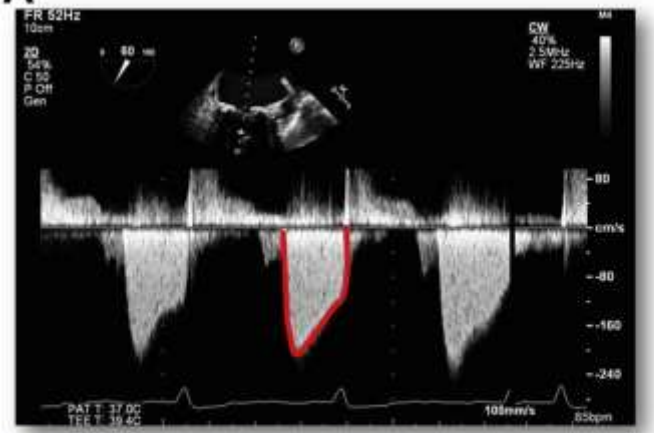


http://1.bp.blogspot.com/-RJ1nkDRY6Rc/TzJPB9zVHsI/AAAAAAAADqM/9tzJ5p0XUJA/s1600/Obraz1.jpg http://www.heart-vessels.com/images/aortic-insufficiency.jpg

Diagnosis
(Mitral Stenosis)

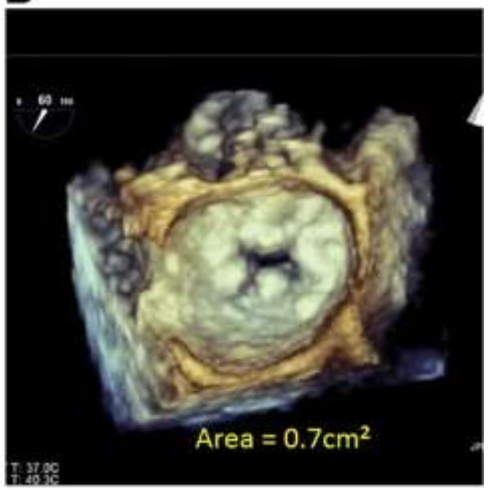


A



Doppler mean gradient 9.5mmHg
MVA 1.5cm^2 (Pressure half-time method)

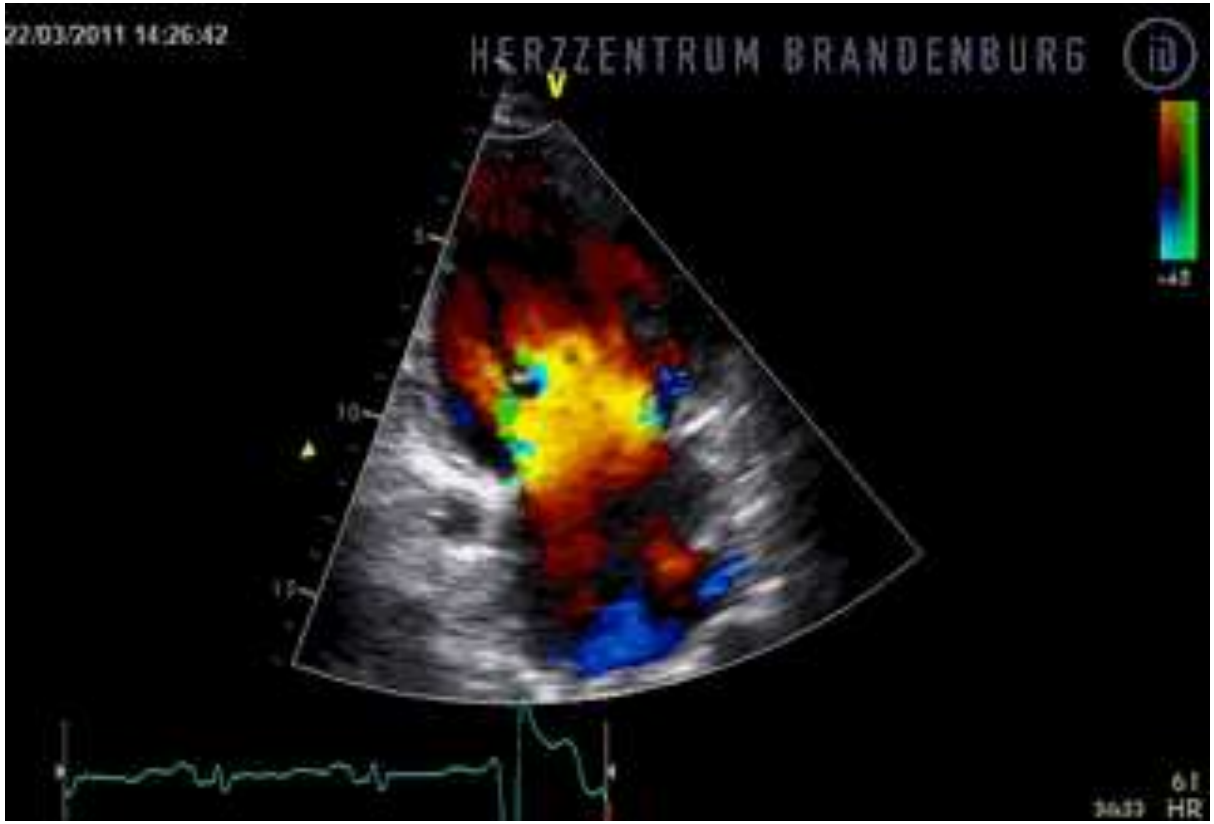
B



Severe MV Stenosis

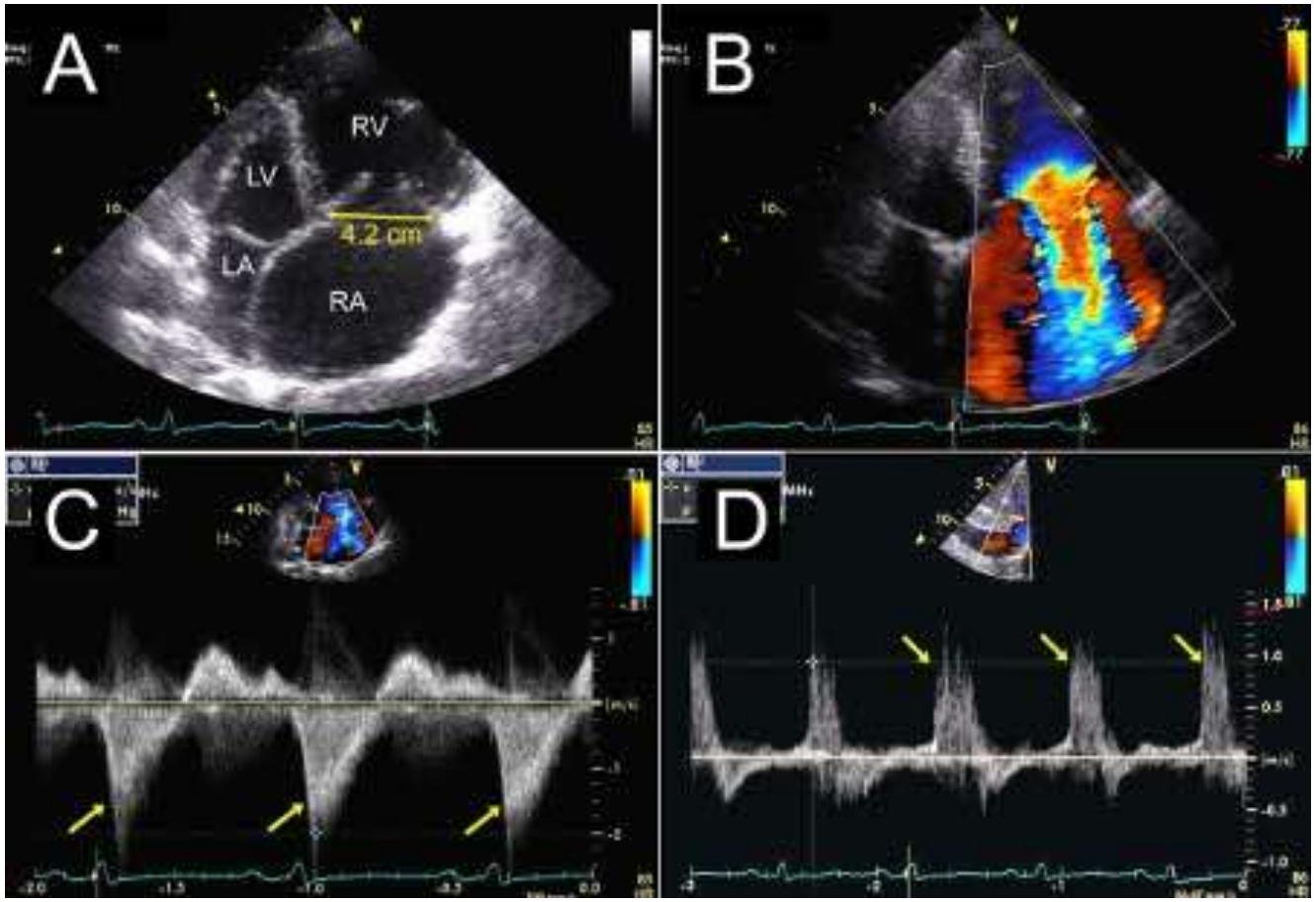
content.onlinejacc.org/data/Journals/JAC/928699/81619_gr4.jpeg clevelandclinicmeded.com/medicalpubs/diseasemanagement/cardiology/mitral-valve-disease/images/figure-8.jpg

Diagnosis
(Mitral Regurgitation)



herzzentrum.immanuel.de/fileadmin/user_upload/IK_Bernau/03_Abteilungen/03_07_Herzzentrum/03_07_02_Leistungen/02_1_Krankheitsbilder

Diagnosis
(Tricuspid Regurgitation)



http://bestpractice.bmj.com/best-practice/images/bp/en-gb/472-2_default.jpg

Treatment
(Aortic Stenosis)

- No treatment in asymptomatic patients.
- If symptomatic, treated with aortic valve replacement surgery.
- Medical therapy and percutaneous balloon valvuloplasty have relatively poor effect:
  - any angina is treated with short-acting nitrovasodilators, beta-blockers and/or calcium blockers;
  - any hypertension is treated aggressively, but caution must be taken in administering beta-blockers;
  - Any heart failure is treated with diuretics, nitrovasodilators and, if not contraindicated, cautious inpatient administration of ACE inhibitors.

https://en.wikipedia.org/wiki/Valvular_heart_disease

Treatment
(Aortic Regurgitation)

- If stable and asymptomatic - conservative treatment such as low sodium diet, diuretics, vasodilators (e.g. (hydralazin or prazosin), ACE inhibitors/angiotensin II receptor antagonists, calcium blockers and avoiding very strenuous activity.
- Aortic valve replacement in symptomatic patients (NYHA II-IV) or progressive LV dilation or systolic ventricular diameter >55 mm on echocardiography, immediately if acute.
- Endocarditis prophylaxis is indicated before dental, gastrointestinal or genitourinary procedures.

https://en.wikipedia.org/wiki/Valvular_heart_disease

Treatment
(Mitral Stenosis)

- No therapy is required for asymptomatic patients.
- Diuretics for any pulmonary congestion or edema.
- If stenosis is severe, surgery is recommended.
- Any atrial fibrillation is treated accordingly (rate or rrhythm control, and chronic anticoagulant administration).
- Prophylaxis of infective endocarditis .
- Surgically, by mitral valvuloplasty with a percutaneously inserted balloon, unless significant mitral regurgitation or too much calcification (indicated in ostium area < 1-1.2 $cm^{2)}$.
- Other options include valvulotomy or mitral valve replacement by open_surgery.

https://en.wikipedia.org/wiki/Valvular_heart_disease

Treatment
(Mitral Regurgitation)

- Medically:
  - afterload reduction with vasodilators;
  - any hypertension is treated aggressively, e.g. by diuretics and low sodium diet;
  - antiarrhythmics;
  - chronic anticoagulation in concomitant mitral valve prolapse or atrial fibrillation.
- In acute cases - intra-aortic balloon pump (IABP) as temporary solution until surgery.
- Surgery by either mitral valve repair or mitral valve replacement, indicated if very symptomatic (NYHA III), ventricular dilation or decreasing ejection fraction.

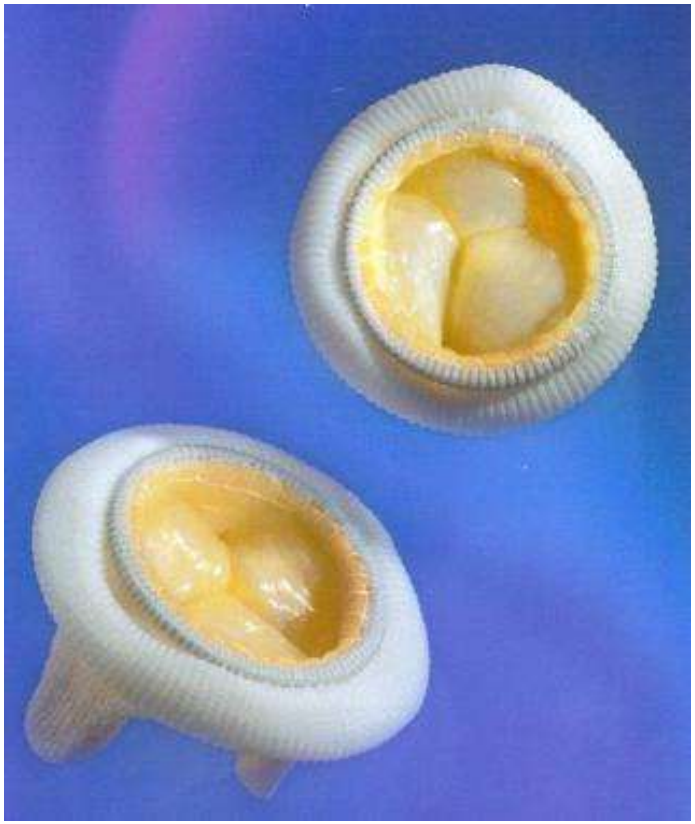
https://en.wikipedia.org/wiki/Valvular_heart_disease

Treatment
(Tricuspid Regurgitation)

- Treatment of underlying cause.
- Surgery:
  - tricuspid valvular repair;
  - Valvuloplasty;
  - valve replacement(rarely performed).

https://en.wikipedia.org/wiki/Valvular_heart_disease

Treatment
(Prosthetic Heart Valves)



- Bioprosthetic valves used in heart valve replacement generally offer functional properties (e.g., hemodynamics, resistance to thrombosis) that are more similar to those of native valves.
- Implantation of prosthetic cardiac valves to treat hemodynamically significant aortic or mitral valve disease has become increasingly common.

http://emedicine.medscape.com/article/780702-overview

Treatment
(Prosthetic Heart Valves Malfunction)

- Acute prosthetic valve failure: sudden onset of dyspnea, syncope, or precordial pain.
- Acute aortic valve failure: sudden death; survivors have acute severe dyspnea, sometimes accompanied by precordial pain, or syncope.
- Subacute valvular failure: symptoms of gradually worsening congestive heart failure; they also may present with unstable angina or, at times, may be entirely asymptomatic.
- Embolic complications: symptoms related to the site of embolization (e.g., stroke, myocardial infarction, sudden death, or symptoms of visceral or peripheral embolization).
- Anticoagulant-related hemorrhage: symptoms related to the site of hemorrhage.

http://emedicine.medscape.com/article/780702-overview

Prognosis

- The prognosis for patients with valvular heart disease has improved substantially over the past 15 years.
- A better understanding of the proper timing of surgery is one of the key reasons.
- In general, surgery for stenotic valvular disease can be delayed until symptoms appear.
- Conversely, in regurgitant valvular heart disease, prognostically important left ventricular dysfunction may develop in the absence of symptoms, and thus valve surgery for some asymptomatic patients is entirely appropriate.

http://www.nejm.org/doi/full/10.1056/NEJM199707033370107

Prophylaxis

- Prompt treatment of strep infections can prevent rheumatic fever, which damages the heart valves.
- An exercise, a heart-healthy diet, and medicines that lower cholesterol might prevent aortic stenosis (thickening and stiffening of the aortic valve).
- Heart-healthy eating, physical activity, other heart-healthy lifestyle changes, and medicines aimed at preventing a heart attack, high blood pressure, or heart failure also may help prevent heart valve disease.

https://www.nhlbi.nih.gov/health/health-topics/topics/hvd/prevention

Abbreviations

ACE - angiotensin converting enzyme

AR – aortic regurgitation

AS - aortic valve stenosis

ECG - electrocardiogram

ERO - effective regurgitant orifice

IABP - intra-aortic balloon pump

IE - infective endocarditis

LA - left atrium

LVEF - left ventricular ejection fraction

LVESD - left ventricular end-systolic dimension

MS - mitral valve stenosis

MVA - mitral valve area

PAWP pulmonary artery wedge pressure

MR – mitral regurgitation

PR – pulmonary regurgitation

VHD - valvular heart disease

Diagnostic and treatment guidelines

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

Guidelines on the management of valvular heart disease (version 2012)

Prosthetic Heart Valves

Infective Endocarditis

Plan of the Lecture

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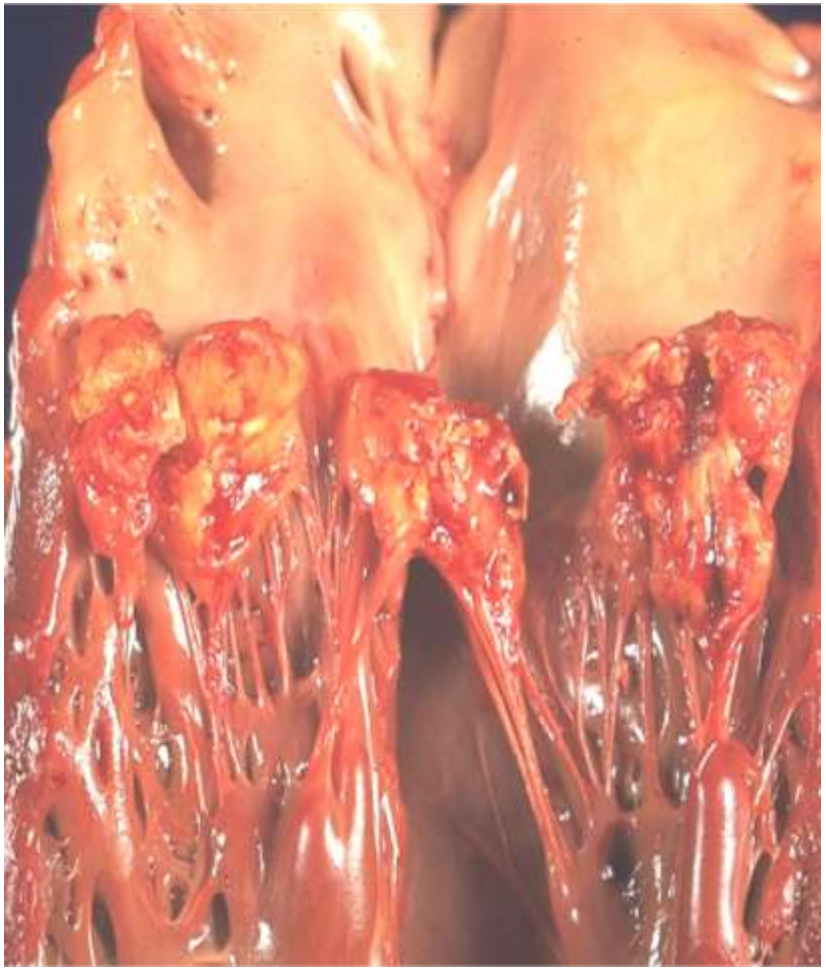
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines



https://mileon.files.wordpress.com/2010/07/sin-titulo4.png

Definition

Infective endocarditis (IE) is a potentially lethal disease caused largely by bacteria that enter the bloodstream and settle in the heart, which may include one or more heart valves, the mural endocardium, or a septal defect or a blood vessel, with intracardiac effects that include severe valvular insufficiency and intractable congestive heart failure and myocardial abscesses.

emedicine.medscape.com/article/216650-overview circ.ahajournals.org/content/early/2015/09/15/CIR.0000000000000296

Epidemiology

- IE is an uncommon infectious disease with an annual incidence ranging from 3 to 7 per 100000 person-years in the most contemporary population surveys.
- Although relatively rare, IE continues to be characterized by increased morbidity and mortality and is now the third or fourth most common life-threatening infection syndrome, after sepsis, pneumonia, and intra-abdominal abscess.
- Characteristics of IE patients have shifted toward an increased mean patient age, a higher proportion of prosthetic valves and other cardiac devices, and a decreasing proportion of rheumatic heart disease.
- The proportion of IE patients undergoing surgery has increased over time to reach ≈50%.

http://circ.ahajournals.org/content/early/2015/09/15/CIR.0000000000000296

Risk Factors

- Artificial heart valves.
- Intracardiac devices.
- Unrepaired cyanotic congenital heart defects.
- History of infective endocarditis.
- Chronic rheumatic heart disease.
- Age-related degenerative valvular lesions.
- Hemodialysis.
- Coexisting conditions, especially ones that suppress immunity (diabetes mellitus, alcohol abuse, HIV/AIDS, and intravenous drug).
- Etc.

https://en.wikipedia.org/wiki/Infective_endocarditis

Etiology

- Many microorganisms can cause infective endocarditis.
- These are generally isolated by blood culture, where the patient's blood is removed, and any growth is noted and identified.
- The term bacterial endocarditis (BE) commonly is used, reflecting the fact that most cases of IE are due to bacteria; however, infective endocarditis (IE) has become the preferred term.

https://en.wikipedia.org/wiki/Infective_endocarditis

Etiology
(Bacterial)

- *Staphylococcus aureus* followed by *Streptococci* of the viridans group and coagulase negative Staphylococci are the three most common organisms responsible for infective endocarditis.
- Other *Streptococci* and *Enterococci* are also a frequent cause of infective endocarditis.
- *Enterococcus* can enter the bloodstream as a consequence of abnormalities in the gastrointestinal or genitourinary tracts.
- Some organisms, when isolated, give valuable clues to the cause, as they tend to be specific.
- Less commonly reported etiological bacteria are *Pseudomonas, S. bovis, Clostridium septicum*, *Bartonella*, *Chlamydia psittaci*, *Coxiella etc*.

https://en.wikipedia.org/wiki/Myocarditis#Causes

Etiology
(Fungal)

- *Candida albicans*, a yeast, is associated with endocarditis in IV drug users and immunocompromised patients.
- Other fungi demonstrated to cause endocarditis are *Histoplasma capsulatum* and Aspergillus.
- Endocarditis with *Tricosporon asahii* has also been reported.

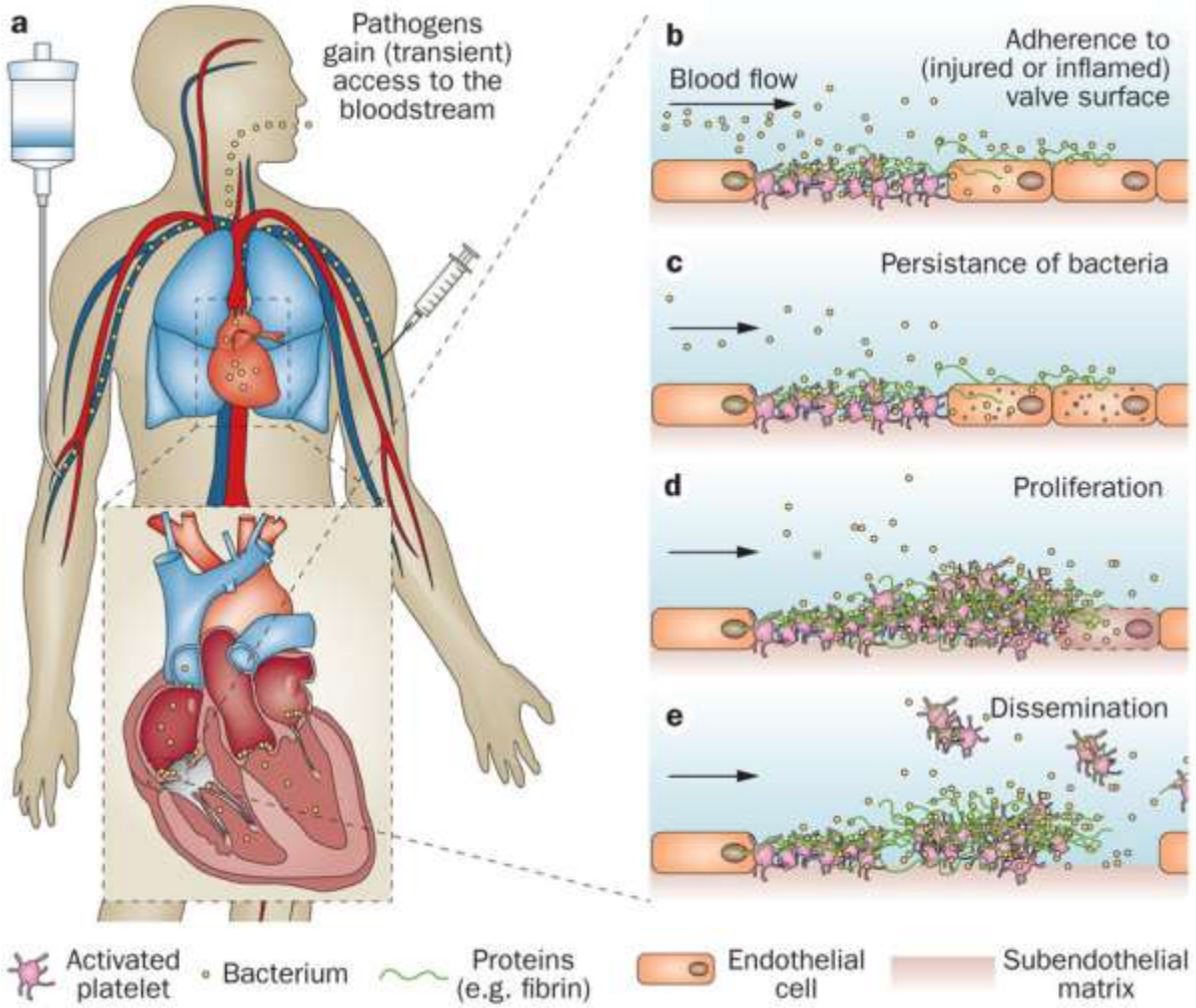
https://en.wikipedia.org/wiki/Myocarditis#Causes

Mechanisms

- Damaged valves and endocardium contribute to the development of IE.
- The damaged part of a heart valve forms a local blood clot, a condition known as non-bacterial thrombotic endocarditis (NBTE); the platelet and fibrin deposits that form as part of the blood clotting process allow bacteria to take hold and form vegetations.
- Damage to the valves and endocardium can be caused by altered, turbulent blood flow, more likely in high pressure areas; catheters, electrodes, and other intracardiac prosthetic devices; solid particles from repeated intravenous injections, chronic inflammation.
- The complications of acute BE result from intracardiac disease and metastatic infection produced by suppurative emboli.
- Because of their shortened course, immunological phenomena are not a part of acute IE.

http://emedicine.medscape.com/article/216650-overview#a3 https://en.wikipedia.org/wiki/Myocarditis#Causes

Mechanisms
(pathogen–host interaction and risk states)



http://www.nature.com/nrcardio/journal/v11/n1/fig_tab/nrcardio.2013.174_F1.html

Classification
(International Classification of Diseases (ICD))

133 Acute and subacute endocarditis

I33.0 Acute and subacute infective endocarditis

Endocarditis (acute)(subacute):bacterial

infective NOS

lenta

malignant

septic

ulcerative.

I33.9 Acute endocarditis, unspecified.

apps.who.int/classifications/icd10/browse/2016/en#/I46

Classification
(the Rate of Progression and Severity of Disease)

- *Subacute bacterial endocarditis* (SBE) is often due to streptococci of low virulence (mainly viridans streptococci) and mild to moderate illness which progresses slowly over weeks and months and has low propensity to hematogenously seed extracardiac sites.
- *Acute bacterial endocarditis* (ABE) is a fulminant illness over days to weeks, and is more likely due to *Staphylococcus aureus* which has much greater virulence, or disease-producing capacity and frequently causes metastatic infection.
- Prosthetic valvular endocarditis (PVE) develops in 2 to 3% of patients within 1 yr. after valve replacement and in 0.5%/yr. thereafter.
- The terms *short incubation* (meaning less than about six weeks), and *long incubation* (greater than about six weeks) are preferred.

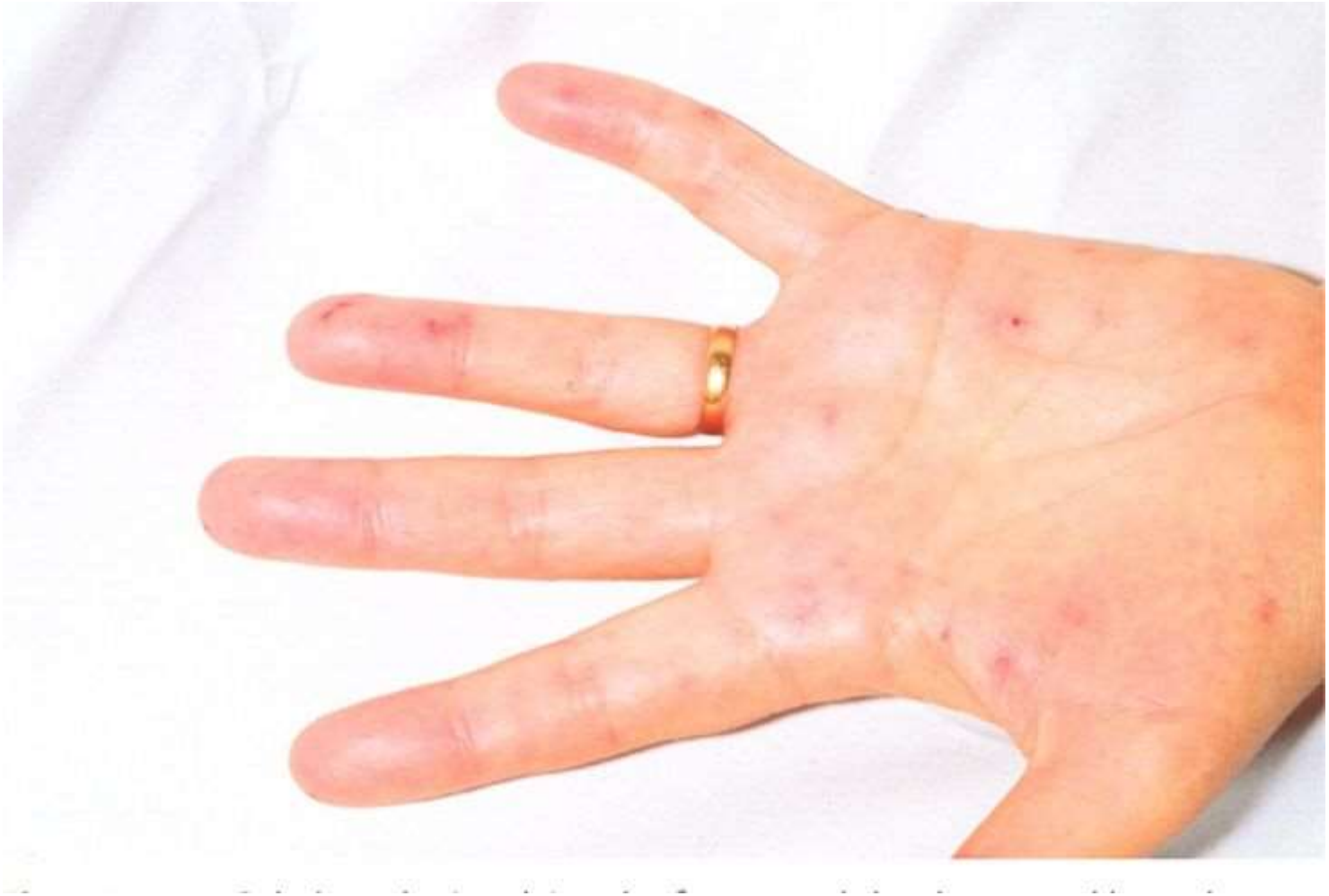
http://www.merckmanuals.com/professional/cardiovascular-disorders/endocarditis/infective-endocarditis https://en.wikipedia.org/wiki/Infective_endocarditis

Clinical Investigation
(Signs and Symptoms)

- Fever (97% of patients), malaise and endurance fatigue (90% of patients).
- A new or changing heart murmur, weight loss, and coughing (35% of patients).
- Vascular phenomena: septic embolism (causing stroke or gangrene of fingers), Janeway lesions (painless hemorrhagic cutaneous lesions on the palms and soles), intracranial hemorrhage, conjunctival and splinter hemorrhages, kidney and splenic infarcts.
- Immunologic phenomena: glomerulonephritis , Osler's nodes (painful subcutaneous lesions in the distal fingers), Roth's spots on the retina, positive serum rheumatoid factor)
- Other signs: night sweats, rigors, anemia, etc.

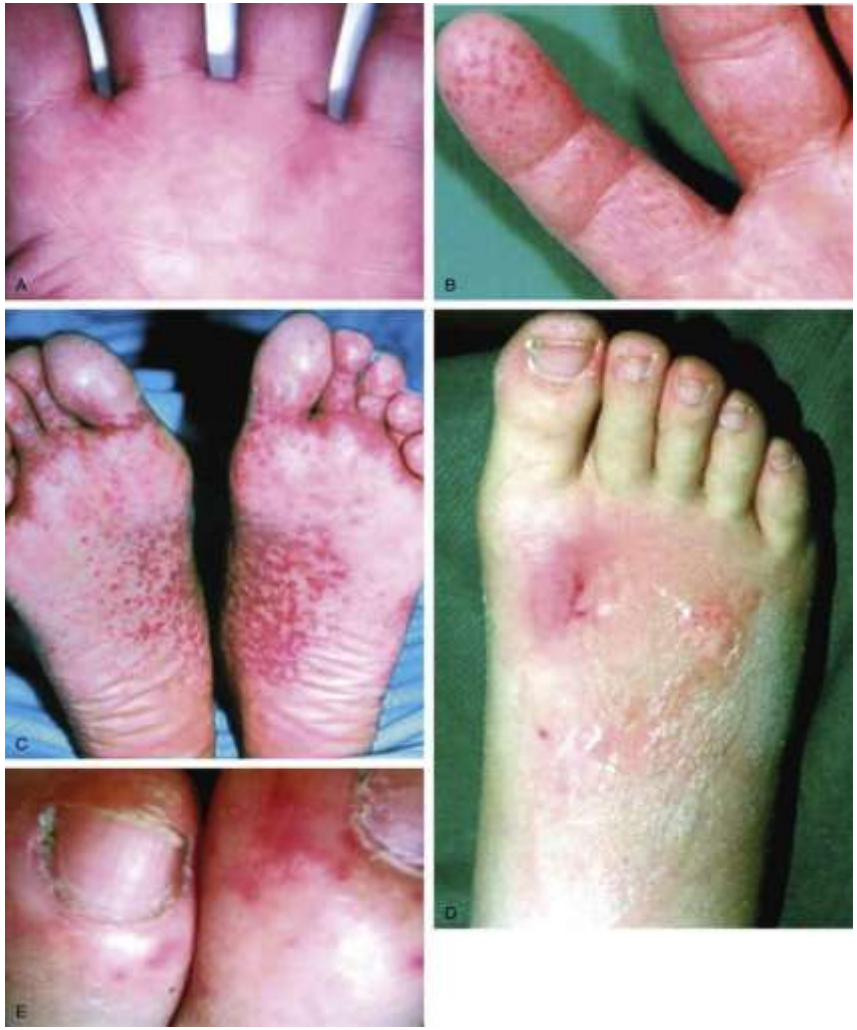
https://en.wikipedia.org/wiki/Infective_endocarditis

Clinical Investigation
(Janeway lesions)



https://s-media-cache-ak0.pinimg.com/736x/89/bc/e9/89bce950c573e31574d2ebf4731ec3a7.jpg

Clinical Investigation
(Skin Lesions)

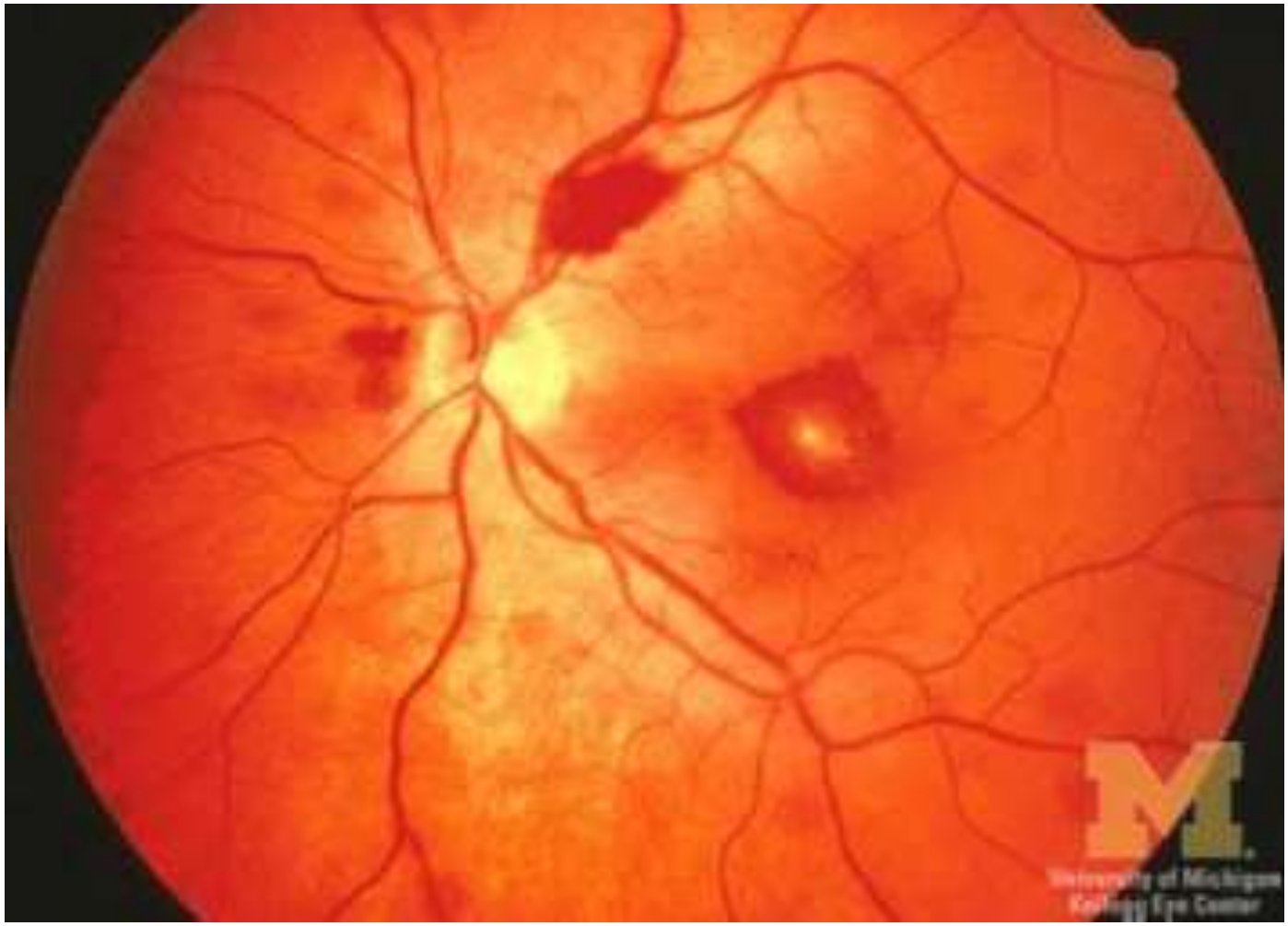


http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/infectious-disease/infective-endocarditis/

Clinical Investigation
(Osler's Nodes)

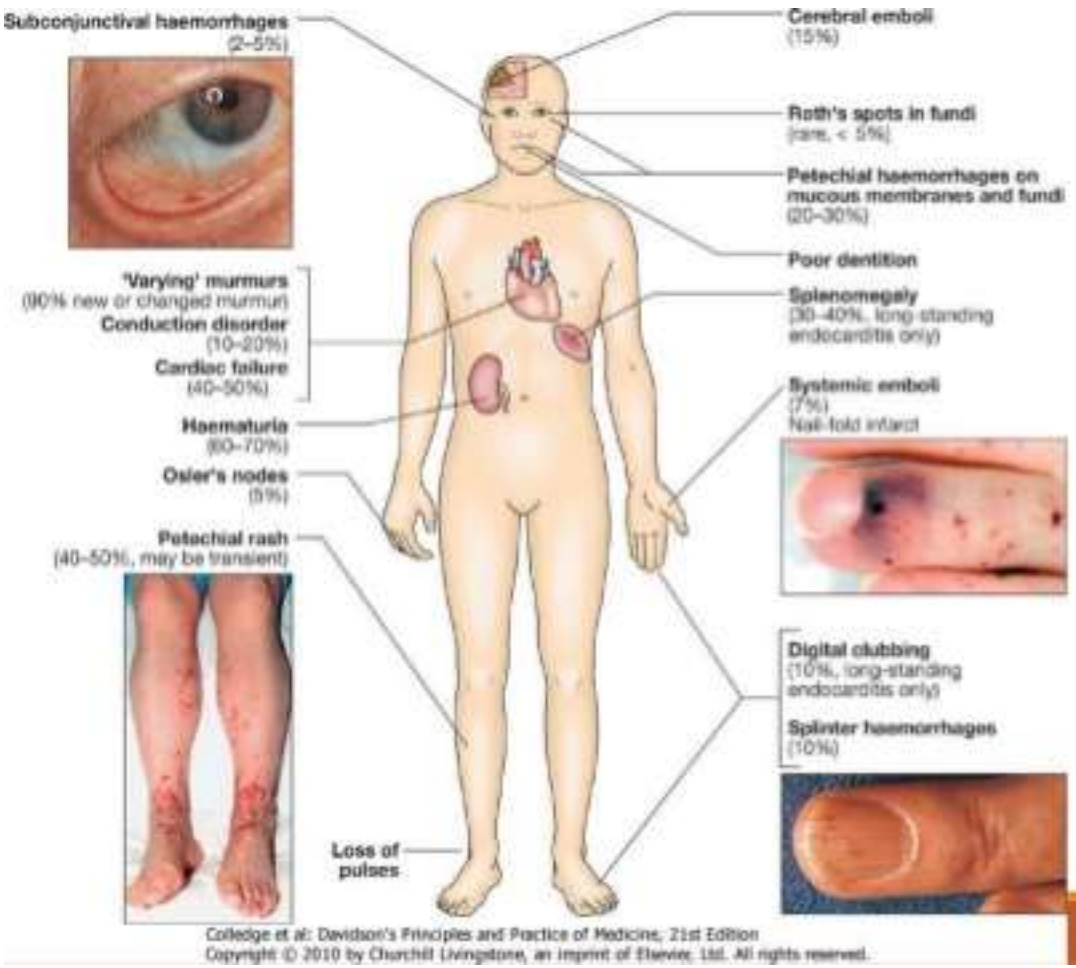
http://yxzl.baiduyy.com/chm11/jzyxtp/Ch.13_files/image012.jpg

Clinical Investigation
(Roth's spots)



http://medlibes.com/uploads/Screen%20shot%202010-07-17%20at%205.12.22%20PM.png

Clinical Investigation
(Sub-acute IE clinical symptoms)



Sub-acute Endocarditis

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

- Embolic Stroke
- Peripheral arterial embolism

- Other features

http://image.slidesharecdn.com/infectiveendocarditis-130201001609-phpapp02/95/infective-endocarditis-11-638.jpg?cb=1359678043

Diagnosis

- The diagnosis of IE is straightforward in the minority of patients who present with a consistent history and classic oslerian manifestations: sustained bacteremia or fungemia, evidence of active valvulitis, peripheral emboli, and immunological vascular phenomena.
- In most patients, however, the “textbook” history and physical examination findings may be few or absent.
- Acute IE may evolve too quickly for the development of immunological vascular phenomena, which are more characteristic of the later stages of the more insidious subacute form of untreated IE.
- The variability in clinical presentation of IE and the importance of early accurate diagnosis require a diagnostic strategy that is both sensitive for disease detection and specific for its exclusion across all forms of the disease.
- In 1994, Durack and colleagues23 from the Duke University Medical Center proposed a diagnostic schema that stratified patients with suspected IE into 3 categories: definite, possible, and rejected cases.

http://circ.ahajournals.org/content/early/2015/09/15/CIR.0000000000000296

Diagnosis
(the Modified Duke Criteria: Definite, Possible, and Rejected Cases)

Definite IE

Pathological criteria: microorganisms demonstrated by culture or 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, 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

Firm alternative diagnosis explaining evidence of IE; or resolution of IE syndrome with antibiotic therapy for ≤4 d; or no pathological evidence of IE at surgery or autopsy with antibiotic therapy for ≤4 d; or does not meet criteria for possible

IE as above IE indicates infective endocarditis.

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Diagnosis
(the Modified Duke Criteria: Major Criteria)

Blood culture positive for IE (2 separate blood cultures: Viridans streptococci, Streptococcus bovis, HACEK (Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens, and Kingella species) group, Staphylococcus aureus; or community-acquired enterococci in the absence of a primary focus, or microorganisms consistent with IE from persistently positive blood cultures defined as follows: at least 2 positive cultures of blood samples drawn >12 h apart or all 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1 h apart).

Single positive blood culture for Coxiella burnetii or anti–phase 1 IgG antibody titer ≥1:800.

Evidence of endocardial involvement (echocardiogram positive for IE (TEE recommended for patients with prosthetic valves, rated at least possible IE by clinical criteria, or complicated IE).

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Diagnosis
(the Modified Duke Criteria: Minor Criteria)

Predisposition, predisposing heart condition, or IDU (injection drug use)

Fever, temperature >38°C.

Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions.

Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor.

Microbiological evidence: positive blood culture but does not meet a major criterion as noted above (excludes single positive cultures for coagulase negative staphylococci and organisms that do not cause endocarditis) or serological evidence of active infection with organism consistent with IE.

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Diagnosis
(Laboratory Investigations and Biomarkers)

- Sepsis severity may be indicated by the demonstration of a number of laboratory investigations, including the degree of leucocytosis/leucopoenia, the number of immature white cell forms, concentrations of C-reactive protein (CRP) and procalcitonin, erythrocyte sedimentation rate (ESR) and markers of end-organ dysfunction (lactataemia, elevated bilirubin, thrombocytopenia and changes in serum creatinine concentration); however, none are diagnostic for IE.
- Further, certain laboratory investigations are used in surgical scoring systems relevant to risk stratification in patients with IE, including bilirubin, creatinine and platelet count and creatinine clearance.
- The pattern of increase in inflammatory mediators or immune complexes may support, but not prove, the diagnosis of IE.

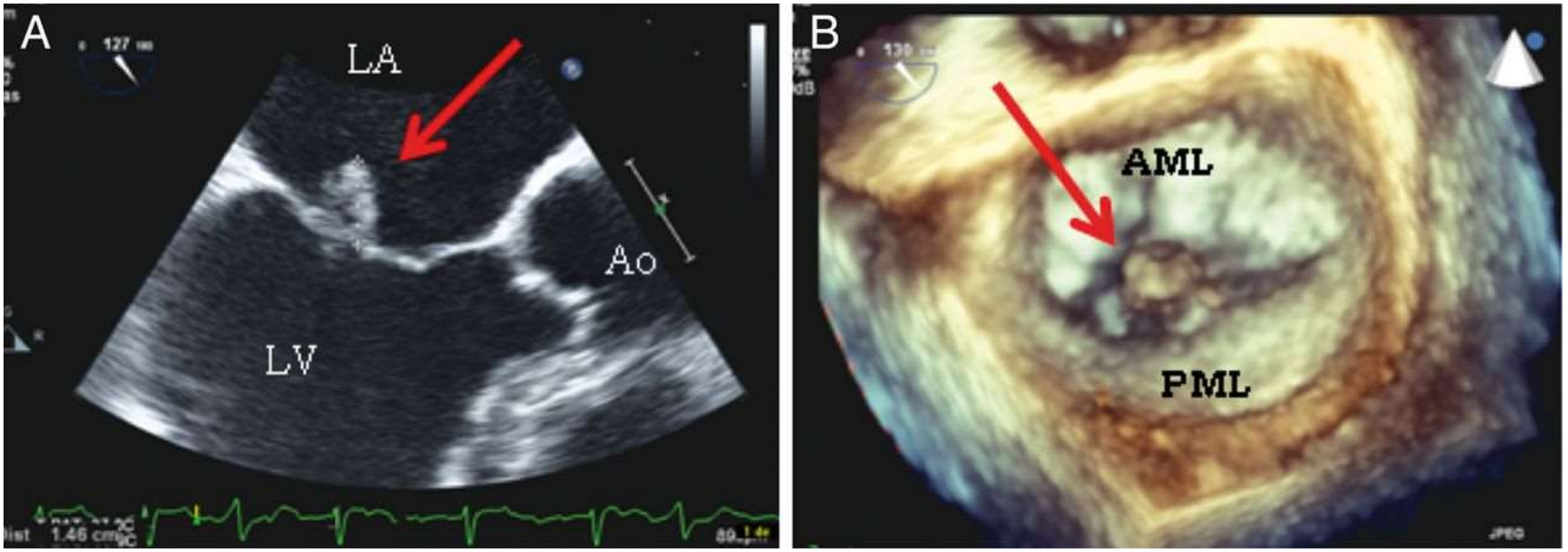
http://eurheartj.oxfordjournals.org/content/early/2015/08/28/eurheartj.ehv319

Diagnosis
(Imaging Techniques)

- Imaging plays a key role in both the diagnosis and management of IE.
- Echocardiography is useful for the prognostic assessment of patients with IE, for its follow-up under therapy and during and after surgery.
- Echocardiography is particularly useful for initial assessment of the embolic risk and in decision making in IE.
- Transoesophageal echocardiography (TEE) plays a major role both before and during surgery (intraoperative echocardiography).
- The evaluation of patients with IE is no longer limited to conventional echocardiography, but should include several other imaging techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET)/computed tomography (CT), etc.

http://eurheartj.oxfordjournals.org/content/early/2015/08/28/eurheartj.ehv319

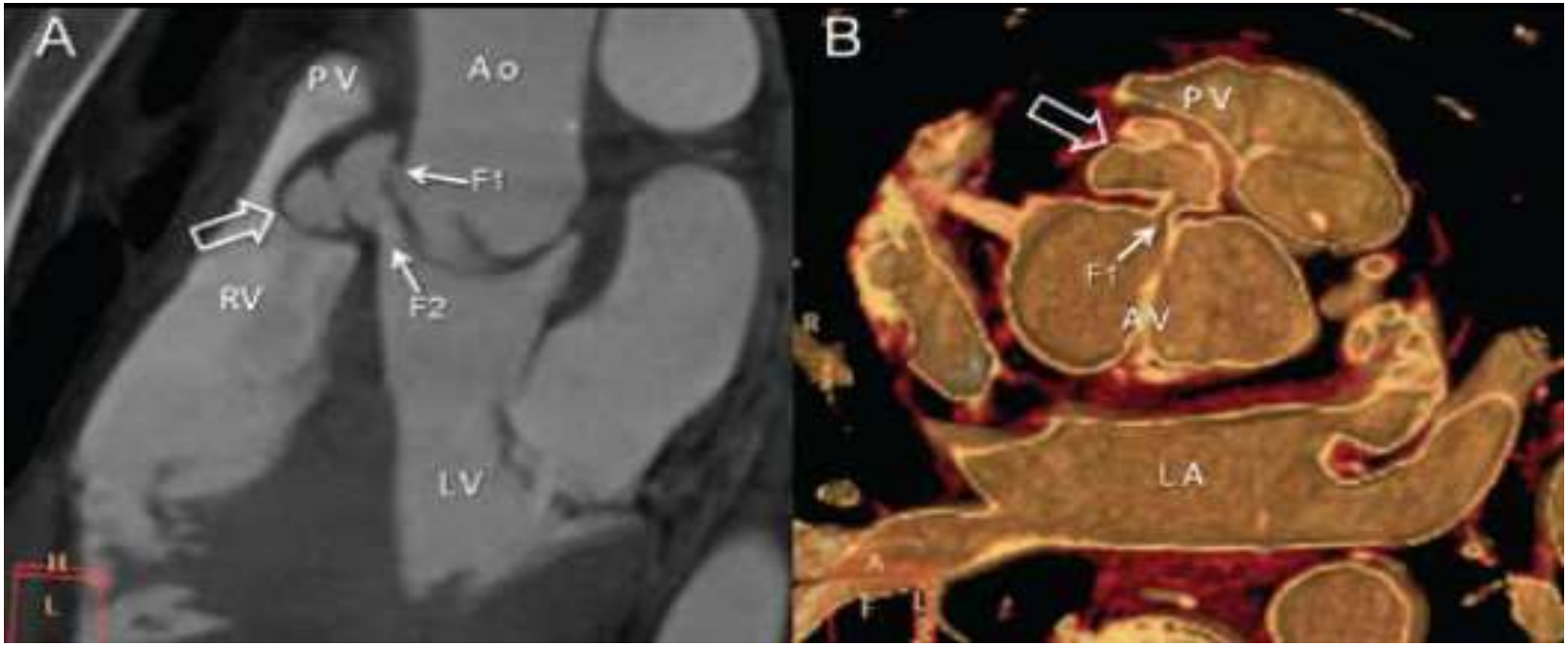
Diagnosis
(Echocardiography as the Reference Method)



Large vegetation on the posterior mitral leaflet (arrow) (transoesophageal echocardiography) (*A*) two-dimensional transoesophageal echocardiography —(*B*) three-dimensional transoesophageal echocardiography. LA, left atrium; LV, left ventricle; Ao, aorta; AML, anterior mitral leaflet; PML, posterior mitral leaflet.

http://eurheartj.oxfordjournals.org/content/35/10/624

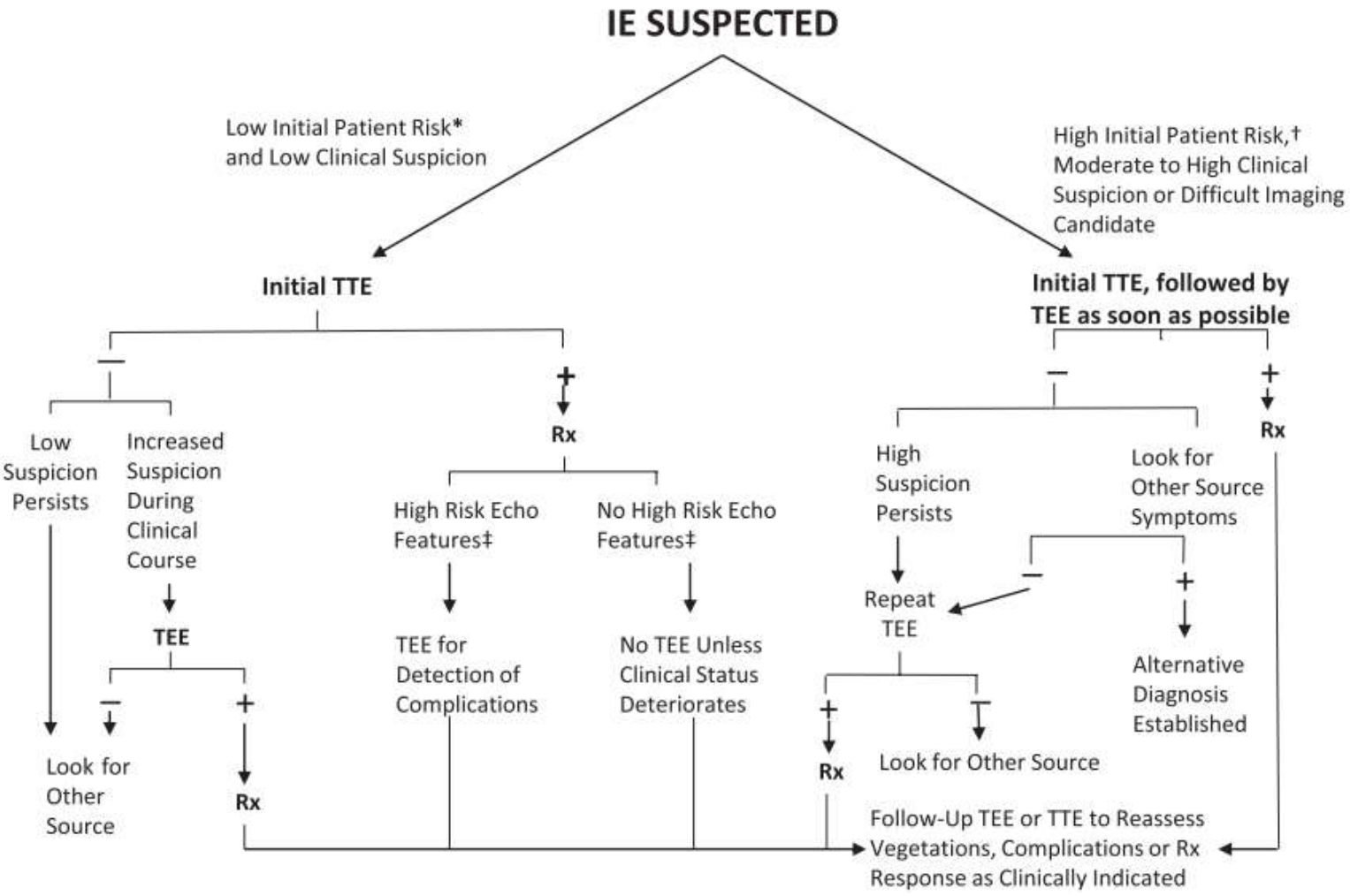
Diagnosis
(Cardiac Computed Tomography)



Cardiac computed tomography (CT) multi-planar reconstruction. The abscess cavity (hollow arrow) communicates with the aortic root (F1) and LV outflow tract (F2) to form a fistula. The abscess presses forward into the right ventricular outflow tract displacing the pulmonary valve (PV) superiorly. B: Cardiac CT blood pool inversion image. The bicuspid aortic valve (AV) is clearly seen with a fistulous connection (F1) to the abscess cavity (hollow arrow)

https://bjcardio.co.uk/2012/03/aortic-root-fistula-complicating-infective-endocarditis-role-of-64-multi-detector-ct-cardiac-angiography/

Diagnosis
(the Diagnostic Use of Echocardiography)



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Diagnosis
(Differential)

- Systemic Lupus Erythematosus.
- Cardiac tumours, e.g. atrial myxoma.
- Lyme disease.
- Antiphospholipid syndrome.
- Polymyalgia rheumatica.
- Reactive arthritis.

http://patient.info/doctor/systemic-lupus-erythematosus-pro

Treatment
(Antimicrobial Therapy: Principles)

- The primary goal of antibiotic treatment is to eradicate infection, including sterilizing vegetations, although the unique characteristics of infected vegetations (focal infection with high bacterial density, slow rate of bacterial growth within biofilms, and low microorganism metabolic activity, impaired immunity) can pose a variety of challenges.
- Antibiotics may fail to eradicate infection as a result of increased binding of the drug to serum proteins, perturbations of antibiotic penetration into the vegetation, and unique antibiotic pharmacokinetic/pharmacodynamic (PK/PD) features.
- Therefore, prolonged, parenteral, bactericidal therapy is required for attempted infection cure.

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Treatment
(Antimicrobial Therapy: Inoculum Effect)

- The effect of high bacterial densities on antimicrobial activity is called the inoculum effect in which certain groups of antimicrobials commonly used to treat IE such as β-lactams and glycopeptides (and, to a lesser extent, lipopeptides such as daptomycin) are less active against highly dense bacterial populations.
- The effective minimum inhibitory concentration (MIC) at the site of infection with bacterial densities of 108 to 1011 colony-forming units per 1 g tissue can be much higher than anticipated by in vitro susceptibility tests that use a standard inoculum (105.5 colony-forming units per milliliter).

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Treatment
(Antimicrobial Therapy: Bactericidal Drugs)

- Data from clinical investigations support the need for bactericidal antibiotics to sterilize vegetations in IE with high bacterial densities.
- For enterococci, bactericidal activity can be achieved by the combination of certain β-lactam antibiotics (e.g., penicillin, ampicillin, and piperacillin) with an aminoglycoside.
- The bactericidal effect achieved by a combination of antibacterial drugs that alone only inhibit bacterial growth is called synergy.
- The rate of bactericidal activity against some other organisms can also be enhanced by a combination of a β-lactam antibiotic plus an aminoglycoside.

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Treatment
(Antimicrobial Therapy: Duration)

- The duration of therapy in IE must be sufficient to ensure complete eradication of microorganisms within vegetations.
- When the bactericidal activity is known to be more rapid or the likely vegetation bacterial burden is lower, then the clinician may prescribe a shorter duration of antimicrobial therapy in unique instances.
- Combination therapy with penicillin or ceftriaxone and an aminoglycoside for 2 weeks is highly effective in viridans group streptococci (VGS) IE in very select patients with uncomplicated infection.
- Both β-lactam therapy alone and combination therapy with nafcillin and an aminoglycoside for only 2 weeks have been effective in patients with uncomplicated right-sided IE caused by S aureus; monotherapy with a β-lactam would be selected for use in cases of uncomplicated IE.

http://circ.ahajournals.org/content/early/2015/09/15/CIR.0000000000000296

Treatment
(Fungi)

- Fungal IE is rare but can develop in a wide range of patients.
- A 2-phase treatment of fungal IE has evolved. The initial or induction phase consists of control of infection. Treatment includes a combination of a parenteral antifungal agent, usually an amphotericin B–containing product, and valve surgery.
- Antifungal therapy usually is given for >6 weeks.

http://circ.ahajournals.org/content/early/2015/09/15/CIR.0000000000000296

Treatment
(Long-Term Follow-Up)

- Months to years after completion of medical therapy for IE, patients should have ongoing observation for and education about recurrent infection and delayed onset of worsening valve dysfunction.
- Daily dental hygiene should be stressed, with serial evaluations by a dentist who is familiar with this patient population.
- Patients should be questioned about symptoms of heart failure, and a thorough physical examination should be done.
- Additional evaluation with echocardiography is indicated in selected patients with positive findings from history and physical examination.
- Patients should be instructed to seek immediate medical evaluation for persistent fever.

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Treatment
(The ‘Endocarditis Team’)

- IE is not a single disease, but rather may present with very different aspects depending on the first organ involved, the underlying cardiac disease (if any), the microorganism involved, the presence or absence of complications and the patient's characteristics, so no single practitioner will be able to manage and treat it.
- Very high level of expertise is needed from practitioners from several specialties, including cardiologists, cardiac surgeons, internal diseases specialists, microbiologists, neurologists, neurosurgeons, experts in coronary heart disease and others.
- About half of the patients with IE undergo surgery during the hospital course.

http://eurheartj.oxfordjournals.org/content/early/2015/08/28/eurheartj.ehv319

Prognosis

- Prognosis largely depends on whether or not complications develop.
- If left untreated, IE is generally fatal.
- Early detection and appropriate treatment of this uncommon disease can be lifesaving.
- The overall mortality rate has remained stable at 14.5%.
- Increased mortality rates are associated with increased age, infection involving the aortic valve, development of congestive heart failure, central nervous system (CNS) complications, and underlying disease such as diabetes mellitus
- Acute endocarditis due to *S aureus* is associated with a high mortality rate (30-40%), except when it is associated with IV drug use.

http://emedicine.medscape.com/article/216650-overview#a6

Prophylaxis

- There is no clinical evidence that it reduces the incidence of IE and there are negative effects (e.g. allergy and increased bacterial resistance) of taking antibiotics that may outweigh the benefits.
- Antibiotics were historically commonly recommended to prevent IE in those with heart problems undergoing dental procedures (known as dental antibiotic prophylaxis) and in now days they are less commonly recommended for this procedure.
- Preventive dental examination and therapy before surgery to repair heart valves or congenital heart lesions is recommended.

http://www.merckmanuals.com/professional/cardiovascular-disorders/endocarditis/infective-endocarditis https://www.nice.org.uk/guidance/published?type=cg

Key Points

- Because the normal heart is relatively resistant to infection, endocarditis occurs when there is a predisposing abnormality of the endocardium.
- Predisposing abnormalities include congenital heart defects, rheumatic valvular disease, bicuspid or calcific aortic valves, mitral valve prolapse, hypertrophic cardiomyopathy, prior endocarditis, and presence of a prosthetic valve.
- Local cardiac consequences include myocardial abscess, conduction system abnormalities, and sudden, severe valvular regurgitation.
- Systemic consequences include immune phenomena and septic emboli, which may affect any organ put particularly the lungs, kidneys, spleen, central nervous system (CNS), skin, and retina.
- Diagnose using blood cultures and Duke criteria.
- Treat with a prolonged course of antimicrobial therapy; surgery may be needed for mechanical complications or resistant organisms.
- Give antimicrobial prophylaxis for patients at high risk of an adverse outcome from infective endocarditis.

http://www.merckmanuals.com/professional/cardiovascular-disorders/endocarditis/infective-endocarditis

Abbreviations

ABE - acute bacterial endocarditis

ACE - angiotensin converting enzyme

BE - bacterial endocarditis

CMR - cardiac magnetic resonance

CNS – central nervous system

CRP - C-reactive protein

CT - computed tomography

ECG - electrocardiogram

ESR - erythrocyte sedimentation rate

IDU - injection drug use

IE - infective endocarditis

HIV - human immunodeficiency virus

MIC - minimum inhibitory concentration

MRI - magnetic resonance imaging

NBTE - non-bacterial thrombotic endocarditis

LVADs - left ventricular assistive devices

PK/PD - pharmacokinetic/pharmacodynamic

SBE - subacute bacterial endocarditis

TEE - transesophageal echocardiography

TTE - transthoracic echocardiography

PET - positron emission tomography

Diagnostic and treatment guidelines

2015 ESC Guidelines for the management of infective endocarditis

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures

Infective Endocarditis

Infective Endocarditis

Cardiac imaging in infectious endocarditis