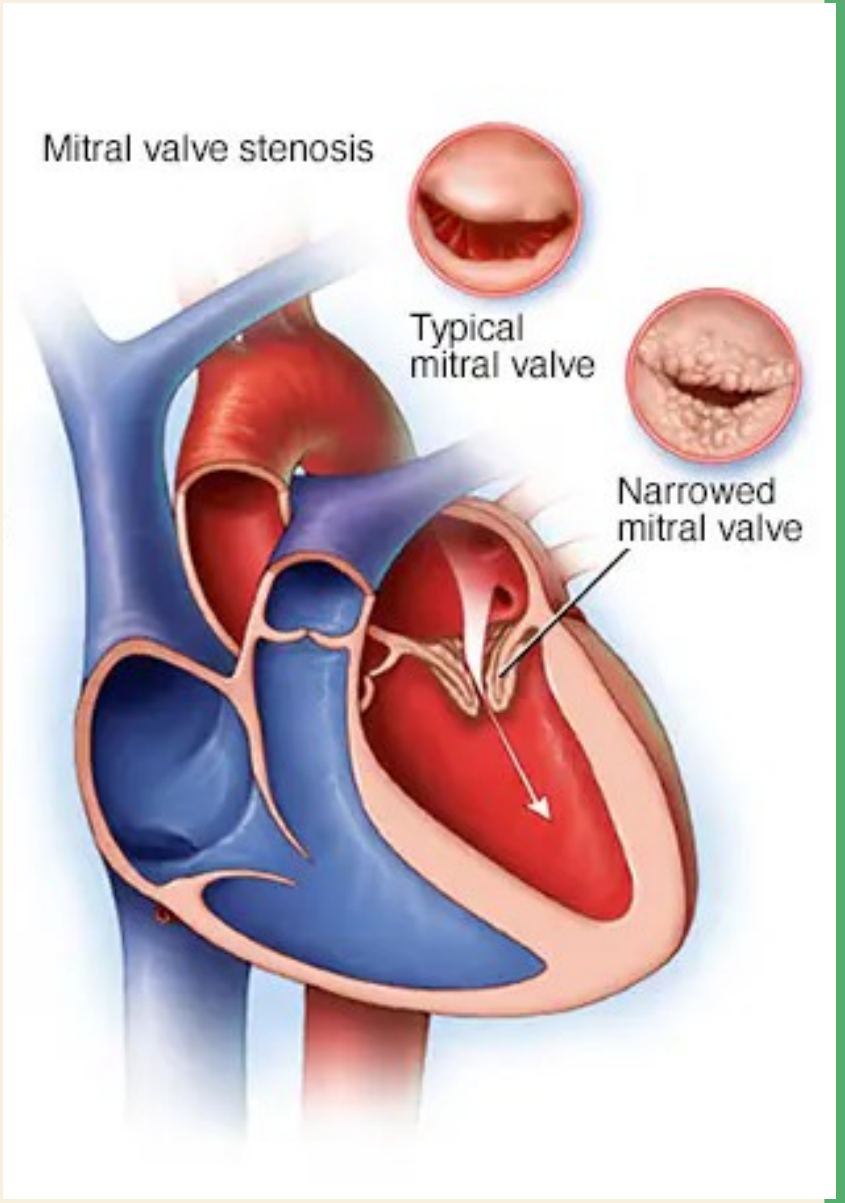
VALVULAR HEAT DISEASE

BY: DR. YASER AREF HAMAM

MITRAL STENOSIS (MS)

- Mitral stenosis (MS) is a structural anomaly of the mitral valve resulting in a decreased cross-sectional area of the valve.



CAUSES

1. Most commonly due to rheumatic fever
2. Calcification of the mitral valve annulus
3. Autoimmune diseases: systemic lupus erythematosus (SLE), rheumatoid arthritis
4. Congenital
5. Bacterial endocarditis
6. Left atrial myxoma

PATHOPHYSIOLOGY

- Mitral valve stenosis → obstruction of blood flow into the left ventricle (LV) → limited diastolic filling of the LV (↓ end-diastolic LV volume) → decreased stroke volume → decreased cardiac output (COP)
- Mitral valve stenosis → increase in left atrial pressure → backup of blood into lungs → increased pulmonary capillary pressure → pulmonary edema → pulmonary hypertension → right ventricular hypertrophy and heart failure

SYMPTOMS

- Patients typically remain asymptomatic for years until the mitral valve area becomes critically reduced (< 2 cm2) [Normal mitral valve area 4-6 cm2]

❑ Progressive dyspnea

❑ Fatigue

❑ Low cardiac output symptoms (dizziness, syncope, fainting, tinnitus, blurred vision, headache, intermittent claudication, coldness, sweating, oliguria)

❑ Recurrent chest infection (Pneumonia)

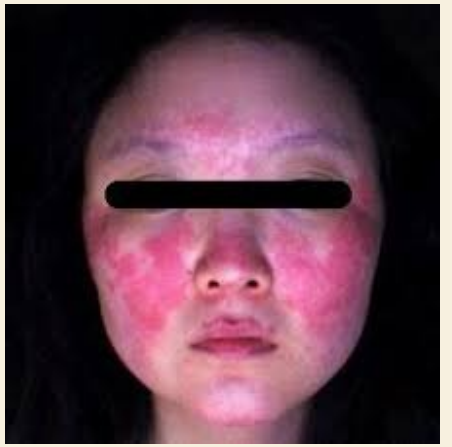
❑ Palpitations

❑ Symptoms of embolic disease (e.g., stroke, mesenteric ischemia)

❑ Later stages:

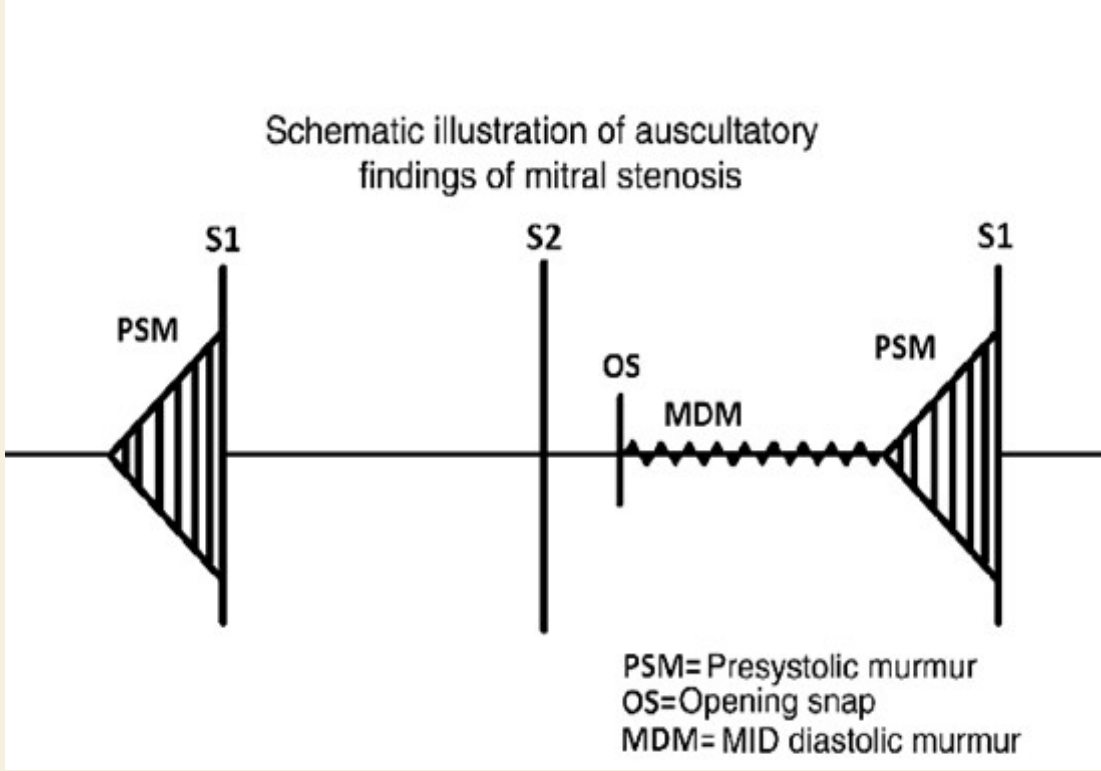
- Symptoms of right heart failure (Ascites, lower limb edema, weight gain, fatigue, hepatosplenomegaly)
- Orthopnea
- Hemoptysis

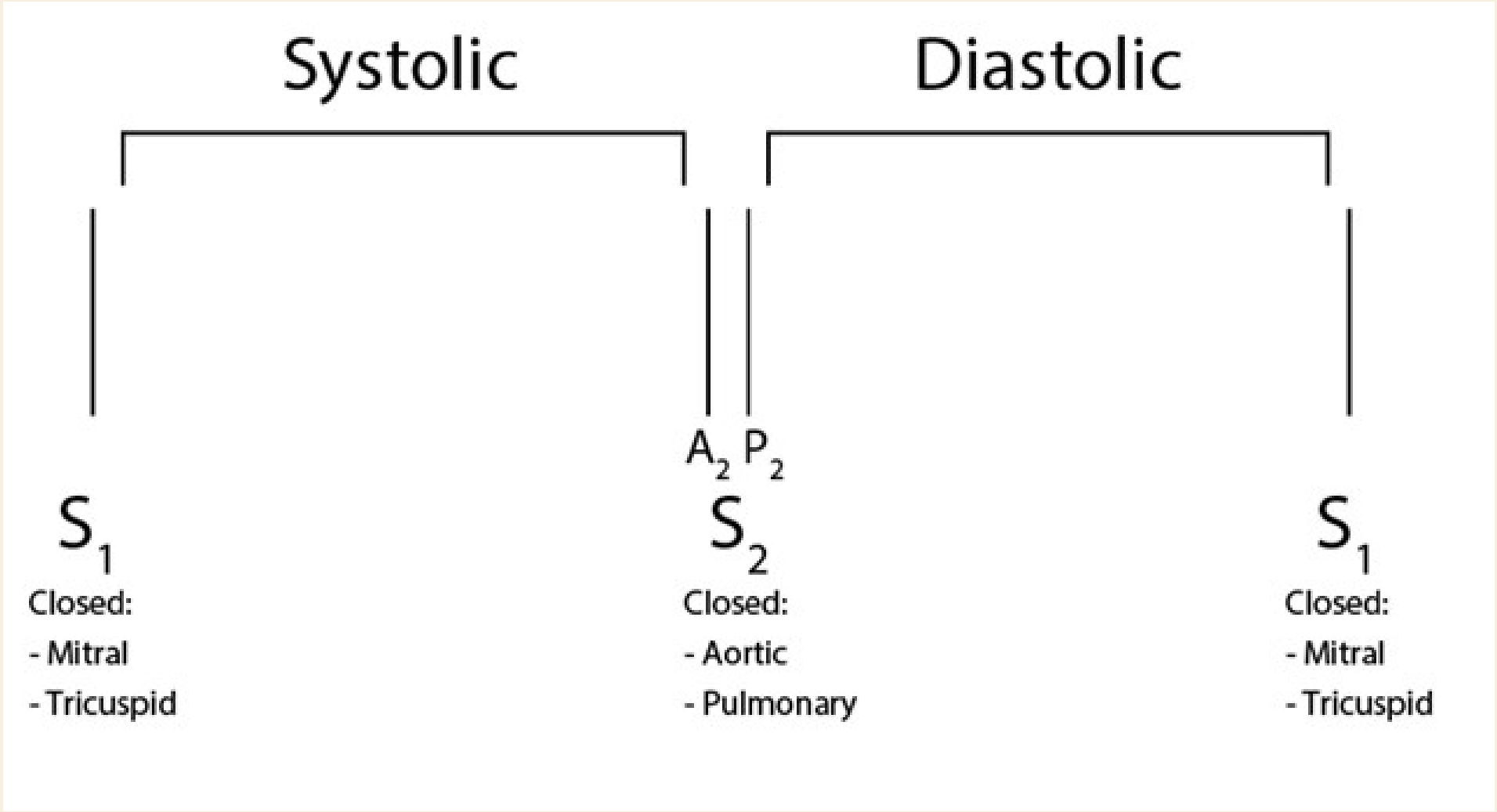
EXAMINATION FINDINGS



- Irregular heart rhythm secondary to atrial fibrillation
- Mitral facies [refers to the abnormal flushing of the cheeks that occurs from cutaneous vasodilation in the setting of severe mitral valve stenosis]
- **Auscultation:**

➢ Mid-diastolic murmur




Systolic
Diastolic
A2 P2
S1
Closed:
- Mitral
- Tricuspid
S2
Closed:
- Aortic
- Pulmonary
S1
Closed:
- Mitral
- Tricuspid

DIAGNOSIS

- **History and Physical examination**
- **Echocardiography**:

- Is the most important test for diagnosing and guiding the treatment of mitral stenosis.

- Characteristic findings include:

❑ Reduced mitral valve area (MVA): ≤ 1.5 cm2 is considered to be severe MS

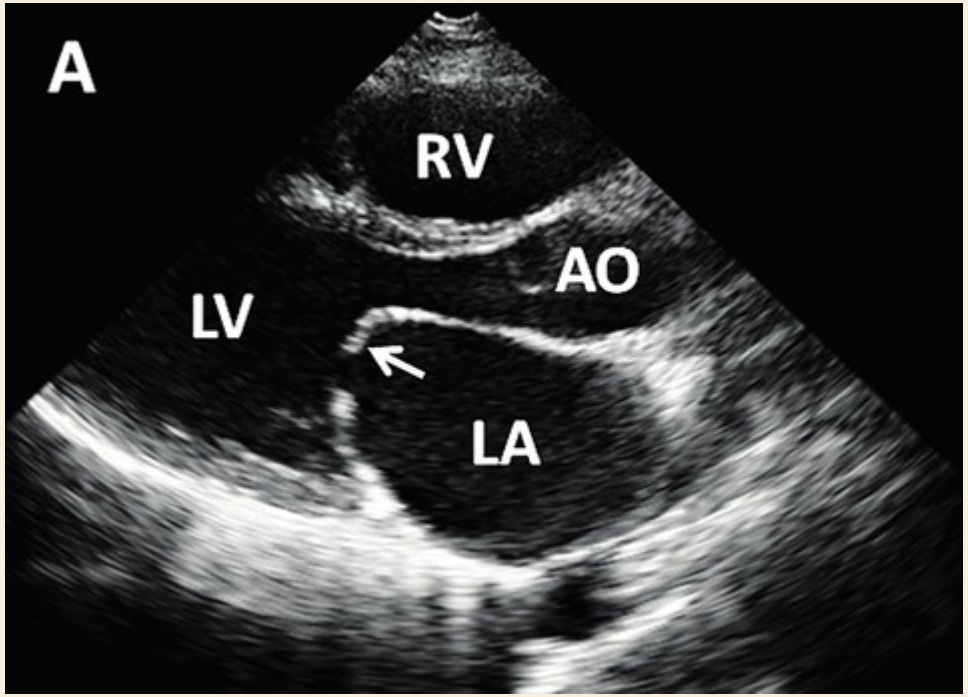
❑ Thickened, calcified leaflets with commissural fusion

❑ Increased mean diastolic pressure gradient across the mitral valve

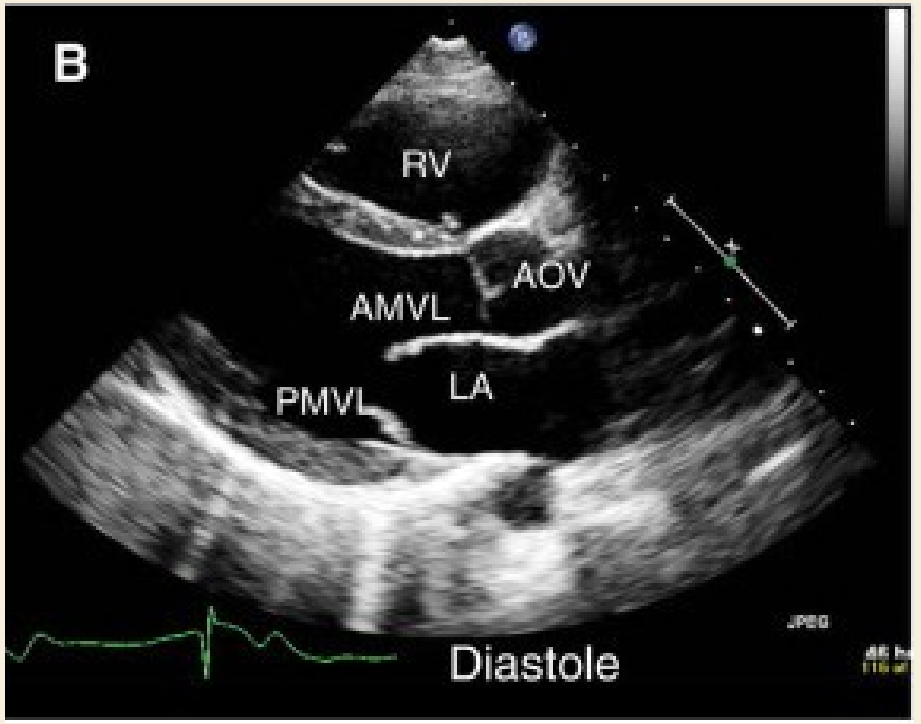
❑ RV dilation

❑ LA enlargement

ECHOCARDIOGRAPHY



Mitral Valve Stenosis



Normal Mitral Valve

DIAGNOSIS

- **Chest x-ray:**

✓ Left atrial enlargement.

✓ Features of pulmonary congestion.

✓ Features of right ventricular enlargement.

- **ECG:**

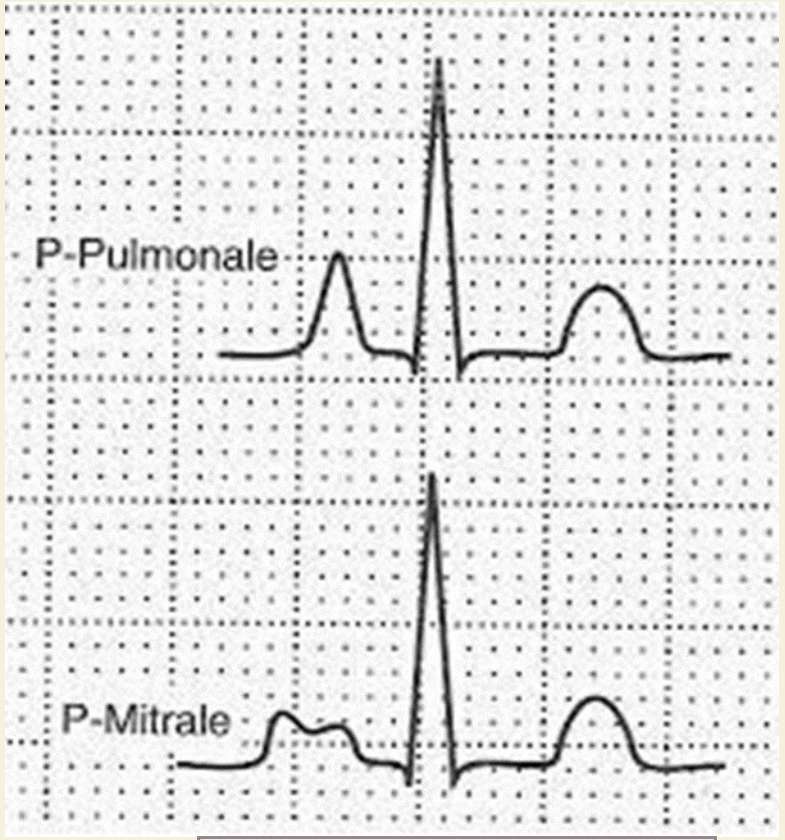
✓Left atrial enlargement / P mitrale

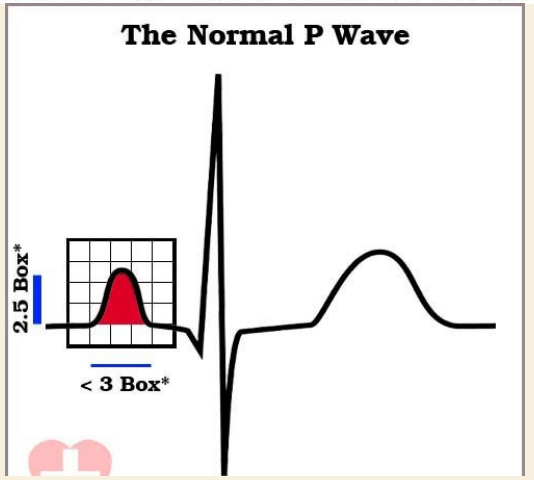
✓Atrial fibrillation

✓Right ventricular hypertrophy (e.g., right axis deviation, dominant R wave in lead V1)

- **P pulmonale is very common, which is a big, tall, peaked P waves.**

- Normal P wave = up to 0.12 sec in duration(< 3 small boxes), and up to 0.25 mV (< 2.5 small boxes)

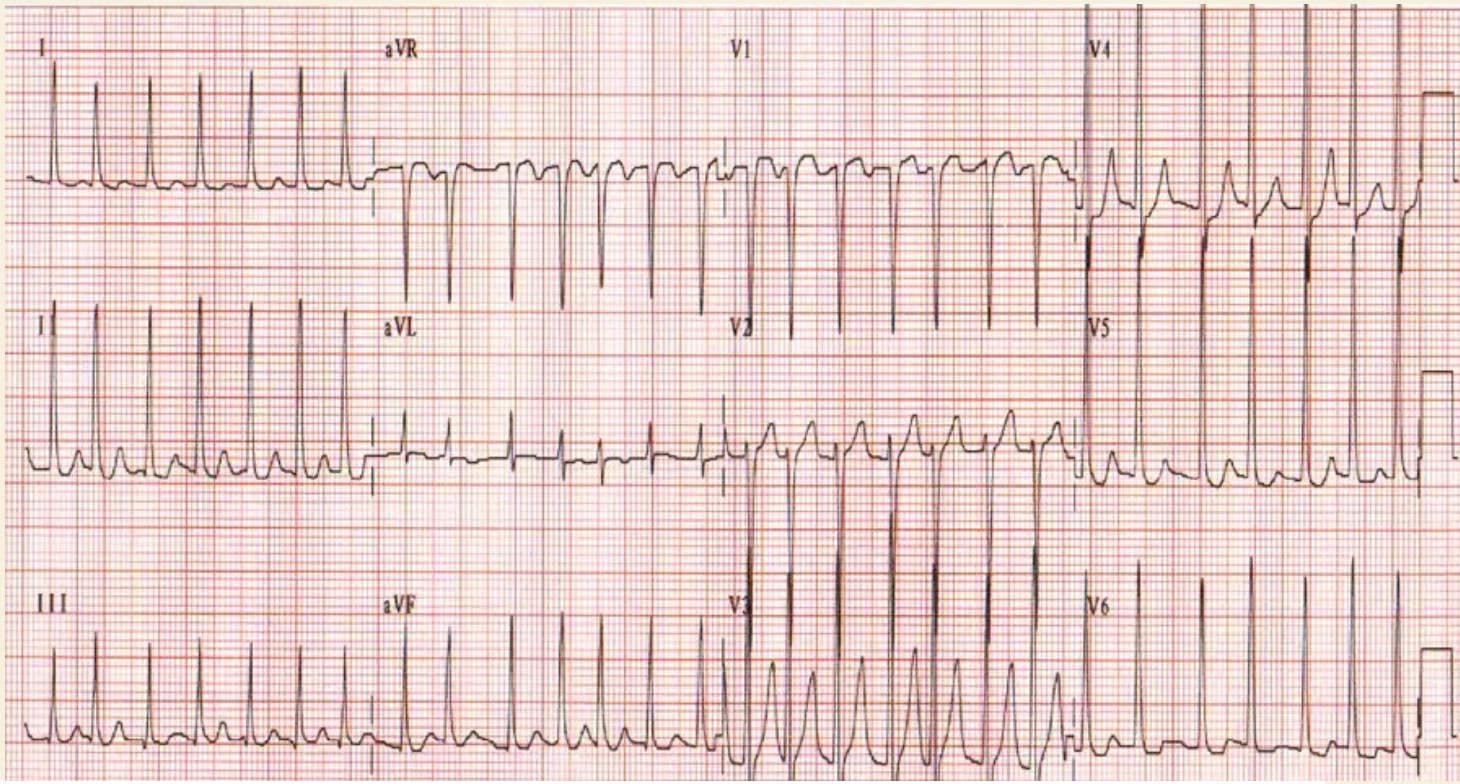


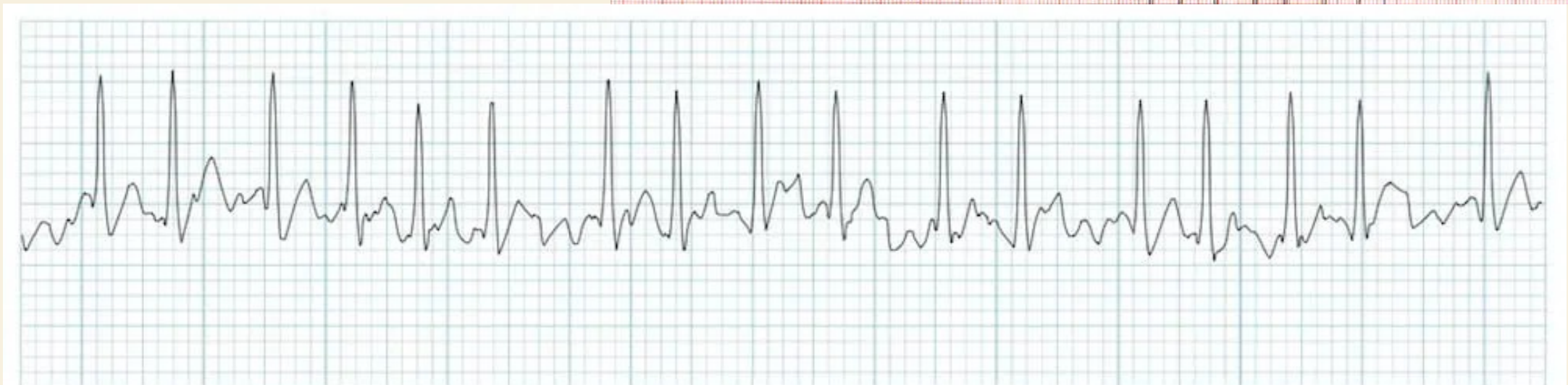


- ECG Features of Atrial Fibrillation

1. Irregular rhythm => Variable ventricular rate
2. No P waves
3. Absence of an isoelectric baseline
4. Heart rate (typically 110-140 beats/min, rarely >160-170 beats/min)

Note: Fibrillatory waves may mimic P waves leading to misdiagnosis

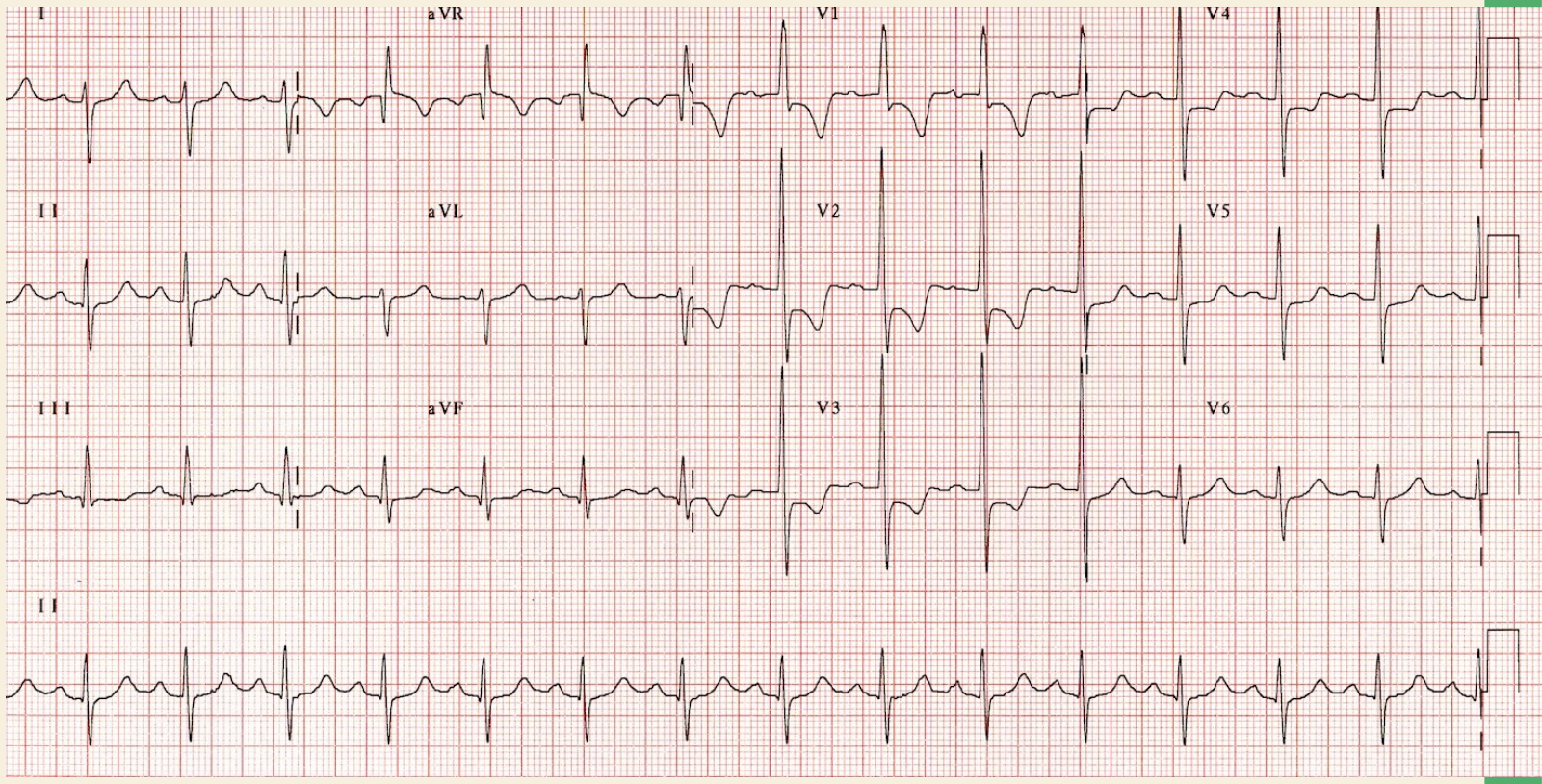


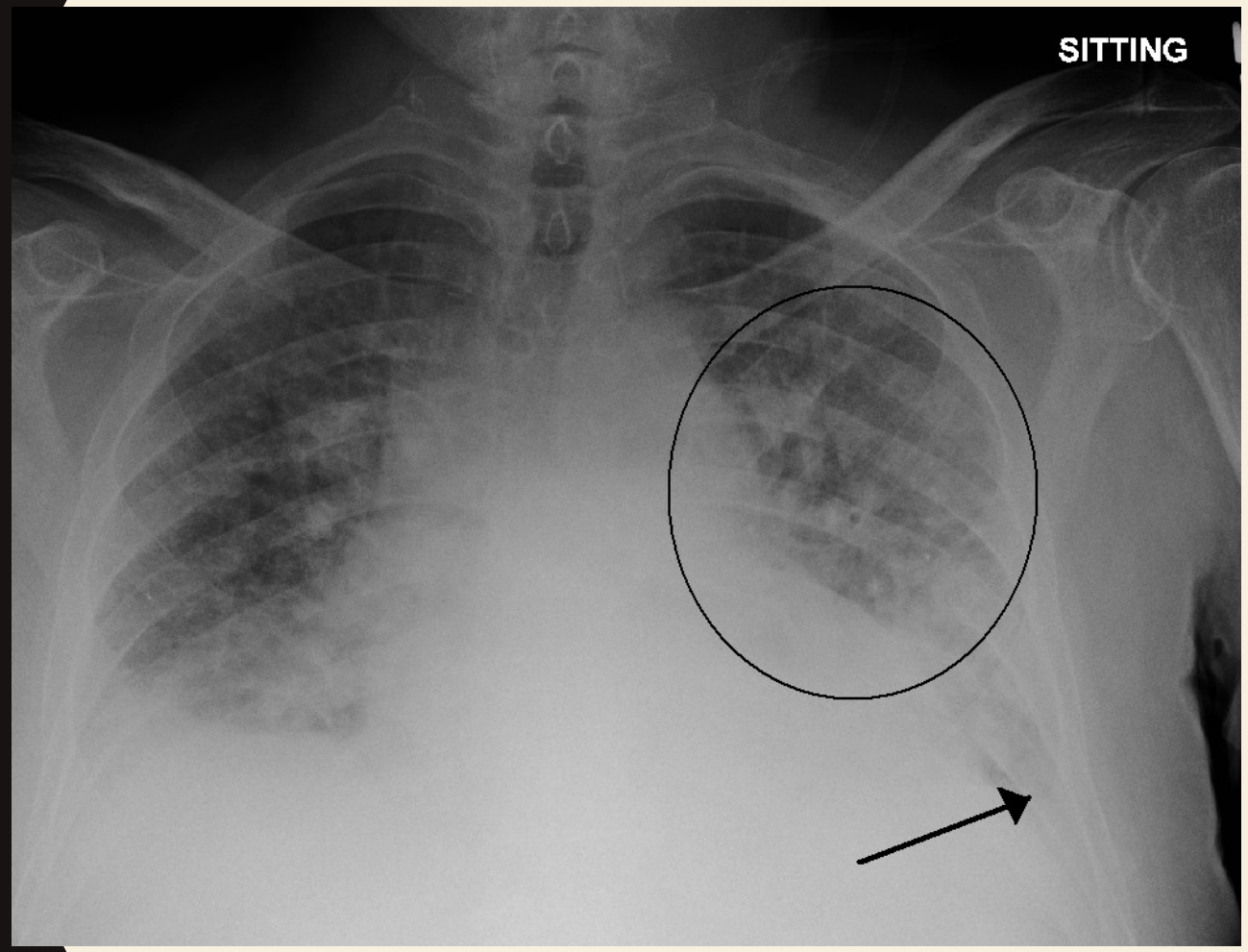


RVH

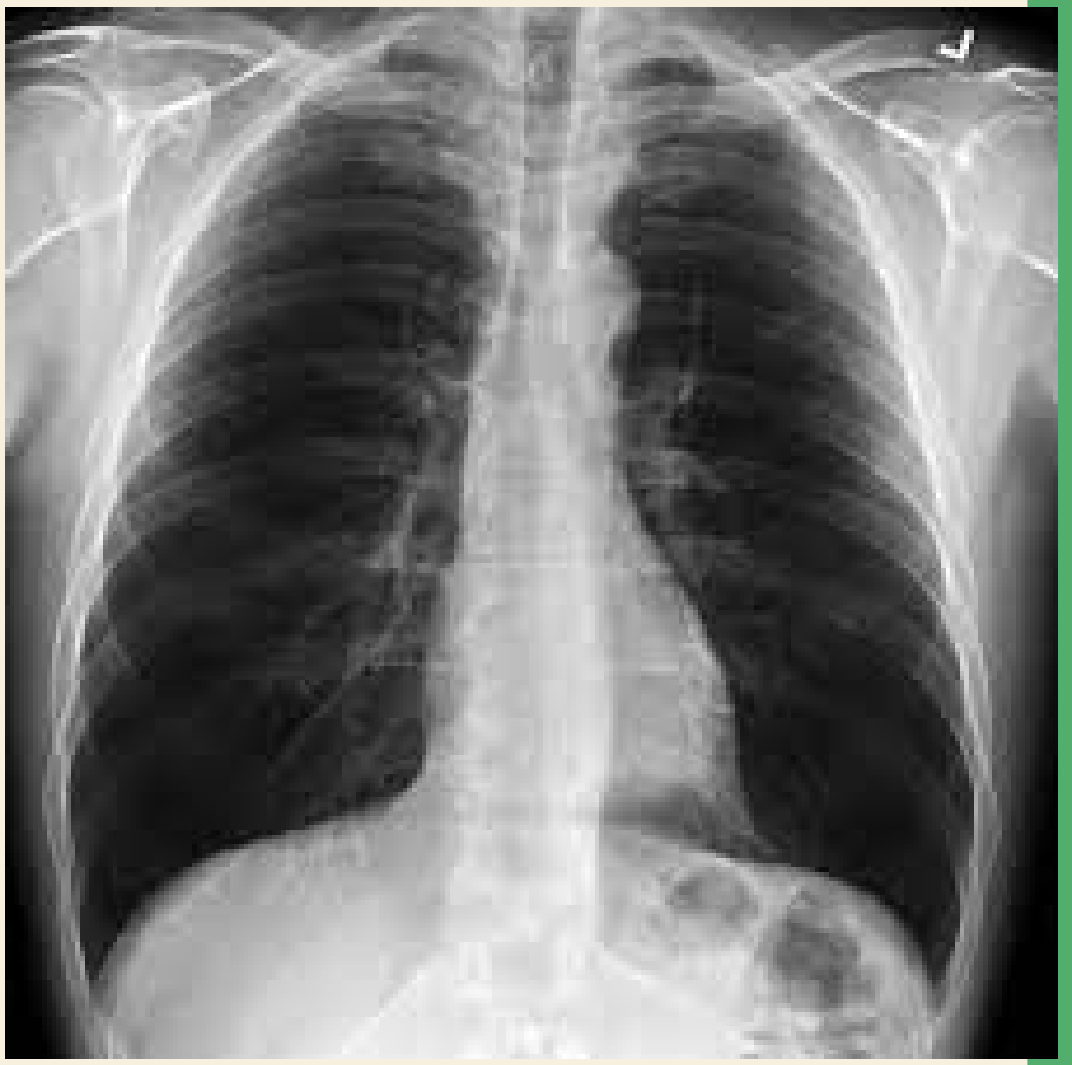
- **ECG changes in right ventricular hypertrophy**

1. larger R-waves and smaller S-waves in in right sided leads (V1, V2)
2. Right axis deviation is almost present.
3. R/S ratio in v1 > 1
4. R in v2 > 7 ml





Congested lung = pulmonary edema



Normal chest X-ray

TREATMENT

Medical treatment:

- **Asymptomatic** → follow-up
- **Symptomatic:**

✓ Treat atrial fibrillation with rate control (Beta blockers) and Anticoagulation (Warfarin)

✓ Heart failure symptoms are managed using standard therapy, e.g., diuretics.

TREATMENT

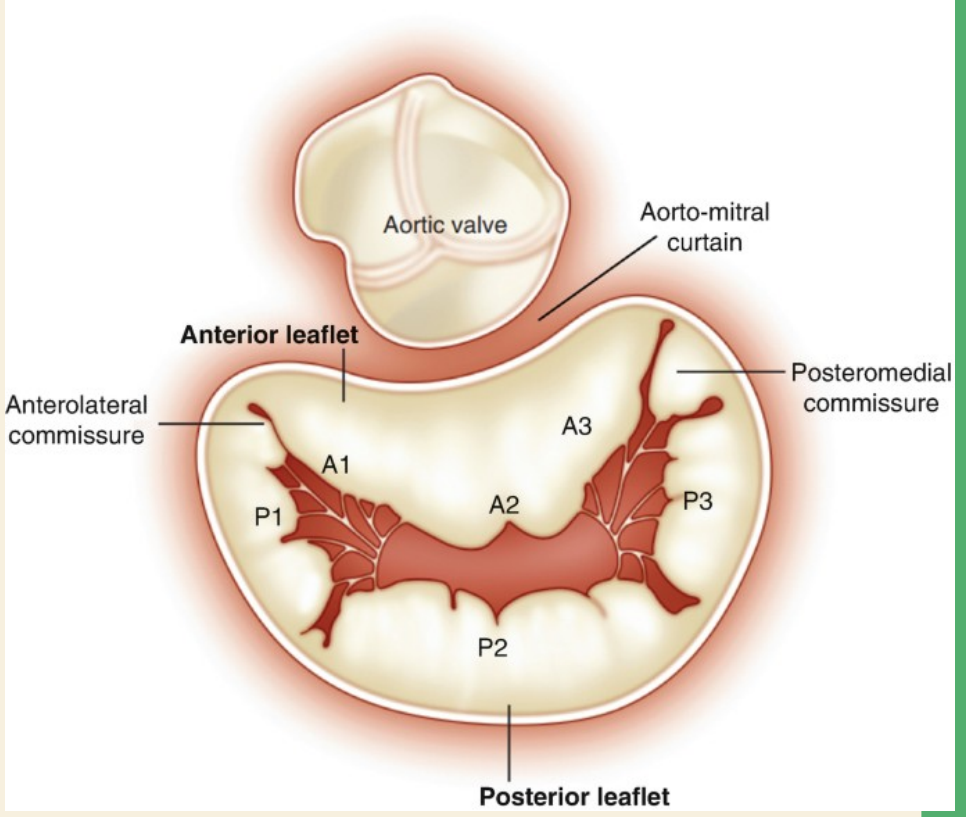
Surgical treatment

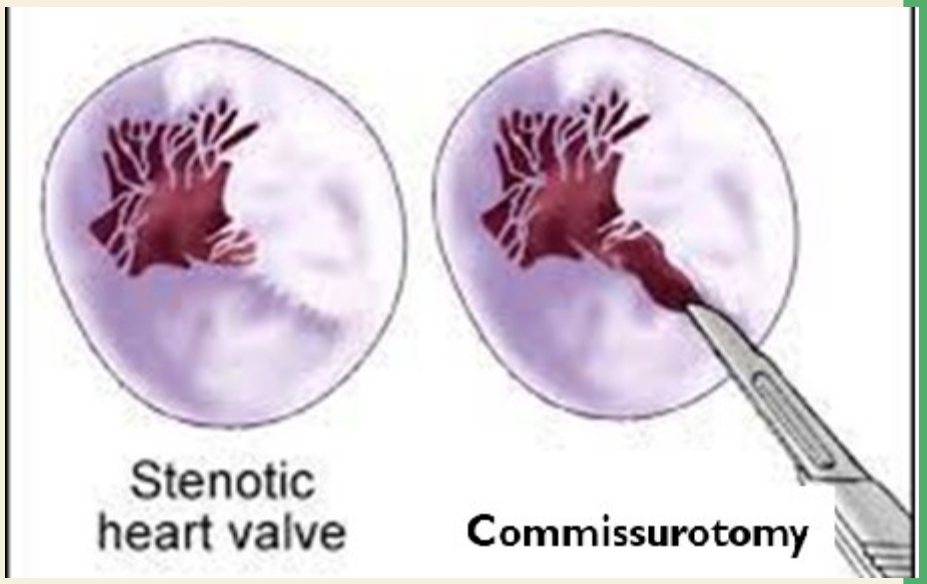
Indication for surgery:

1. Sever symptoms despite medical treatment
2. Patient undergoing other cardiac surgery
3. Pulmonary artery systolic pressure > 50 mm Hg
4. Asymptomatic patients with mitral valve area ≤ 1.5 cm2
5. Mean Pressure gradient across the valve > 12 mmHg

Surgical options:

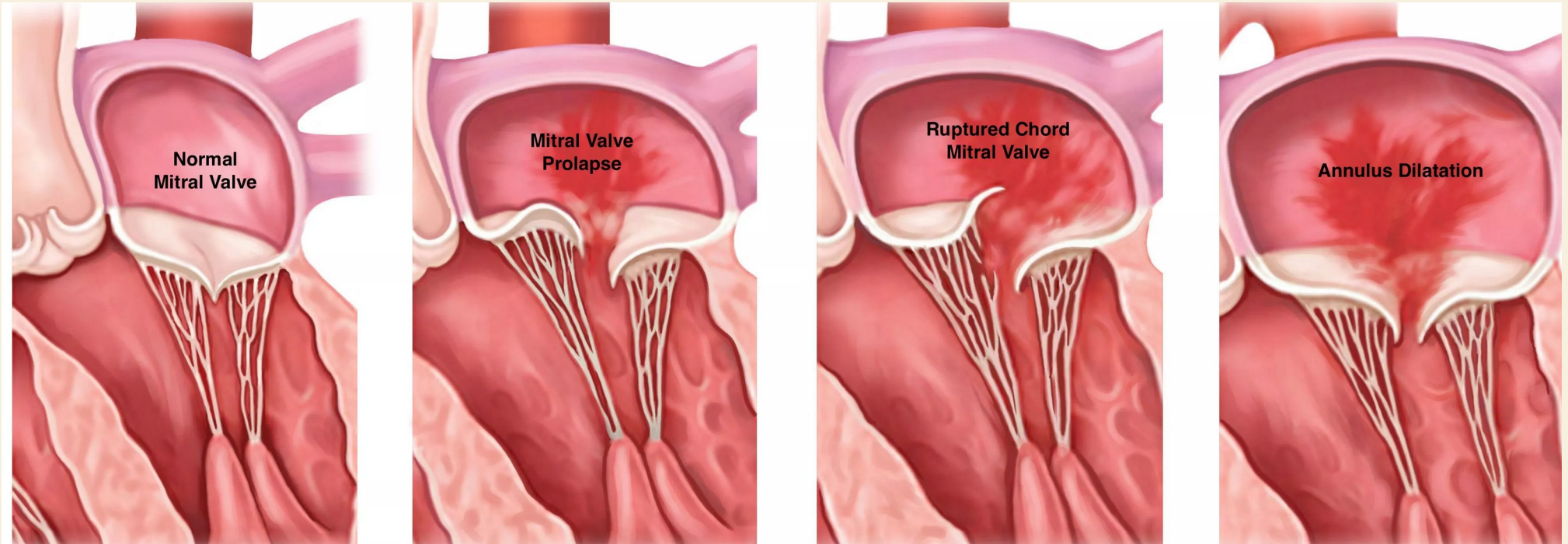
6. **Mitral valve replacement:** for associated with regurgitation, severely calcified valve.
7. **Mitral valvuloplasty** (Commissurotomy)





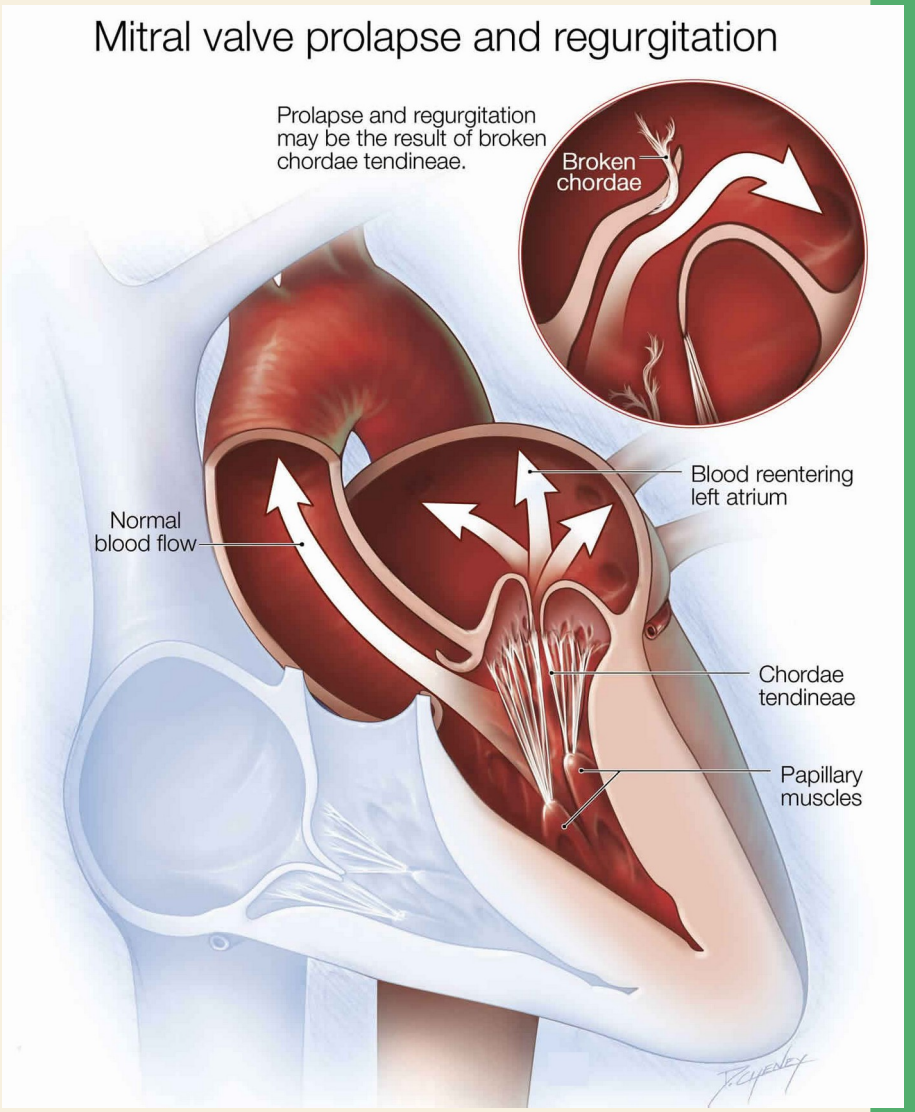
MITRAL REGURGITATION (MR)

- Mitral regurgitation (MR) is the leakage of blood from the left ventricle into the left atrium due to incomplete closure of the mitral valve during systole.



CAUSES

- **Primary MR (organic): mitral regurgitation caused by direct involvement of the valve**
  - ➢ Congenital (Mitral valve prolapse = MVP)
  - ➢ Mitral annular calcification
  - ➢ Rheumatic fever
  - ➢ Infective endocarditis
- **Secondary MR (functional): caused by changes of the left ventricle that lead to valvular incompetence**
  - ➢ Coronary artery disease or prior myocardial infarction causing papillary muscle rupture
  - ➢ Dilated cardiomyopathy



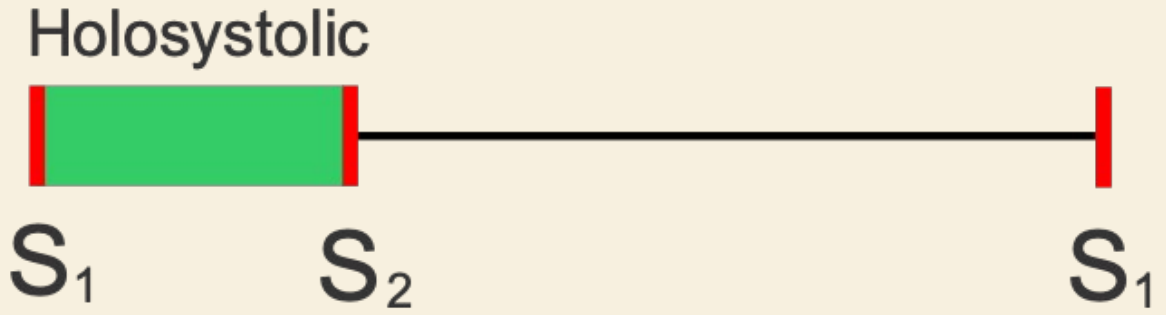
PATHOPHYSIOLOGY

- **Acute MR:** ↑ left atrial volume → rapid ↑ in LA and pulmonary pressures → pulmonary venous congestion → pulmonary edema

- **Chronic MR:** progressive LV enlargement and myocardial dysfunction → ↓ stroke volume → ↑ LV and LA pressure → pulmonary congestion, possible acute pulmonary edema, pulmonary hypertension, and right ventricular hypertrophy → right-sided heart failure

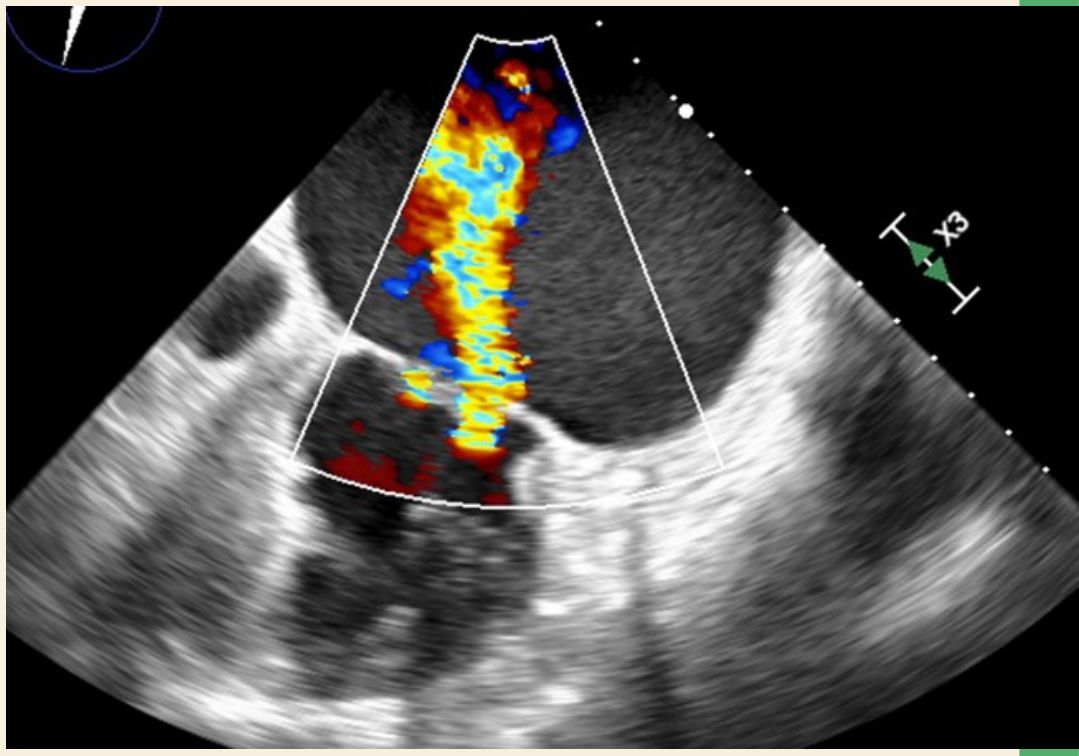
CLINICAL FEATURES

- Dyspnea (including exertional dyspnea), dry cough
- Fatigue
- Palpitations
- In late stages, symptoms of right-sided heart failure
- **Auscultation:** == > **Systolic murmur**



DIAGNOSIS

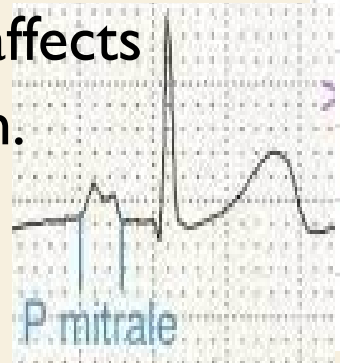
- **Echocardiography:**
  - Modality of choice for the initial assessment of all patients with suspected valvular abnormality
  - Characteristic findings include:
    - Dilated left atrium and left ventricle
    - Regurgitation Jet into Left atrium
- **ECG:**
  - Left ventricular hypertrophy (50% of patients)
  - P mitrale
  - Atrial fibrillation

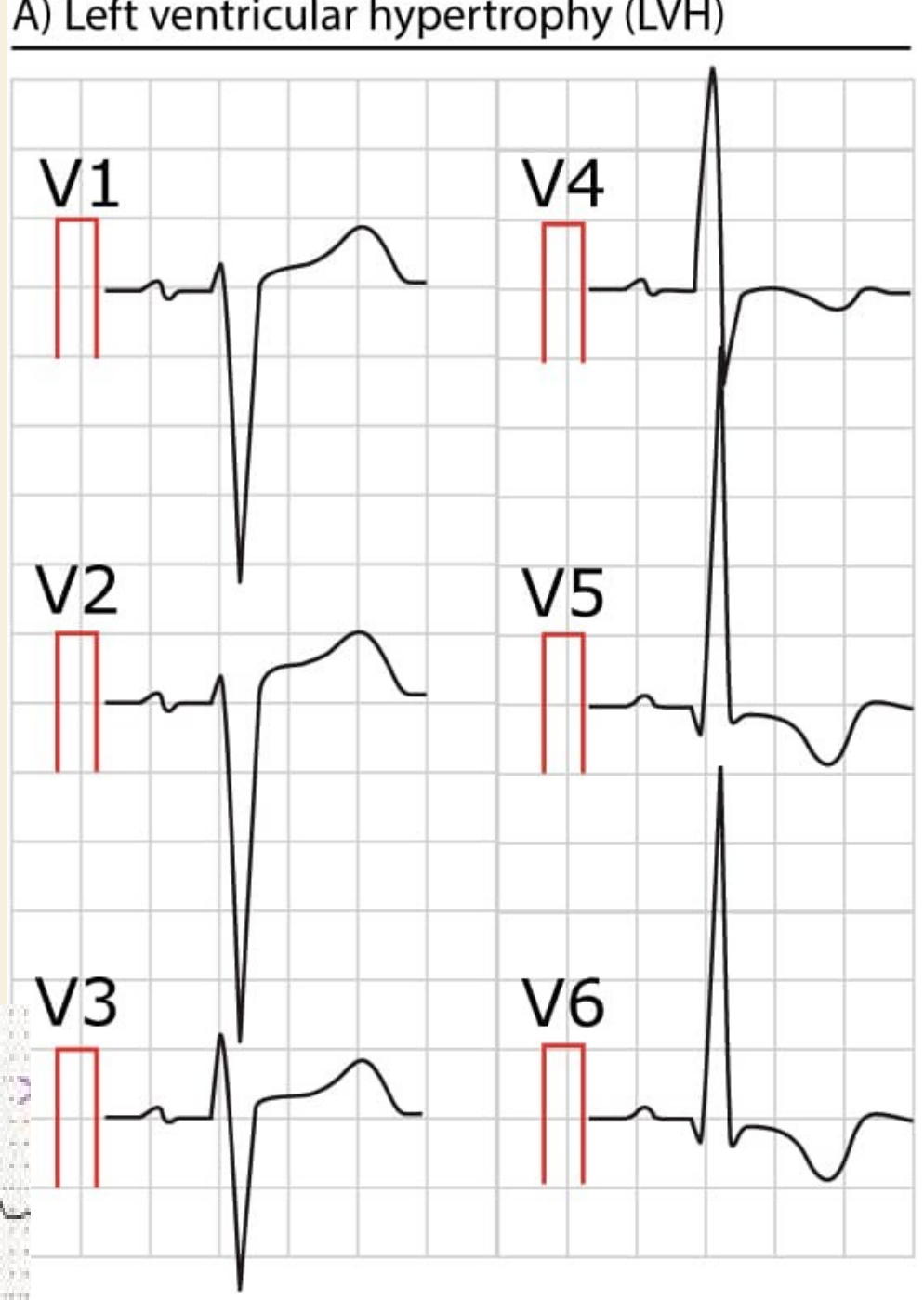


LVH

- **ECG changes in left ventricular hypertrophy (LVH)**

1. Large R-waves in left sided leads (V5, V6, I and aVL) and deep S-waves in right sided leads (V1, V2) indicate that the vector of the left ventricle is amplified.
2. Left axis deviation – is common in LVH.
3. P mitrale = bifid P wave in lead II, due to Left atrial enlargement, as the LVH affects the hemodynamics of the left atrium.





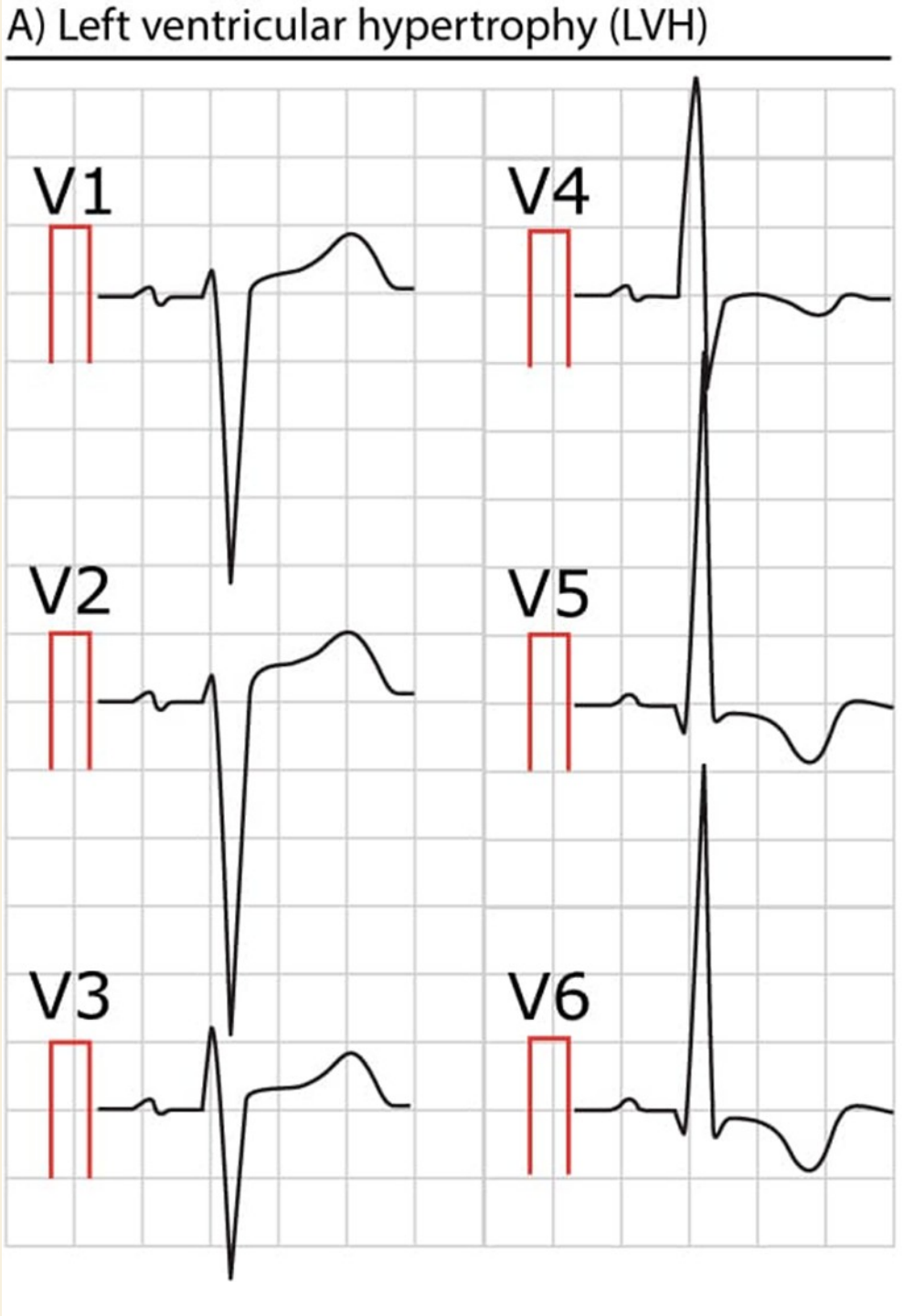
ECG CITERIA/INDEX FOR LEFT VENTRICULAR HYPERTROPHY (LVH)

- **Sokolow-Lyon criteria:**

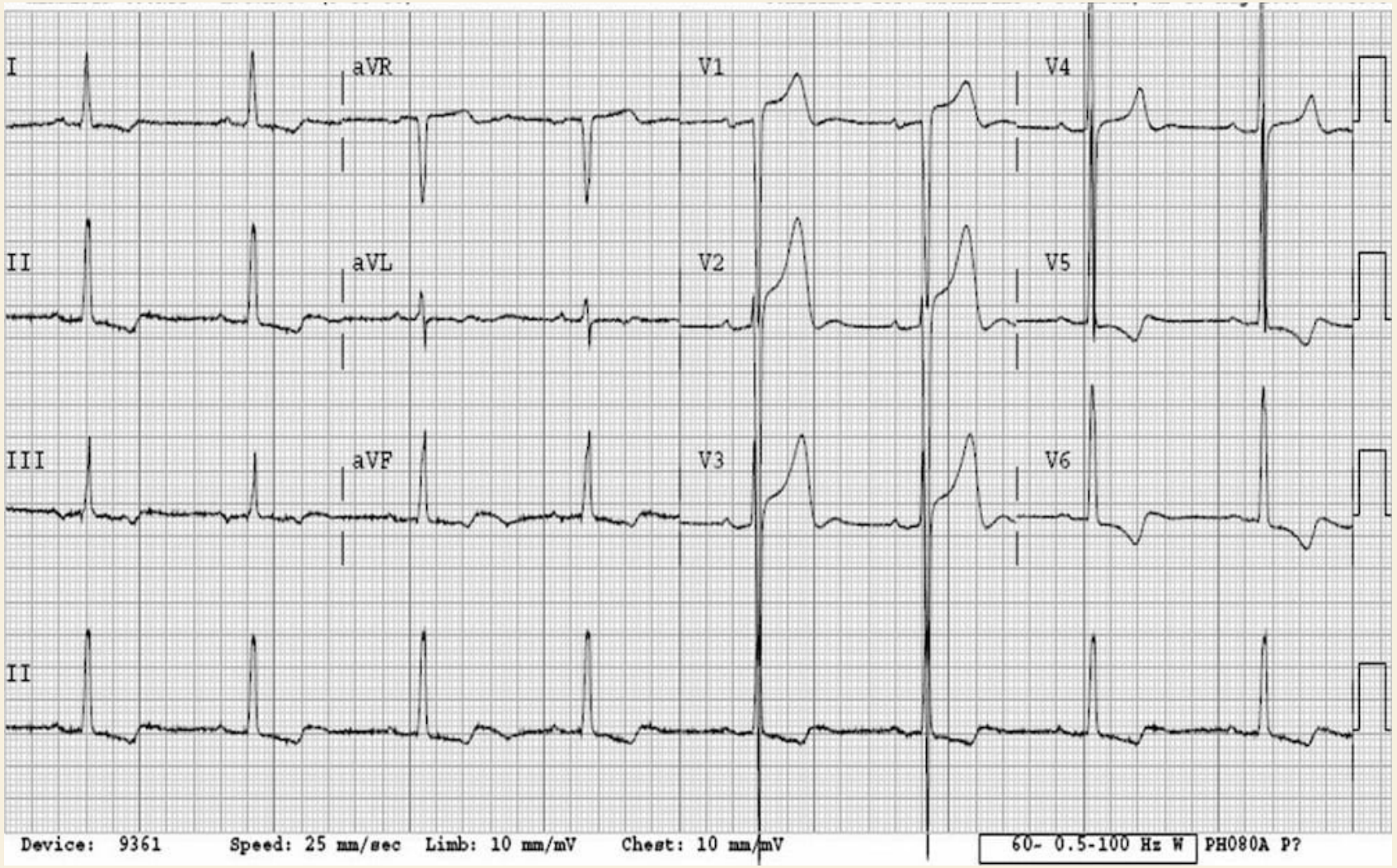
1. (R v5 or R v6) + (S v1 or S v2) > 35 mm or
2. RaVL > 11 mm

- **Cornell-voltage criteria:**

1. Men: S(V3) + R(aVL) > 28mm
2. Women: S(V3) + R(aVL) > 20 mm



LVH


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Device: 9361
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
60- 0.5-100 Hz W
PH080A P?

DIAGNOSIS

- **Chest x-ray:**
  - Features of pulmonary congestion.
  - Features of left atrium and left ventricle enlargement.
  - Annular calcification over the valve area

MANAGEMENT

- **Medical management**

○ Identify and treat any underlying cause

○ Symptomatic treatment:

➔ Heart failure management: - Diuretics (e.g., furosemide)

- ACE inhibitors (e.g., lisinopril)

- Beta blockers (e.g., metoprolol)

MANAGEMENT

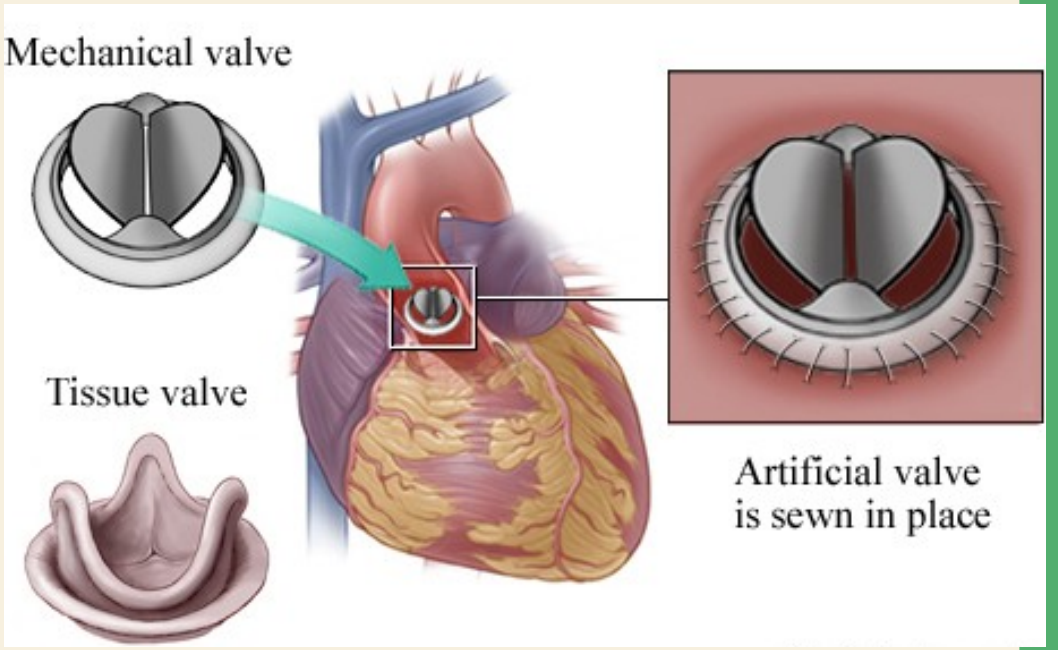
- **Surgical management:**

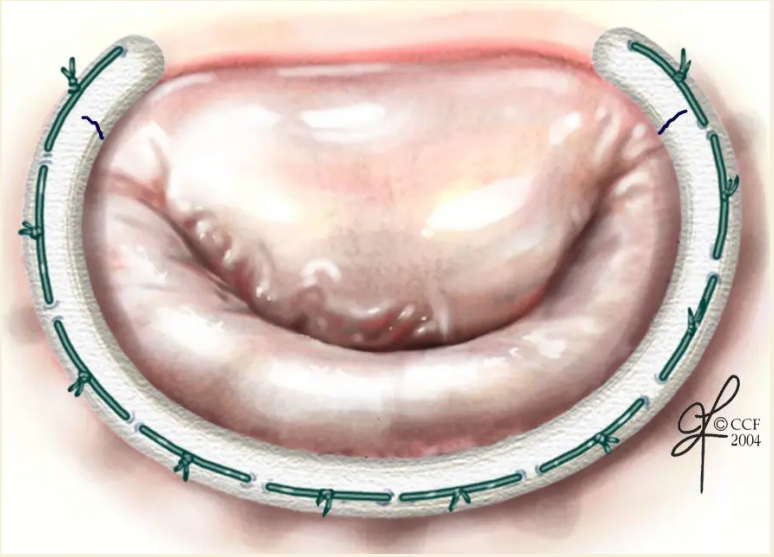
Indication for surgery:

1. Sever symptoms despite medical treatment
2. Patient undergoing other cardiac surgery
3. Pulmonary artery systolic pressure > 50 mm Hg
4. Ejection fraction < 50%
5. Left ventricle "end-diastolic" diameter > 4.5 cm2

Surgical option considered on an individual basis:

- Mitral valve replacement





AORTIC STENOSIS (AS)

- Aortic valve stenosis (AS) is a valvular heart disease characterized by narrowing of the aortic valve.
- Most common valvular heart disease in industrialized countries
- Frequently associated with aortic regurgitation

CAUSES

1. Degenerative Aortic valve stenosis

- Dur to calcification and fibrosis of aortic valve leaflets
- Most common cause of aortic stenosis

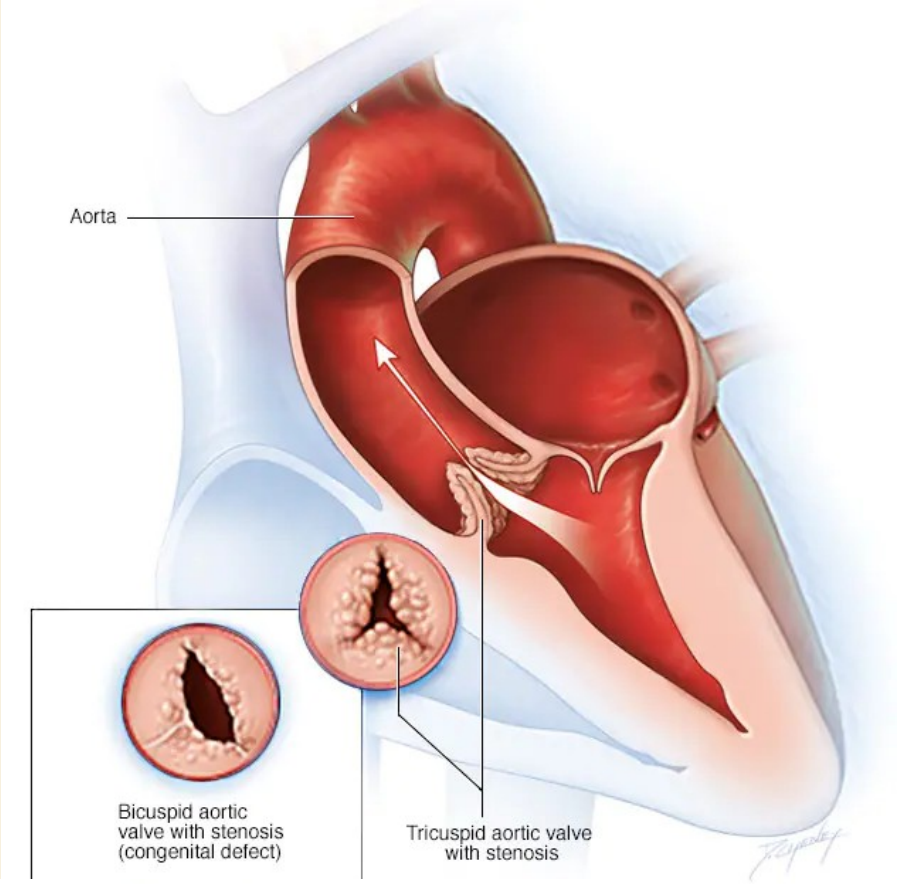
2. Bicuspid aortic valve (BAV):

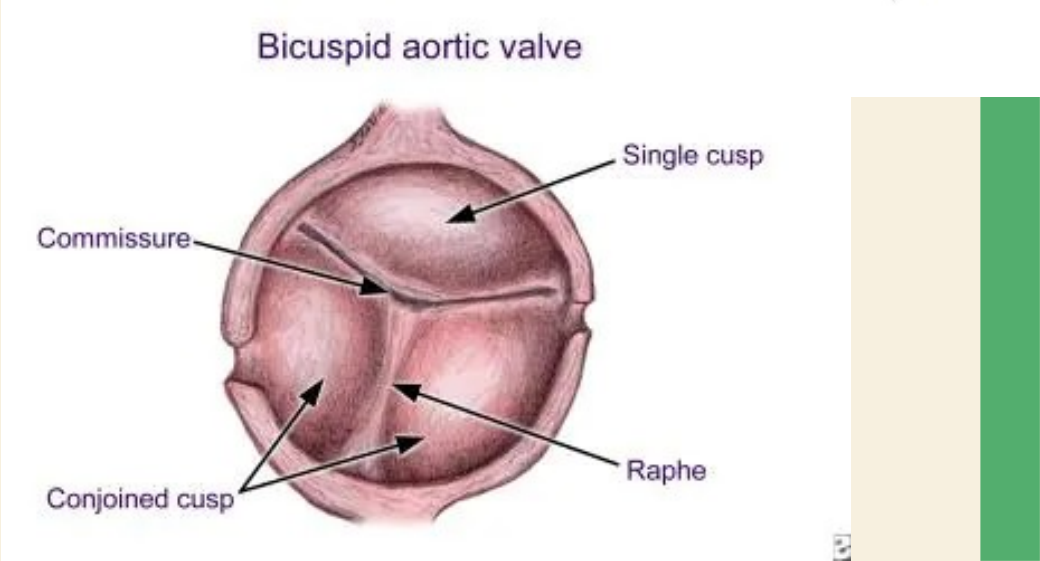
- = Fusion of two of the three aortic-valve leaflets in utero
- Most common congenital heart valve malformation

3. Rheumatic fever

4. Infective endocarditis

5. Collagen disease (e.g., rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis),





PATHOPHYSIOLOGY

- Narrowed opening area of the aortic valve during systole → obstruction of blood flow from left ventricle (LV) → increased LV pressure → decrease the cardiac output (COP) and left ventricular hypertrophy, **which leads to:**
  - **Impaired ventricular filling during diastole** → left atrium dilatation
  - **Later,** that will cause backflow of blood into the pulmonary veins and capillaries (pulmonary edema) → pulmonary hypertension → right ventricular hypertrophy → right heart failure

CLINICAL FEATURES

- Aortic stenosis may remain asymptomatic for years.
- Symptoms usually start to develop when the disease progresses to severe AS.
- **The 3 cardinal signs of AS:**

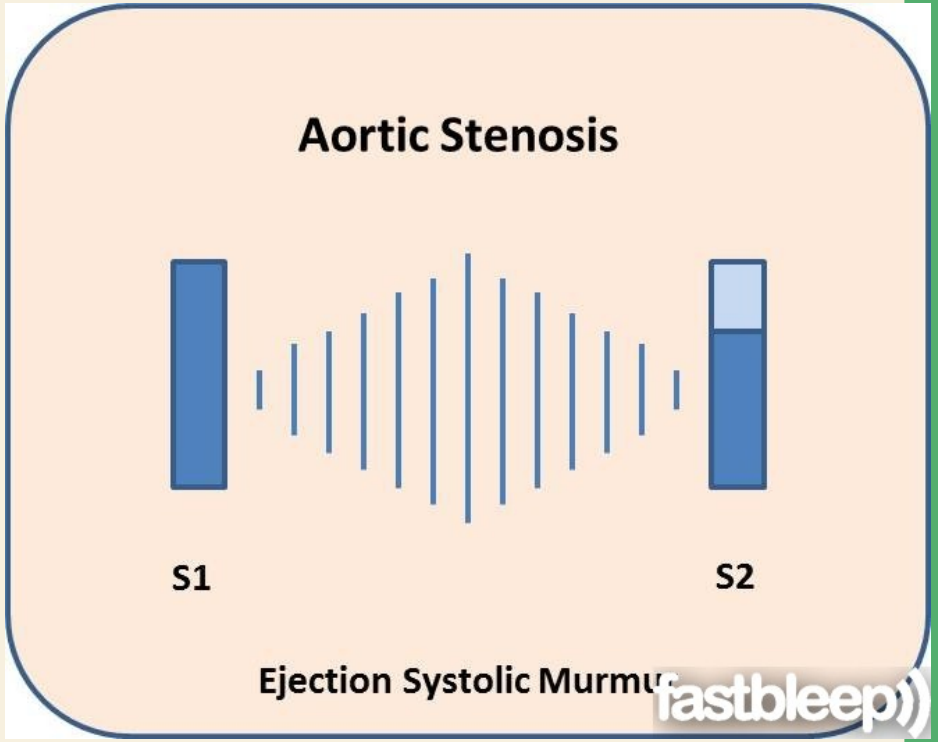
1. Dyspnea (typically exertional)
2. Angina pectoris
3. Dizziness and syncope

- At later stages of the disease, patient may develop left sided heart failure, which if not treated properly will lead to right side heart failure.

CLINICAL FEATURES

Auscultation

- **Mid-systolic murmur**

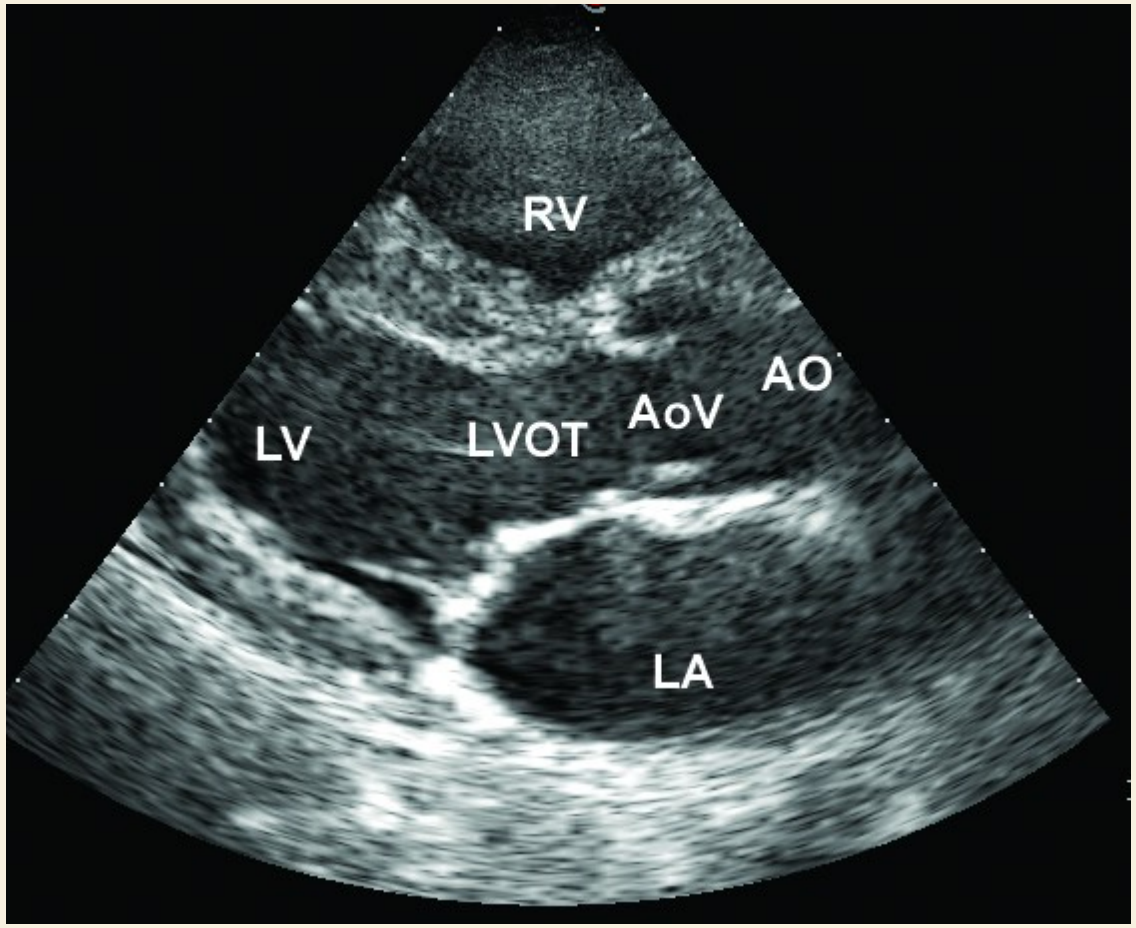


DIAGNOSIS

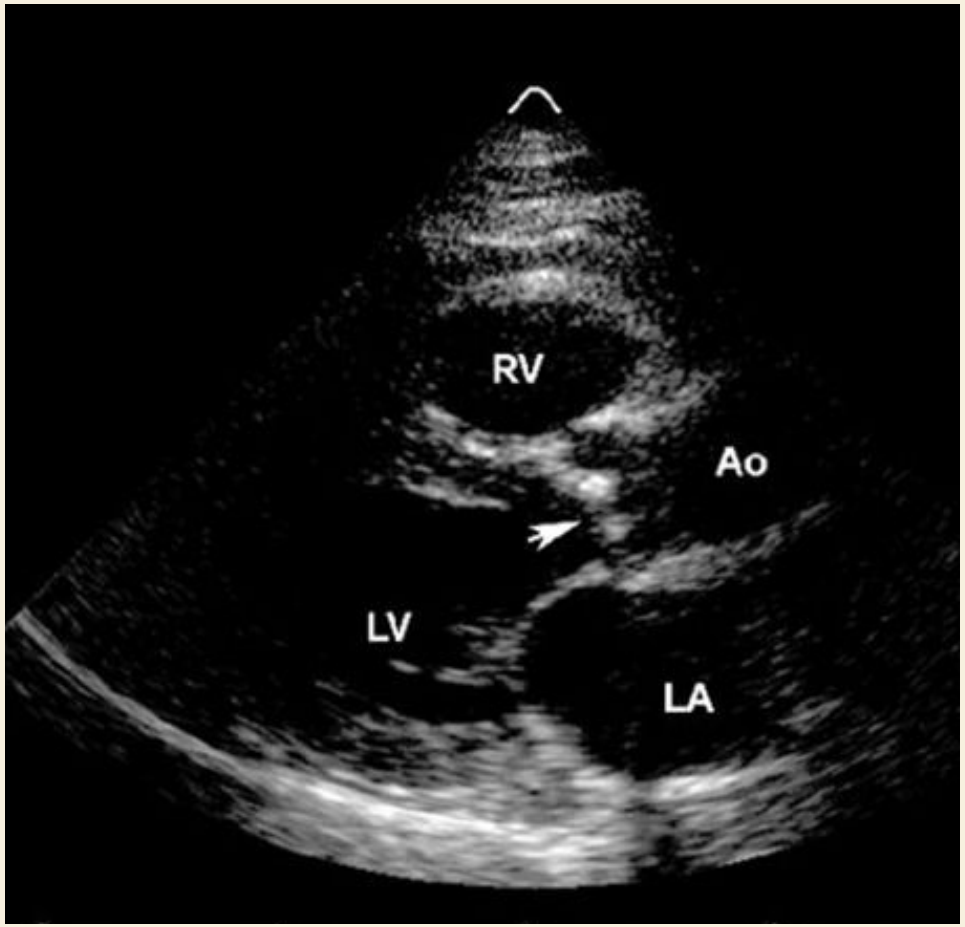
- **Echocardiography:** supportive findings

1. Calcification and narrowing of the aortic valve
2. Increased mean aortic pressure gradient and transvalvular velocity
3. Left ventricle hypertrophy

- **ECG:** shows signs of LVH and left atrium dilatation.
- **Chest X-ray:** signs of LVH, pulmonary congestion, pulmonary edema



Normal Aortic Valve



Aortic Valve stenosis

TREATMENT

Medical management

- Identify and treat any underlying cause
- Symptomatic treatment:

➔ Heart failure management: - Diuretics (e.g., furosemide)

- ACE inhibitors (e.g., lisinopril)
- Beta blockers (e.g., metoprolol)

TREATMENT

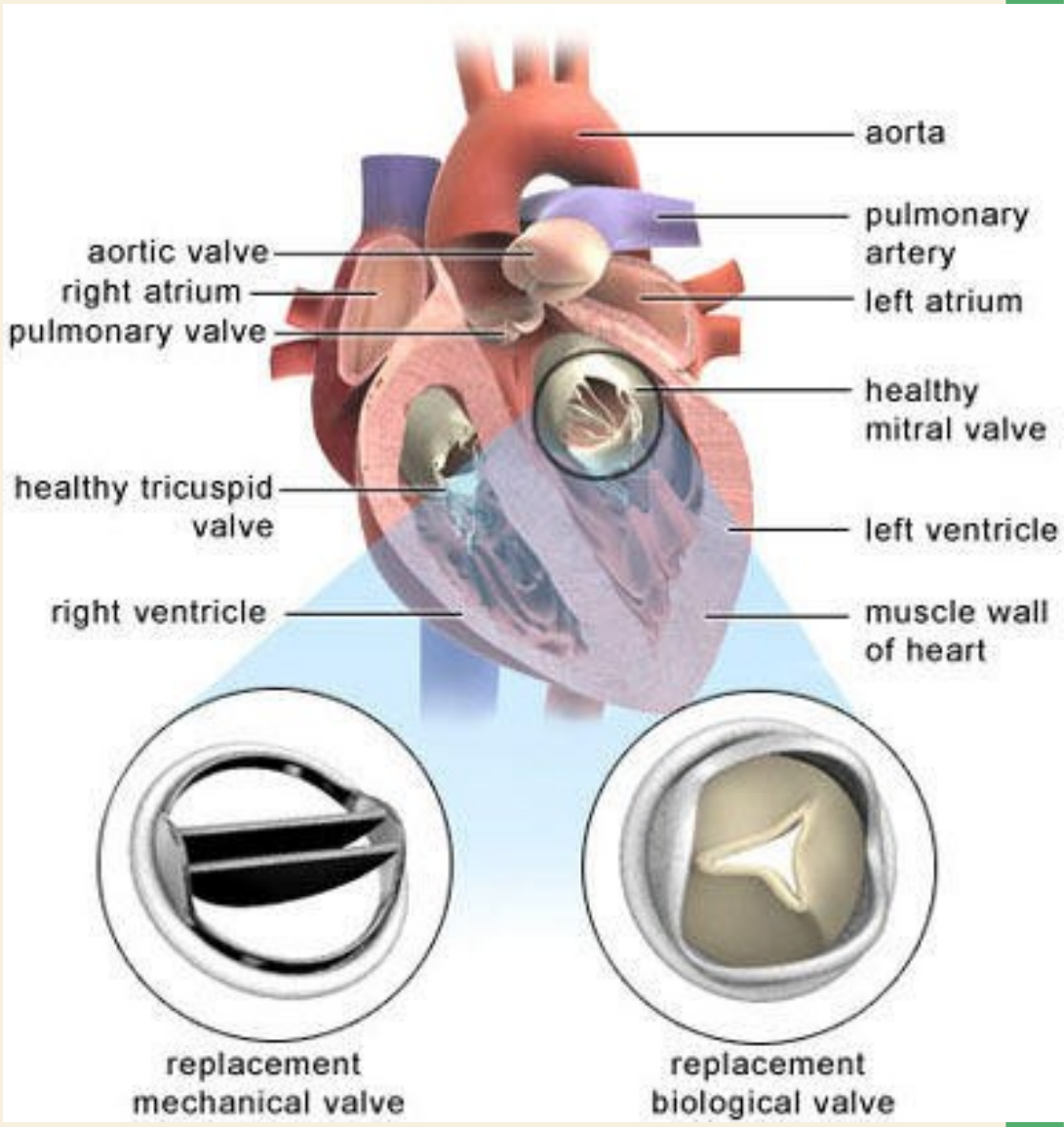
Surgical treatment

Indication for surgery:

1. Sever symptoms despite medical treatment
2. Patient undergoing other cardiac surgery
3. Pulmonary Hypertension (Pulmonary artery systolic pressure > 50 mm Hg)
4. Mean Pressure gradient across the valve > 50 mmHg
5. Aortic valve area < 0.8 cm2

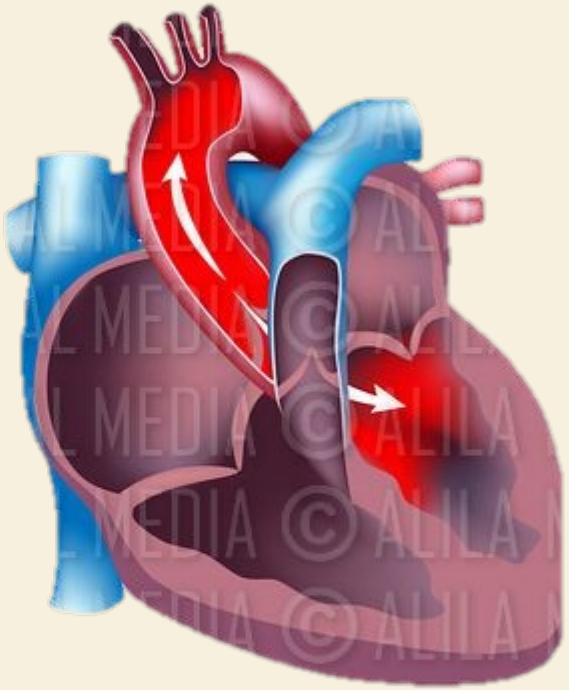
Surgical options:

6. **Aortic valve replacement:** for associated with regurgitation, severely calcified valve.
7. **Aortic valvuloplasty** (Commissurotomy)



AORTIC REGURGITATION (AR)

- Aortic regurgitation (AR) is a valvular heart disease characterized by incomplete closure of the aortic valve leading to the reflux of blood from the aorta into the left ventricle (LV) during diastole.



CAUSES

1. **Degenerative Aortic valve regurgitation**
2. **Rheumatic fever**
3. **Infective endocarditis**
4. **Collagen disease** (e.g., rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis)
5. **Bicuspid aortic valve (BAV)**
6. **Aortic dilatation: due to**

- Connective tissue disorders (e.g., Marfan syndrome, Ehlers-Danlos syndrome)
- Chronic hypertension
- Aortitis of any etiology (e.g., tertiary syphilis)
- Thoracic aortic aneurysm

PATHOPHYSIOLOGY

Acute AR

- Because LV cannot sufficiently dilate in response to regurgitant blood, LV end-diastolic pressure increases rapidly → pressure transmits backwards into left atrium, then to pulmonary circulation → pulmonary edema and dyspnea.
- Causes of Acute AR include: Aortic dissection, Endocarditis, Traumatic rupture of the valve leaflets, and Iatrogenic (as a complication of procedures such as aortic balloon valvotomy)

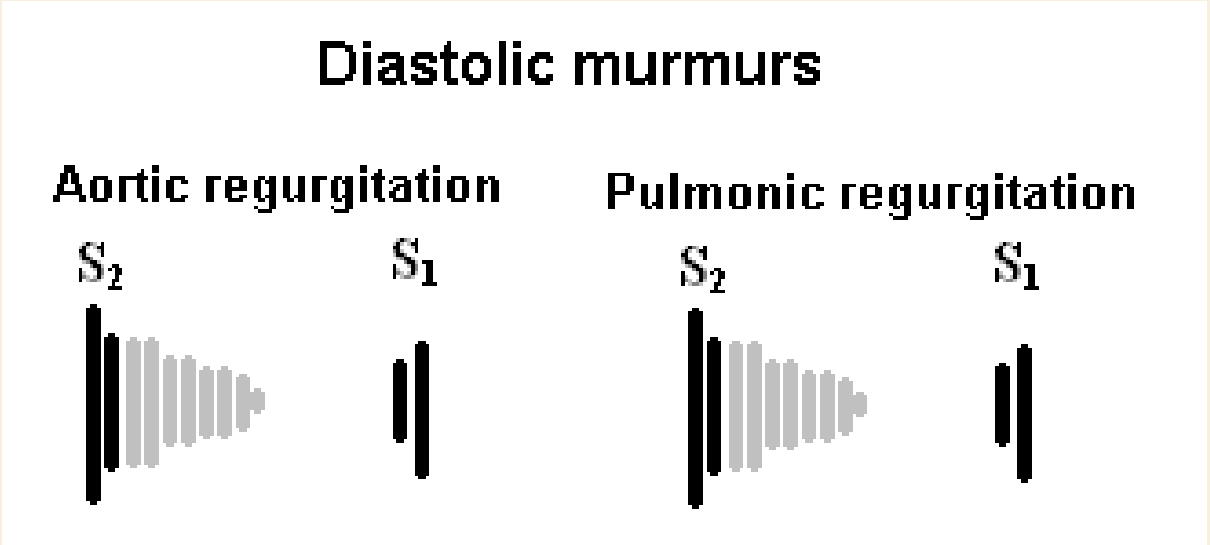
Chronic AR

- Over time, increased left ventricular end-diastolic volume → LV enlargement and hypertrophy → left ventricular systolic dysfunction → left side heart failure

CLINICAL FEATURES

Acute aortic regurgitation

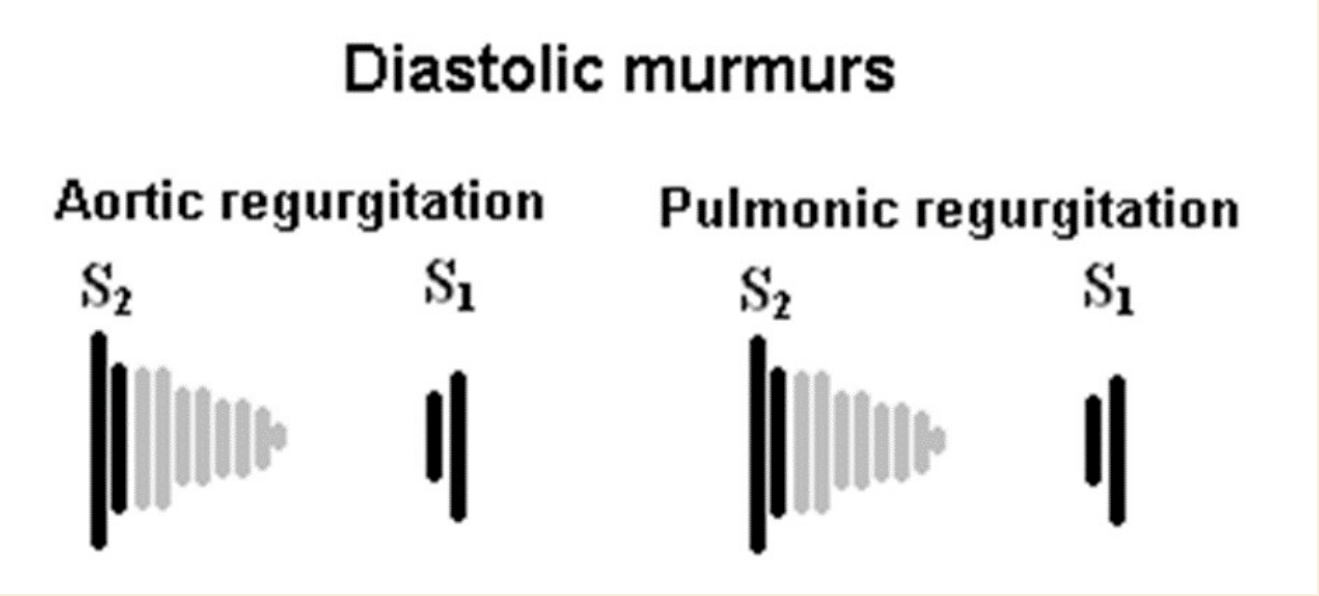
1. Sudden, severe dyspnea due to pulmonary edema
2. Symptoms related to underlying disease (e.g., fever due to endocarditis, chest pain due to aortic dissection)
3. **Auscultation** ➔ early diastolic murmur



CLINICAL FEATURES

Chronic aortic regurgitation

- Symptoms of left heart failure
  - Exertional dyspnea
  - Angina
  - Orthopnea
  - Easy fatigability
  - Syncope
- **Auscultation** ➔ Early diastolic murmur (decrescendo)



CLINICAL FEATURES

Chronic aortic regurgitation

- May be asymptomatic for up to decades despite progressive LV dilation
- Palpitations
- **Symptoms of high pulse pressure:**
  - **Water hammer pulse of peripheral arteries** characterized by rapid upstroke and downstroke
  - **Corrigan pulse:** pulse of carotid arteries characterized by rapid upstroke and downstroke
  - **Duroziez sign:** to-and-fro bruit over the femoral artery that is heard when slight pressure is applied with a stethoscope
  - **Quincke sign:** visible capillary pulse when pressure is applied to the tip of a fingernail
  - **De Musset sign:** rhythmic nodding or bobbing of the head in synchrony with heartbeats

DIAGNOSIS

- **Echocardiography:** supportive findings

1. Abnormal aortic valve leaflets
2. Regurgitant AR jet on Doppler flow tracing
3. Reduced cardiac output
4. increased LV size and volume

- **ECG:** shows signs of LVH

- **Chest x-ray:**
  - **Acute AR:**

1. Normal heart
2. signs of pulmonary congestion or edema

  - **Chronic AR:** X-ray shows signs of LVH

TREATMENT

Medical management

- Identify and treat any underlying cause
- Symptomatic treatment:

➔ Heart failure management: - Diuretics (e.g., furosemide)

- ACE inhibitors (e.g., lisinopril)
- Beta blockers (e.g., metoprolol)

TREATMENT

- **Surgical management:**

Indication for surgery:

1. Sever symptoms despite medical treatment
2. Patient undergoing other cardiac surgery
3. Pulmonary hypertension (pulmonary artery systolic pressure > 50 mm Hg)
4. Ejection fraction < 55%
5. Left ventricle "end-systolic" diameter > 5.5 cm2

Surgical option considered on an individual basis:

- Aortic valve replacement
- Aortic valvuloplasty

S3 vs. S4 heart sound(s):

S3-"ventricular gallop"	S4-"atrial gallop"
Occurs in early diastole	Occurs in late diastole
Occurs during passive LV filling	Occurs during active LV filling
May be physiologic at times	Almost always pathological
Requires a very compliant LV	Requires a non-compliant LV
Can be a sign of systolic CHF	Can be a sign of diastolic CHF
Associated with mitral & aortic regurgitation	Associated with aortic stenosis

S3 caused by rapid inflow of blood into the ventricle during early diastole

S4 caused by contraction of the atrium against non-compliant left ventricle

THANKS

VASCULITIS

VASCULITIS

- **Vasculitis** is a general term for vessel wall inflammation with manifestations depending on the vascular bed affected

- Besides the findings referable to **the specific tissues involved**, the clinical manifestations typically include constitutional signs and symptoms associated with systemic inflammation, such as fever, myalgias, arthralgias, and malaise.

classifications

- the disease could either be primary or secondary to another disease , drug or malegnancy

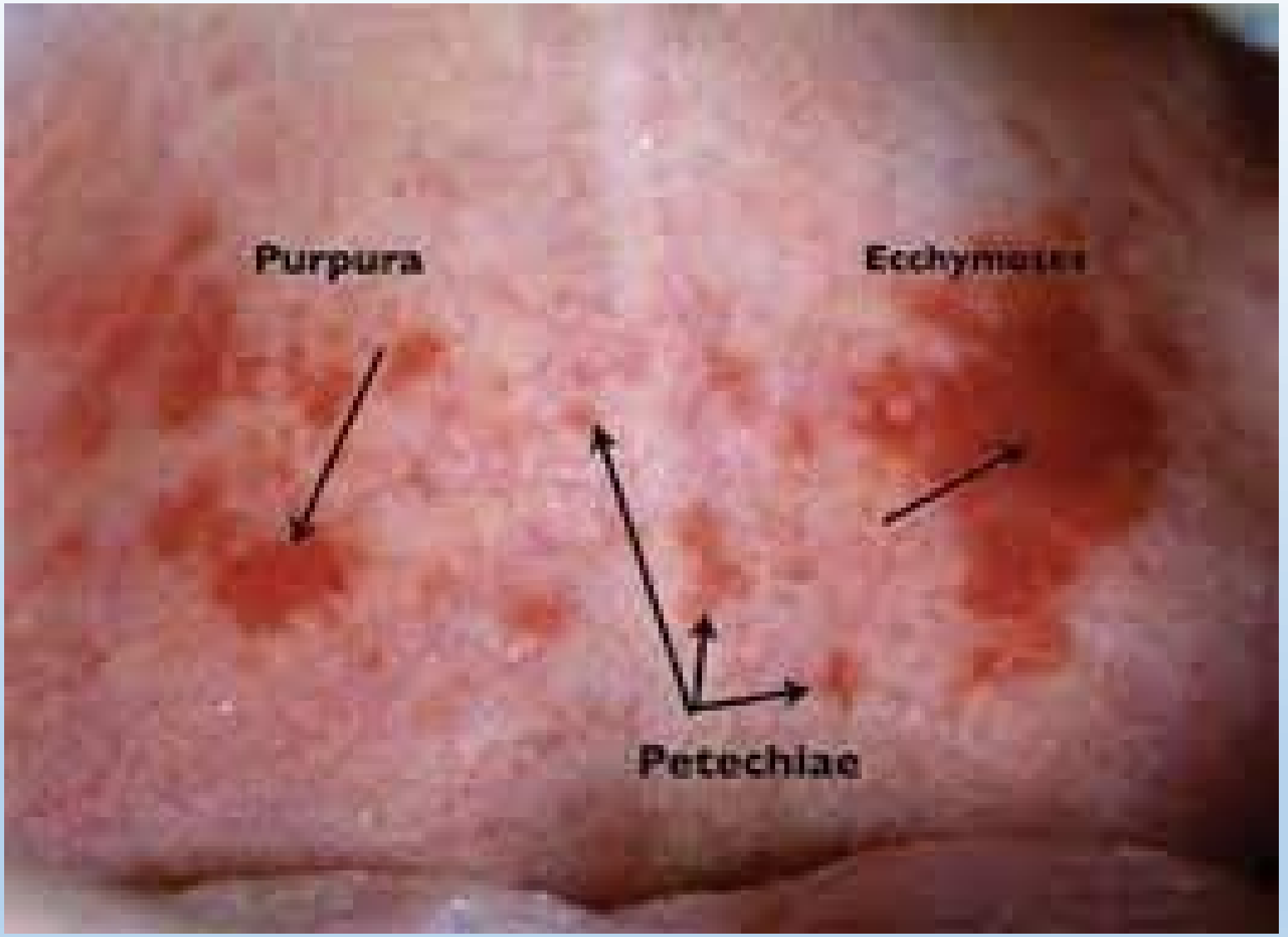
- primary vasculitis can be classified to the size of blood vessel affected :

✓Large vessel vascilitis :ex. aorta and its main branches

✓Medium vessel vasculitis : ex renal arterie

✓Small vessel vasculitis : ex arteriols , capillaries

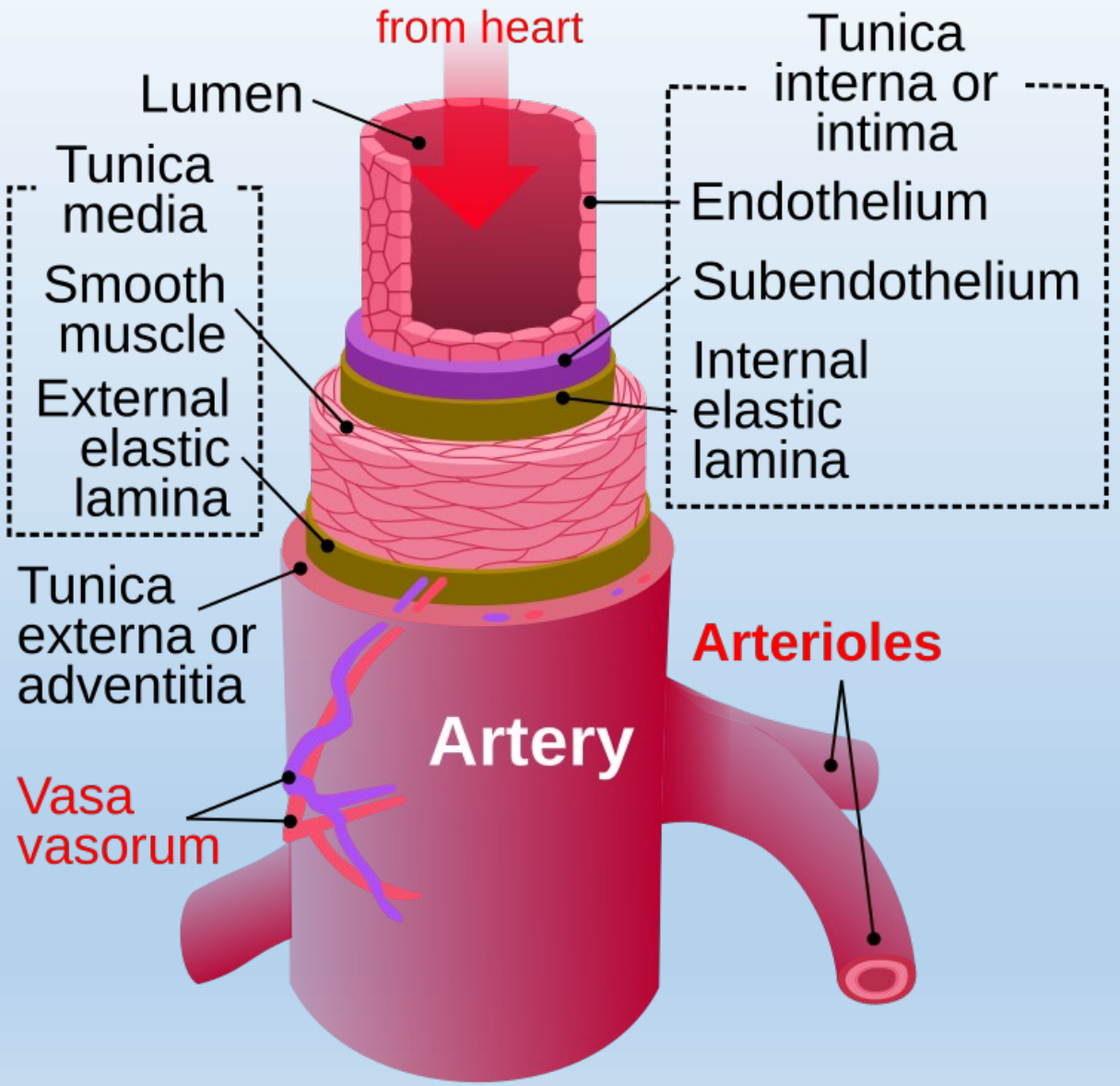
- Medium and small vessel vasculitis present with cutaniuos finding (purpura and patichea) as they are more superficial to the skin

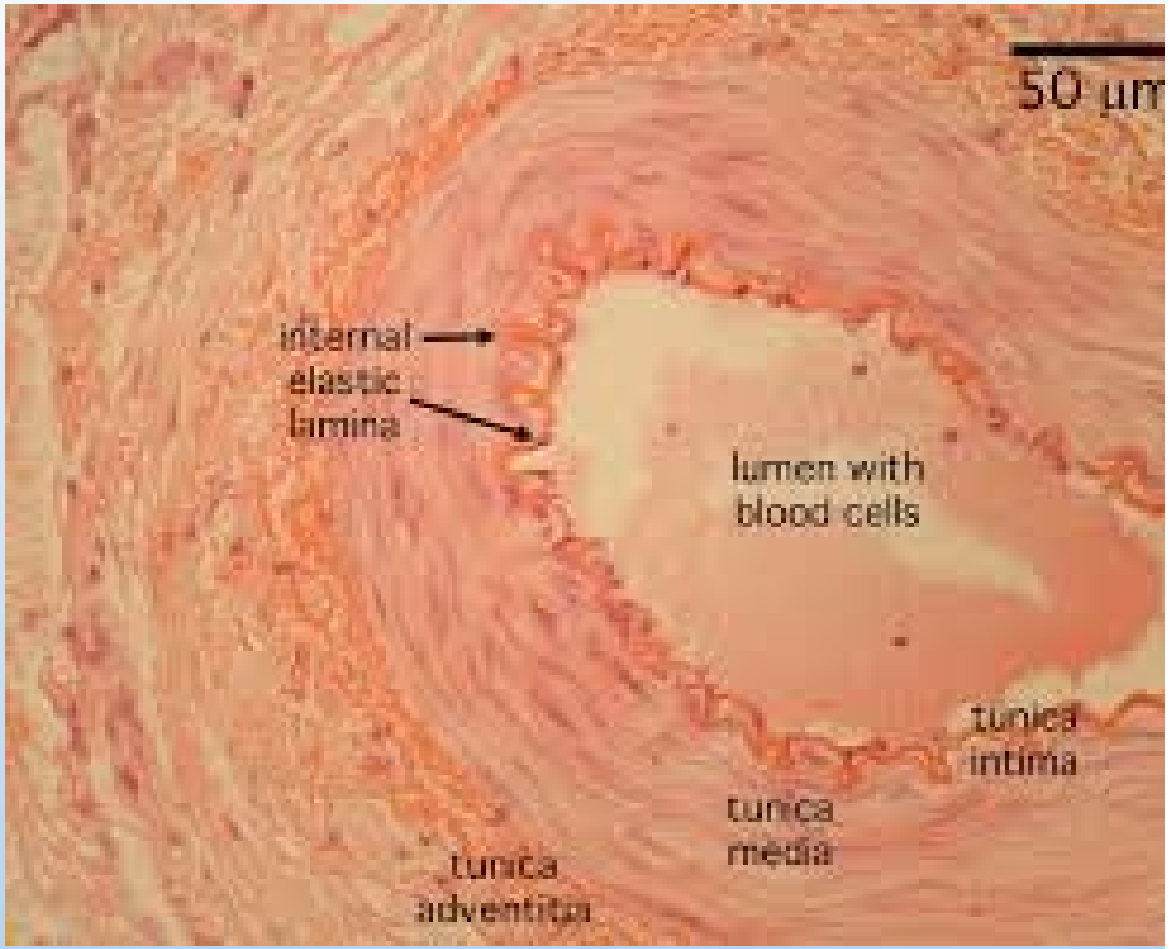

Purpura
Ecchymoses
Petechiae

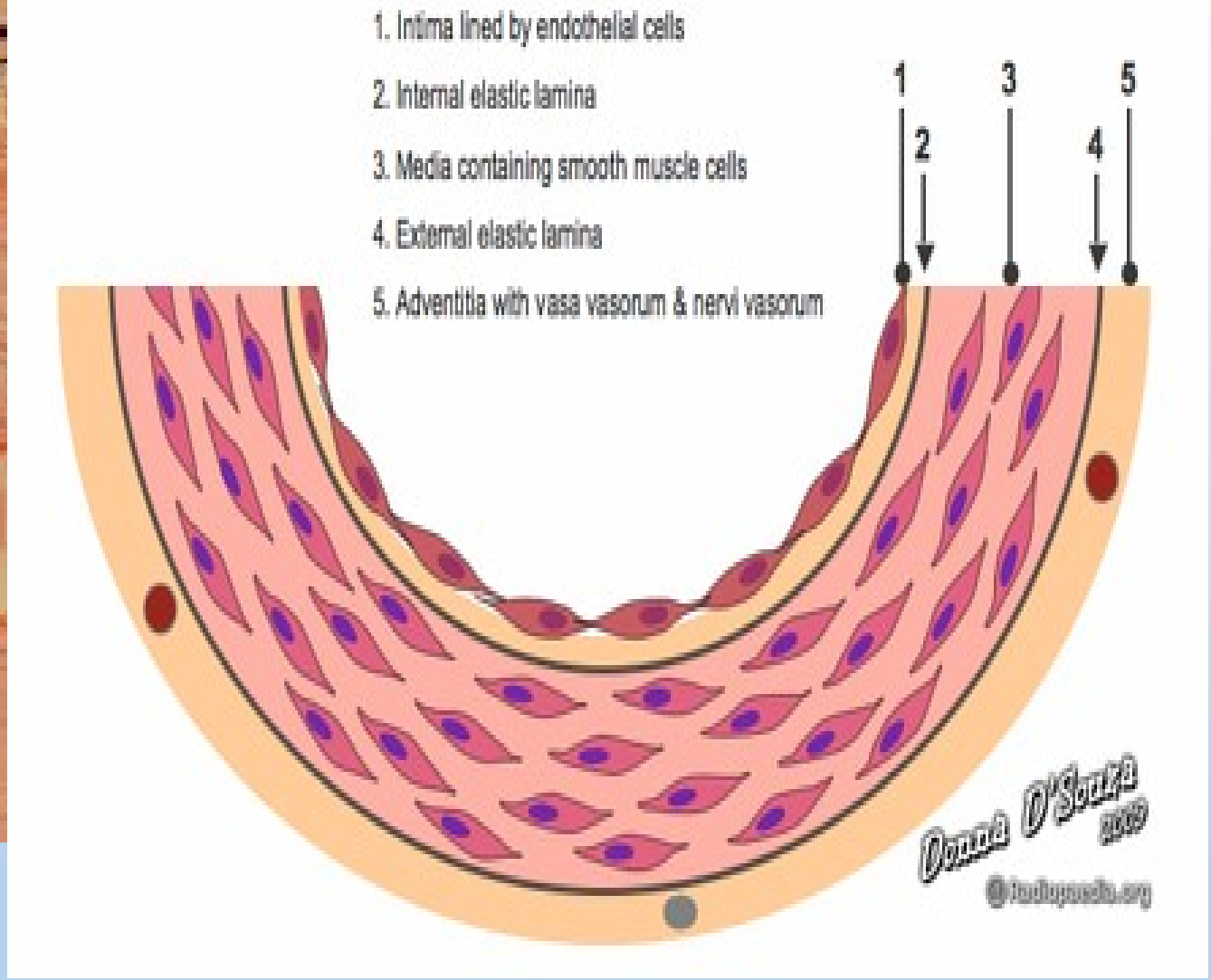
pathogenesis

- The two pathogenic mechanisms of vasculitis are
  - immune-mediated inflammation
  - direct invasion by infectious pathogens.

- Infections can also indirectly induce a noninfectious vasculitis, for example, by generating immune complexes or triggering vascular cross-reactivity


from heart
Lumen
Tunica media
Smooth muscle
External elastic lamina
Tunica externa or adventitia
Vasa vasorum
Tunica interna or intima
Endothelium
Subendothelium
Internal elastic lamina
Arterioles
Artery


50 µm
internal elastic lamina
lumen with blood cells
tunica intima
tunica media
tunica adventitia


1. Intima lined by endothelial cells
2. Internal elastic lamina
3. Media containing smooth muscle cells
4. External elastic lamina
5. Adventitia with vasa vasorum & nervi vasorum
1
2
3
4
5

Noninfectious Vasculitis

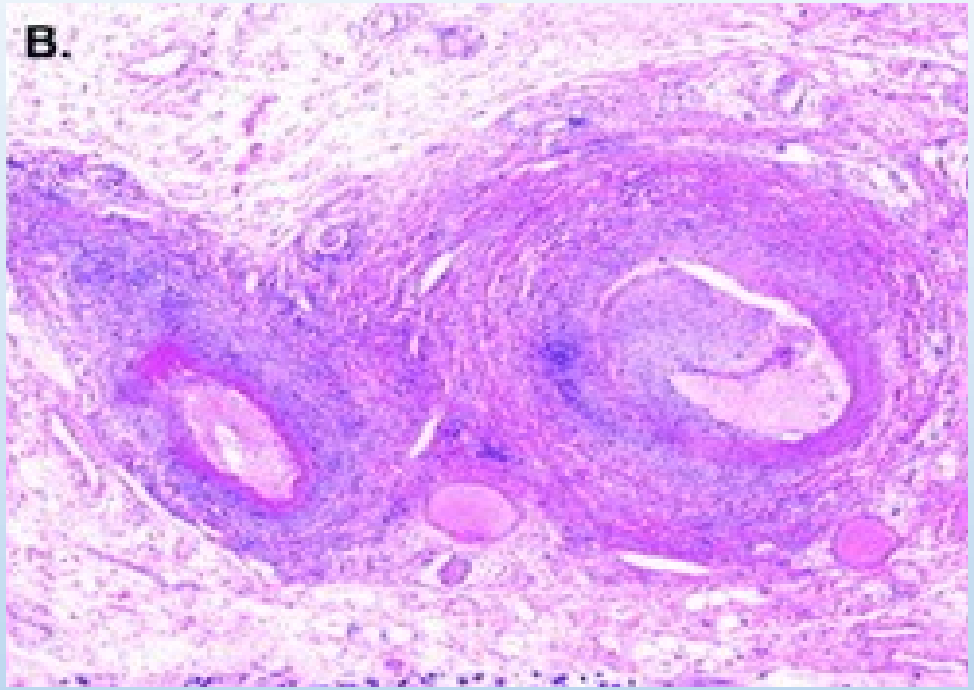
- The main Immunologic mechanisms underlying noninfectious vasculitis are:
- Immune complex deposition
- Antineutrophil cytoplasmic antibodies (ANCAs)
- Anti-EC antibodies
- Autoreactive T cells

❖ Immune Complex–Associated Vasculitis

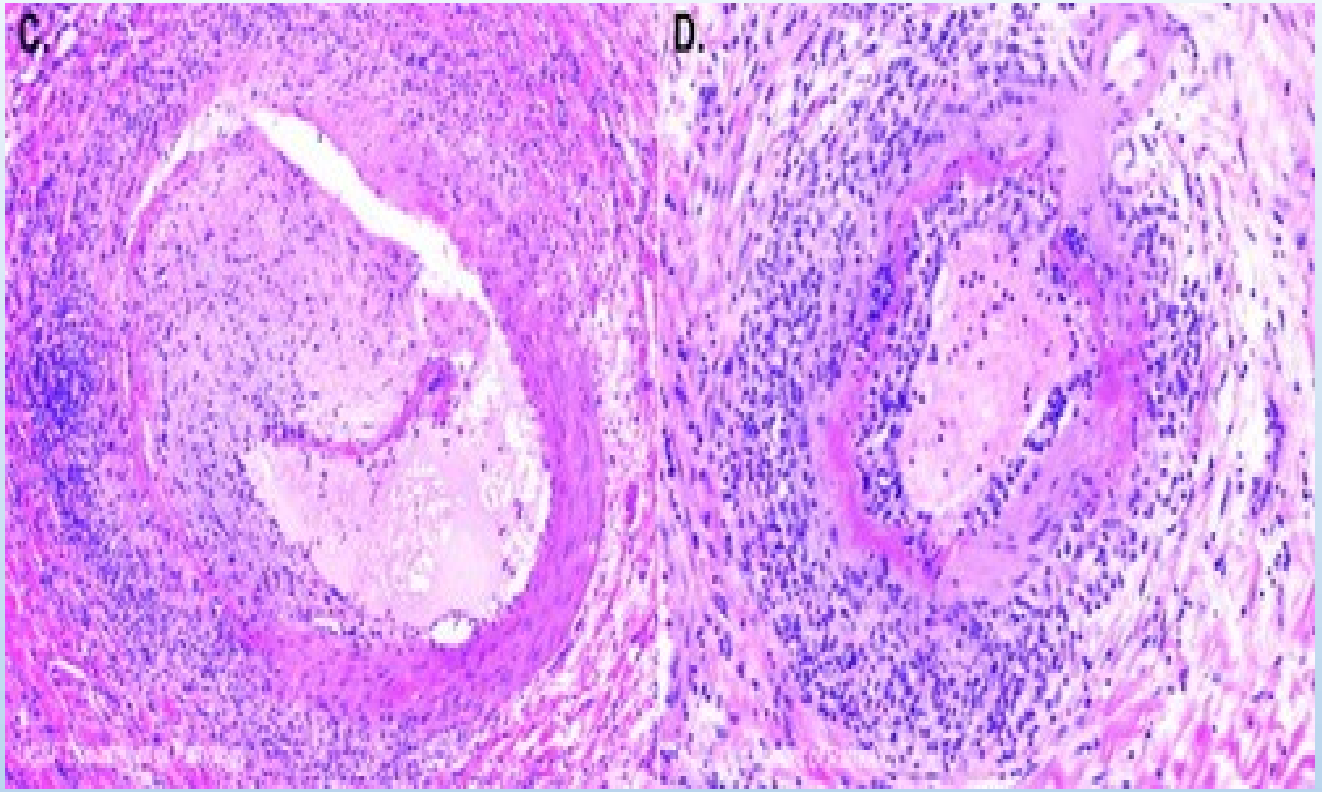
- This form of vasculitis can be seen in immunologic disorders that are associated with autoantibody production(ex. systemic lupus erythematosus)

- The specific antigen responsible for immune complex formation is only rarely identified.
- Immune complexes can occasionally be detected in the blood, but in most cases it is not clear whether the pathogenic complexes are deposited from the circulation or form in situ.
- the sensitivity and specificity of circulating immune complex assays in such diseases are extremely low.

SLE vasculitis



b, Marked acute vasculitis in small to medium vessels .



C, Intraluminal thrombi within the vessel involved by vasculitis and extensivel lymphocytic infiltrate in the vessel wall.

D, Fibrinoid necrosis of the vessel wall

Immune Complex–Associated Vasculitis

- **Drug hypersensitivity vasculitis.**

Antibodies directed against the drug-modified proteins or foreign molecules result in immune complex formation

The clinical manifestations can be mild and self-limiting or severe and even fatal; skin lesions are most common.

discontinuation of the offending agent usually leads to resolution.

- **Vasculitis secondary to infections**.

Antibodies to microbial constituents can form immune complexes that circulate and deposit in vascular lesions

❖ Antineutrophil Cytoplasmic Antibodies

- Many patients with vasculitis have circulating antibodies that react with neutrophil cytoplasmic antigens—ANCAs.
- ANCAs are a heterogeneous group of autoantibodies directed against constituents (mainly enzymes) of neutrophil primary granules, monocyte lysosomes, and ECs
- their titers generally mirror clinical severity,

- ANCAs are grouped according to the intracellular distribution of the target antigens :

✓(cytoplasmic [c-ANCA], now called Anti-proteinase-3 (PR3-ANCA)associated with granulomatosis with polyangiitis

✓ perinuclear [p-ANCA]), now called Anti-myeloperoxidase (MPO-ANCA) are associated with microscopic polyangiitis and Churg-Strauss syndrome

Mechanism for ANCA vasculitis

- Drugs or cross-reactive microbial antigens induce ANCA formation or, leukocyte surface expression or release of PR3 and MPO (in the setting of infections) incites ANCA development in a susceptible host.
- cytokines such as tumor necrosisfactor [TNF] upregulate the surface expression of PR3 and MPO on neutrophils and other cell types.
- ANCAs react with these cytokine-activated cells, causing either direct injury (e.g., to ECs) or further activation (e.g., of neutrophils) causing tissue injury due to release of reactive oxygen species and proteolytic enzymes.

➢ ANCAassociated vasculitides are often described as **pauci-immune** as ANCA autoantibodies are directed against cellular constituents and do not form circulating immune complexes, the vascular lesions do not typically contain demonstrable antibody and complement.

Anti–Endothelial Cell Antibodies

- Antibodies to ECs, perhaps induced by defects in immune regulation, may predispose to certain vasculitides, for example, Kawasaki disease

LARGE-VESSEL VASCULITIS

1. Giant Cell (Temporal) Arteritis

- chronic, classically granulomatous inflammation of large- to small-sized arteries principally affects arteries in the head
- classically involves branches of the carotid artery
- Temporal (hence the name), Vertebral and ophthalmic arteries, as well as the aorta (giant cell aortitis), also can be involved

➢it is the most common form of vasculitis among elderly adults

Pathogenesis

- T cell–mediated immune response to an uncharacterized vessel wall antigen.
- Proinflammatory cytokines (especially TNF) and anti-EC antibodies also contribut

Morphology

- intimal thickening (with occasional thromboses) reducing the luminal diameter
- medial granulomatous inflammation centered on the internal elastic membrane with elastic lamina fragmentation;
- infiltrate of T cells and macrophages
- lesions are only focally distributed along the vessel, and segments of relatively normal artery may be interposed

➢ The healed stage is marked by medial attenuation and scarring with intimal thickening,

fragmentation of greater than 30% of the circumference of the internal elastic lamina, and adventitial fibrosis.

MORPHOLOGY

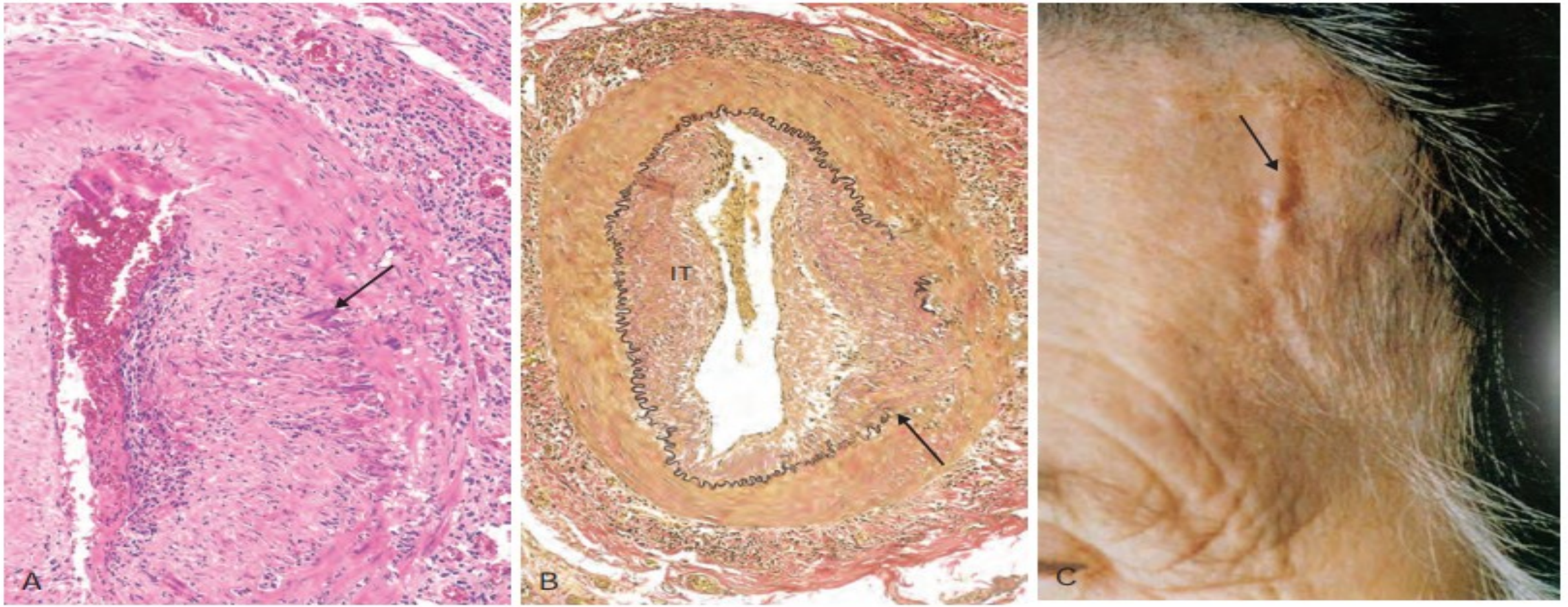


Figure 11.25 Giant cell (temporal) arteritis. (A) Hematoxylin-and-eosin stain of section of temporal artery showing giant cells at the degenerated internal elastic membrane in active arteritis *(arrow)*. (B) Elastic tissue stain demonstrating focal destruction of internal elastic membrane *(arrow)* and intimal thickening *(IT)* characteristic of long-standing or healed arteritis. (C) The temporal artery of a patient with classic giant cell arteritis shows a thickened, nodular, and tender segment of a vessel on the surface of head *(arrow)*. (C, From Salvarani C, et al. Polymyalgia rheumatica and giant-cell arteritis, *N Engl J Med* 347:261, 2002.)

Clinical Features

- headache (temporal artery involvement),
- visual disturbances (ophthalmic artery involvement),
- jaw claudication.
- Flu-like symptoms with joint and muscle pain (polymyalgia rheumatica)

❖rare before the age of 50 yrs

- **Diagnosis**: biopsy and histologic confirmation.

➢adequate biopsy requires at least a 1-cm segment and a negative biopsy result does not exclude the diagnosis, because lession can be extremely focal within an artery.

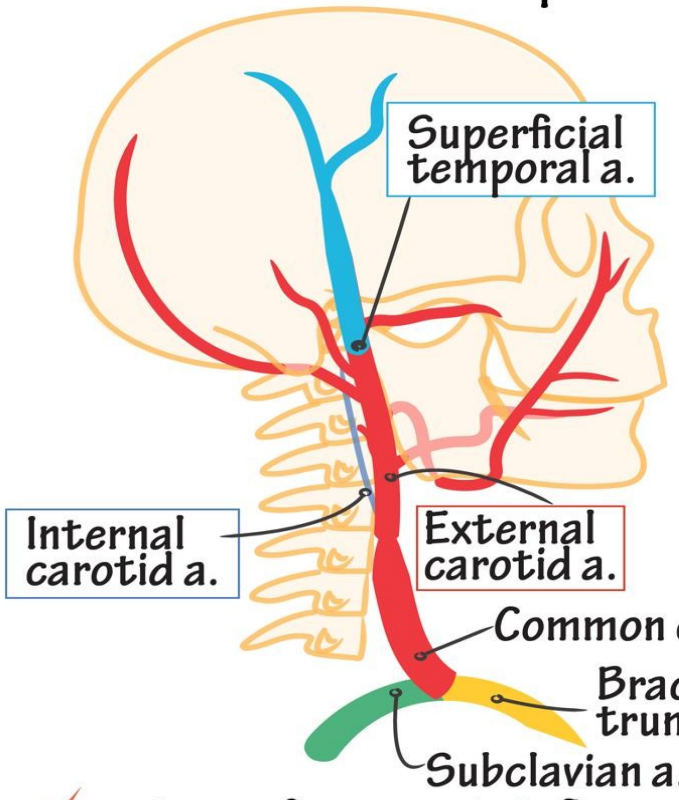
- **treatment** : Corticosteroids, high risk of blindness without treatment

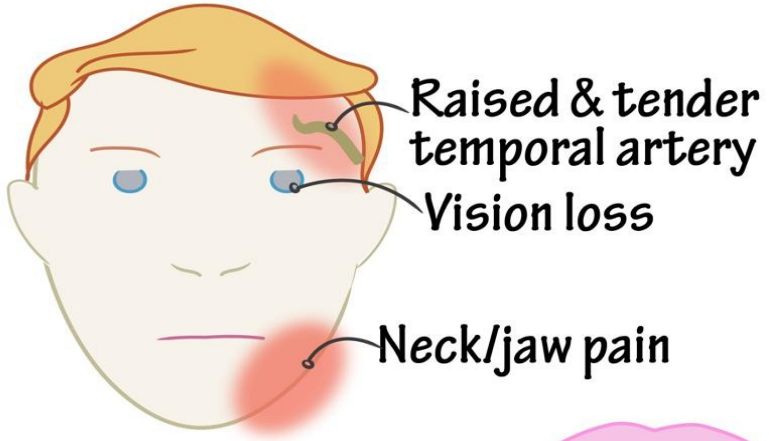
Giant cell arteritis

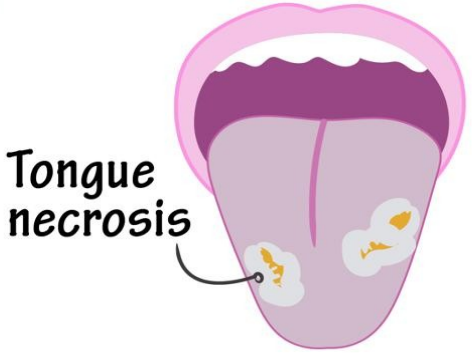
(aka, Temporal arteritis, Horton disease)

Granulomatous Disease

- ✓ Affects aorta and its large branches (esp. external carotid arteries).
  - Vessels of head/scalp



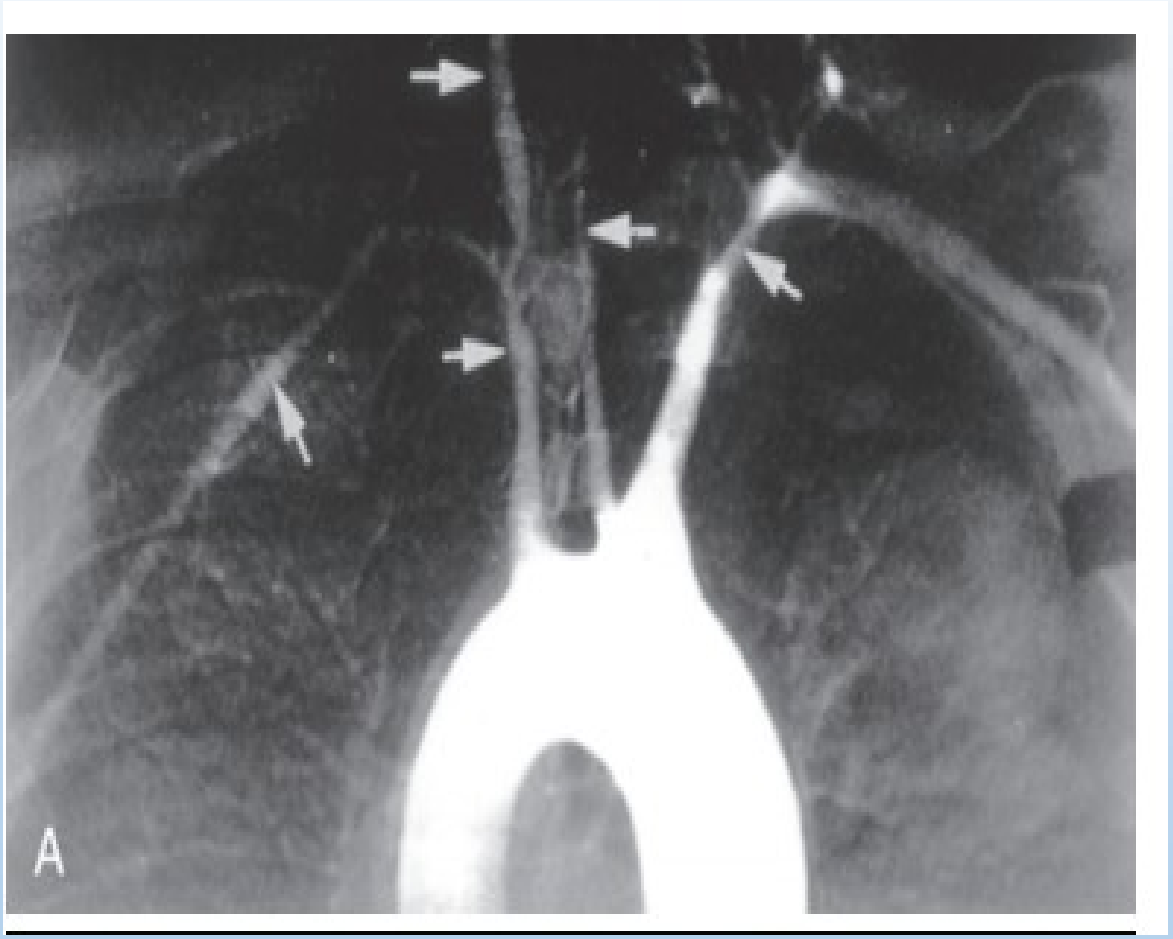




- ✓ + signs of systemic inflammation (fatigue, fever, weight loss)
- ✓ Most common in > 55 y.o., Women, Nordic ancestry
  - * Assoc. w/ polymyalgia rheumatica
- ✓ Complications: Aortic aneurysm, stroke, blindness.

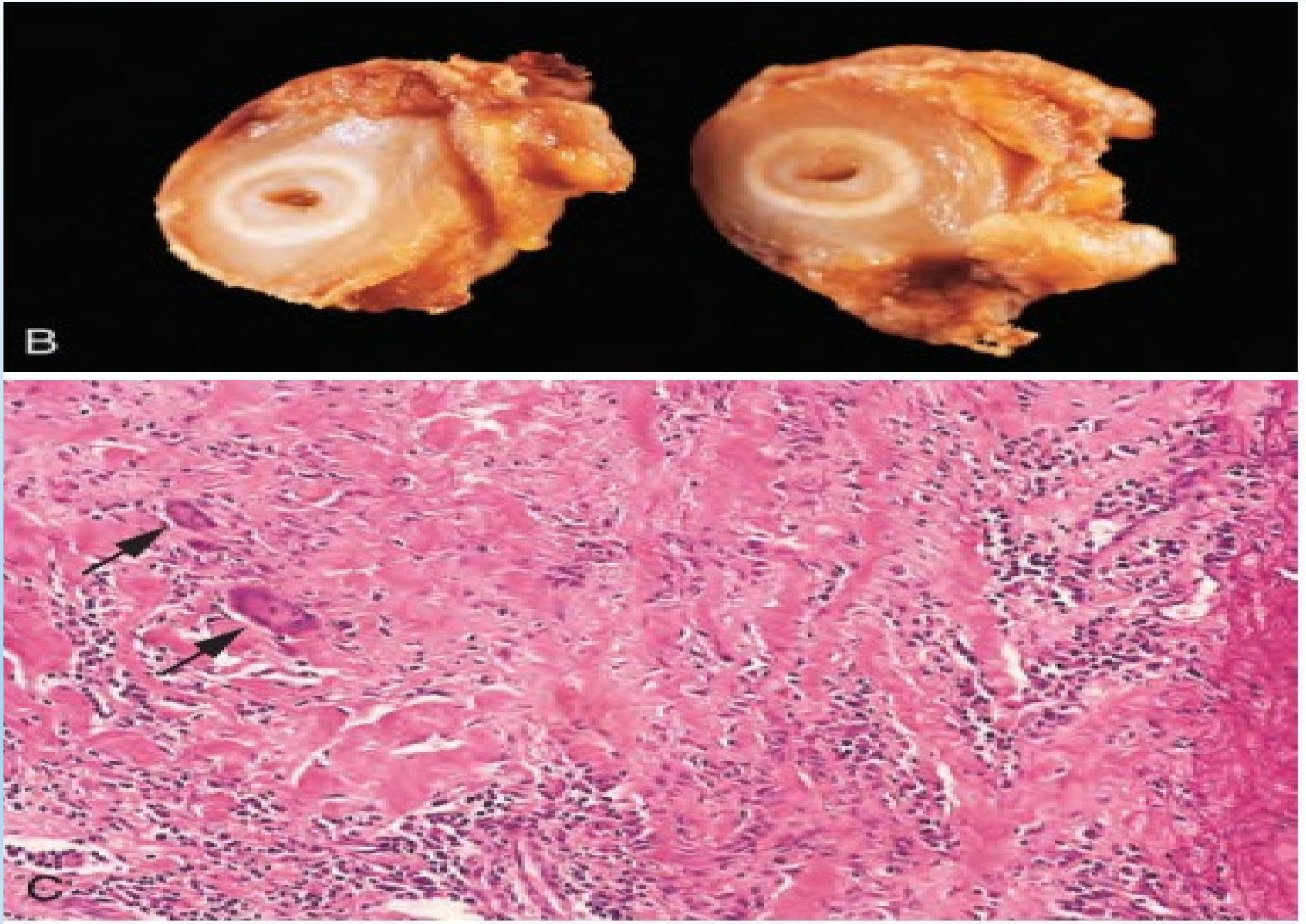
2. Takayasu Arteritis

- Takayasu arteritis is a granulomatous vasculitis of medium and larger arteries characterized principally by ocular disturbances and marked weakening of the pulses in the upper extremities
- arteritis manifests with transmural fibrous thickening of the aorta—particularly the aortic arch and great vessels—with severe luminal narrowing of the major branch vessels
- An autoimmune etiology is likely.



Morphology

- irregular thickening of the vessel wall with intimal hyperplasia; when the aortic arch is involved, the great vessel lumens can be markedly narrowed or even obliterated
- Histologically : changes range from adventitial mononuclear infiltrates with cuffing of the vasa vasorum to intense mononuclear inflammation in the media
- Granulomatous inflammation, with giant cells and patchy medial necrosis, is also seen


B
C

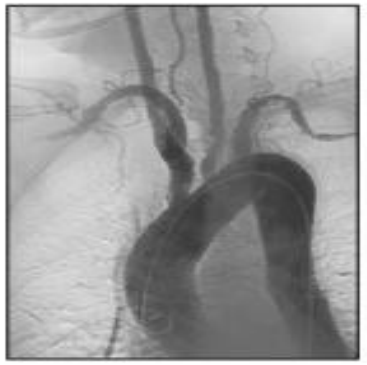
Clinical Features

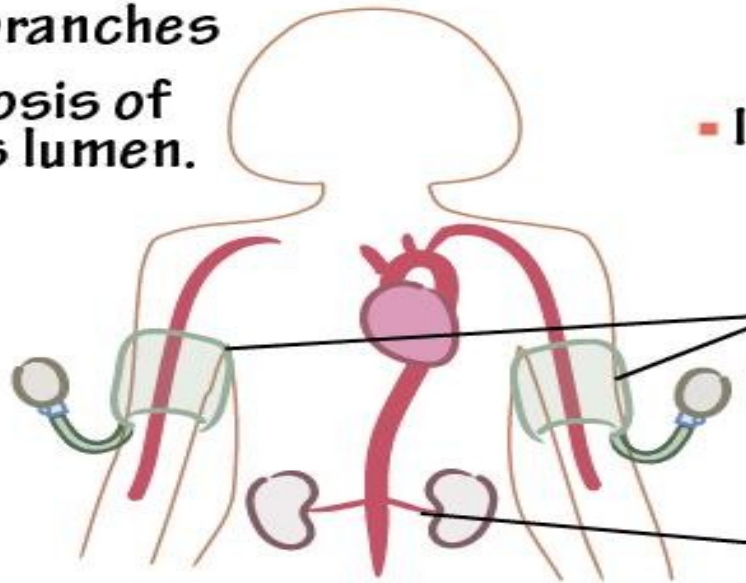
- Presents in adults < 50 years old (classically, young Asian females)
- nonspecific symptoms , including fatigue, weight loss, and fever.
- With progression, vascular symptoms appear including reduced blood pressure and weaker pulses in the upper extremities.
- ocular disturbances, including visual defects, retinal hemorrhages, and total blindness.
- Narrowing of the coronary ostia may lead to myocardial infarction.
- involvement of the renal arteries leads to systemic hypertension in roughly half of patients.

- **Treatment is corticosteroids.**

Takayasu arteritis
(aka, Pulseless disease)
Granulomatous Disease

- ✓ Aorta and its large branches
  - Thickening and fibrosis of vessel wall narrows lumen.

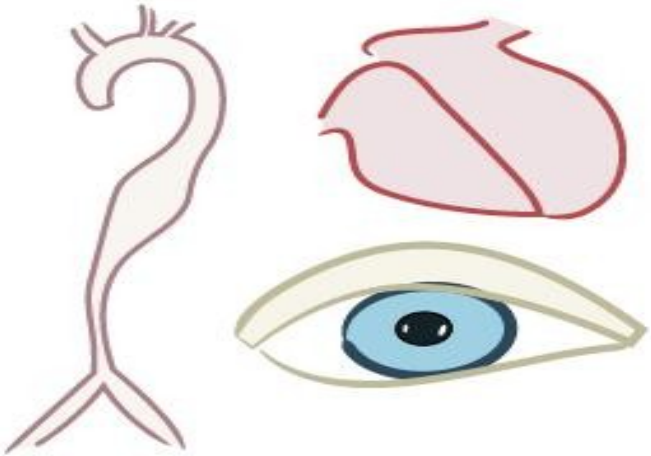




- Ischemia produces:
  - "Pulseless disease" Weak/absent pulse.
  - Different pressures in upper extremities.
  - Claudication in limbs, chest pain.
  - Poss. hypertension (renal art. stenosis)

  - Nonspecific symtpoms assoc. with inflammation:
    Weakness, fatigue, fever, weight loss, arthralgia.

- ✓ Poss. complications:
  Aneurysm, aortic regurgitation, retinopathy.



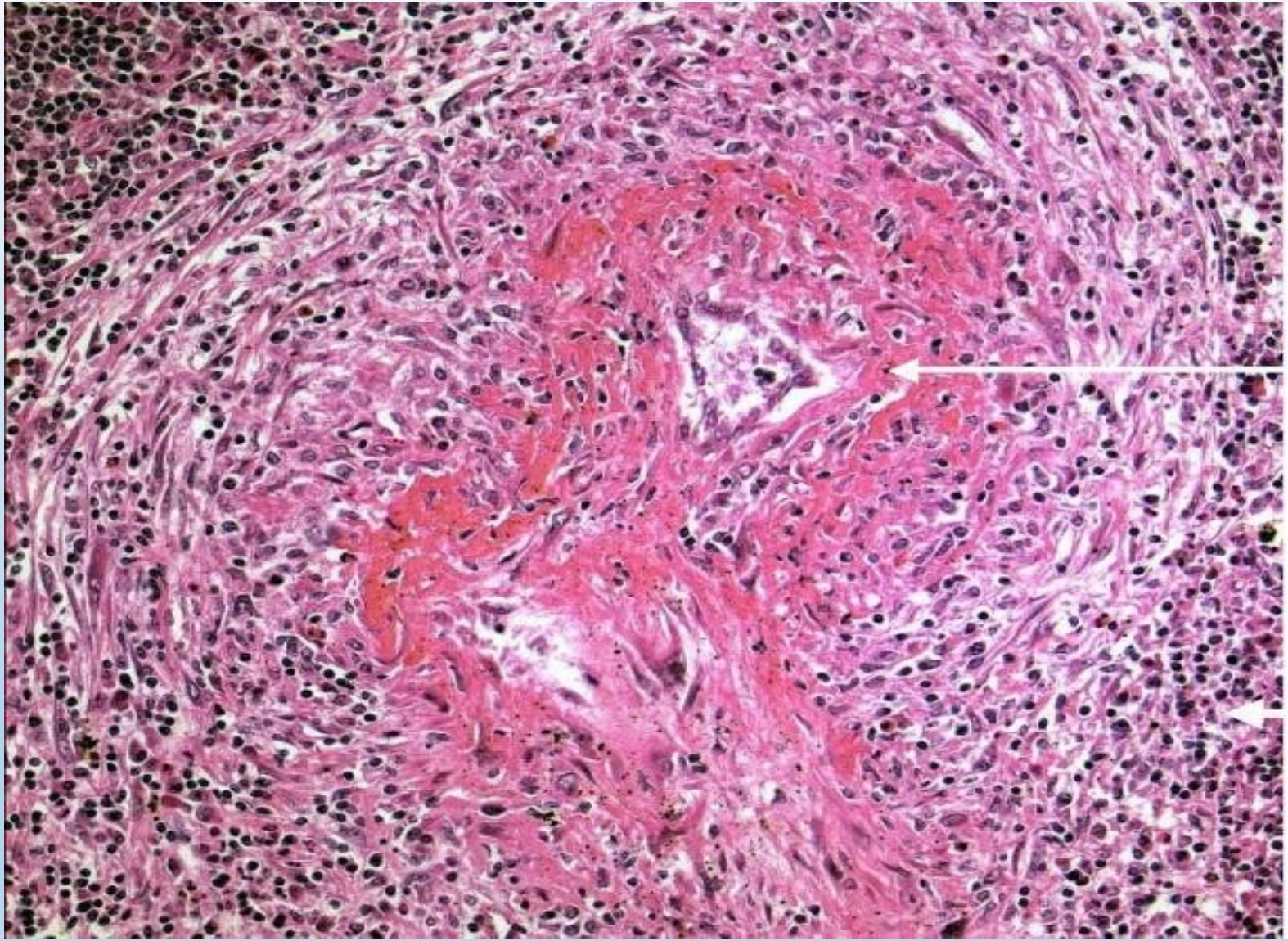
- ✓ Most common in women < 40 y. o.; esp. Asian ancestry.

MEDIUM-VESSEL VASCULITIS

- **Polyarteritis Nodosa**
- PAN is a systemic vasculitis of small- or medium-sized muscular arteries that typically affects renal and visceral vessels but spares the pulmonary circulation
- immune complex mediated vasculitis , a third of patients with PAN have chronic hepatitis B, which leads to the formation of HBsAg-HbsAb complexes that deposit in affected vessels, The cause remains unknown in the majority of cases

MORPHOLOGY

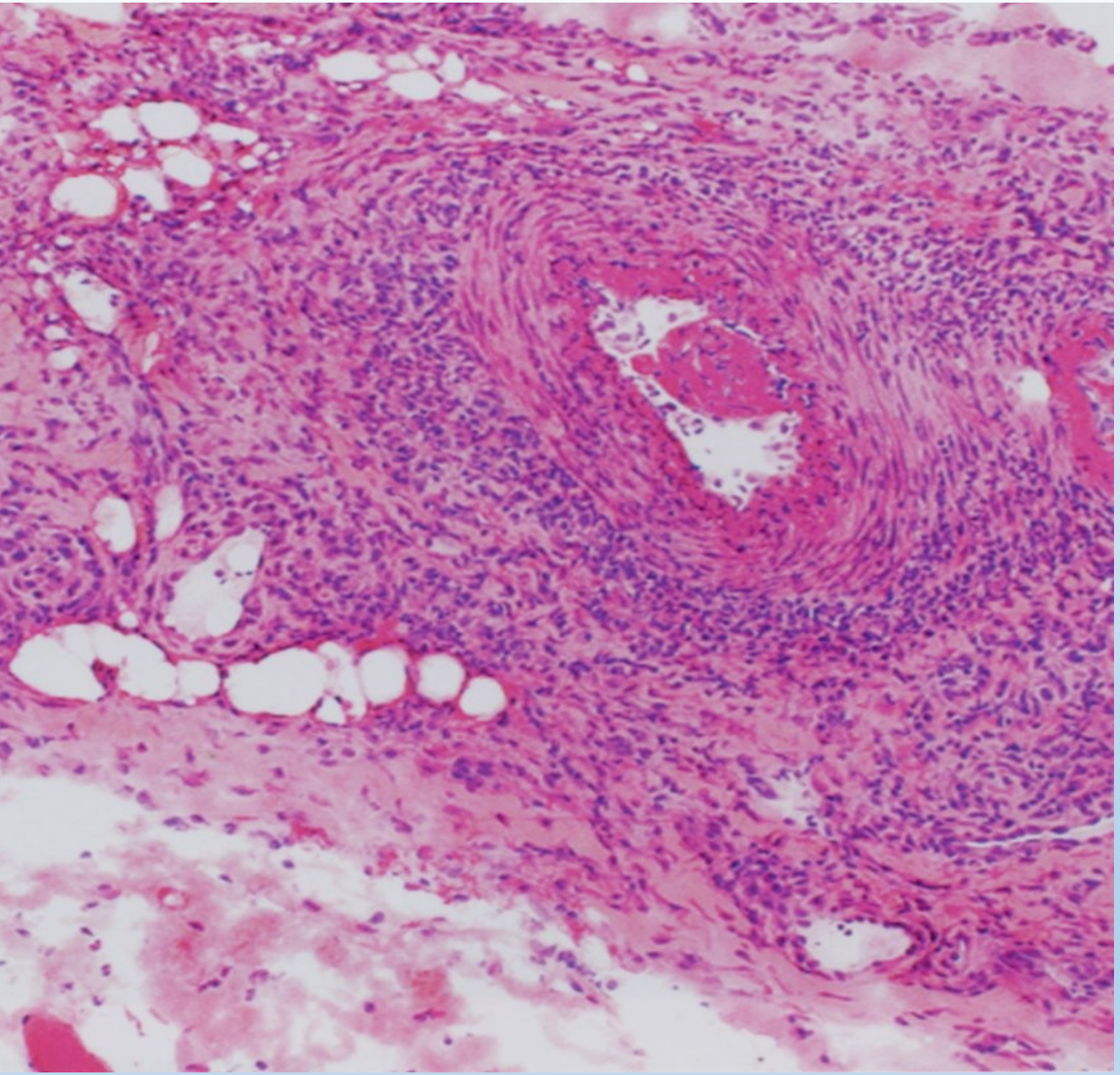
- transmural inflamatory infiltrate of neutrophils, eosinophils, and mononuclear cells
- fibrinoid necrosis and luminal thrombosis
- Lesions usually involve only part of the vessel circumference
- Older lesions show fibrous thickening of the vessel wall extending into the adventitia.
- Characteristically, all stages of activity (from early to late) coexist suggesting on going injury

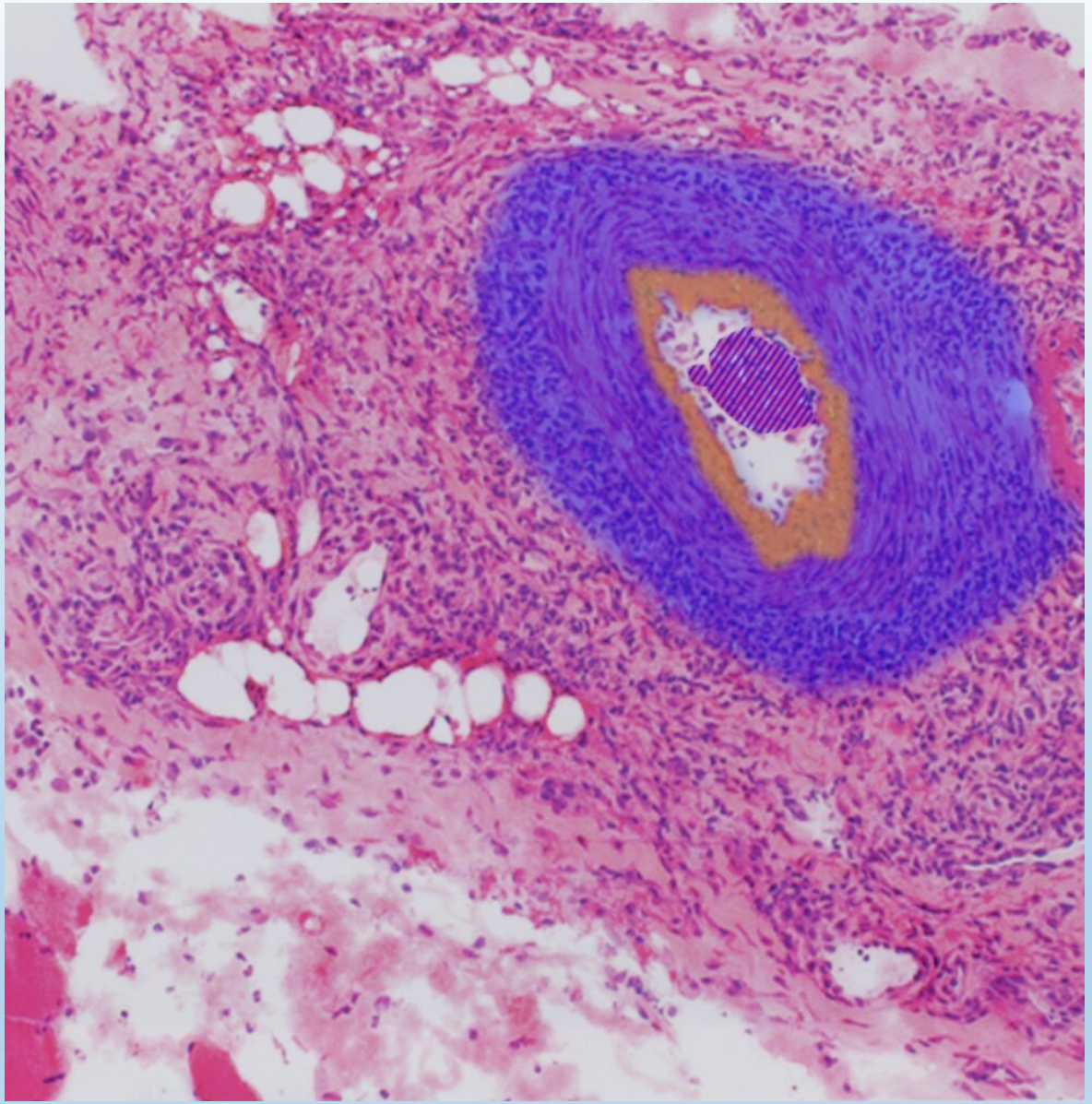


Case 1: Polyarteritis nodosa

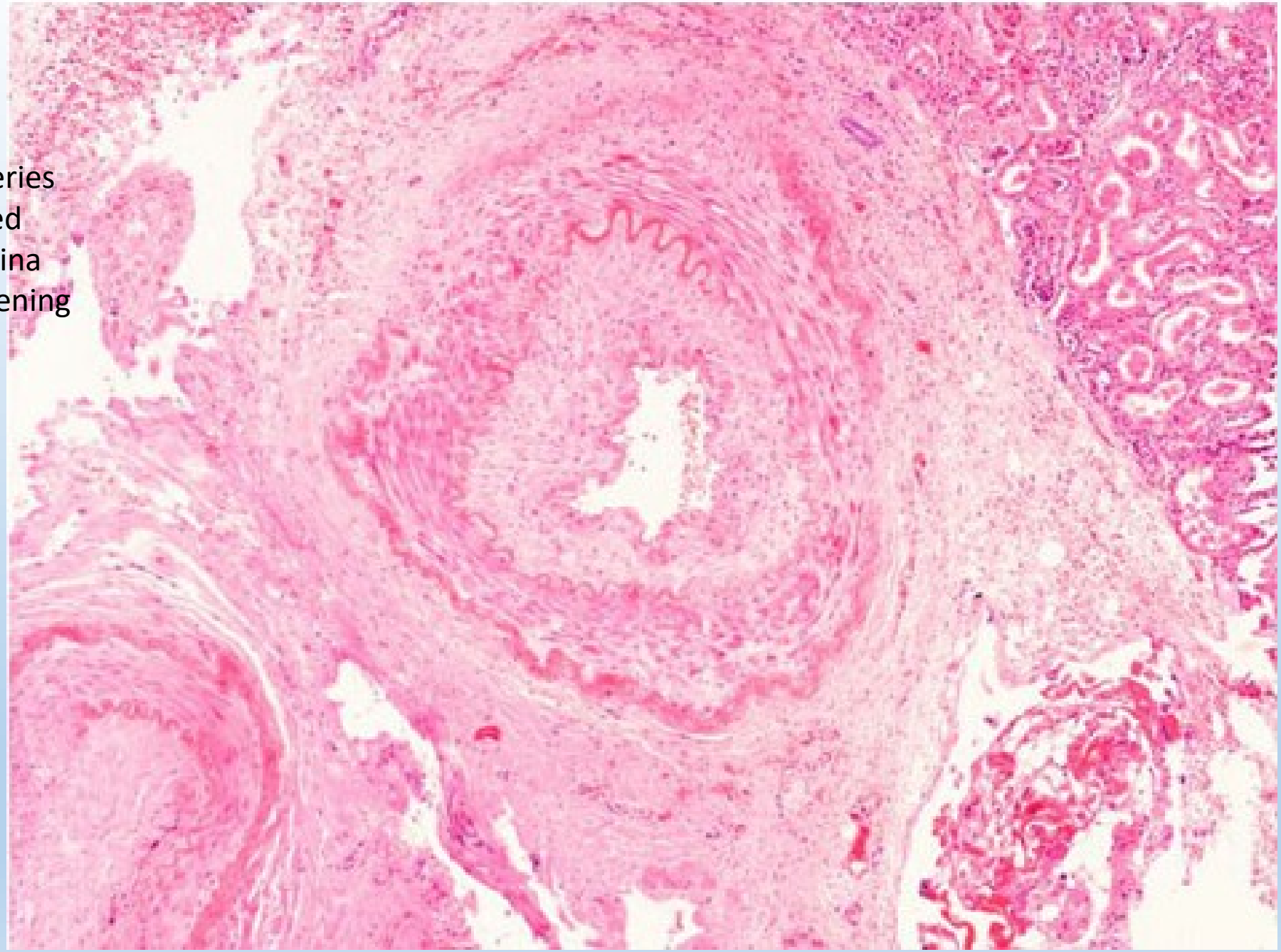
fibrinoid necrosis of the vessel wall

lymphocytes, plasma cells and macrophages





Very abnormal medium-sized arteries are present, consistent with healed vasculitis with internal elastic lamina rupture, fibrosis and intimal thickening but no active vasculitis



Clinical Features

- PAN is primarily a disease of young adults but can occur in all age groups, The course is frequently remitting and episodic, with long symptom-free intervals.

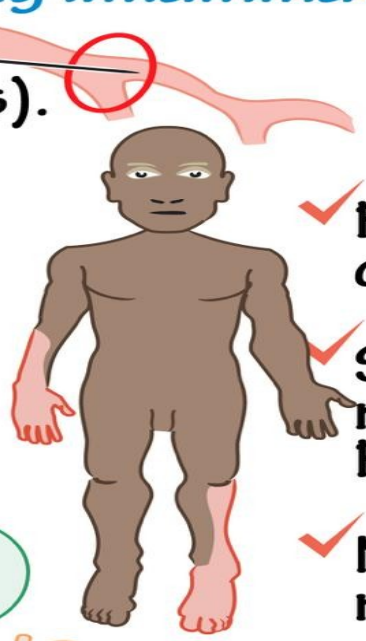
- rapidly accelerating hypertension due to renal artery involvement;
- abdominal pain and bloody stools caused by vascular gastrointestinal lesions;
- diffuse myalgias; and peripheral neuritis, predominantly affecting motor nerves.
- Renal involvement is often a major cause of mortality

- Treatment is corticosteroids and cyclophosphamide; fatal if not treated

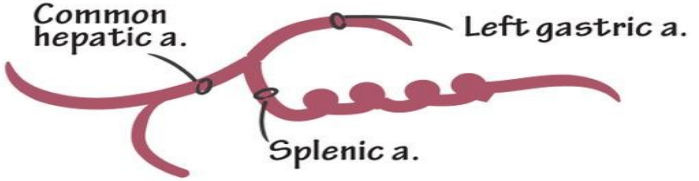
Polyarteritis nodosa

Necrotizing inflammation

- Medium muscular arteries, esp. at branch points (not veins).

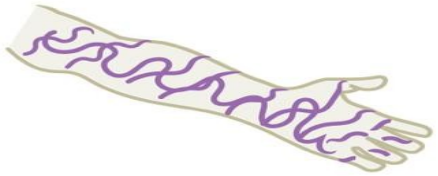


- Ischemia most often affects:
  - Nervous system
    Mononeuritis multiplex or asymmetric polyneuropathy.
    Median, ulnar, fibular nerves; Sensory and motor deficits.
  - Renal
    Hypertension, oliguria, may lead to renal failure.
  - GI
    Abd. pain, malabsorption; aneurysm poss. fatal.
  - Skin



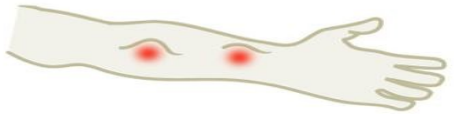
- PAN can be systemic or cutaneous.
- Some secondary forms are related to HBV, HBC, or Rheumatoid arthritis.
- Most commonly affects men > 50 y.o.

Livedo reticularis



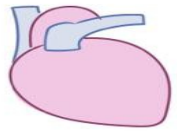
Ulcers

Subcutaneous nodules



Gangrene

- Heart
  Heart failure -> coronary artery obstruction.



- Kawasaki Disease
- is an acute, febrile, usually self-limited illness of infancy and childhood,80% of the patients are younger than 4 years of age

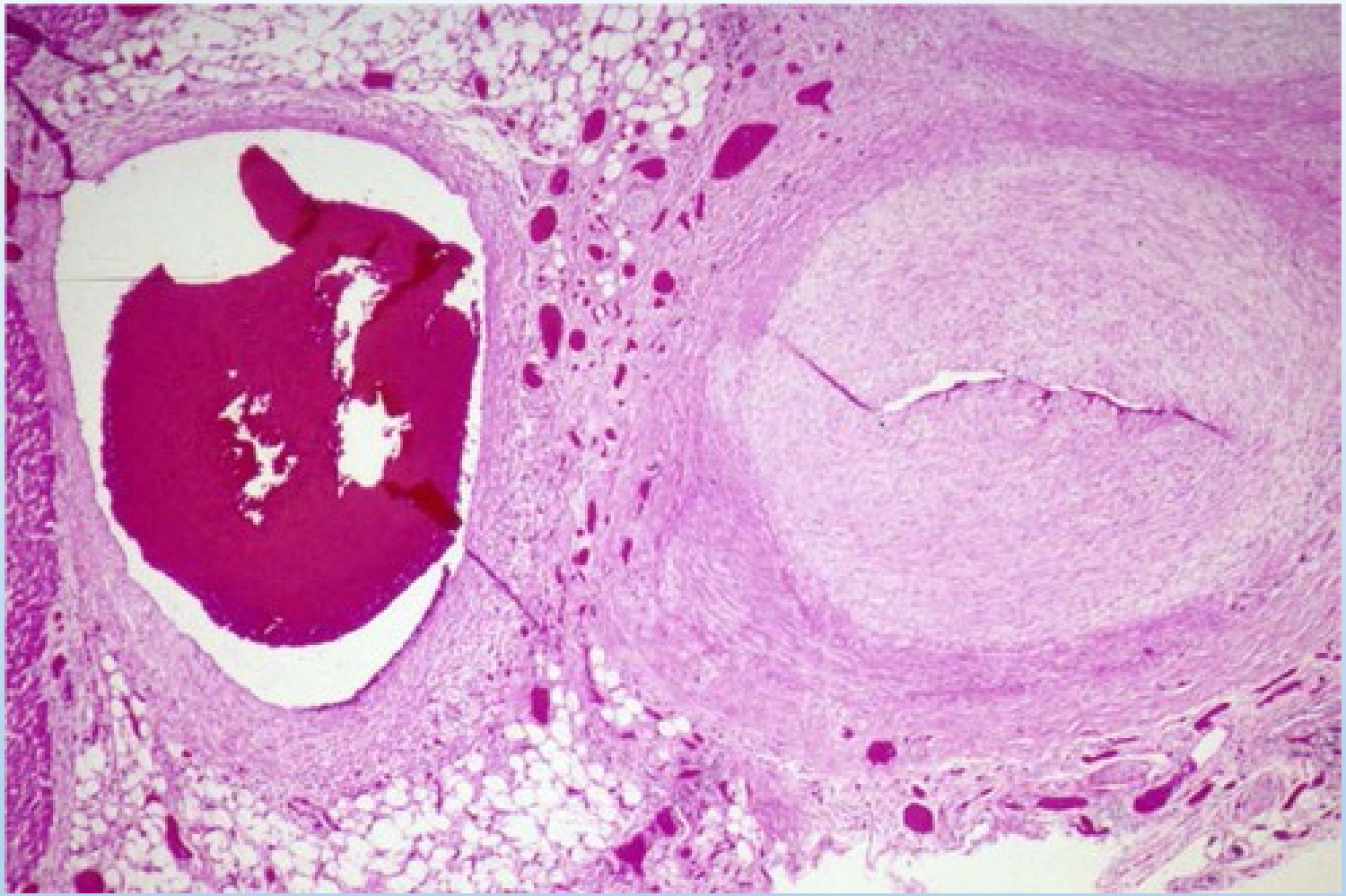
- The vasculitis may result from a delayed-type hypersensitivity response directed against cross-reactive or newly uncovered vascular antigens.
- Subsequent cytokine production and polyclonal B-cell activation result in autoantibodies to ECs and SMCs that precipitate the vasculitis.

- Its clinical significance stems from the involvement of coronary arteries and leads to risk for (1) thrombosiswith myocardial infarction and (2) aneurysm with rupture.

Morphology

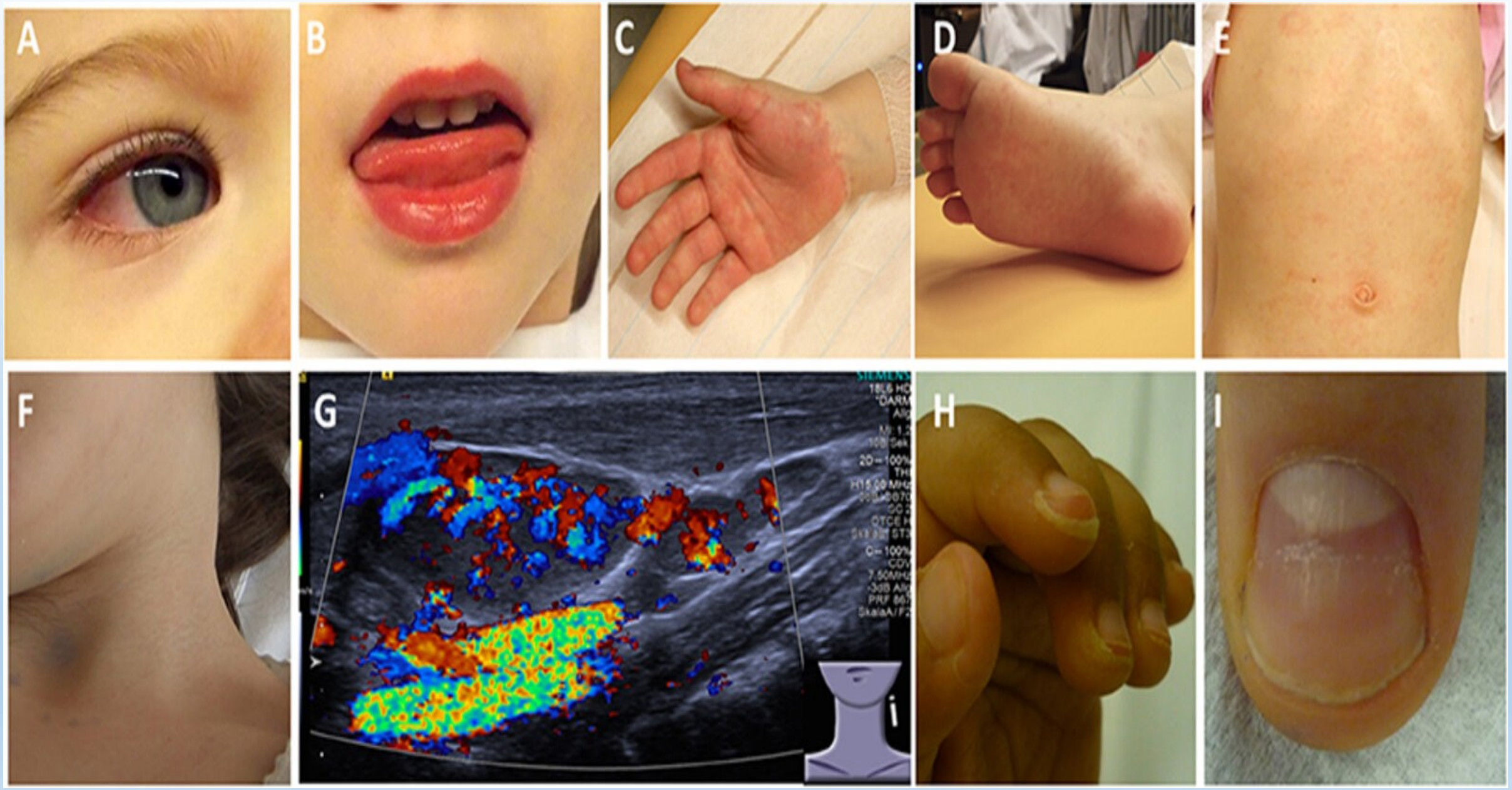
- a dense transmural inflammatory infiltrate
- vascultis resembles that seen in PAN although the fibrinoid necrosis is usually less prominent than in PAN
- healed lesions can also exhibit obstructive intimal thickening.

the coronary artery shows almost complete occlusion by luminal myofibroblastic proliferation with a fine slit-like lumen.



clinical features

- patients typically present with
- fever
- conjunctivitis
- mucus membrane erythema and blistering
- desquamative rash of palms and soles
- edema of palms and soles
- enlarged cervical lymph nodes
- 20% of untreated patients develop cardiovascular sequelae, ranging from asymptomatic coronary arteritis, to coronary artery ectasia, to giant coronary artery aneurysms
- Treatment is aspirin and IVIG(decrease the risk of symptomatic CAD to 4%)


A
B
C
D
E
F
G
H
I

• Thromboangiitis Obliterans (Buerger Disease)

- Thromboangiitis obliterans is characterized by segmental, thrombosing, acute and chronic inflammation of medium and small-sized arteries, especially the tibial and radial arteries, that often leads to vascular insufficiency, typically of the extremities

- Highly associated with heavy smoking

- **Pathogenesis**
- direct EC toxicity caused by some tobacco component or an immune response to the same agents that have modified host vascular wall proteins

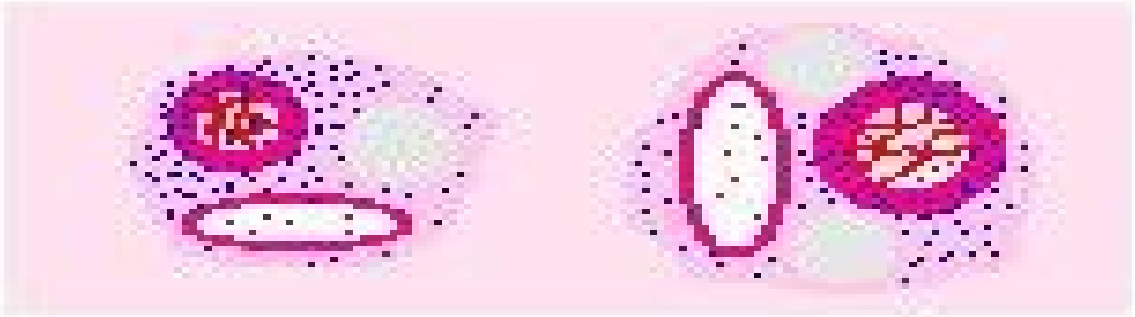
MORPHOLOGY

- vessels of thombangitis obliterans show acute and chronic inflammation, accompanied by luminal thrombosis
- The thrombus can contain small microabscesses composed of neutrophils surrounded by granulomatous inflammation and may eventually organize and recanalize
- **The inflammatory process extends into contiguous veins and nerves (rare with other forms of vasculitis), and with time all three structures can be encased in fibrous tissue.**

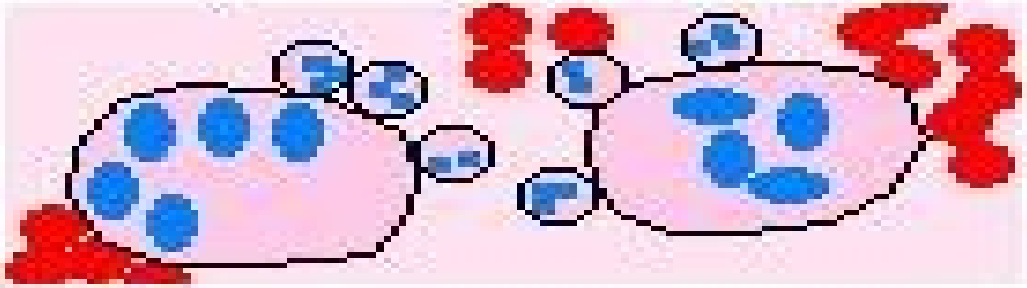
Buerger's Thromboangiitis Obliterans

Pathologists look for:

1. Inflamed / scarred neurovascular bundles



2. Neutrophils adjacent to epithelioid giant cells deep inside thrombi



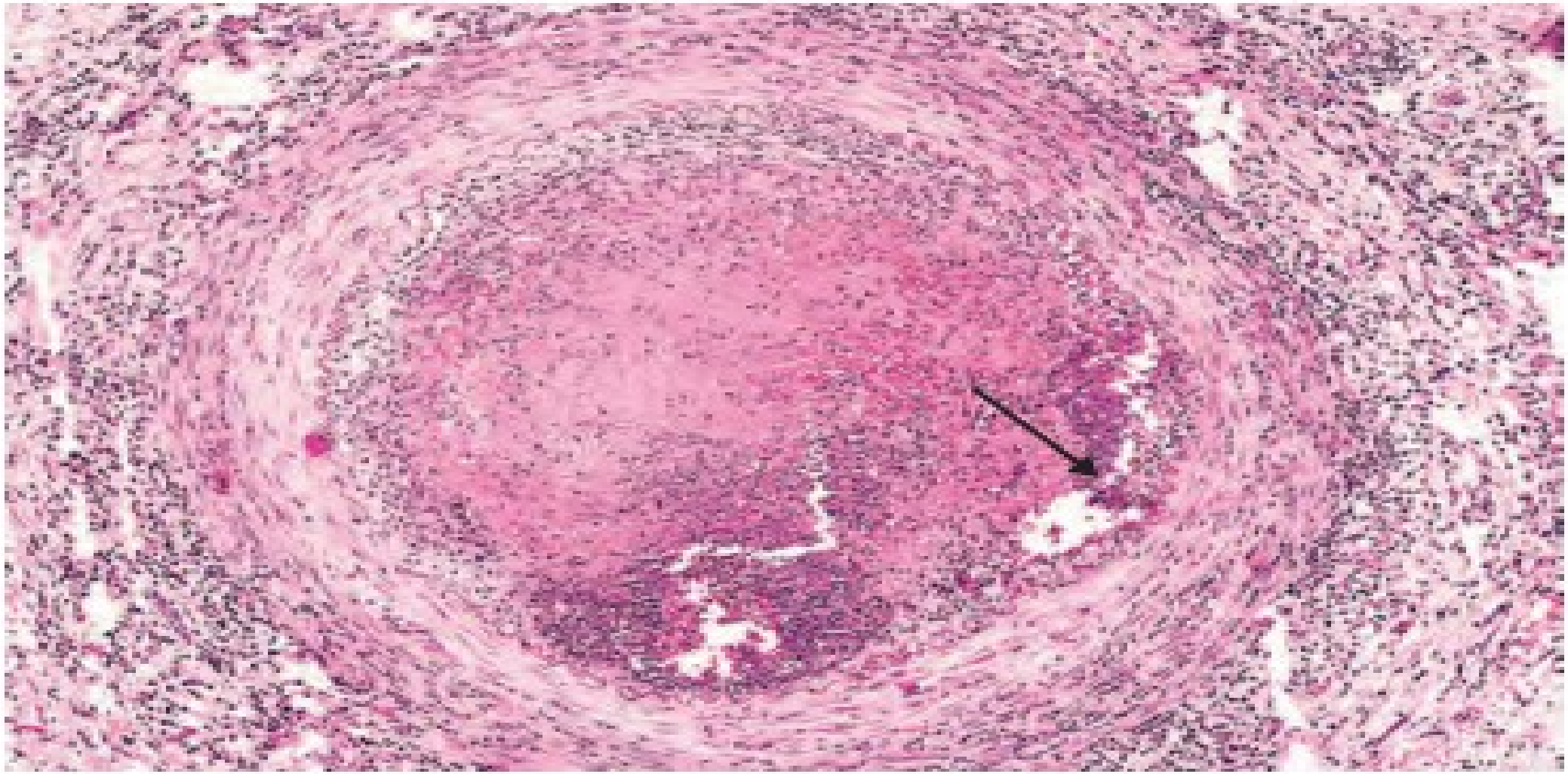
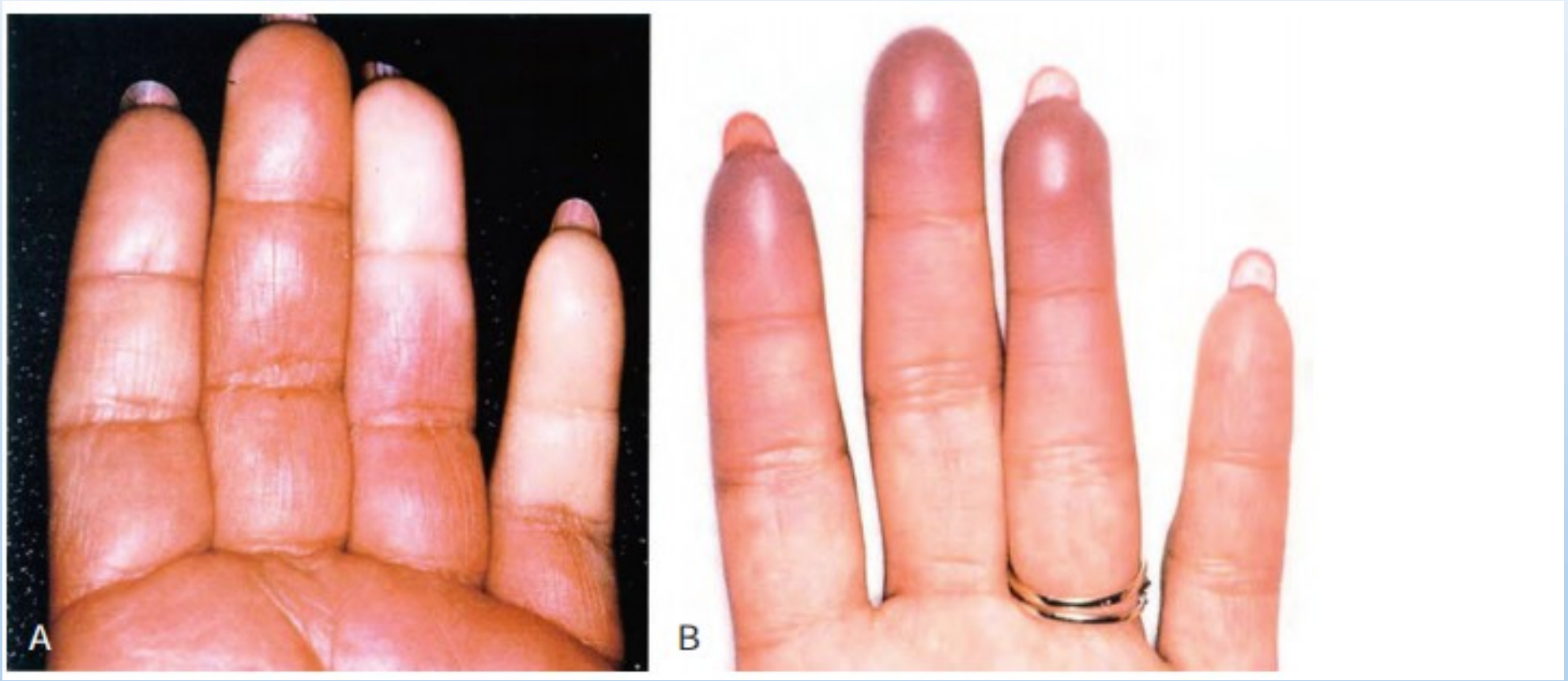


Figure 11.29 Thromboangiitis obliterans (Buerger disease). The lumen is occluded by a thrombus containing abscesses *(arrow)*, and the vessel wall is infiltrated with leukocytes.

clinical features

- Early manifestations include Raynaud phenomenon
- instep foot pain induced by exercise, and a superficial nodular phlebitis (venous inflamation)
- vascular insufficiency tends to be accompanied by severe pain—even at rest—undoubtedly due to the neural involvement
- extremity ulcerations can develop, progressing over time to frank gangrene and autoamputation of fingers and toe
- treatment is smoking cessation

Figure 1 Hands lesions – August 2013 : distal melanoma


A
B


Raynaud's Phenomenon
White due to lack of blood flow
Blue due to lack of oxygen
Red when blood flow returns

SMALL-VESSEL VASCULITIS

- Microscopic Polyangiitis

a necrotizing vasculitis that generally affects capillaries as well as small arterioles and venules

- The skin, mucous membranes, lungs, brain, heart, gastrointestinal tract, kidneys, and muscle all can be involved

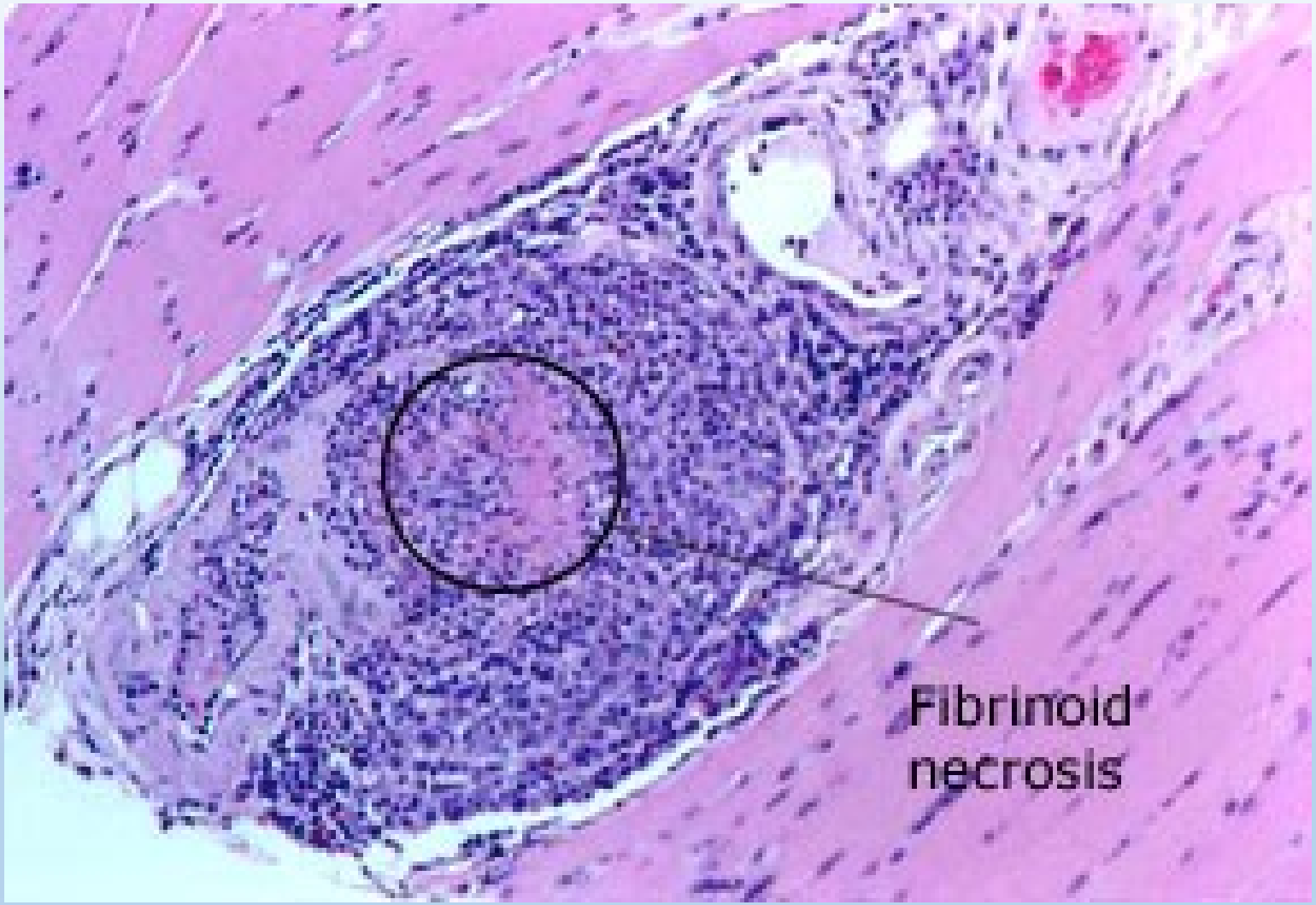
- necrotizing glomerulonephritis (90% of patients) and pulmonary capillaritis are particularly common

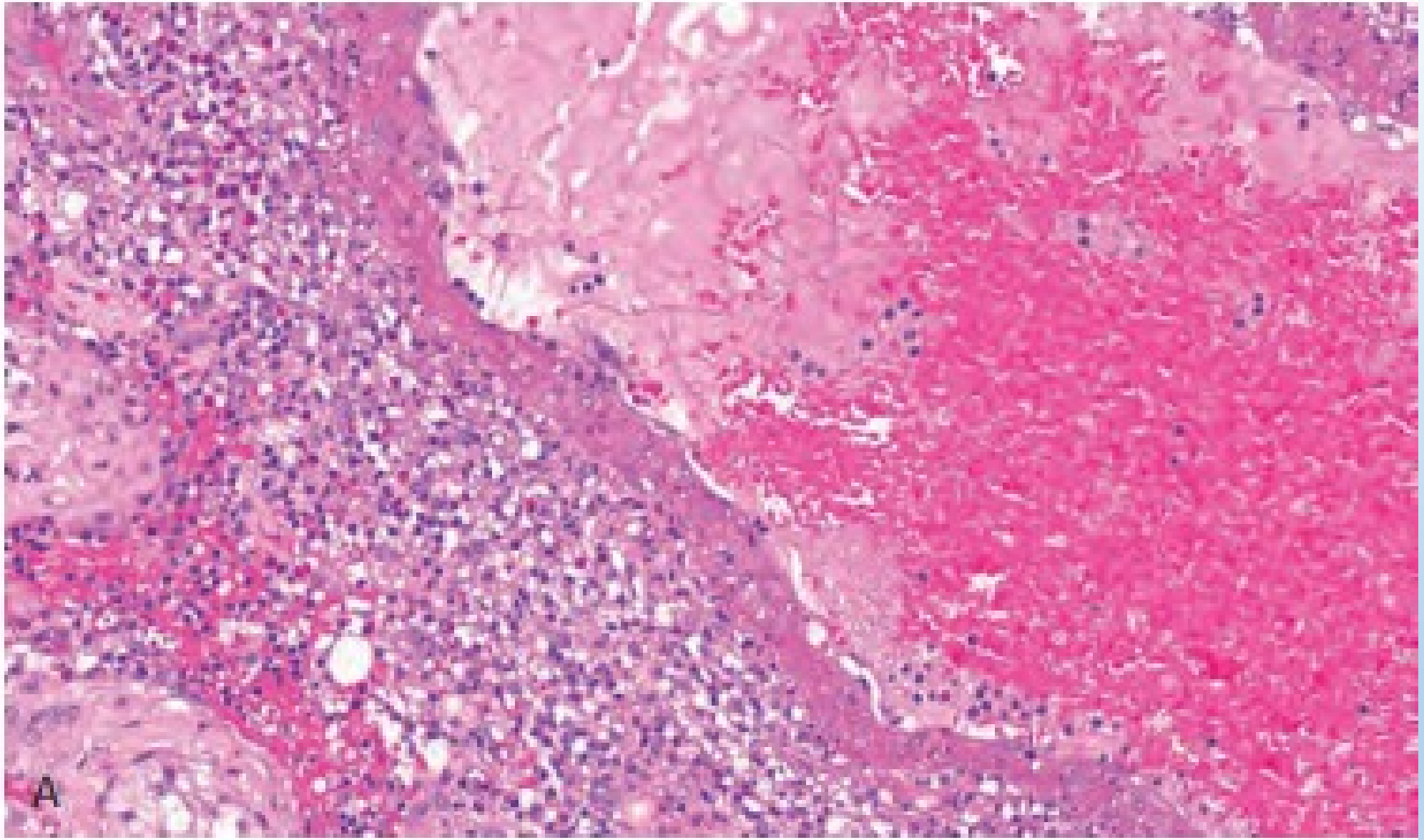
- can be a feature of a number of immune disorders

- **pathogenesis** :
- most cases are associated with MPO-ANCA.
- Recruitment and activation of neutrophils within affected vascular beds is likely responsible for the disease manifestations.

MORPHOLOGY

- segmental fibrinoid necrosis of the media with focal transmural necrotizing lesions
- granulomatous inflammation is absent
- morphologically resemble PAN but typically spare medium-sized and larger arteries>macroscopic infarcts are uncommon
- In some areas , only infiltrating and fragmenting neutrophils are seen, (leukocytoclastic vasculitis)
- little or no immunoglobulin can be seen in most lesions (pauci-immune injury)


Fibrinoid
necrosis


A

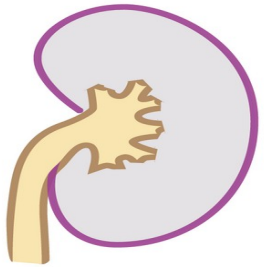
Clinical features

- major clinical features include
  - hemoptysis
  - hematuria and proteinuria,
  - bowel pain or bleeding,
  - muscle pain or weakness,
  - palpable cutaneous purpura
- Treatment is corticosteroids and cyclophosphamide;
- Serum p-ANCA levels correlate with disease activity.

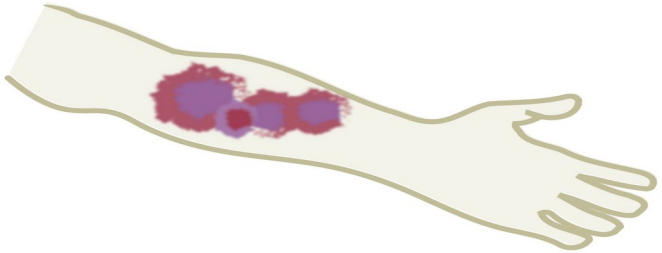
Microscopic Polyangiitis

ANCA- Associated; Necrotizing pauci-immune, and no granulomas

- ✓ Affects mostly small vessels, including venules and capillaries.
- ✓ Kidneys
  - Glomerulonephritis with rapid progression to renal failure.



- ✓ Skin
  - Purpuric rash



- ✓ Lungs are less commonly invovled
  - Alveolar hemrrohage, fibrosis possible.
- ✓ Tends to occur in adults 50-60 y.o.

- Granulomatosis With Polyangiitis (GPA)/ Wegener Granulomatosis

GPA is a necrotizing vasculitis characterized by a triad of:

- Acute necrotizing granulomas of the upper respiratory tract (ear, nose, sinuses, throat) or the lower respiratory tract (lung) or both

- Necrotizing or granulomatous vasculitis affecting small- to medium-sized vessels , most prominent in the lungs and upper airways but affecting other sites as well

- Focal necrotizing, often crescentic, glomerulonephritis

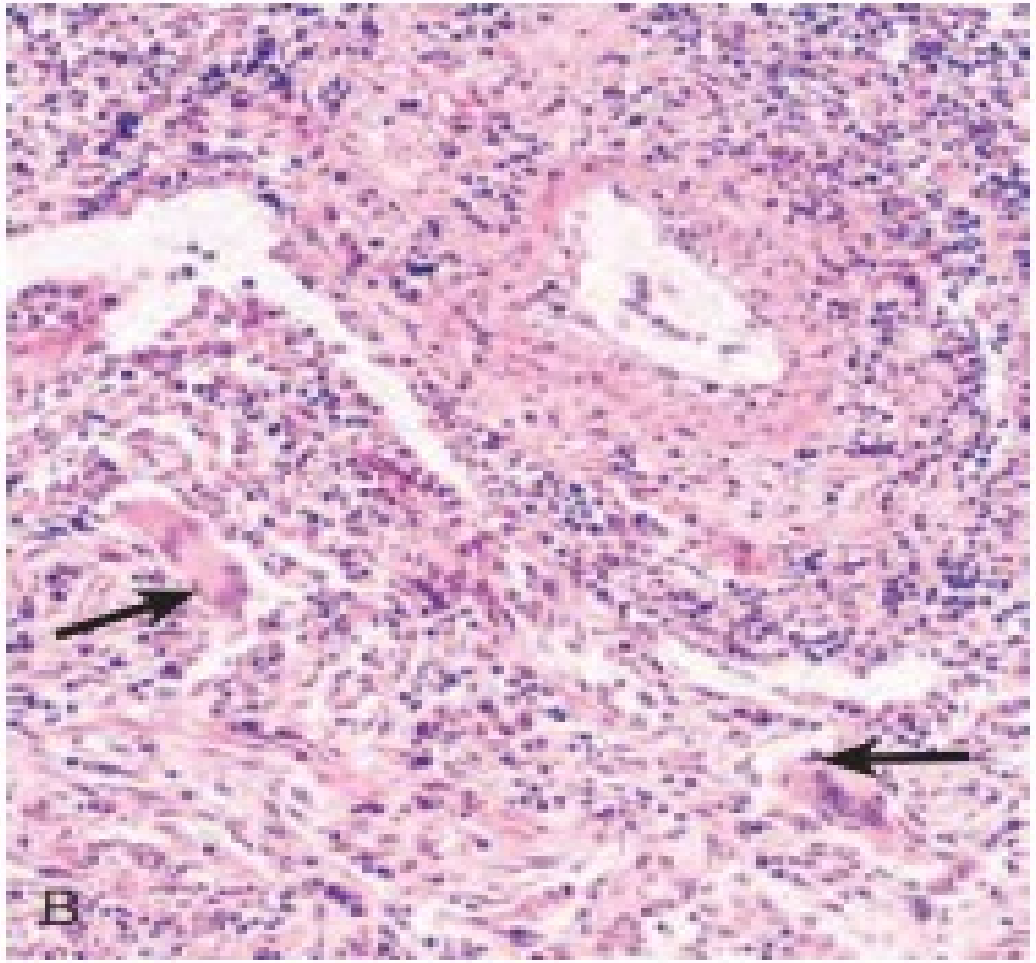
Pathogenesis

- GPA likely represents a form of T cell–mediated hypersensitivity response to normally “innocuous” inhaled microbial or other environmental agents

- PR3-ANCAs (c-ANCA) are also present in up to 95% of cases; they are a useful marker of disease activity and may participate in disease

MORPHOLOGY

- Upper respiratory tract lesions range from inflammatory sinusitis with mucosal granulomas to ulcerative lesions of the nose, palate, or pharynx.
- The necrotizing granulomas are surrounded by a zone of proliferating fibroblasts with giant cells and leukocyte infiltrate
- Multiple granulomata can coalesce to produce radiographically visible nodules
- late-stage disease may be marked by extensive necrotizing granulomatous involvement of the parenchyma , and alveolar hemorrhage
- Renal ivolvement ranges from focal and segmental necrotizing glomerulonephritis to crescentic glomerulonephritis(diffuse necrosis with parietal cell proliferation)



Vasculitis of a small artery with adjacent granulomatous inflammation including epithelioid cells and giant cells (arrows)

granulomatosis with polyangiitis demonstrating large, nodular, centrally cavitating lesions

Clinical Features

- Males are affected more often than females

Classic features include :

- bilateral pneumonitis with nodules and cavitary lesions (95%),
- chronic sinusitis (90%),
- mucosal ulcerations of the nasopharynx (75%),
- renal disease (80%)
- untreated, the disease is usually rapidly fatal with 80%

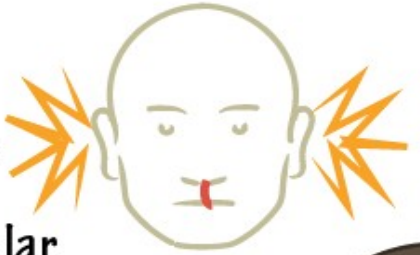
- mortality within 1 year
- **Treatment** is cyclophosphamide and steroids; relapses are common

Granulomatosis with Polyangiitis
(aka, Wegener's)

ANCA- Associated;
Necrotizing granulamatous inflammation

✓ Granulomas with giant cells, plasma cells, lymphocytes, neutrophils, and eosinophils form in Small vessels.

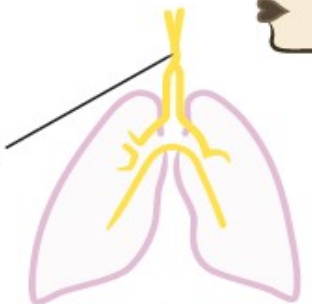
- Respiratory tract



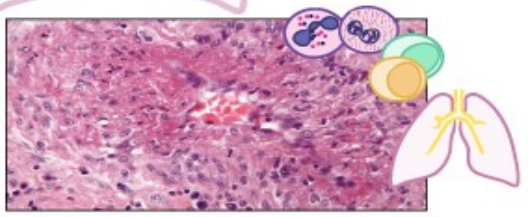
Sinusitis, otitis media, rhinorrhea, epistaxis

Mucosa becomes granular, with crusted ulcers.

Nasal bridge can collapse from tissue necrosis and septum erosion.



Tracheobroncial stenosis (airway obstruction)



Lung involvement: coughing, difficulty breathing, hemoptysis, poss. hemorrhage.

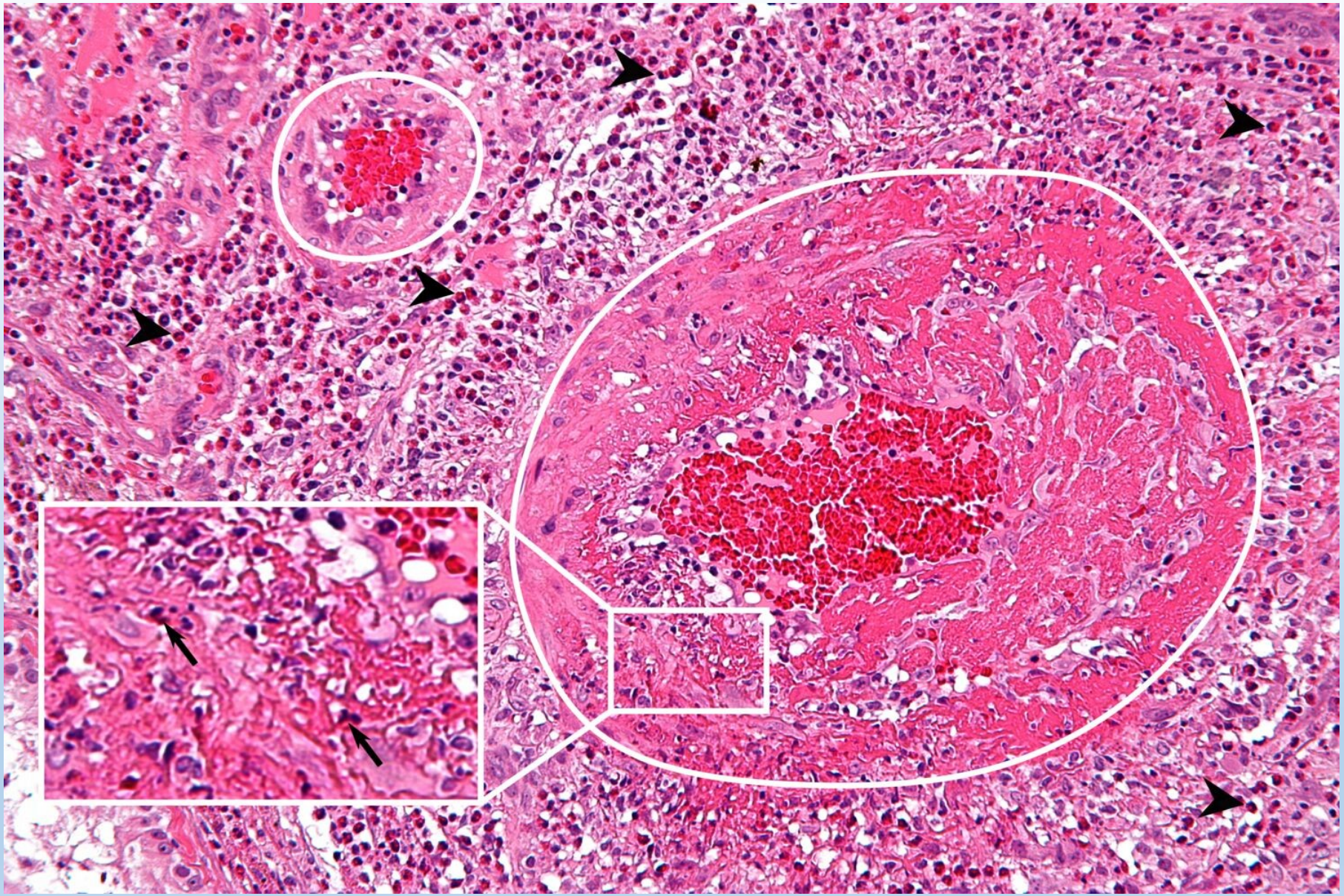
- Churg-Strauss Syndrome (also called allergic granulomatosis and angiitis)

- a small-vessel necrotizing vasculitis classically associated with asthma, allergic rhinitis, lung infiltrates, peripheral eosinophilia, extravascular necrotizing granulomas, and a striking eosinophilic infiltration of vessels and tissues.
- Pathogenesis :

is likely a consequence of hyperresponsiveness to some normally innocuous allergic stimulus.

MPO-ANCAs are present in a minority of cases.

❖ Serum p-ANCA levels correlate with disease activity



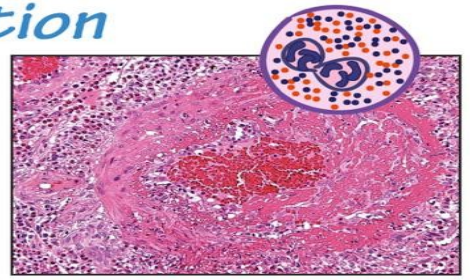
Clinical Features:

- Cutaneous involvement (with palpable purpura),
- gastrointestinal bleeding
- renal disease (primarily as focal and segmental glomerulosclerosis)
- myocardial eosinophilic infiltrates often leads to cardiomyopathy;
- cardiac involvement is seen in 60% of patients and is a major cause of morbidity and death.

Eosinophilic Granulomatosis with Polyangiitis

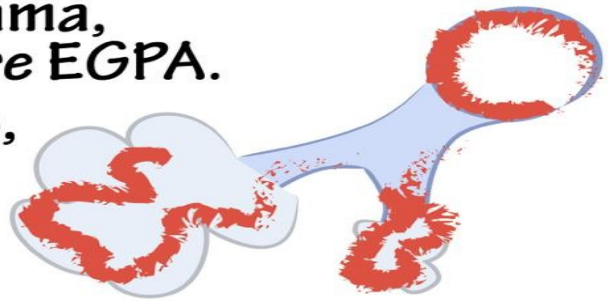
(aka, Churg-Strauss)

ANCA- Associated;
Necrotizing granulamatous inflammation



- Vascular and extravascular necrotizing granulomas
  - Eosinophil blood and tissue infiltrations.

- Allergic
  - Many patients develop asthma, possibly several years before EGPA.
    Also: Sinusitis, hemoptysis, pulmonary infiltrates.

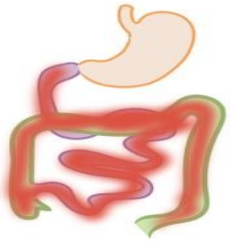


  - Eosinophilic 
  - Vasculitic

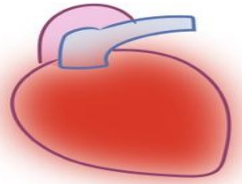
    Neurologic — Multiple mononeuropathy is most common.

    Skin — Extensor surfaces w/nodules or papules.

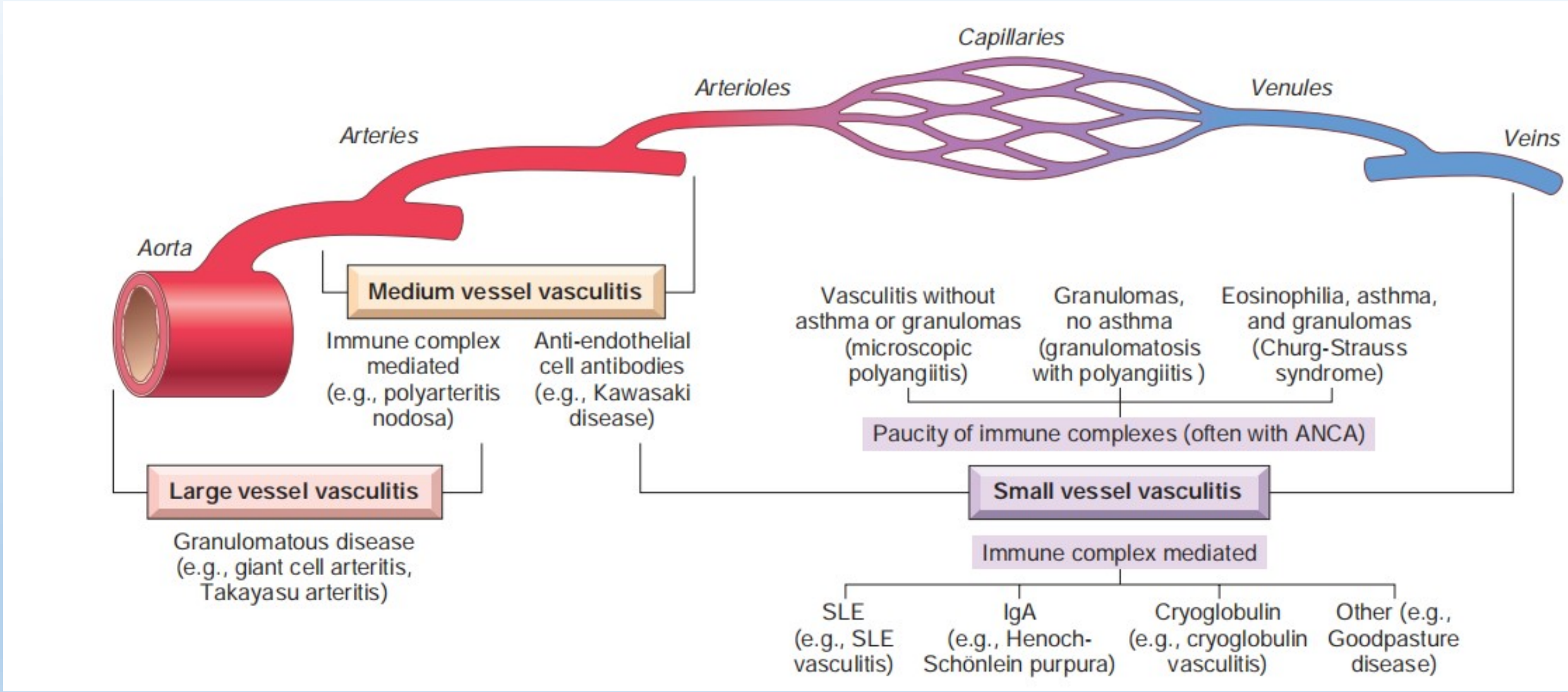
    GI — Pain, diarrhea, bleeding.



    Heart — Inflammation & cardiomyopathy



- Most commonly affects people in their late 40s.


Capillaries
Arterioles
Venules
Arteries
Veins
Aorta
Medium vessel vasculitis
Immune complex mediated (e.g., polyarteritis nodosa)
Anti-endothelial cell antibodies (e.g., Kawasaki disease)
Large vessel vasculitis
Granulomatous disease (e.g., giant cell arteritis, Takayasu arteritis)
Vasculitis without asthma or granulomas (microscopic polyangiitis)
Granulomas, no asthma (granulomatosis with polyangiitis)
Eosinophilia, asthma, and granulomas (Churg-Strauss syndrome)
Paucity of immune complexes (often with ANCA)
Small vessel vasculitis
Immune complex mediated
SLE (e.g., SLE vasculitis)
IgA (e.g., Henoch-Schönlein purpura)
Cryoglobulin (e.g., cryoglobulin vasculitis)
Other (e.g., Goodpasture disease)

Infectious Vasculitis

- direct invasion of infectious agents, usually bacteria or fungi, and in particular Aspergillus and Mucor species.
- either part of a localized tissue infectionn (e.g., bacterial pneumonia) or, less commonly, can arise from hematogenous spread of microorganisms during septicemia or embolization from infective endocarditis.

- Vascular infections can weaken arterial walls and cul_x0002_minate in mycotic aneurysms or can induce thrombosis and downstream infarction

- RHEUMATIC FEVER & RHEUMATIC HEART DISEASE
- INFECTIVE ENDOCARDITIS

RHEUMATIC FEVER (RF)

- An acute, immunologically mediated multisystem inflammatory disease, occurs a few weeks after an episode of group A β-hemolytic streptococcal pharyngitis, or rarely streptococcal infection of the skin.

RHEUMATIC FEVER (RF)

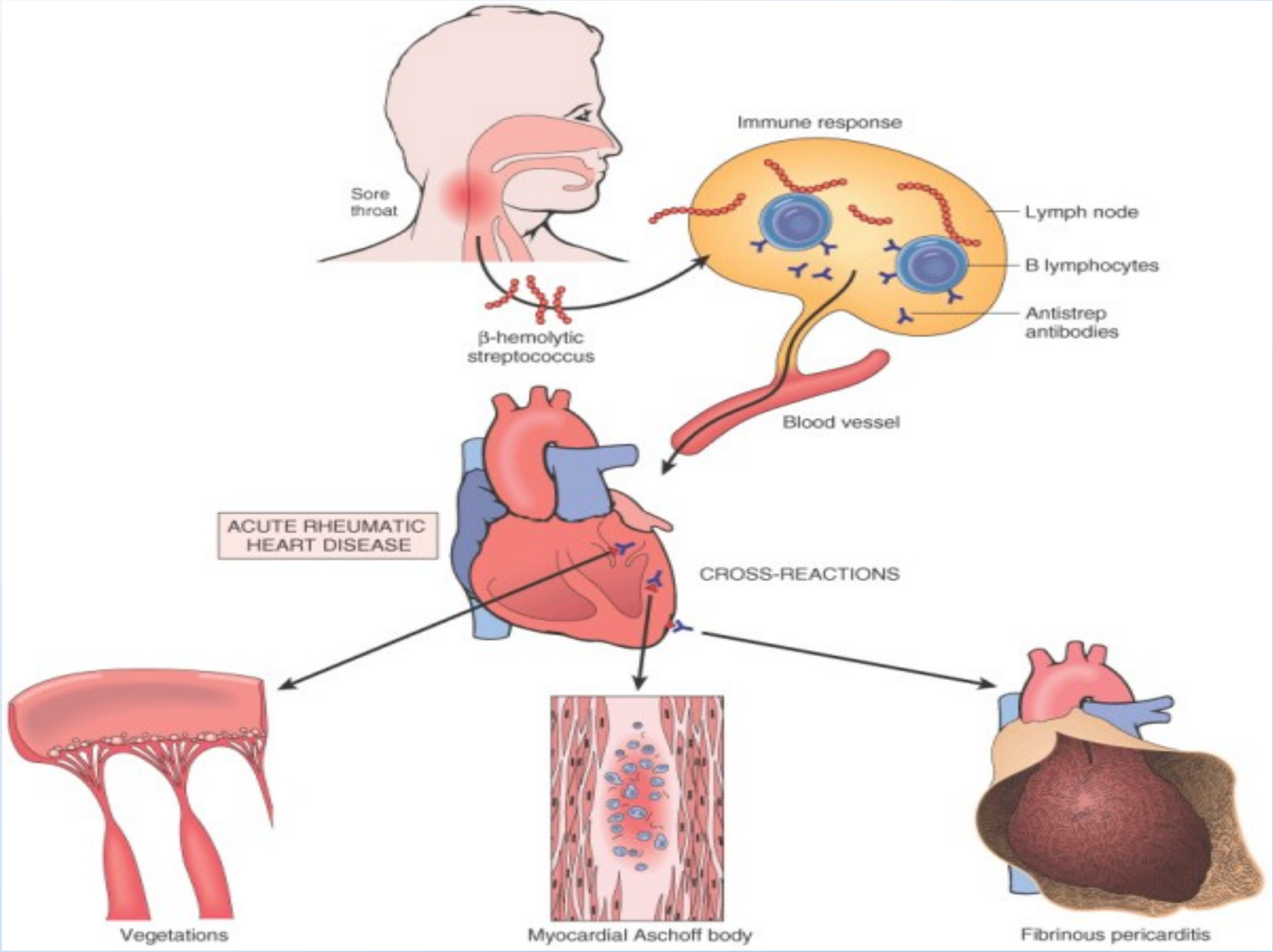
- **pathogenesis**
- Acute RF results from an immune response (type II hypersensitivity reaction) to group A β hemolytic streptococci, (3% of population).
- Antibodies directed against the M proteins of streptococci cross-react with glycoprotein antigens in the heart, joints and other tissues.
- The characteristic 2- to 3-week delay in symptomonset after infection is explained by the time needed to generate an immune response; In particular, antibodies and CD4+ T cells directed against streptococcal M proteins can also in some cases recognize cardiac self antigens

Predisposing factors:

Family history of rheumatic fever

Low socioeconomic status (poverty, poor hygiene, medical deprivation)

Age: 6-15 years


Immune response
Sore throat
Lymph node
B lymphocytes
Antistrep antibodies
β-hemolytic streptococcus
Blood vessel
ACUTE RHEUMATIC HEART DISEASE
CROSS-REACTIONS
Vegetations
Myocardial Aschoff body
Fibrinous pericarditis

Cardiac manifestations

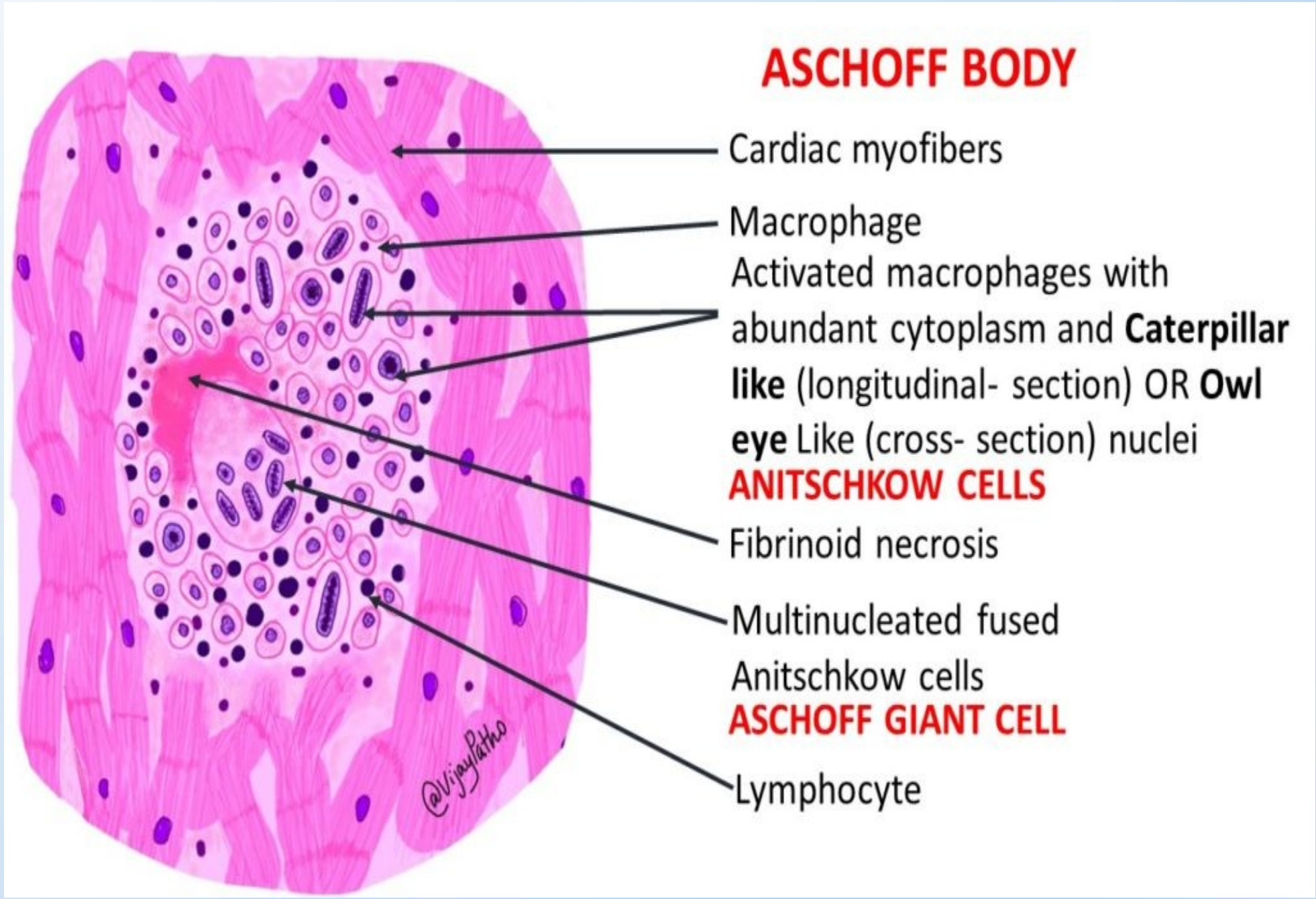
- Acute rheumatic carditis is a manifestation of acute RF.
- May progress to chronic RHD.

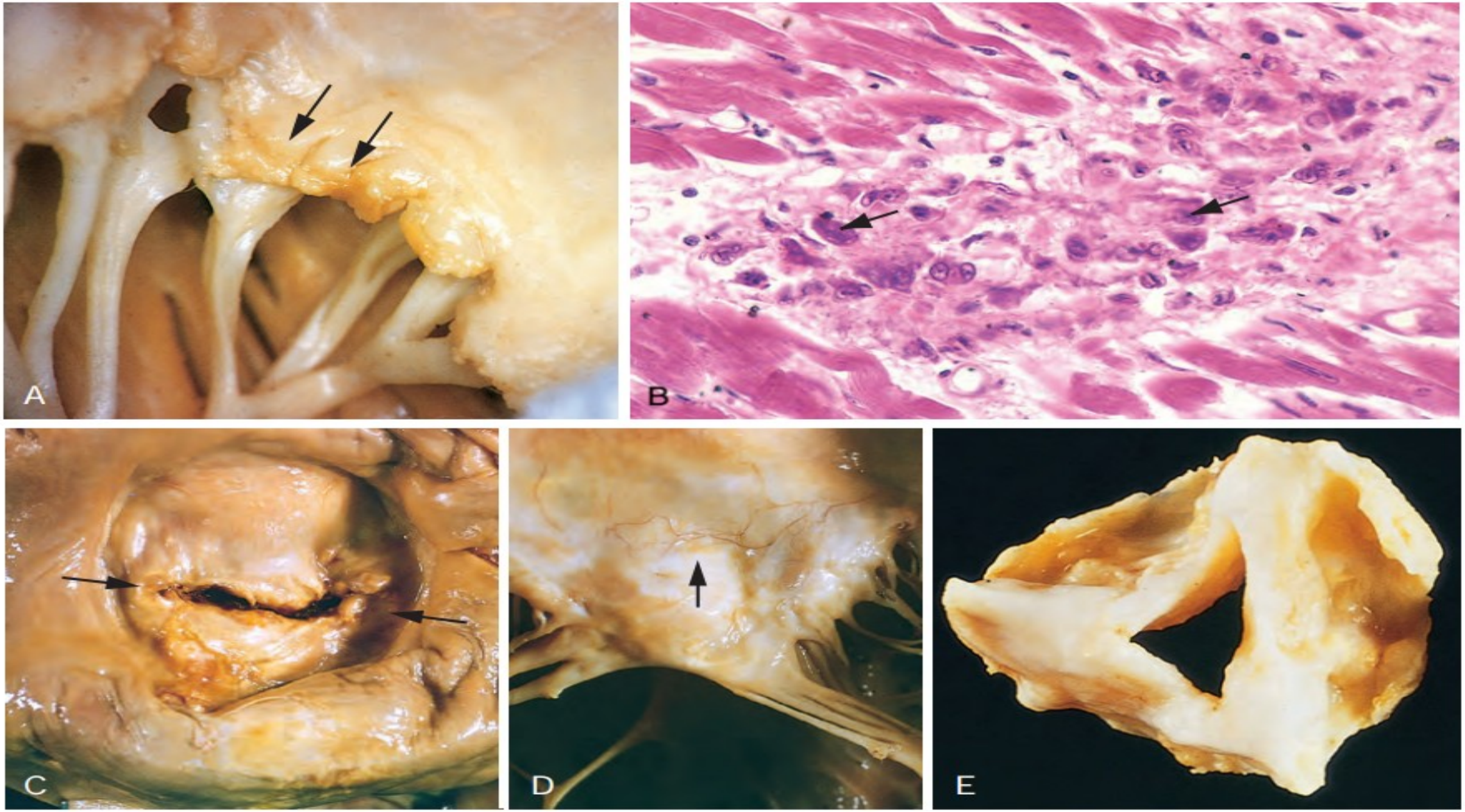
- RHD is characterized by **deforming fibrotic valvular disease**, particularly mitral stenosis.

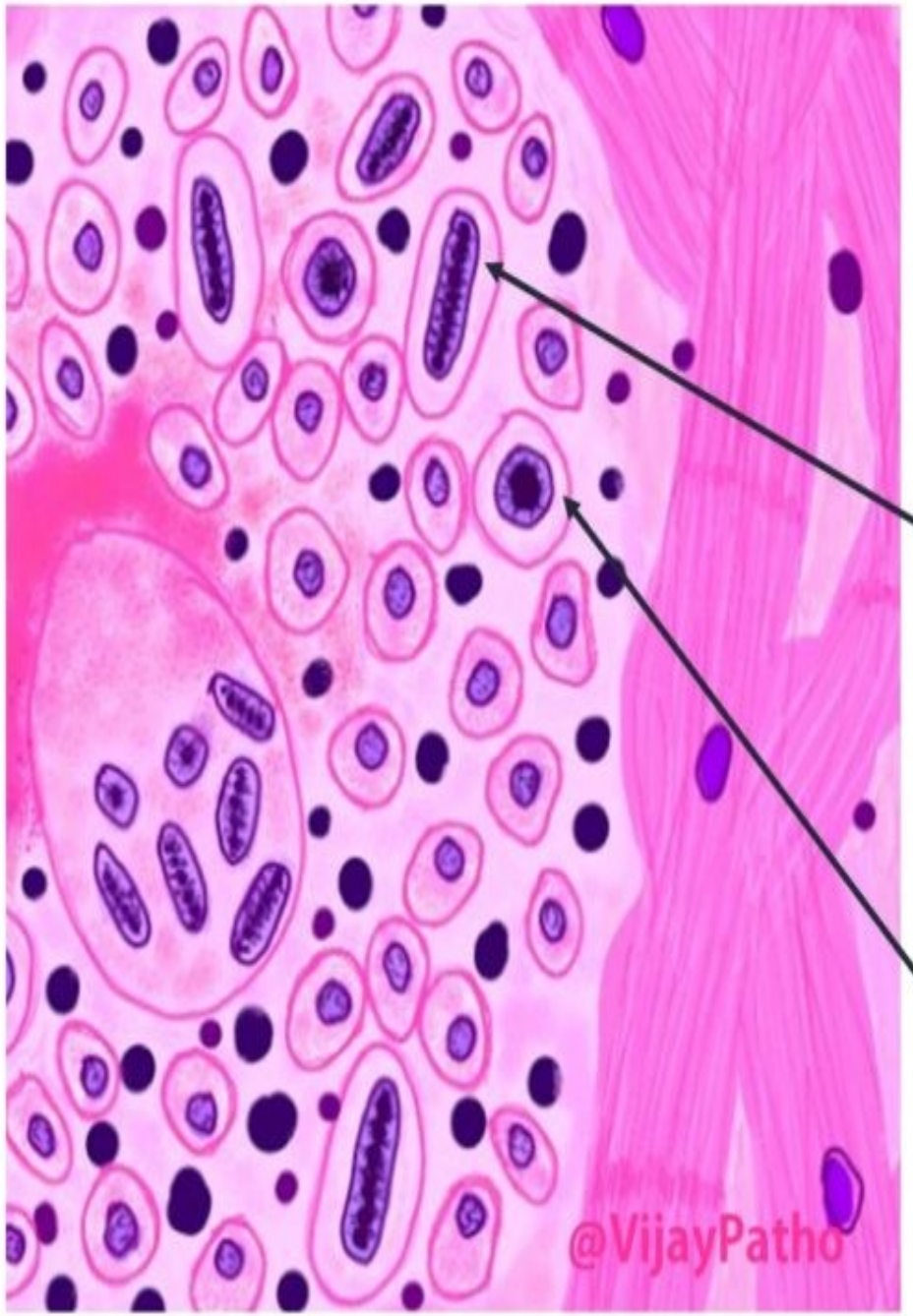
Morphology of acute RF

Aschoff bodies:

- Aschoffbodies—are composed of foci of T lymphocytes, occasional plasmacells, and plump activated macrophages called Anitschkow cells.
- These macrophages have abundant cytoplasm and central roundto-ovoid nuclei (occasionally binucleate) in which the chromatincondenses into a central, slender, wavy ribbon (hence the designation “caterpillar cells”).


ASCHOFF BODY
Cardiac myofibers
Macrophage
Activated macrophages with abundant cytoplasm and **Caterpillar like** (longitudinal- section) OR **Owl eye** Like (cross- section) nuclei
ANITSCHKOW CELLS
Fibrinoid necrosis
Multinucleated fused Anitschkow cells
ASCHOFF GIANT CELL
Lymphocyte
@VijayPatho


A
B
C
D
E



ANITSCHKOW CELLS

Activated macrophages with abundant cytoplasm with,

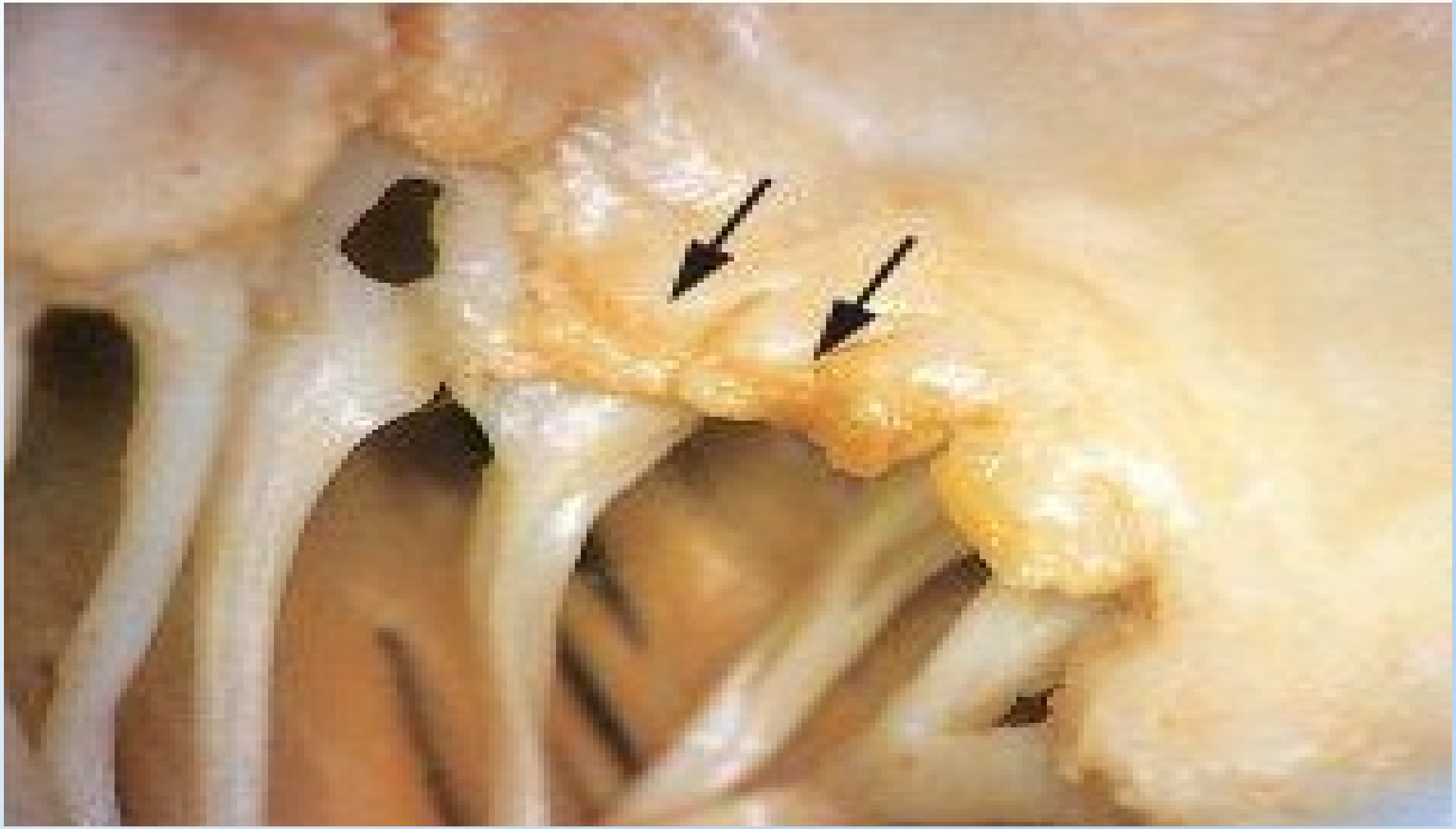
CATERPILLAR like nuclei (longitudinal-section)

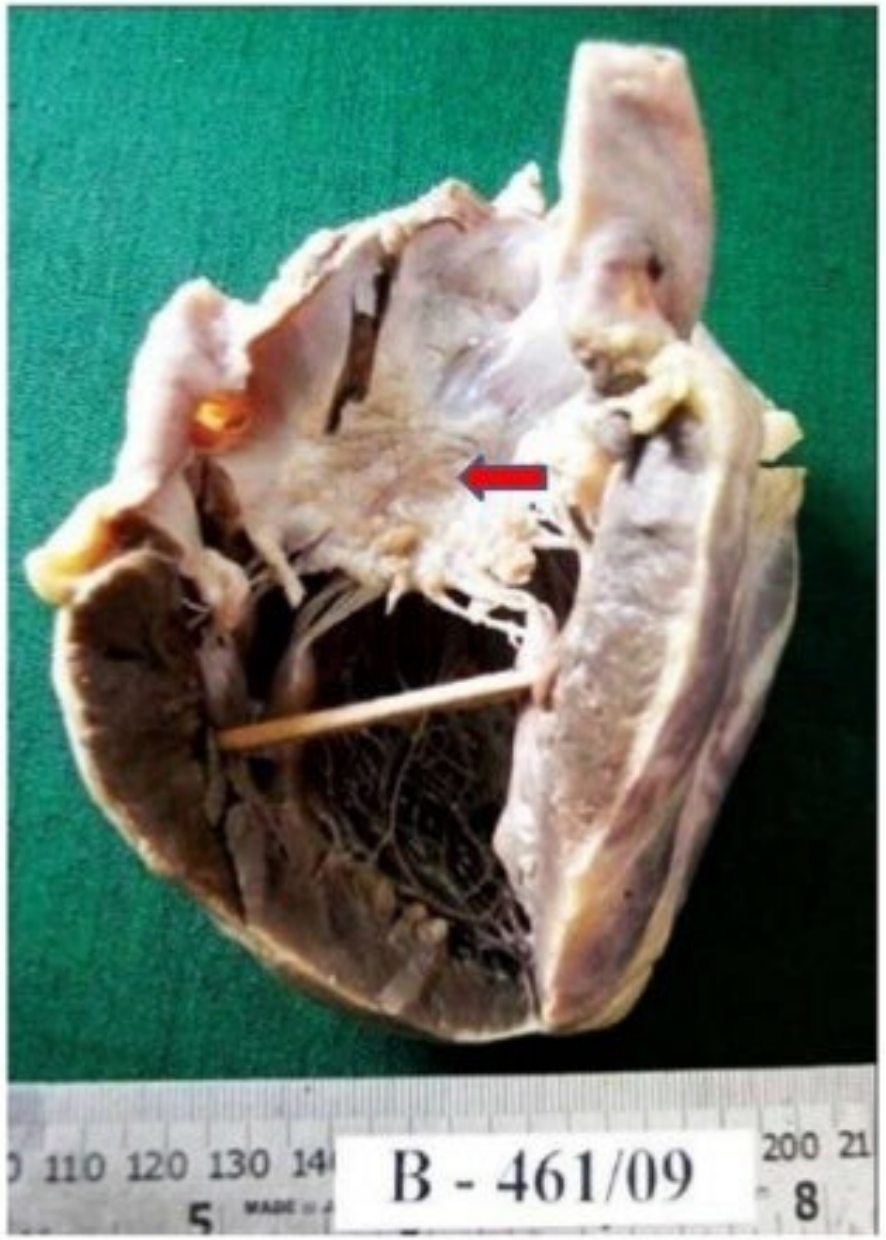
OWL-EYE Like nuclei (cross- section)

- **Morphology of acute RF**
- During acute RF, diffuse inflammation and Aschoff bodies may be found in any of the three layers of the heart, resulting in pericarditis, myocarditis, or endocarditis (pancarditis).
- Inflammation of the endocardium and the left-sided valves typically results in fibrinoid necrosis within the cusps or tendinous cords
- Overlying these necrotic foci and along the lines of closure are small (1 to 2 mm) vegetations, called verrucae

MacCallum plaques:

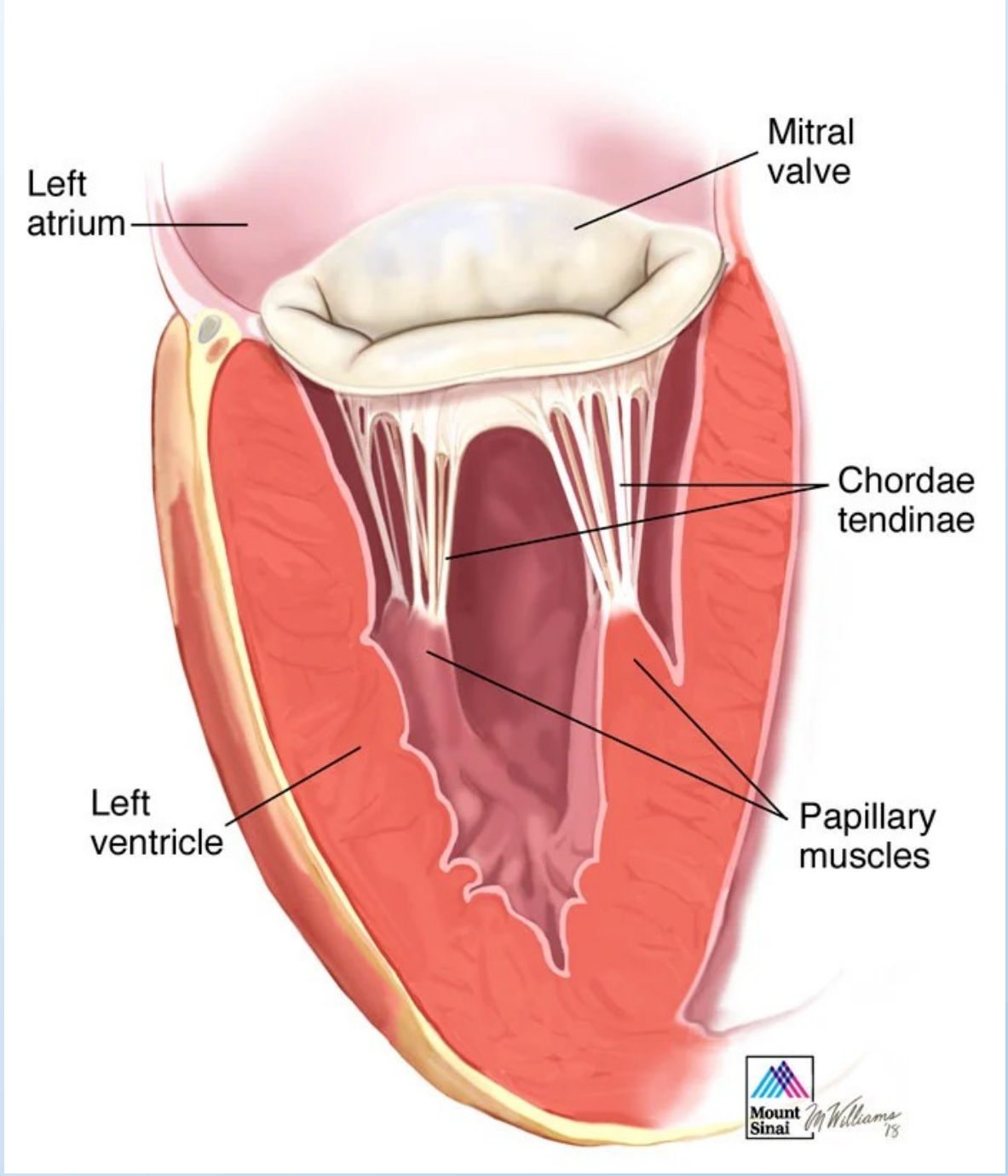
Subendocardial lesions, exacerbated by regurgitant jets, may induce irregular thickenings**, usually in the left atrium.**





Macculum plaques

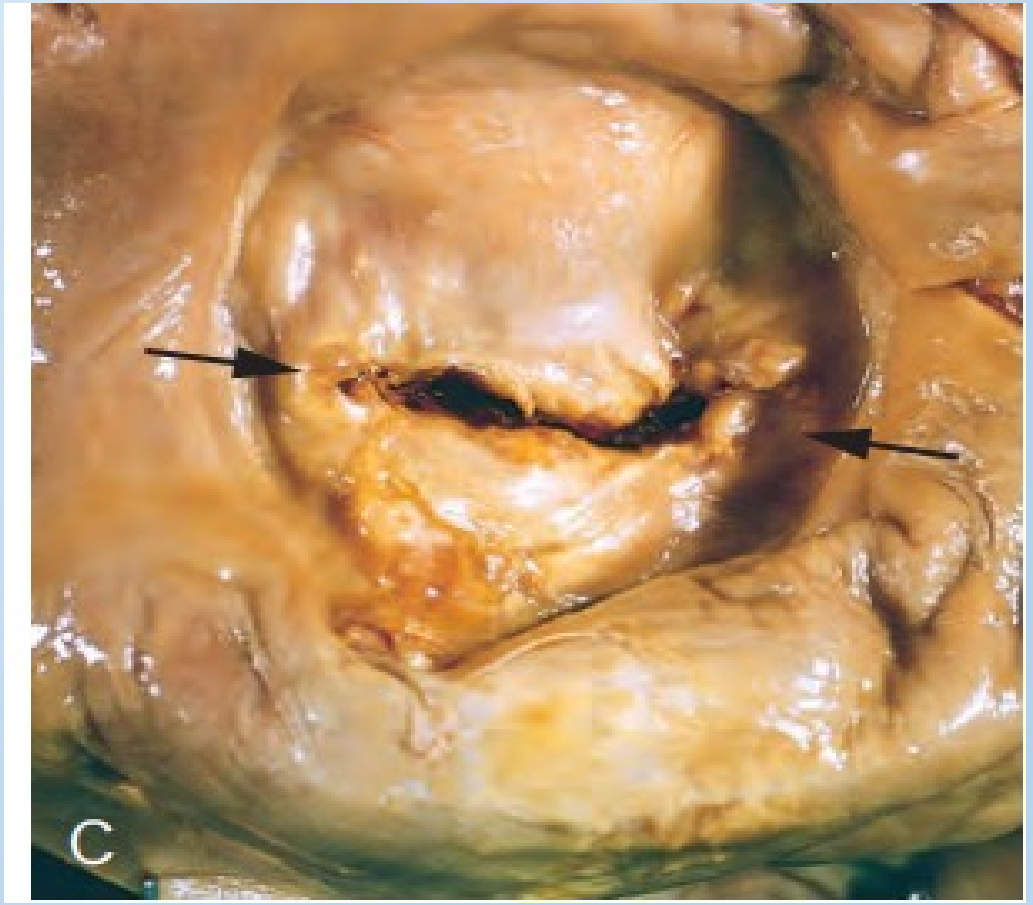
- **irregular thickenings** of endocardium in **left atrium** caused by **regurgitant blood flow**


Mitral valve
Left atrium
Chordae tendinae
Left ventricle
Papillary muscles
Mount Sinai

Morphology of chronic RHD

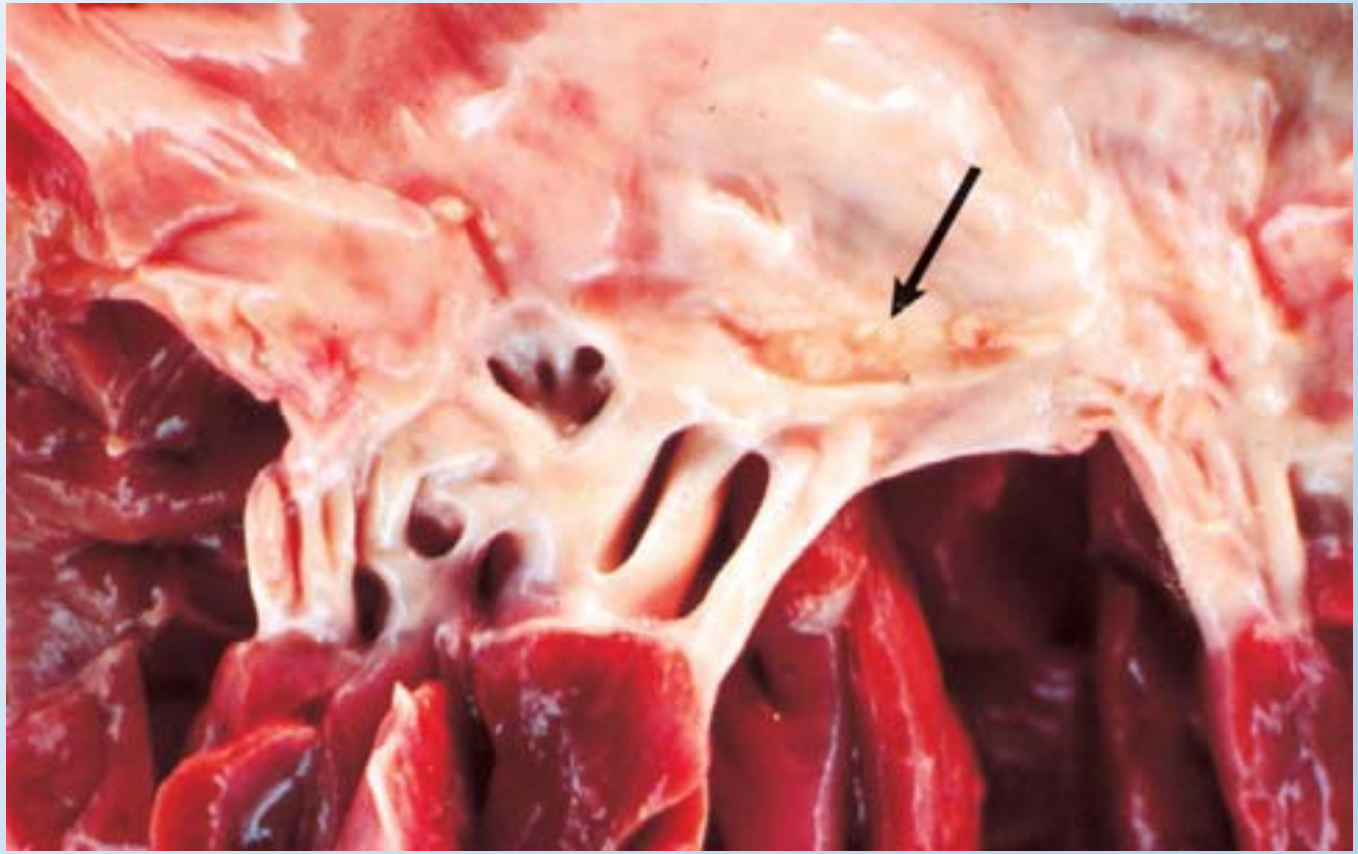
Valve stenosis and/or regurgitation

- . The mitral valve is virtually always involved in chronic RHD; it is affected in isolation in roughly two-thirds of cases, and along with the aortic valve in another 25%
- The cardinal anatomic changes of the mitral valve in chronic RHD are leaflet thickening, commissural fusion and shortening, and thickening and fusion of the tendinous cords



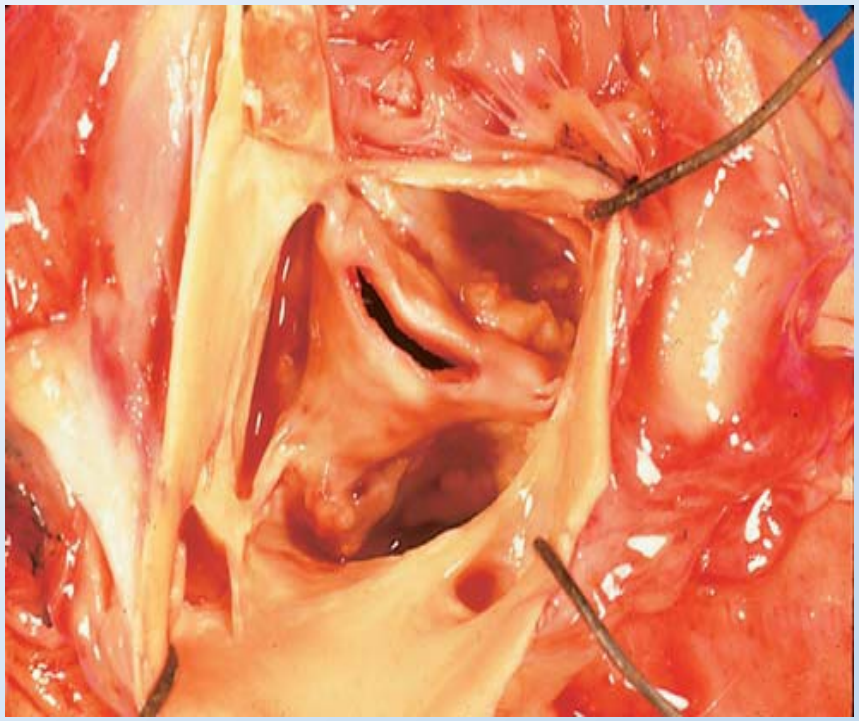
- In rheumatic mitral stenosis, calcification and fibrous bridging across the valvular commissures create “fish mouth” stenoses

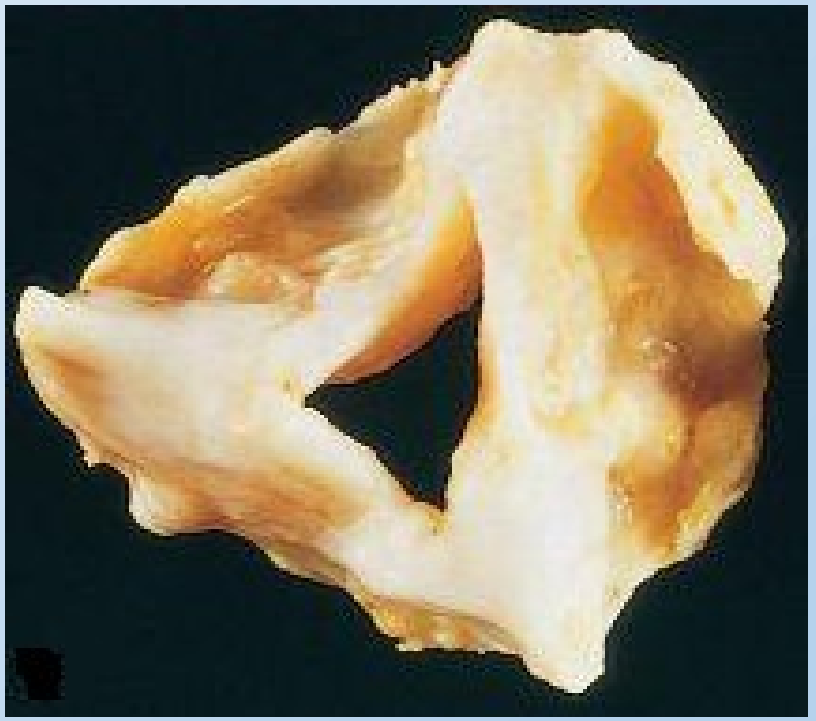
Chronic rheumatic valvulitis



The mitral valve leaflets are thickened and focally calcified (arrow), and the commissures are partially fused.
The chordae tendineae are also short, thick and fused.

Severe rheumatic aortic stenosis





the cusps are rigidly fibrotic and calcified, and extensive fusion of the commissures has narrowed the orifice.

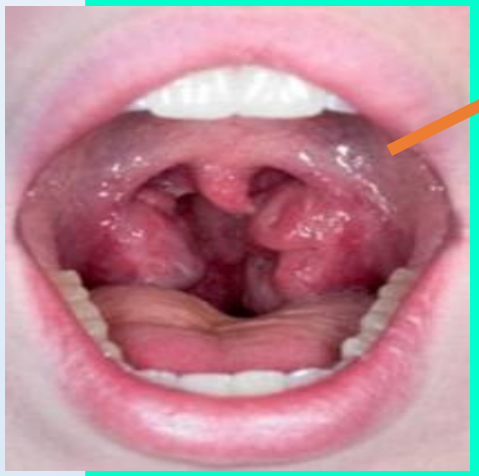
diagnosis

- Acute RF typically appears 10 days to 6 weeks after a group A streptococcal infection in about 3% of patients.
- The diagnosis is established in accordance with the revised Jones criteria: evidence of a preceding group A streptococcal infection, and the presence of two major manifestations, or one major and two minor manifestations
- The peak **age** (6-15 yrs) & **seasonal incidence** of acute rheumatic fever closely parallel those of GABHS infections

- Although pharyngeal cultures for streptococci are negative by the time the illness begins, antibodies to one or more streptococcal enzymes, such as streptolysin O and DNase B, can be detected in the sera of most patients with RF

- Antimicrobial therapy against GABHS: prevents initial episodes of acute rheumatic fever & Long-term, continuous prophylaxis: prevents recurrences of acute rheumatic fever

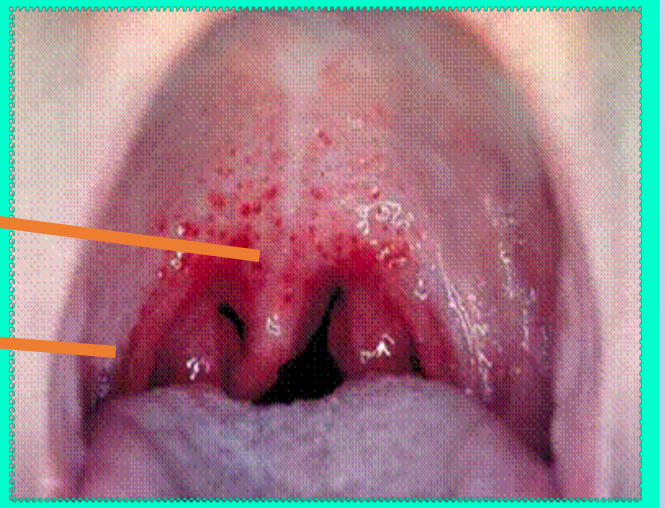
Features suggestive of GABHS infection

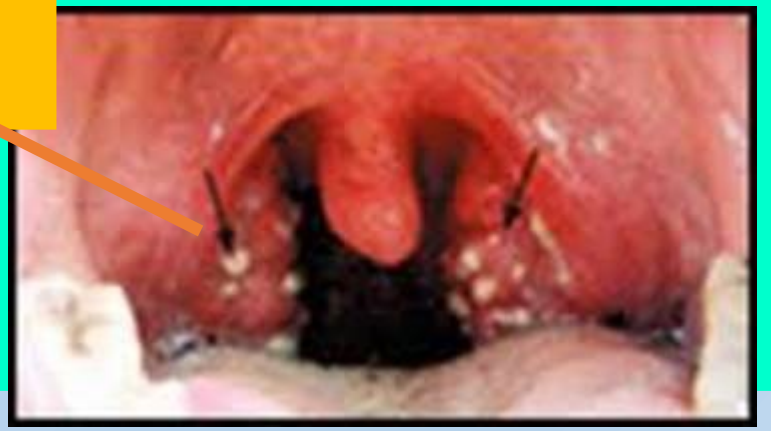


Redness & swelling of throat & tonsils;

Beefy, swollen, red uvula; Soft palate petechiae ("doughnut lesions")

Tonsillopharyngeal erythema & exudates





Sore throat: fever, white draining patches on the throat & swollen or tender lymph glands in the neck

- **Diagnosis is based on Jones criteria.**

1. Evidence of prior group A β- hemolyticstreptococcal infection with the presence of major and minor criteria.

2. Minor criteria are nonspecific and include fever and elevated ESR.

3. Major criteria:

- i. Migratory polyarthritis - swelling and pain in a large joint (e.g., wrist, knees,ankles) that resolves within days and "migrates" to involve another large joint , earliest manifestation
- ii. Pancarditis
- a. Endocarditis - Mitral valve is involved more commonly than the aorticvalve.
- b. Myocarditis with Aschoff bodies; myocarditis is the most common cause of death during the acute phase.
- c. Pericarditis - leads to friction rub and chest pain
- iii. Subcutaneous nodules
- iv. Erythema marginatum - annular, nonpruritic rash with erythematous
- borders, commonly involving trunk and limbs
- v. Sydenham chorea (rapid, involuntary muscle movements)

Migratory Polyarthritis

Most common (75%)

Involves **larger** joints: the knees, ankles, wrists & elbows

Rheumatic joints: hot, red, swollen & tender

- earliest manifestation of acute rheumatic fever

Carditis

- Carditis & chronic rheumatic heart disease: **most serious manifestations** of acute rheumatic fever
- Occurs in 50% of patients
- Rheumatic carditis: **pancarditis** with active inflammation of myocardium, pericardium & endocardium

Clinical features related to acute carditis include pericardial friction rubs, tachycardia, and arrhythmias. Myocarditis can cause cardiac dilation that may culminate in functional mitral valve insuf_x0002_ficiency or even heart failure.

Acute Pericarditis

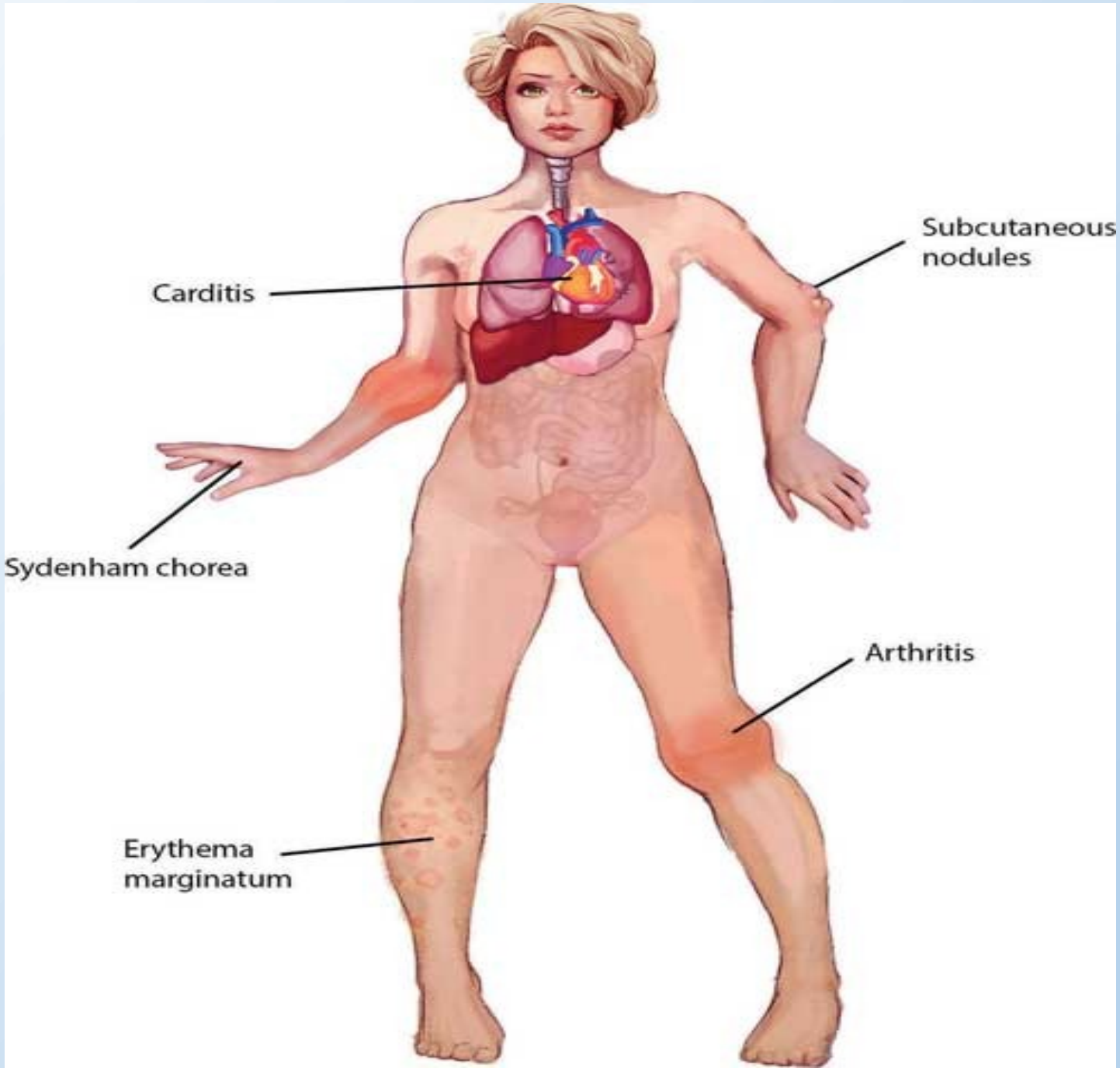
- It is inflammation of the pericardium .Classically, fibrinous material is deposited into the pericardial space and pericardial effusion often occurs

- Chest pain:

Pleuritic and sharp in nature,Exacerbated by inspiration

Worsens when supine and improves upon sitting upright or leaning forward

- Pericardial friction rub
- Diffuse ST segment elevation on ECG
- Pericardial effusion


Subcutaneous nodules
Carditis
Sydenham chorea
Arthritis
Erythema marginatum

Acute Pericarditis

- Fibrinous pericarditis develops with scanty serous exudate in the pericardial sac and excess fibrin deposit on the visceral and parietal pericardium giving the "bread and butter appearance".
- Pericarditis heals by organization.

Chorea

Erythema Marginatum

rare but characteristic rash of acute rheumatic fever

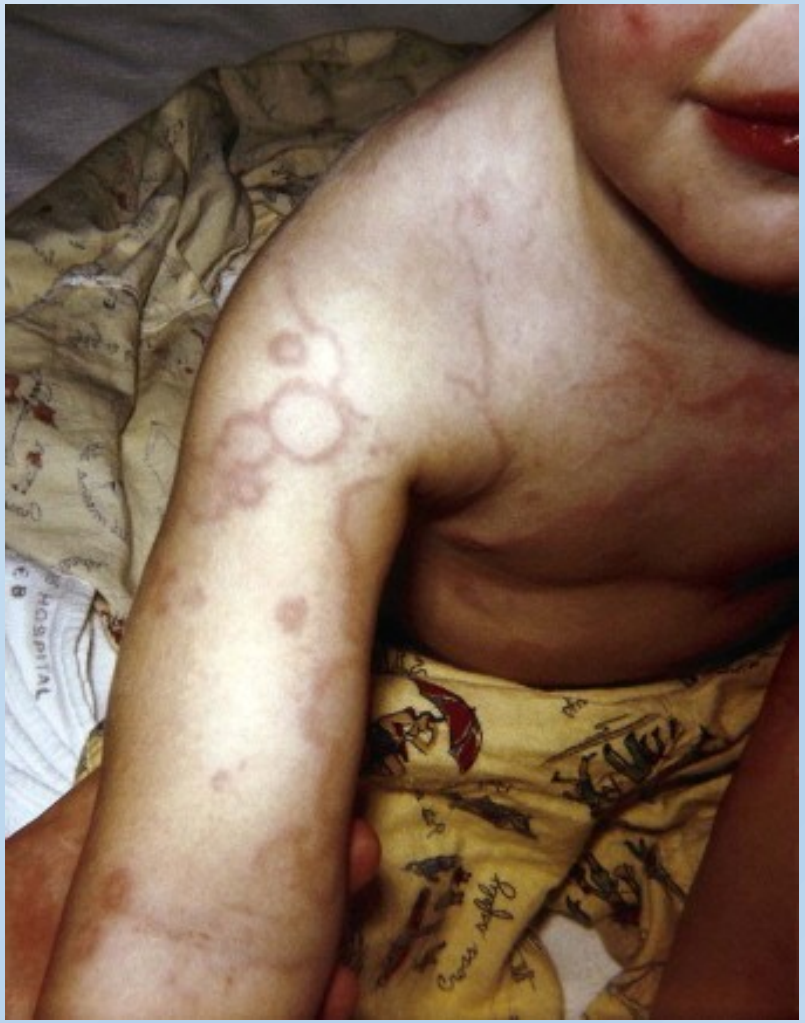
It consists of **erythematous,**

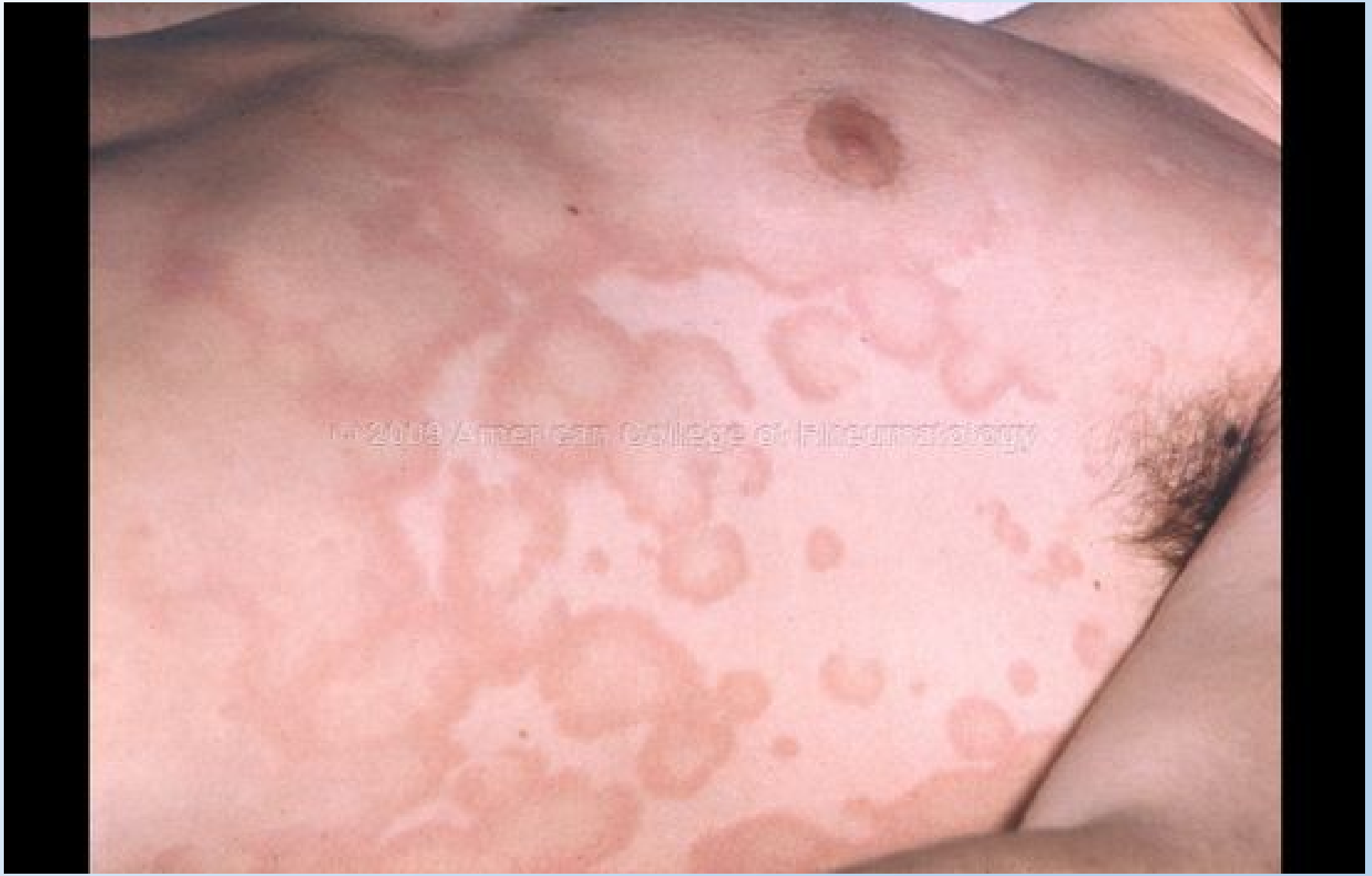
, **macular** lesions with **pale centers** that are **not pruritic**

It occurs primarily on the **trunk**

& extremities, **not on** the face &

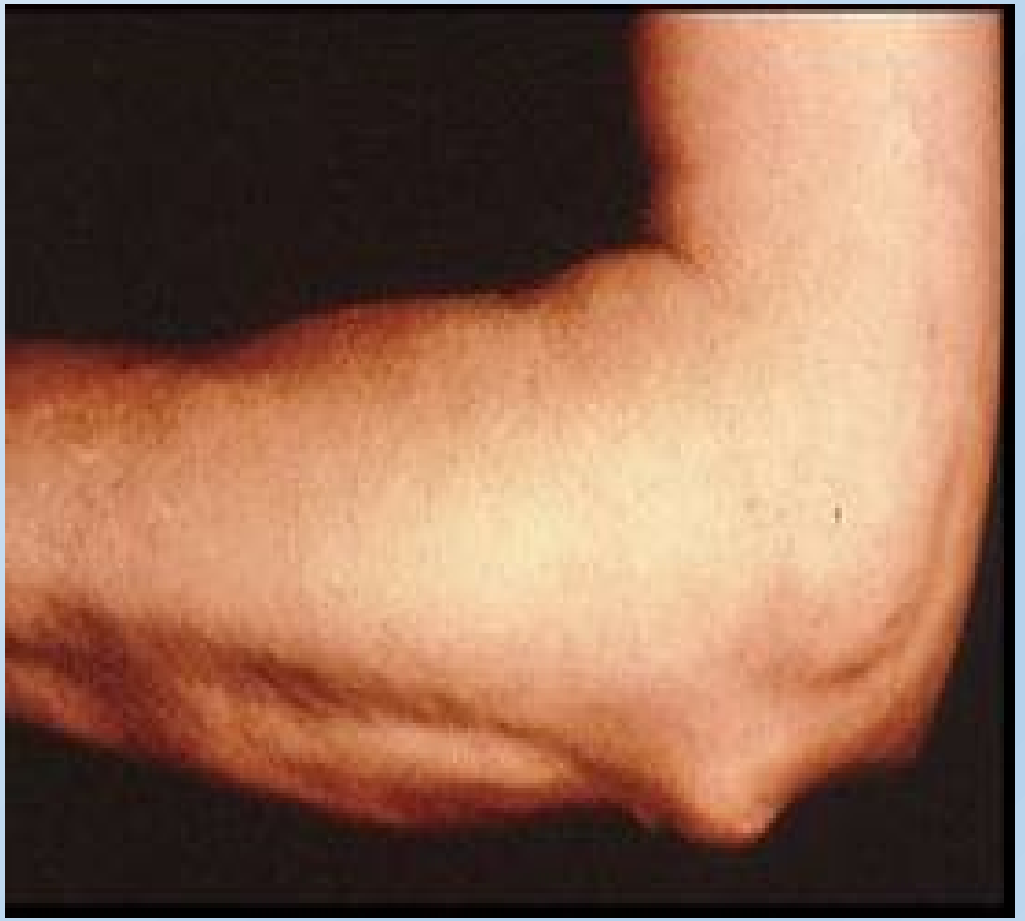
it can be accentuated by warming the skin




(c) 2008 American College of Rheumatology

Subcutaneous Nodules

Consist of firm nodules approximately 1 cm in diameter along the extensor surfaces of tendons near bony prominences



minor criteria

Clinical:

1. Arthralgia (**in the absence** of polyarthritis as a major criterion)

2. Fever

Laboratory minor manifestations:

1.Elevated acute-phase reactants (C-reactive protein, erythrocyte sedimentation rate, polymorphonuclear leukocytosis)

2. Prolonged PR interval on electrocardiogram (1st degree heart block)

DIAGNOSIS

MAJOR MANIFESTATIONS	MINOR MANIFESTATIONS	SUPPORTING EVIDENCE OF ANTECEDENT GROUP A STREPTOCOCCAL INFECTION******
Carditis	Clinical features: Arthralgia Fever	-Elevated or increasing streptococcal antibody titer
Polyarthritis	Laboratory features: Elevated acute phase reactants: ESR, C-reactive protein Prolonged PR interval	**History of (<45 days)** -Positive throat culture or rapid streptococcal antigen test or streptococcal sore throat or scarlet fever)
Erythema marginatum		
Subcutaneous nodules		
Chorea		

INFECTIVE ENDOCARDITIS (IE)

- IE is a microbial infection of the heart valves or the mural endocardium that leads to the formation of vegetations composed of thrombotic debris and organisms, often associated with destruction of the underlying cardiac tissues

- The aorta, aneurysms, other blood vessels, and prosthetic
- devices can also become infected
- all classes of microorganisms can be responsible but most infections are bacterial (bacterial endocarditis)

Acute IE vs Subacute IE

based on severity and microbial virulence, and whether there is underlying valvular pathology Traditionally, IE has been classified on clinical grounds into acute and subacute forms

Acute IE

- **infection of a previously normal heart valve by a highly virulent organism (e.g., Staphylococcus aureus) that rapidly produces destructive lesionsdespite appropriate treatment, there can be substantial morbidity and even mortality**
- **These infections may be difficult to cure with antibiotics alone and often require surgery**

Subacute IE

- **insidious infections of deformed valves with overall less destruction by organisms with lower virulence (e.g., viridans streptococci)**
- **the disease may pursue a protracted course of weeks to months, and cures can often be achieved with antibiotics alone.**

FEATURES OF ACUTE ENDOCARDITIS & SUBACUTE ENDOCARDITIS		
Features	**Acute**	**Subacute**
Duration	<6 weeks	> 6 weeks
Most common organism	Staphylococcus aureus, β- streptococcus	Streptococcus viridans
Virulence of organism	Highly	Less
Valve conditions	Normal	Damaged
Lesion on valves	Invasive, suppurative, destructive	None
Clinical features	Acute systemic infection	Splenomegaly, clubbing of fingers, petechiae

Etiology and Pathogenesis

a variety of cardiac abnormalities increase the risk of developing IE

- Mitral valve prolapse.
- Rheumatic heart disease.
- Degenerative calcific valvular stenosis.
- Bicuspid aortic valve (whether calcified or not).
- Artificial (prosthetic) valves.
- Unrepaired and repaired congenital defects.

The causative organisms

- Streptococcus viridans; normal flora in the oral cavity, in (50% - 60% of cases). Cause IE of native but abnormal valves.
- S. aureus organisms; more virulent, in (10% to 20% of cases) found on the skin.Can infect either healthy or deformed valves. notably,the major offender in IV drug abusers.
- Enterococci(HACEK group)Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, and Kingella> all commensals in the oral cavity
- less commonly , Gram-negative bacilli and fungi can be involved

- **In about 10% of all cases of endocarditis, no organism can be isolated from the blood ("culture-negative" endocarditis); reasons include prior antibiotic therapy, difficulties in isolation, or because deeply embedded organisms within the vegetation are not released into the blood**

prosthetic valve infection

- Prosthetic valve endocarditis occurring in the 1 to 2 months after surgical implantation is typically caused by skin flora (S. aureus and S. epidermidis); prosthetic valve infections 1 year or more after surgery tend to be streptococci and S. aureus

Source of bacteremia

An obvious infection elsewhere.

A dental or surgical procedure.

A contaminated needle shared by IV drug users.

Trivial breaks in the epithelial barriers of the gut, oral cavity, or skin.

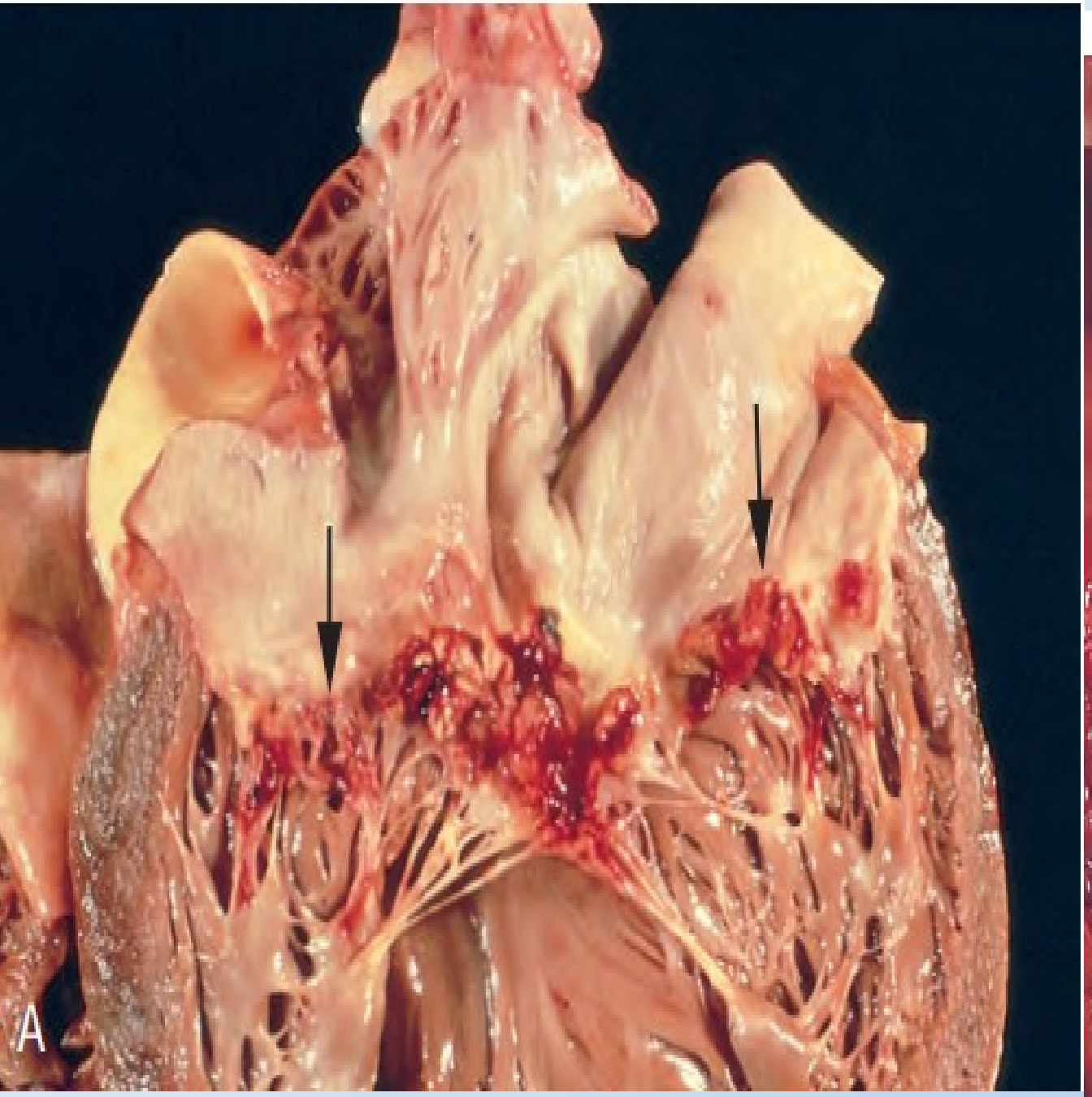
IE risk can be lowered by antibiotic prophylaxis, *in those with predisposing factors*

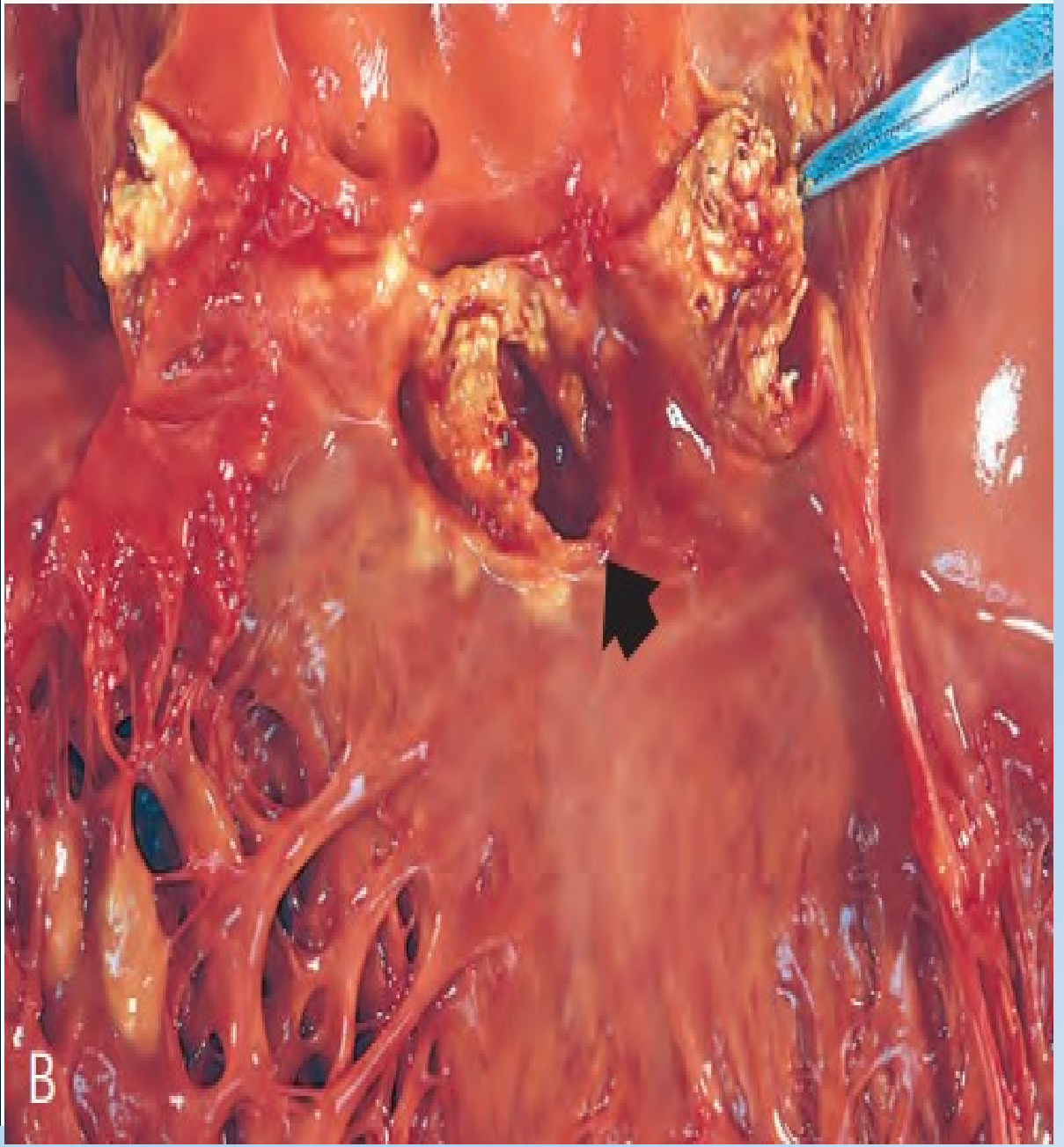
MORPHOLOGY

- the classic hallmark is Vegetations on heart valves ; these are friable, bulky, potentially destructive lesions containing fibrin, inflammatory cells, and bacteria or other organisms
- The aortic and mitral valves are the most common , valves of the right heart may also be involved, particularly in intravenous drug abuser
- May be single or multiple and may involve more than one valve.

May erode into the underlying myocardium and produce an abscess

Emboli may be shed from the vegetations,abscesses frequently develop where they lodge leading to septic infarcts or mycotic aneurysms.


A

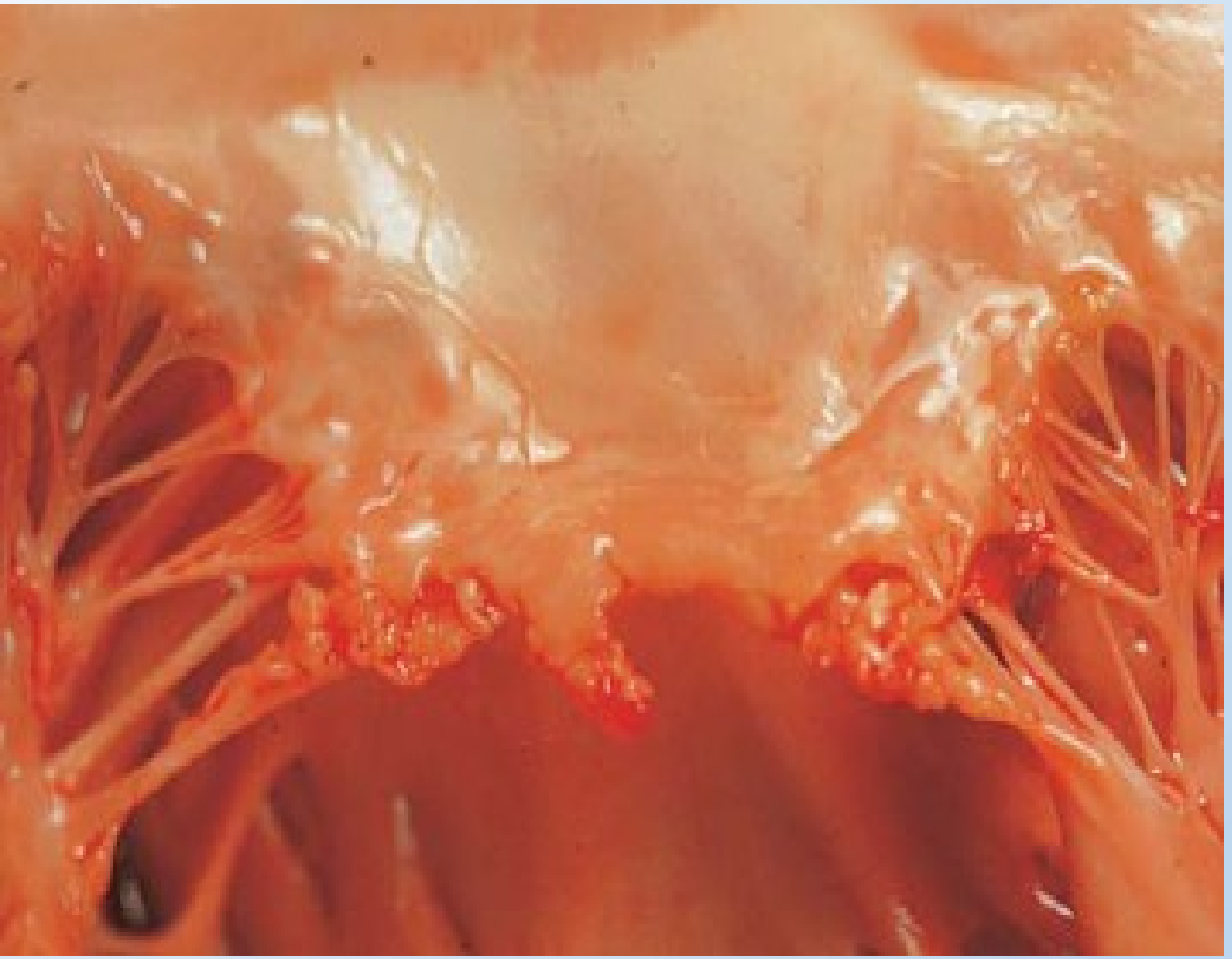

B

- The vegetations of subacute endocarditis are associated with less valvular destruction

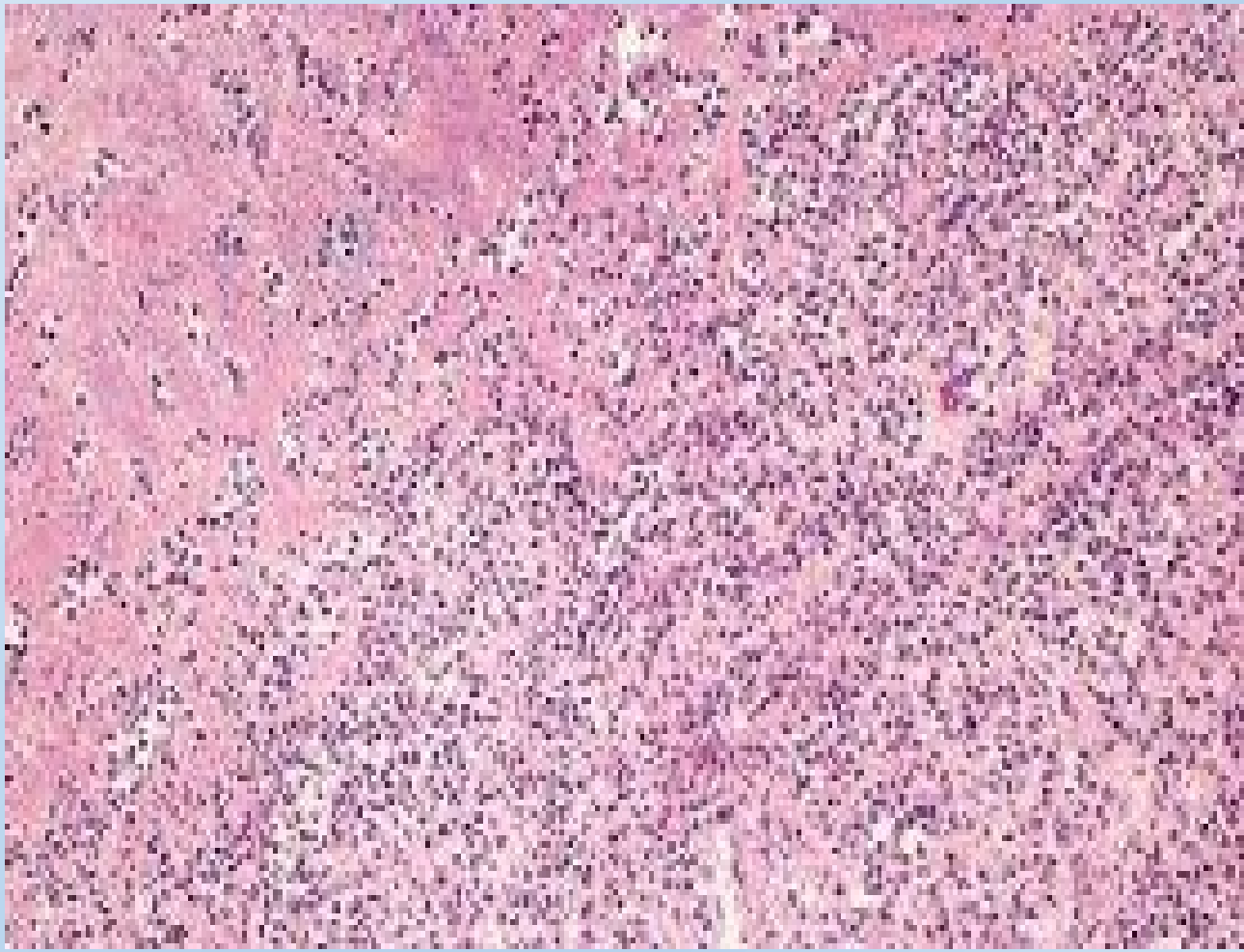
- Microscopically, the vegetations of subacute IE typically exhibit granulation tissue at their bases indicative of healing

- With time, fibrosis, calcification, and a chronic inflammatory infiltrate can develop

The mitral valve shows destructive vegetations, which have eroded through the free margins of the valve leaflets



Extensive acute inflammatory cells and fibrin. Bacterial organisms were demonstrated by tissue Gram stain.



Clinical Features

Acute endocarditis has a stormy onset with rapidly developing fever, chills & weakness.

Fever is the most consistent sign (may be slight or absent in elderly).

and the only manifestations may be nonspecific fatigue, weight loss, and a flulike syndrome

Murmurs are present in 90% of patients (may stem from a new valvular defect or represent a preexisting abnormality).

Positive blood culture & echocardiographic findings.

Complications of IE

- Begin within the first few weeks of onset:

- Glomerulonephritis
  - Caused by deposition of Ag-Ab complexes.
  - Hematuria, albuminuria and renal failure.

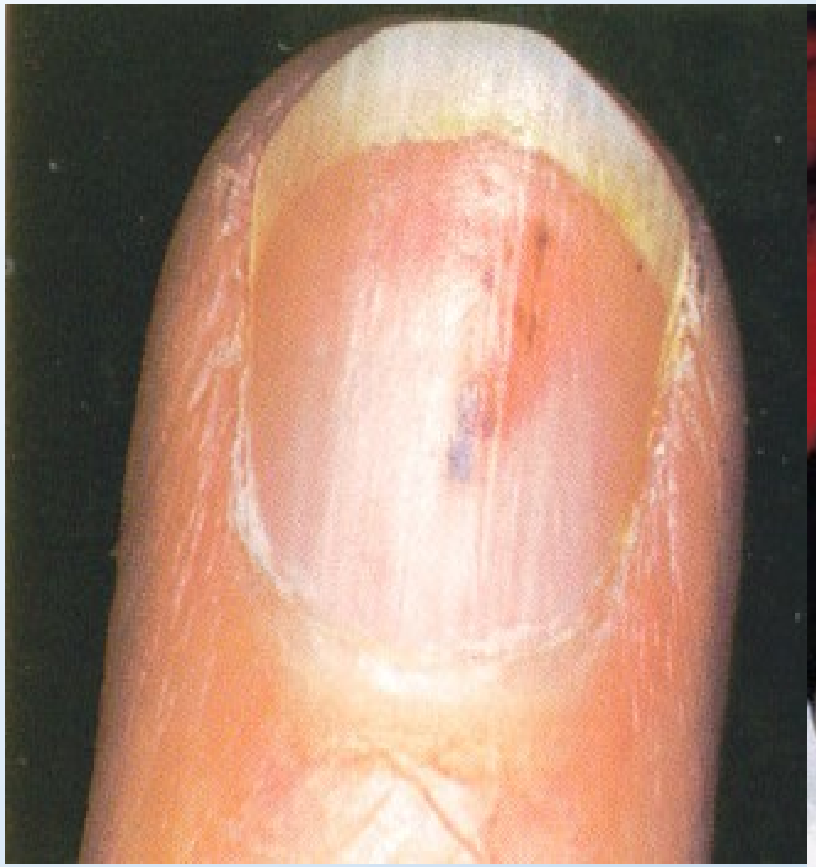
- Septicemia.
- Arrythmia.suggesting invasion into underlying myocardium and conduction system)
- Systemic embolisation.
- if Left untreated, IE generally is fatal

Complications due to microemboli

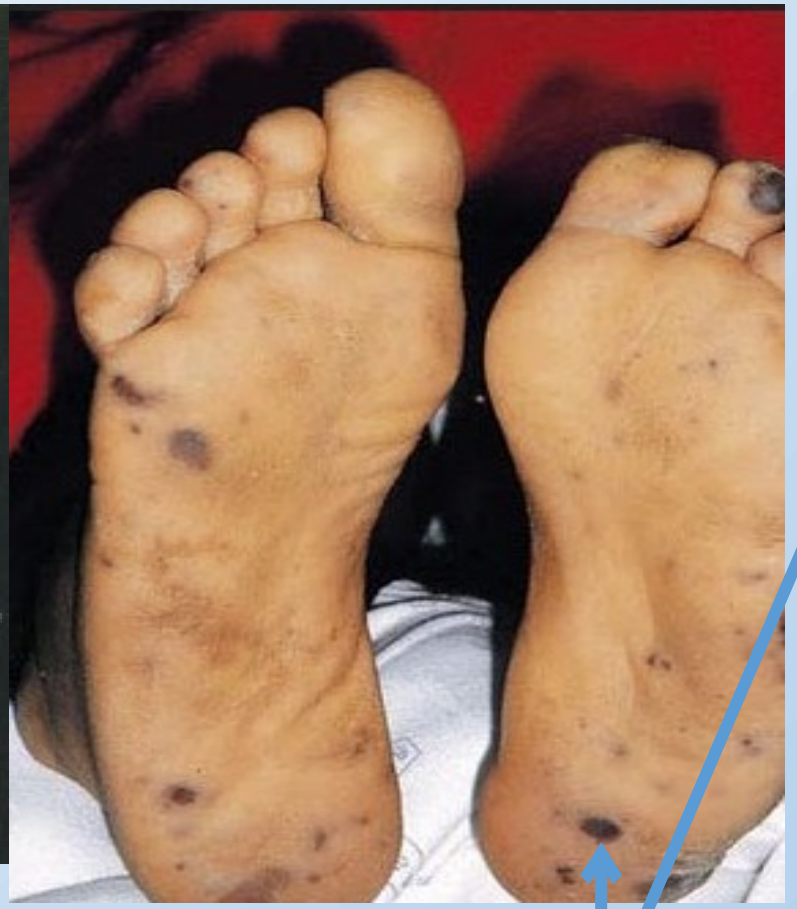
- Splinter or subungual hemorrhages.
- Janeway lesions: erythematous or hemorrhagic nontender lesions on the palms or soles
- Osler nodes: subcutaneous nodules in the pulp of the digits.
- Roth spots: retinal hemorrhages with pale center in the eyes.

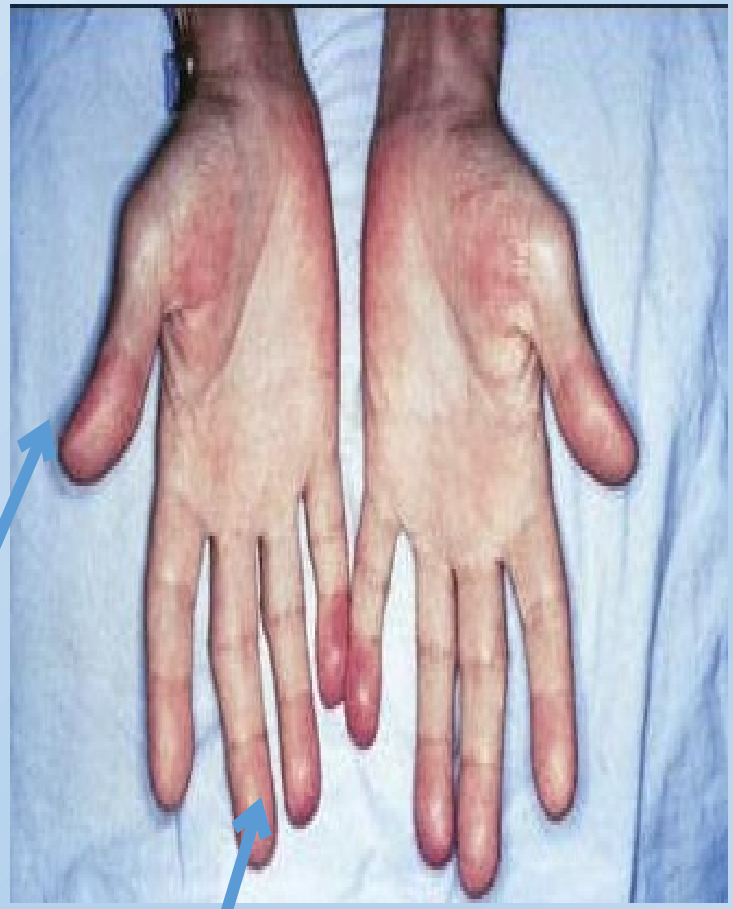
(clinical manifestations of long-standing IE)

Complications of IE



Splinter hemorrhage

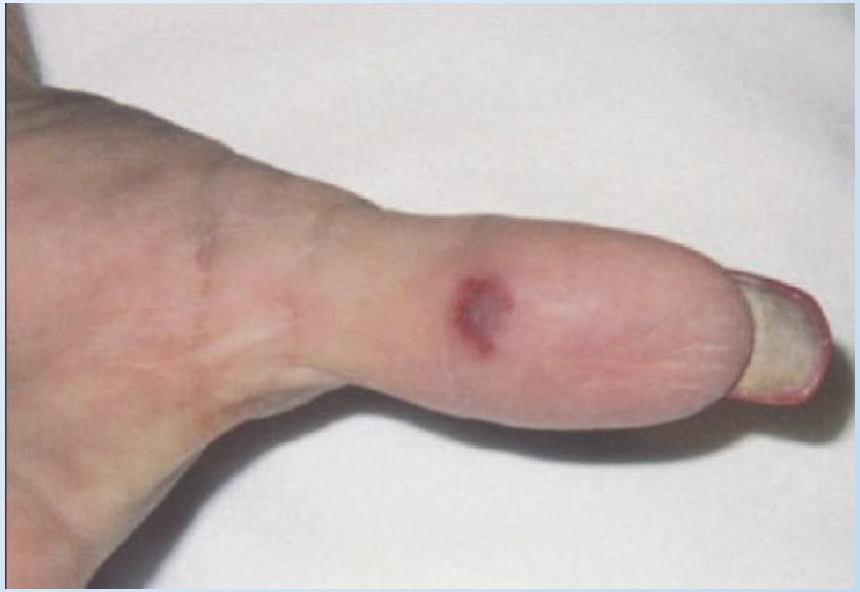




Janeway lesions & Osler nodes

Complications of IE

Osler nodes



Roth spots

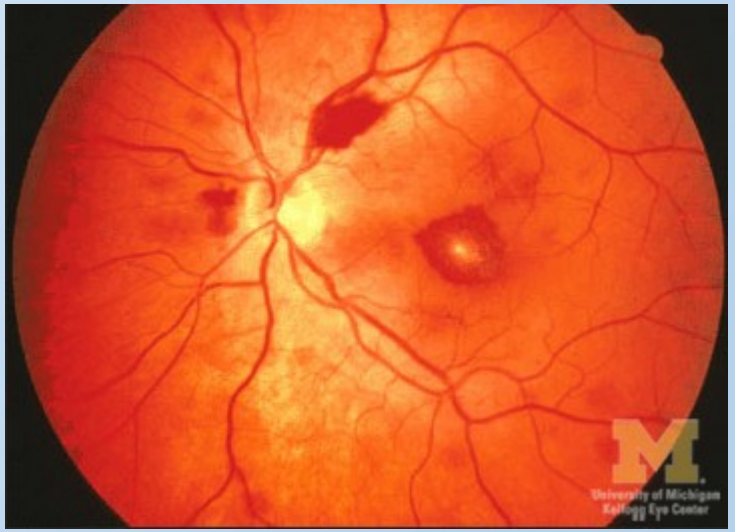


Table 12.9 Diagnostic Criteria for Infective Endocarditis[a]

Pathologic Criteria

Microorganisms, demonstrated by culture or histologic examination, in a vegetation, embolus from a vegetation, or intracardiac abscess

Histologic confirmation of active endocarditis in a vegetation or intracardiac abscess

Clinical Criteria

Major

Blood culture(s) positive for a characteristic organism or persistently positive for an unusual organism

Echocardiographic identification of a valve-related or implant-related oscillating mass or abscess, or partial separation of artificial valve

New valvular regurgitation

Minor

Predisposing heart lesion or intravenous drug use

Fever

Vascular lesions, including major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions[b]

Immunological phenomena, including glomerulonephritis, Osler nodes,[c] Roth spots,[d] and rheumatoid factor

Microbiologic evidence, including a single culture positive for an unusual organism

Diagnosis by these guidelines, often called the Modified Duke Criteria, requires either pathologic or clinical criteria; if clinical criteria are used, 2 major, 1 major +3 minor, or 5 minor criteria are required for definitive diagnosis. “Possible” infective endocarditis diagnosis requires either 1 major +1 minor, or 3 minor

NONINFECTED VEGETATIONS

Noninfected (sterile) vegetations include :

- Nonbacterial thrombotic endocarditis (NBTE).
- The endocarditis of SLE; Libman-Sacks endocarditis (LSE).

Marantic endocarditis
NBTE

- Occur in debilitated patients as cancer.
- Frequently occurs with other findings of hypercoagulable states: DVT & PE.

- Predisposing factors:
- Adenocarcinoma
- Sepsis.
- Endocardial trauma from an indwelling catheter.

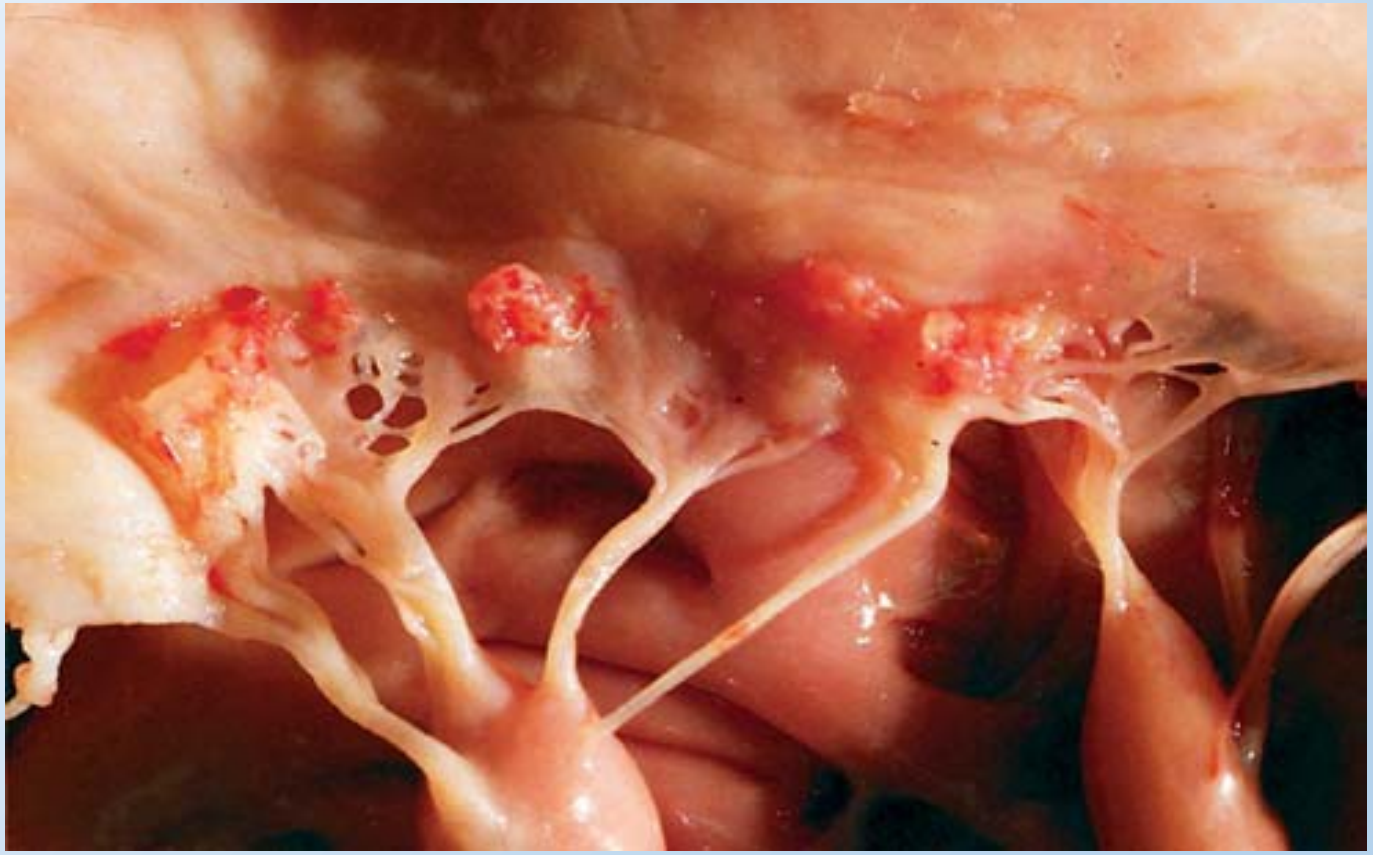
Morphology of NBTE

- The lesions are 1 mm to 5 mm in size.
- Single or multiple along the line of closure of the leaflets or cusps.

- **Microscopic picture:**
  - Bland (sterile) thrombi (platelet & fibrin).
  - Loosely attached to the valve; not invasive.
  - Do not elicit any inflammatory reaction.

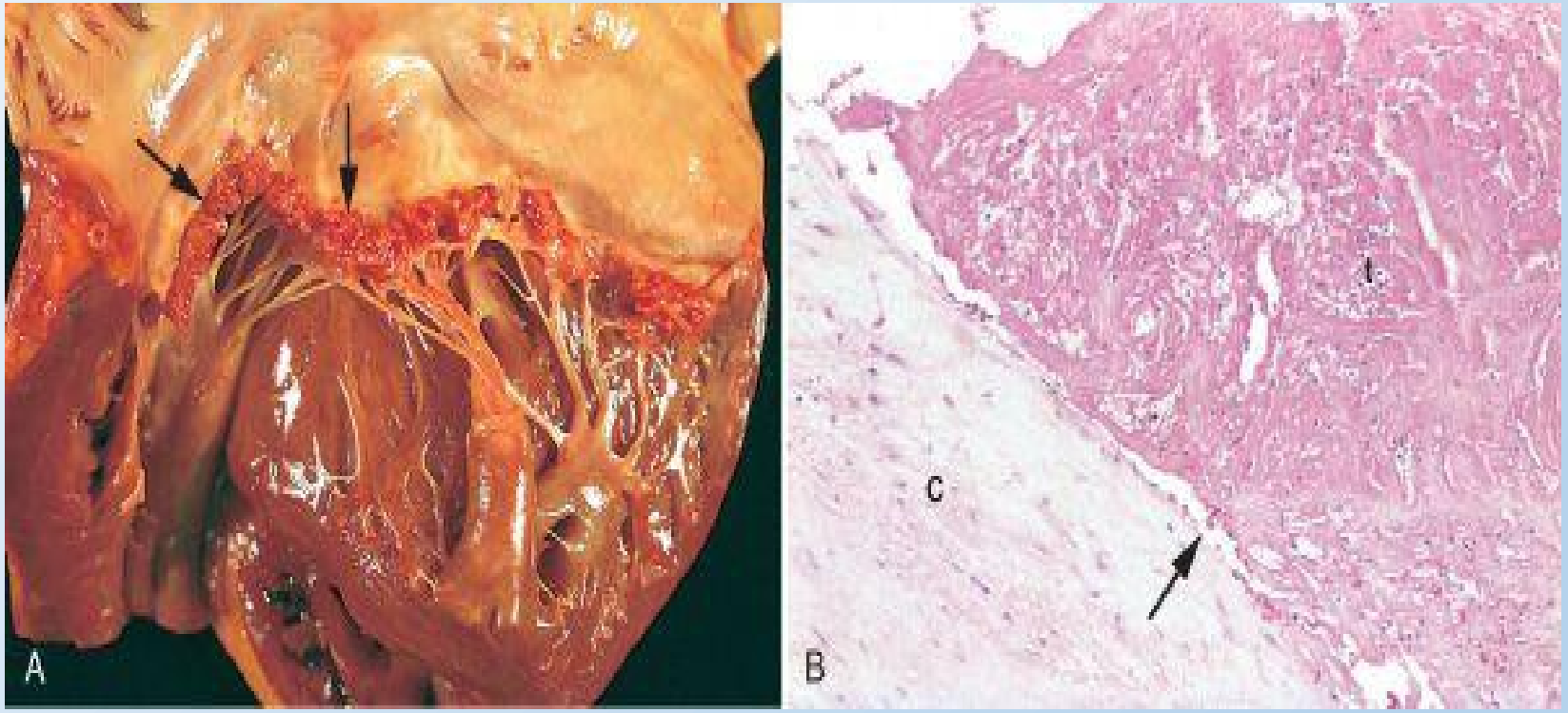
- May be the source of systemic emboli that produce infarcts.

Marantic endocarditis



Sterile platelet–fibrin vegetations are seen on the leaflets of a structurally normal mitral valve.

Marantic endocarditis (NBTE)



A. Nearly complete row of thrombotic vegetations along the line of closure of the mitral valve leaflets (arrows).
B. Bland thrombus, with virtually no inflammation in the valve cusp (c) or the thrombotic deposit (t).

Libman-Sacks Endocarditis

- Sterile vegetations on the valves of patients with SLE especially with antiphospholipid syndrome.
- Caused by immune complex deposition and have associated inflammation.
- Uncommon now due to ↑ use of steroids.
- The mitral valve is more frequently involved than the aortic valve; regurgitation is the usual functional abnormality.

Morphology of LSE

- Small lesions (1-4 mm in diameter).
- Single or multiple.
- Sterile, pink vegetations with warty appearance.

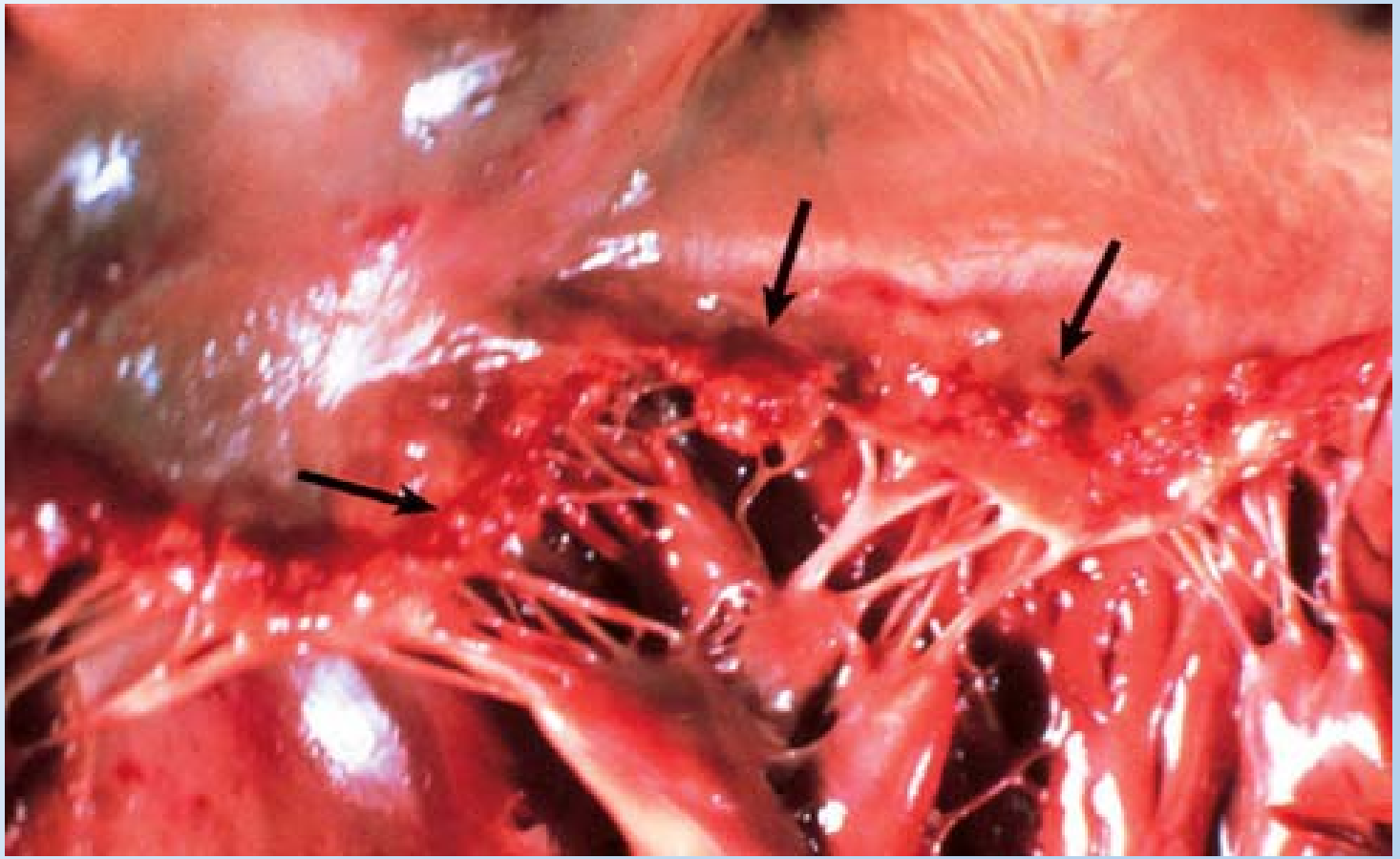
- May be located on either sides including the undersurfaces of the A-V valves, on the chords, or on the endocardium of the valve, atria or ventricles.

Microscopic picture

- Finely granular, fibrinous eosinophilic material that may contain hematoxylin bodies (remnants of nuclei damaged by AbS).

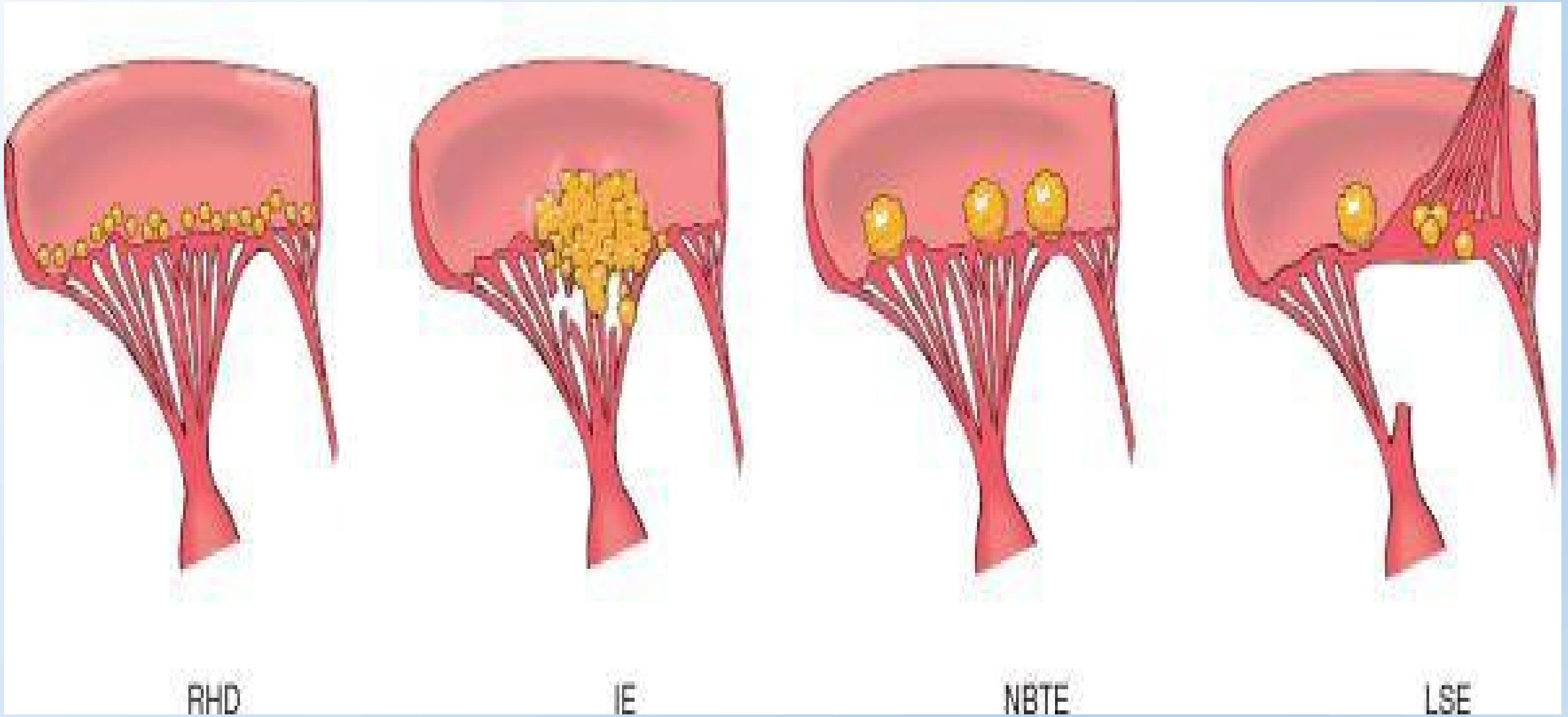
- An intense valvulitis with fibrinoid necrosis of the valve may be present

Libman-Sacks endocarditis



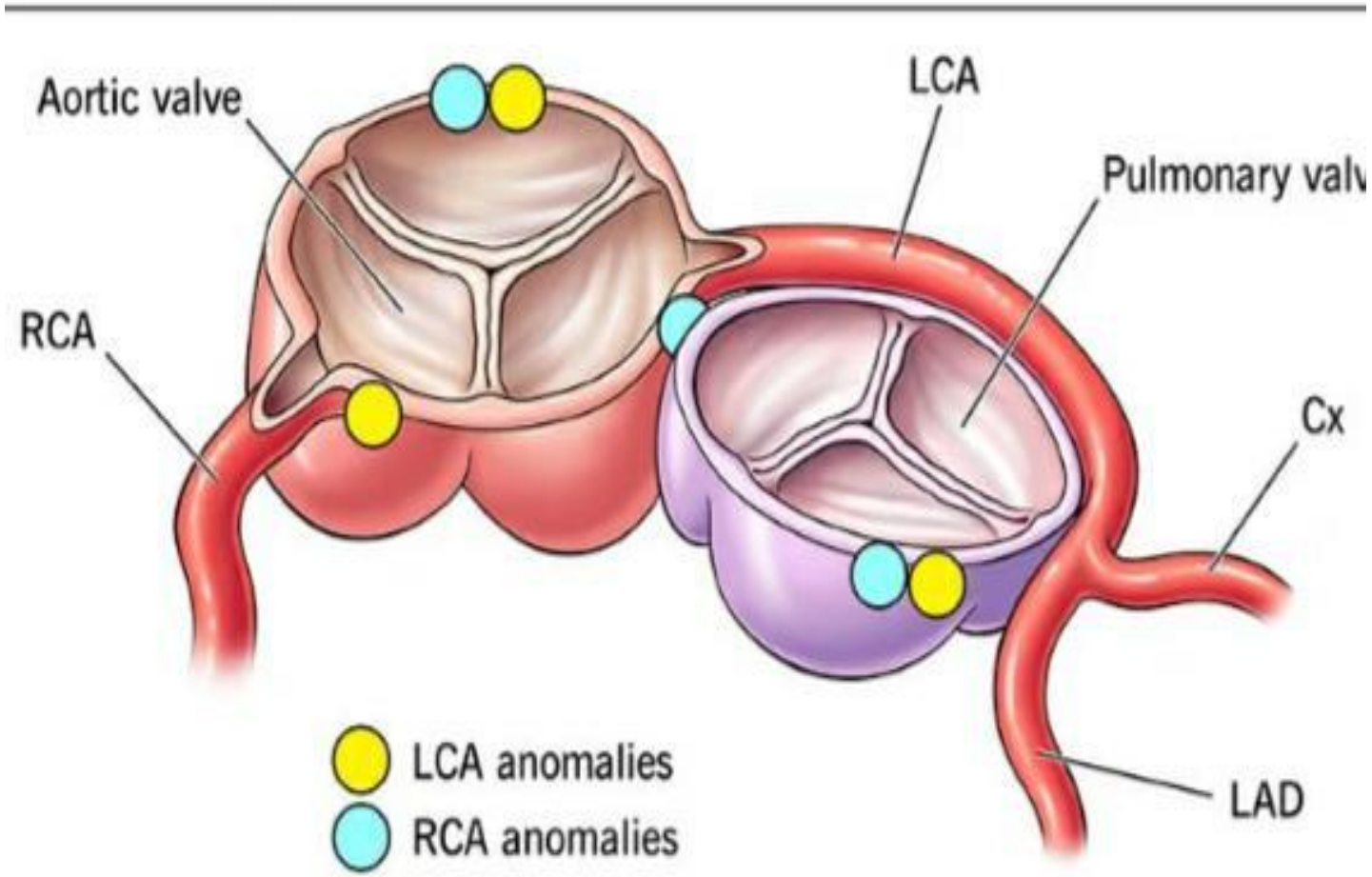
The heart of a patient who died of complications of SLE displays verrucous vegetations (arrows) on the leaflets of the mitral valve

Major forms of vegetations

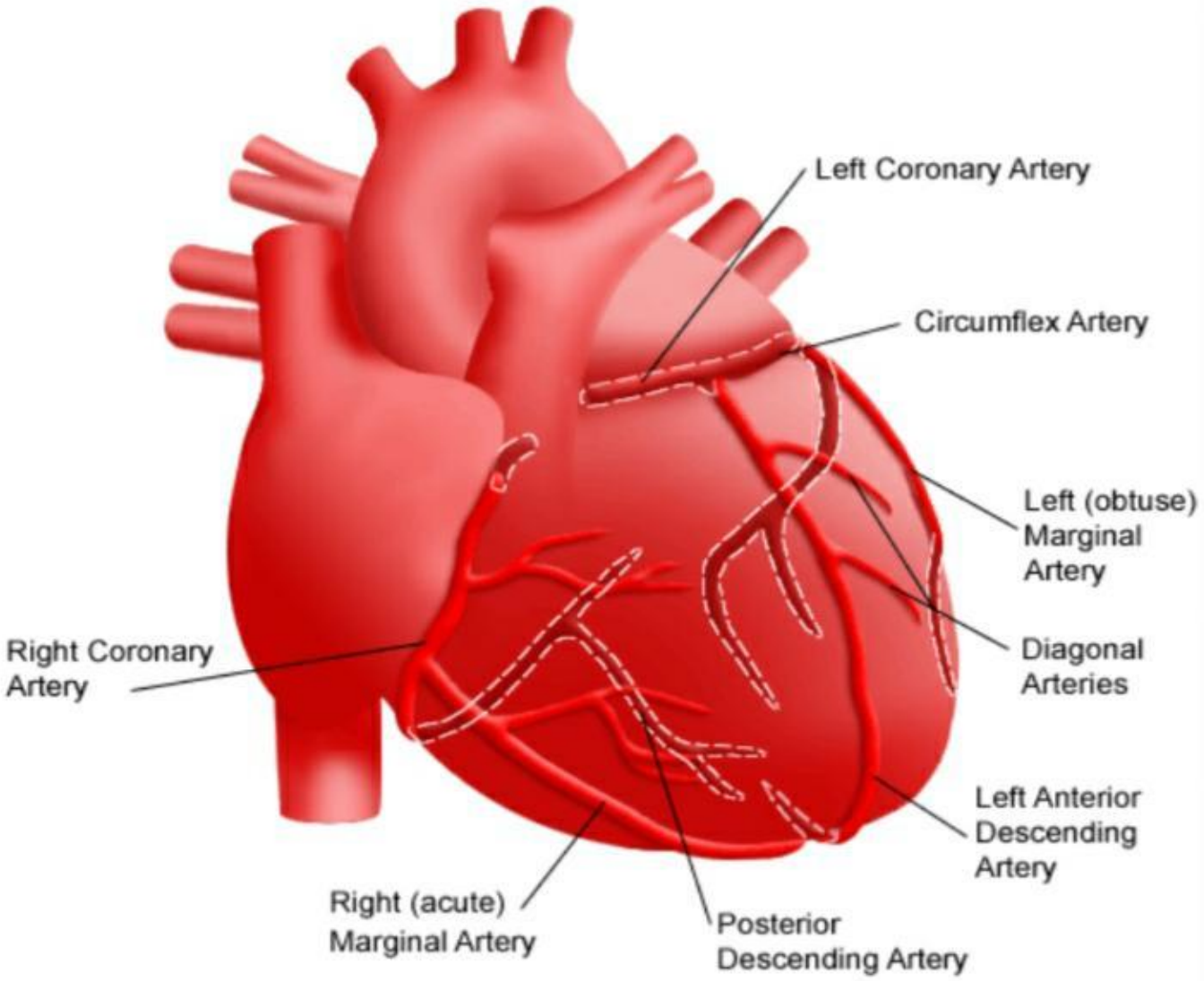


Ischemic heart disease

Dr. Dina Haboush


Aortic valve
LCA
Pulmonary valv
RCA
Cx
LAD
LCA anomalies
RCA anomalies

Coronary Arteries of the Heart



Coronary Circulation

- The coronary arteries arise from the root of the ascending aorta, particularly from the semilunar cusps of The aortic valve (the sinuses of Valsalva)The left and right semilunar cusps give rise to the left and right coronary arteries (respectively).
- The third sinus-which is the posterior semilunar cusp-is notassociated with a coronary vessel and is also called the non-coronary sinus

Lt Coronary Artery

- The left coronary artery typically runs for 2-3 cm, and then bifurcates into the left anterior descending (LAD) and the circumflex artery (Cx)•
- LAD : Runs in anterior interventricular groove, Supplies 2/3 the heart; It gives Septal perforators supplying the ant. Part of septum (2/3), Diagonal Branches Supplying the Ant, Lateral and apical parts of LV
- Circumflex Artery: It gives Optose Marginal (OM) branches supplying lateral, Posterior and inferior segments of LV

Rt Coronary Artery

- Runs in Rt AV groove towards the crux of the heart Gives branches that supply RA, RV and Inferiorposterior aspects of LV
- Branches: Posterior Descending Artery (PDA), Posterior Lateral Branches (PLB), Branch to SAN (60%), Branch to AVN (90%), Right marginal branch(Branch to RV)
- PDA: Runs in posterior IV groove, Supplying the posterior part of IV septum

Coronary Artery Disease

Definition

Imbalance between blood supply by the coronaries and oxygen requirements of myocardium

Etiology

- Atherosclerosis (90%): The most common cause
- Vasospasm
- Inflammation; Vasculitis
- Thromboembolic
- Congenital anomaly of the coronaries

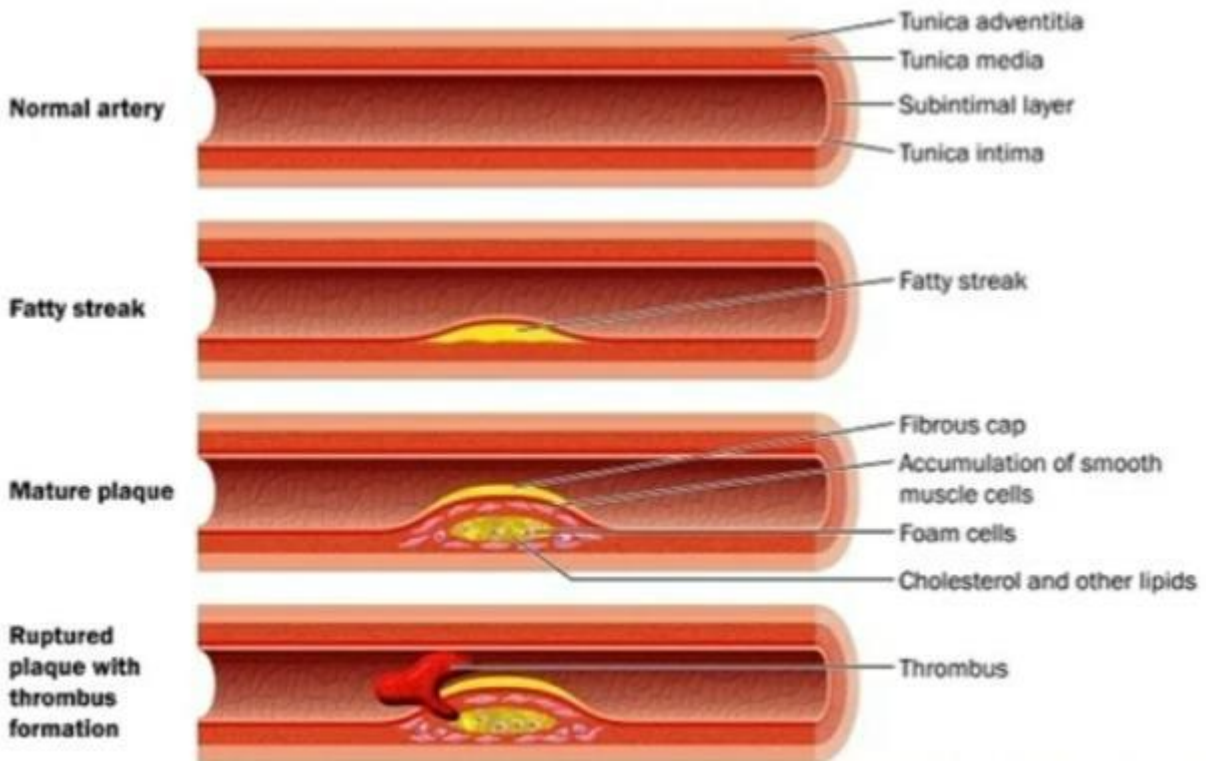
Non-modifiable risk factors	Modifiable risk factors
• Age • Sex • Family history of premature cardiovascular disease	• Hypertension • Diabetes mellitus • Obesity • Cigarette smoking • Physical inactivity • Dyslipidemia

Ischemic heart disease types

- Stable angina
- Unstable angina
- Myocardial infarction (STEMI Vs. NSTEMI)
- Ischemic Heart failure
- Ischemic Arrhythmia
- Sudden Cardiac Death: Unexpected non-traumatic death due to a cardiovascular cause (History of heart disease Or heart disease in autopsy) that occurs within one hour of the onset of symptoms

Pathogenesis

- Atherosclerosis is a progressive pathologic process of the arterial wall that that generally begins in childhood and manifests clinically in middle to late adulthood.
- Atherosclerosis has a multifactorial etiology including endothelial dysfunction and vascular inflammation.
- Caused by sub-intimal buildup of atheromatous

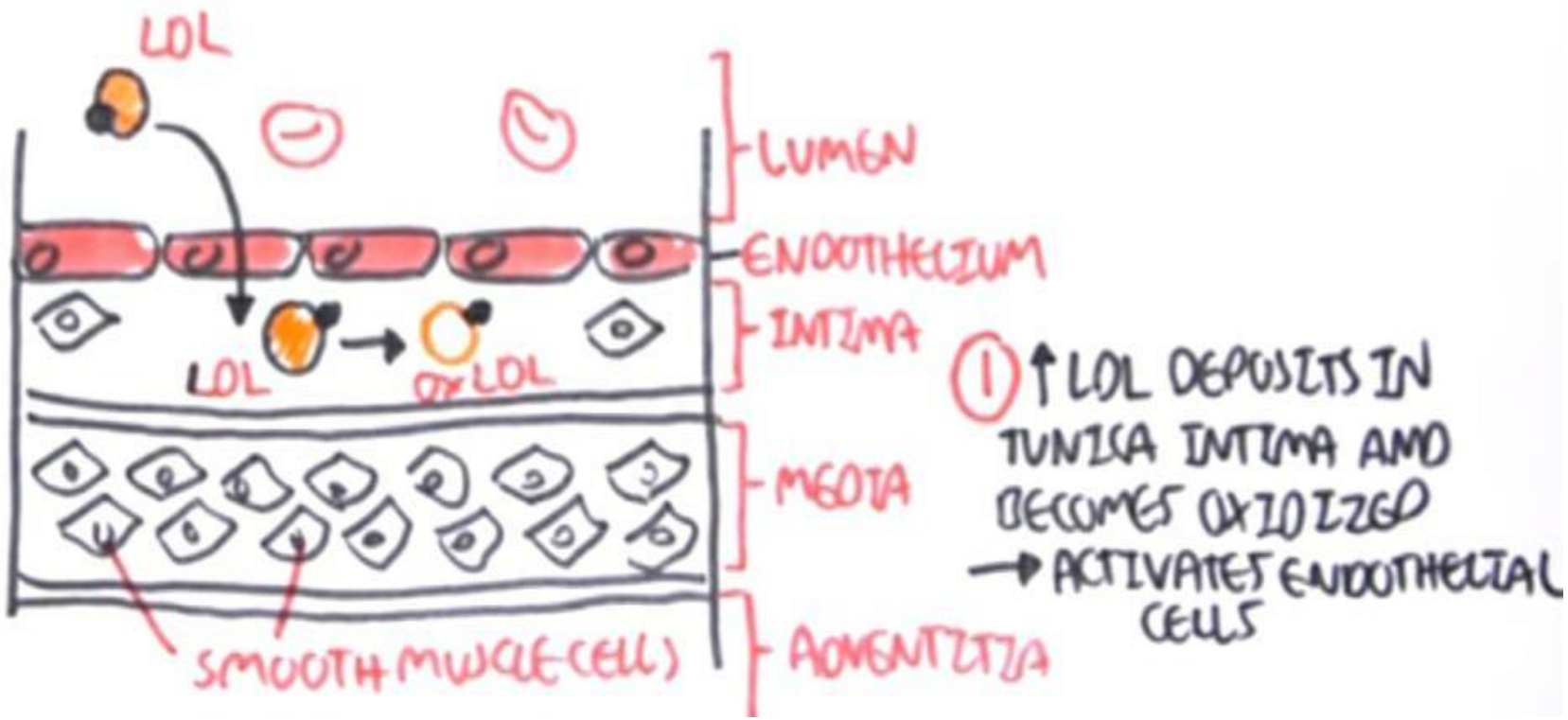

Normal artery
Tunica adventitia
Tunica media
Subintimal layer
Tunica intima
Fatty streak
Fatty streak
Mature plaque
Fibrous cap
Accumulation of smooth muscle cells
Foam cells
Cholesterol and other lipids
Ruptured plaque with thrombus formation
Thrombus

- plaque causing narrowing of coronary lumen and thus impairing tissue perfusion
- Plaques which may require 10-15 years for full development, characteristically occur in regions of branching and where blood undergoes sudden changes in velocity and direction of flow
- Clinically significant plaques tend to occur within the first several centimeters of the LAD and LCX , and along the entire length of the RCA.

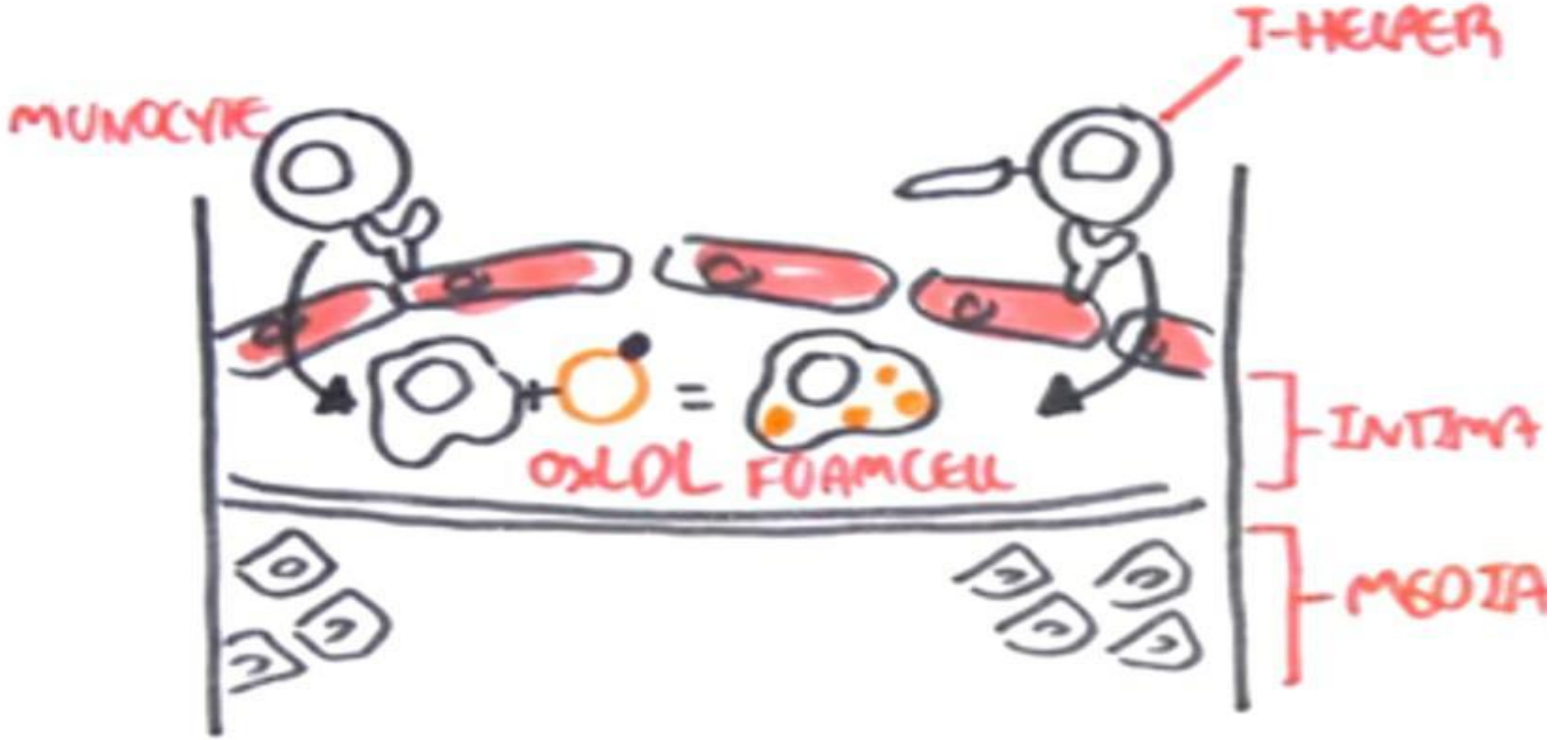
- Plaques are composed of: Core (lipid-laden foam cells, extracellular lipid, and necrotic cellular debris) and fibrous Cap
- The cap is made up of extracellular connective tissue matrix (collagen) synthesized by migrating smooth muscle cells from media

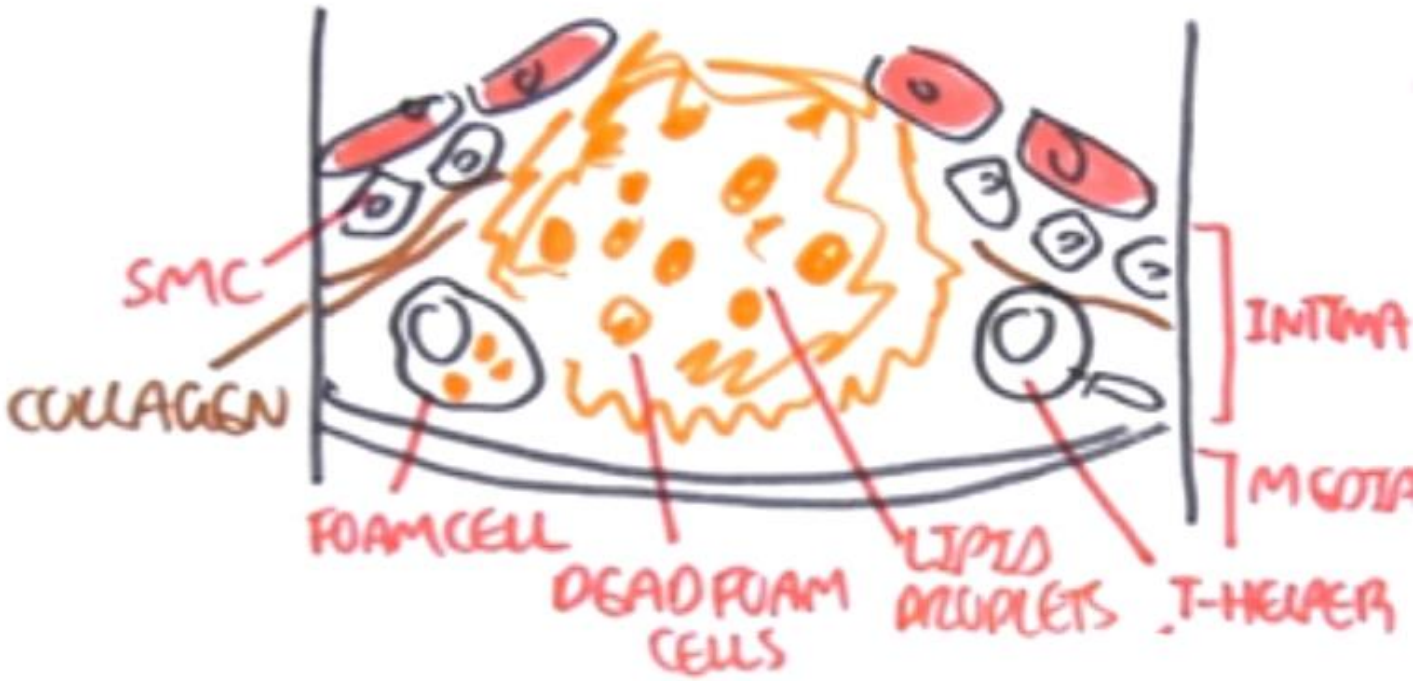
Pathogenesis

- During evolution of an atherosclerotic plaque, monocytes and other inflammatory cells bind to receptors expressed by endothelial cells. Subsequently, they migrate into the intima, and take up lipoprotein particles by phagocytosis to become lipid-laden macrophages or foam cells.
- Extracellular lipid pools appear in the intimal space when foam cells die and release their contents.


LDL
LUMEN
ENDOTHELIUM
INTIMA
LDL
oxLDL
MEDIA
SMOOTH MUSCLE CELL
ADVENTITIA
① ↑ LDL DEPOSITS IN TUNICA INTIMA AND BECOMES OXIDIZED
→ ACTIVATES ENDOTHELIAL CELLS

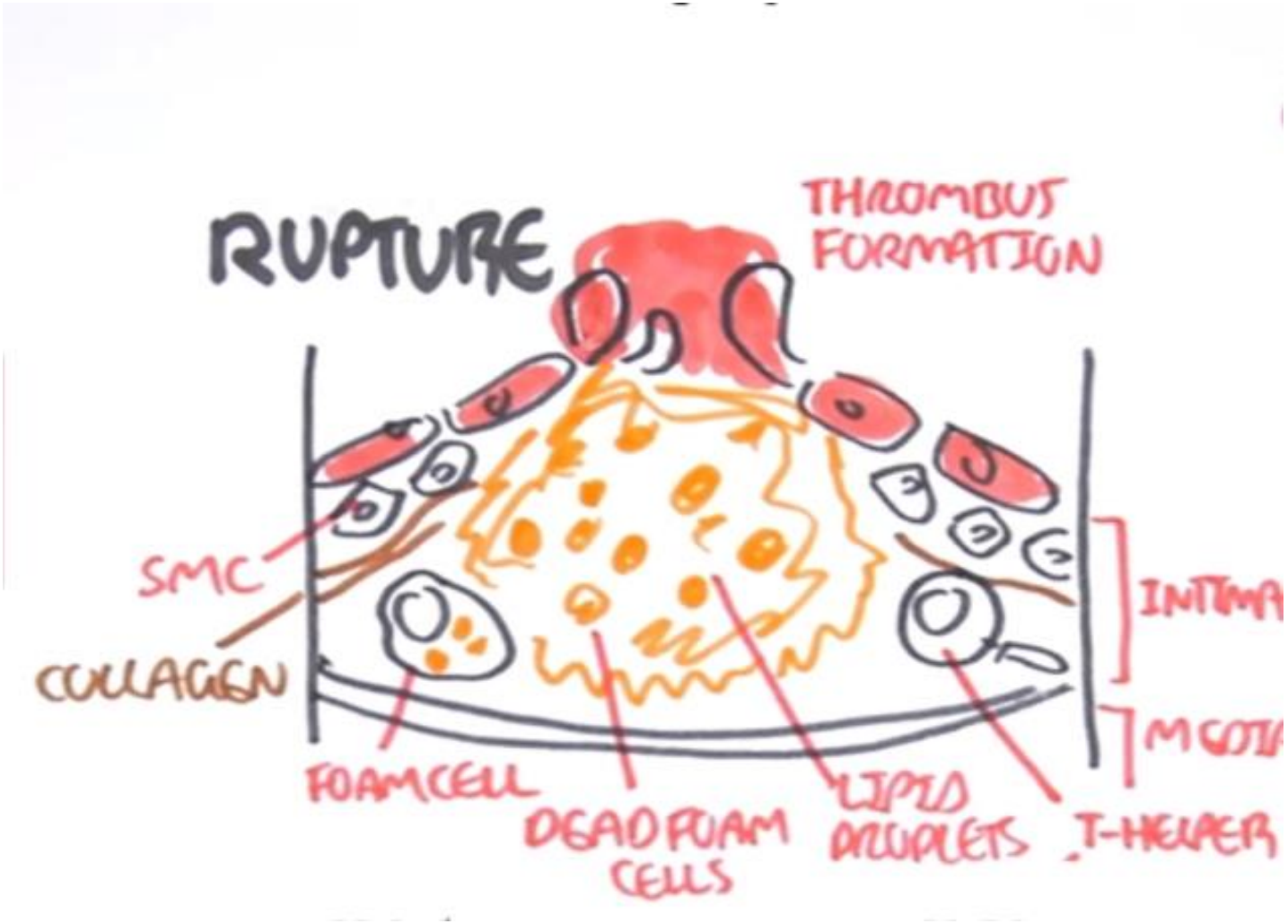
- In response to cytokines and growth factors produced by activated macrophages, smooth muscle cells migrate from the media of the arterial wall into the intima, and change from a contractile to a fibroblastic phenotype, which can stabilize the atherosclerotic lesion.
- If this is successful, the lipid core will be covered by smooth muscle cells and matrix, producing a stable atherosclerotic plaque that will remain asymptomatic until it becomes large enough to obstruct arterial flow.


T-HELPER
MONOCYTE
=
OXLDL FOAMCELL
INTIMA
MEDIA


SMC
COLLAGEN
FOAMCELL
DEAD FOAM CELLS
LIPID DROPLETS
T-HELPER
INTIMA

- In an established atherosclerotic plaque, macrophages mediate inflammation and smooth muscle cells promote repair.If inflammation predominates, the plaque becomes unstable and may be complicated by ulceration and thrombosis. This results in thinning of the protective fibrous cap, making the lesion vulnerable to mechanical stress that ultimately causes erosion, fissuring or rupture of the plaque surface

- Any breach in the integrity of the plaque will expose its contents to blood and will trigger platelet aggregation and thrombosis. This may cause partial or complete obstruction at the site of the lesion, resulting in infarction or ischemia of the affected organ. This common mechanism underlies acute coronary syndromes


RUPTURE
THROMBUS FORMATION
SMC
COLLAGEN
INTIMA
FOAMCELL
DEAD FOAM CELLS
LIPID DROPLETS
T-HELPER

- Fixed obstructions that occlude less than 70% of a coronary vessel lumen typically are asymptomatic, even with exertion.
- Lesions that occlude more than 70% of a vessel lumen generally cause symptoms in the setting of increased demand, certain levels of exertion predictably cause chest pain, and the patient is said to have stable angina .

- A fixed stenosis that occludes 90% or more of a vascular lumen can lead to inadequate coronary blood flow with symptoms even at rest-one of the forms of unstable angina
- subtotal occlusion will cause Subendocardial Infarction (NSTEMI), While total occlusion will cause Transmural Infarction (STEMI)
- The only difference between UA and NSTEMI, is that NSTEMI is associated with elevation of cardiac biomarkers

Angina Pectoris

- Intermittent chest pain caused by transient, reversible myocardial ischemia
- The pain is a consequence of the ischemia-induced release of adenosine, bradykinin, and other molecules that stimulate autonomic nerves.
- There are three major types of angina: Stable angina, Prinzmetal or variant angina, Unstable angina

Stable Angina

- Predictable episodic chest pain associated with particular levels of exertion or some other increased demand (e.g., tachycardia) The pain is described as a heaviness, squeezing or Burning substernal sensation that often radiates down the left arm or to the left jaw
- Pain from above umbilicus (Epigastric pain) To Jaw can be of cardiac origin!
- Duration: Lasts minutes up to 20 minutes
- The pain usually is relieved by rest (reducing demand) or by nitroglycerin, a vasodilator that increases coronary perfusion

Prinzmetal or variant angina

- Myocardial ischemia caused by Coronary artery spasm.
- Although such spasms typically occur on or near existing atherosclerotic plaques, a completely normal vessel can be affected (<1%)
- Patients present with nonexertional chest pain (at rest) with transient ST elevation on the ECG
- Typically responds to vasodilators such as nitroglycerin and calcium channel blockers.

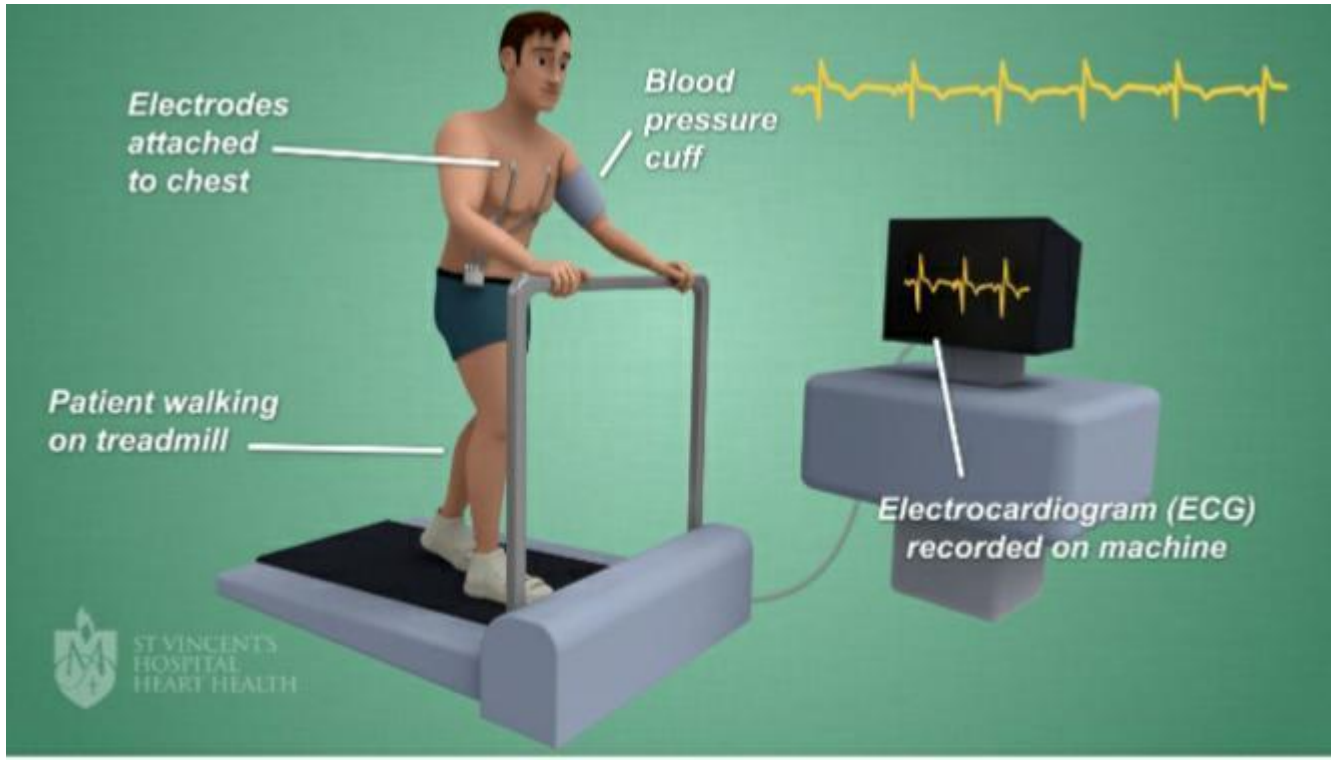
Unstable angina

- Unstable angina is associated with plaque disruption and superimposed thrombosis Considered to be an ACS in which there is myocardial ischemia without detectable myocardial necrosis (ie, cardiac biomarkers of myocardial necrosis -such as CK-MB, troponin, myoglobin-are not released into the circulation) It can be a harbinger of MI, portending complete vascular occlusion

Syndrome X

- The constellation of typical angina on effort, objective evidence of myocardial ischemia on cardiac stress testing, and normal coronary arteries on angiography Many of these patients are women and the mechanism of their symptoms is often unclear. This disorder is poorly understood; it carries a good prognosis but may respond to anti-anginal therapy

Cardiac stress testing



Myocardial Infarction

- Irreversible injury of ischemic myocytes first occurs in the subendocardial zone. This region is especially susceptible to ischemia because it is the last area to receive blood delivered by the epicardial vessels
- With more prolonged ischemia, a wavefront of cell death moves through other regions of the myocardium
- An infarct usually achieves its full extent (transmural infarct) within 3 to 6 hours; in the absence of intervention

Patterns of Infarction

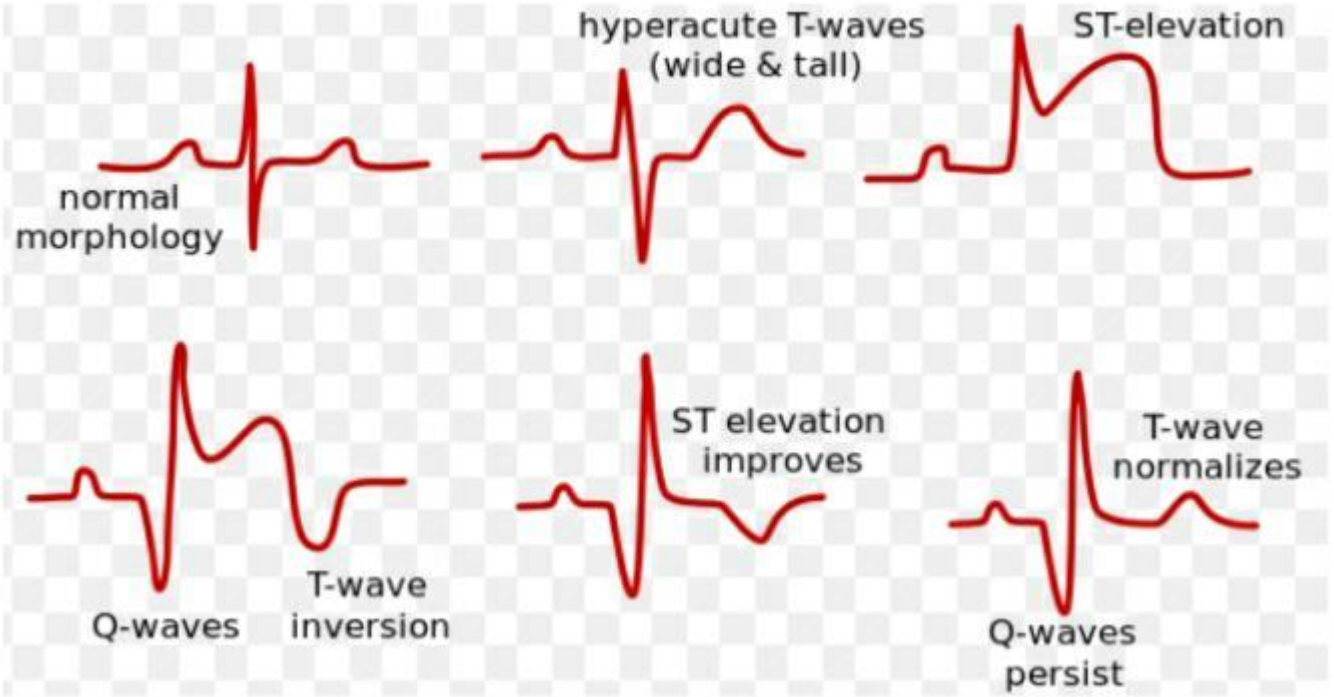
- Proximal LAD occlusion (40%-50%) : Results in infarction of the anterior wall of the left ventricle, the anterior two thirds of the ventricular septum, and most of the heart apex; more distal occlusion of the same vessel may affect only the apex
- Proximal circumflex (15%-20%): Causes necrosis of the lateral left ventricle
- Proximal RCA occlusion (30%-40%): Infarction of inferior wall with or without RV infarction

Clinical Features

- The classic MI is heralded by severe, crushing substernal chest pain (or pressure) that can radiate to the neck, jaw, epigastrium, or left arm.
- In contrast to angina pectoris, the associated pain typically lasts several minutes to hours, and is not relieved by nitroglycerin or rest
- 10% to 15% of patients, MI present with atypical presentation, and may even be entirely asymptomatic.

- Silent MI are particularly common in patients with underlying diabetes mellitus (in which autonomic neuropathy may prevent perception of pain) and in older adults
- Chest pain can be associated with other symptoms; Sweating, Nausea & vomiting, Dyspnea, Dizziness
- Pateints can present with any of the associated symptoms without chest pain (ATYPICAL CASES)
- Angor Animi; Patient's feeling of impeding death

ECG changes


normal morphology
hyperacute T-waves (wide & tall)
ST-elevation
Q-waves
T-wave inversion
ST elevation improves
T-wave normalizes
Q-waves persist

ECG Criteria for the diagnosis of acute STEMI

- New ST segment elevation in at least two anatomically contiguous leads

1. For leads V2-V3: 2 mm in men ≥40 years; 2.5 mm in men <40 years, or 1.5 mm in women regardless of age

2. For all other leads: 1 mm

- New LBB
- True dorsal MI

Cardiac enzymes

	onset	duration
Myoglobin	1-2 hour	1 day
TroponinT,I	3 hours	10 days
CPK(MB)	4 hours	3 days
Ast	6h	7 days
LDH	12 h	14 days

COMPLICATIONS OF ACUTE MI

Early complications: arrhythmia and HB,LVF.early pericarditis and tromboembolic complications.

LATE COMPLICATIONS: post MI angina,late pericarditis, CHF ,LV aneurysm,frozen shoulder , frozen chest,coplications of treatment.

PERICARDITIS

Early pericarditis: 2-3 days – chest pain when lying , relieved with sitting, pericardial rub.- treatment : NSAIDS.

Late pericarditis (Dresslers syndrome): fever, pleurisy,pericarditis ,possible effusion.

Treatment: NSAIDS,AND STEROIDS.

ECG in pericarditis

PERICARDITIS

1. Concave ST elevation
2. Diffuse changes
3. PR deprission,(specific)
4. Late dynamic changes

MI

convex ST

localized change

---

rapid changes.

Thank you

Prepared by :

Dr. Asmaa Alaa Abed

Definition of heart failure

- CHF occurs when the heart cannot generate sufficient output to meet the metabolic demands of the tissues, or can only do so at higher-than-normal filling pressures; in a minority of cases, heart failure is a consequence of greatly increased tissue demands, as in hyperthyroidism, or decreased oxygen carrying capacity, as in anemia *(high-output failure)*
- *Low output failure vs high output failure*

- Heart failure is not a single pathological diagnosis, but a clinical syndrome of group of signs and symptoms. Which caused by structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.

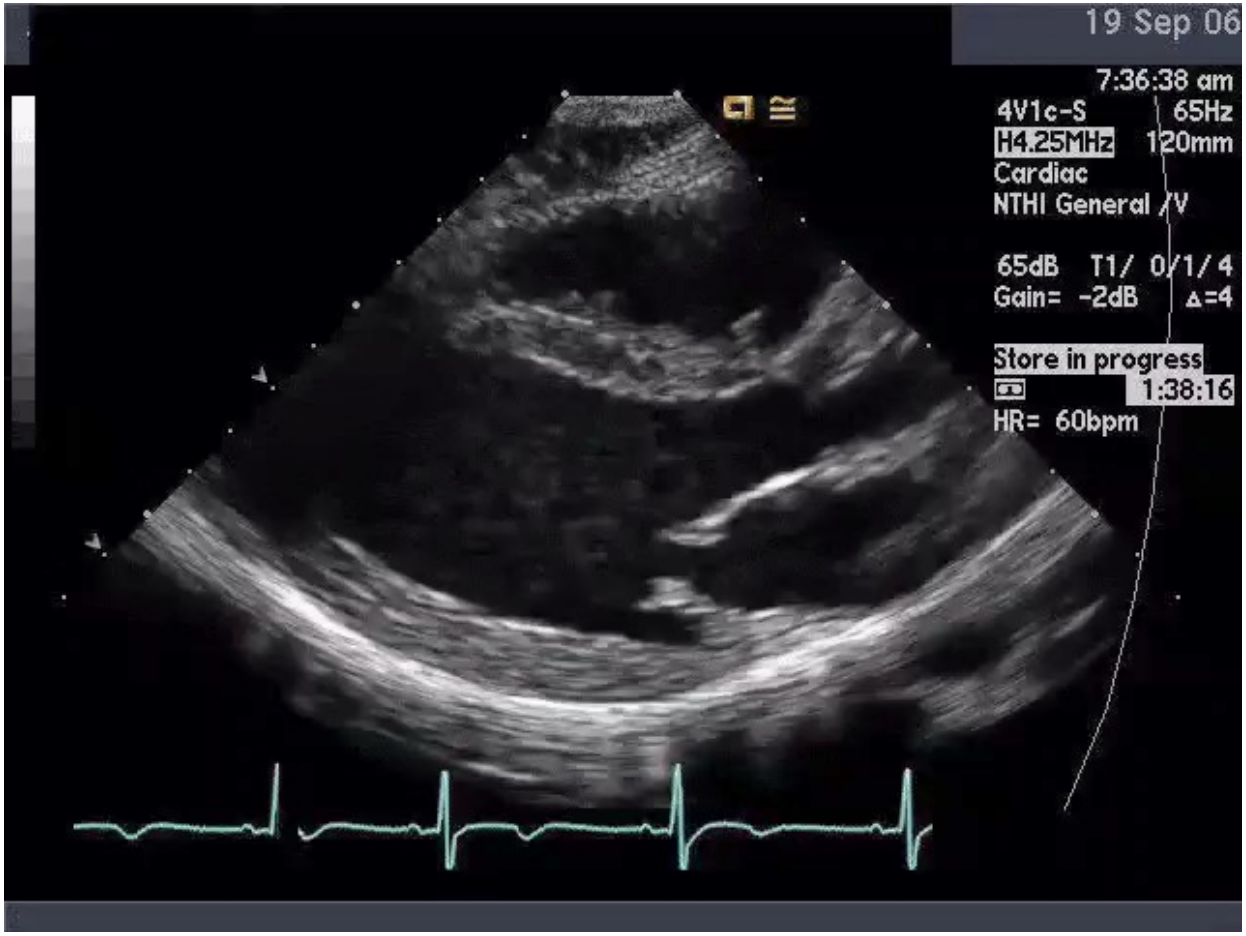
- Identification of the etiology of the underlying cardiac dysfunction is mandatory in the diagnosis of HF as the specific pathology can determine subsequent treatment.

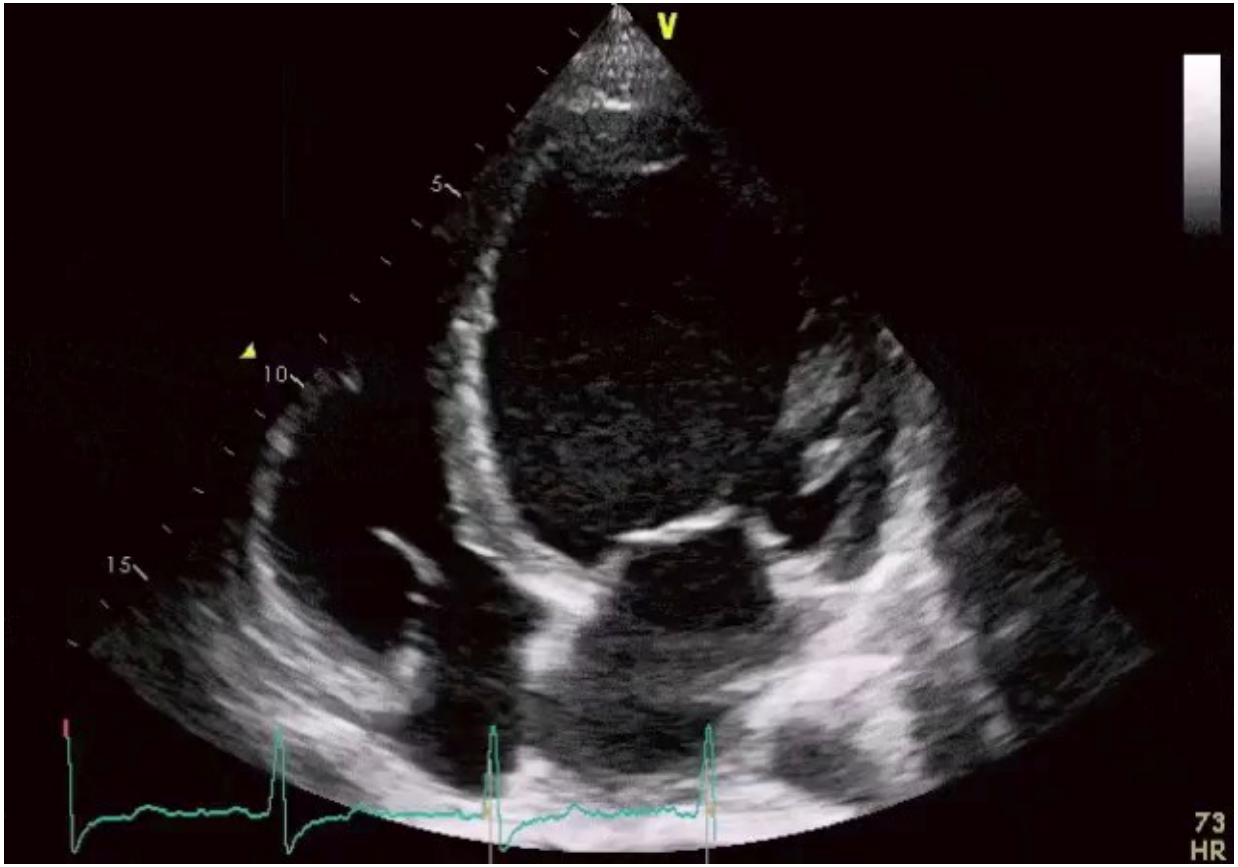
Classifications of heart failure

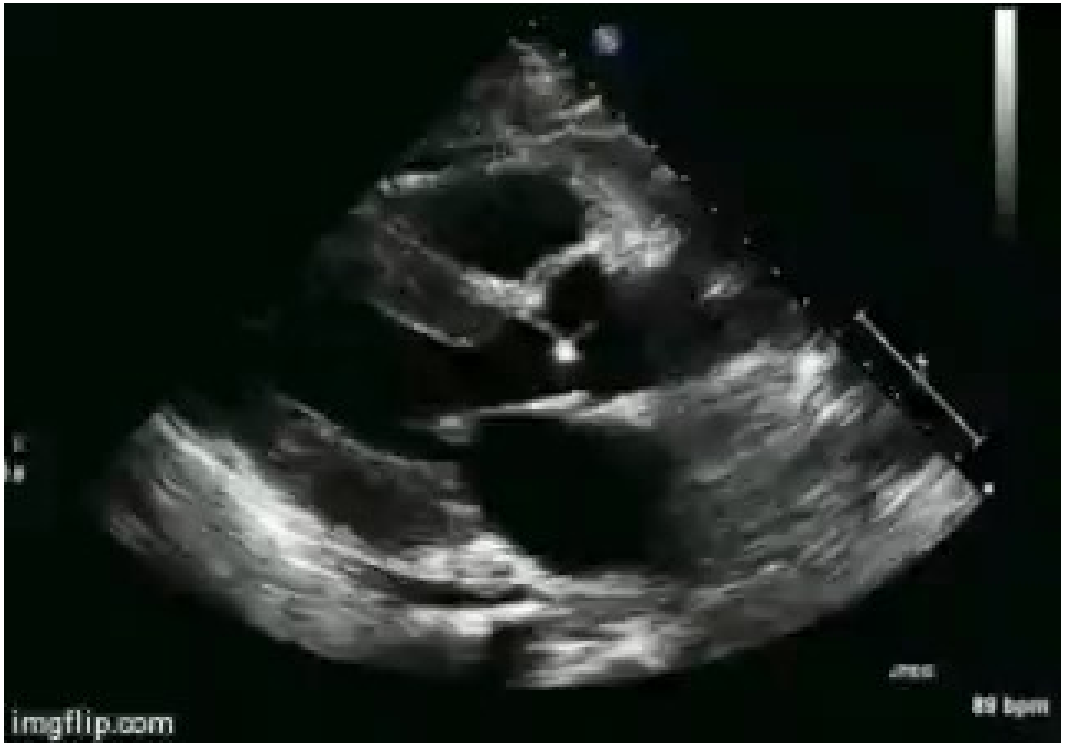
Right sided heart failure vs Left sided heart failure

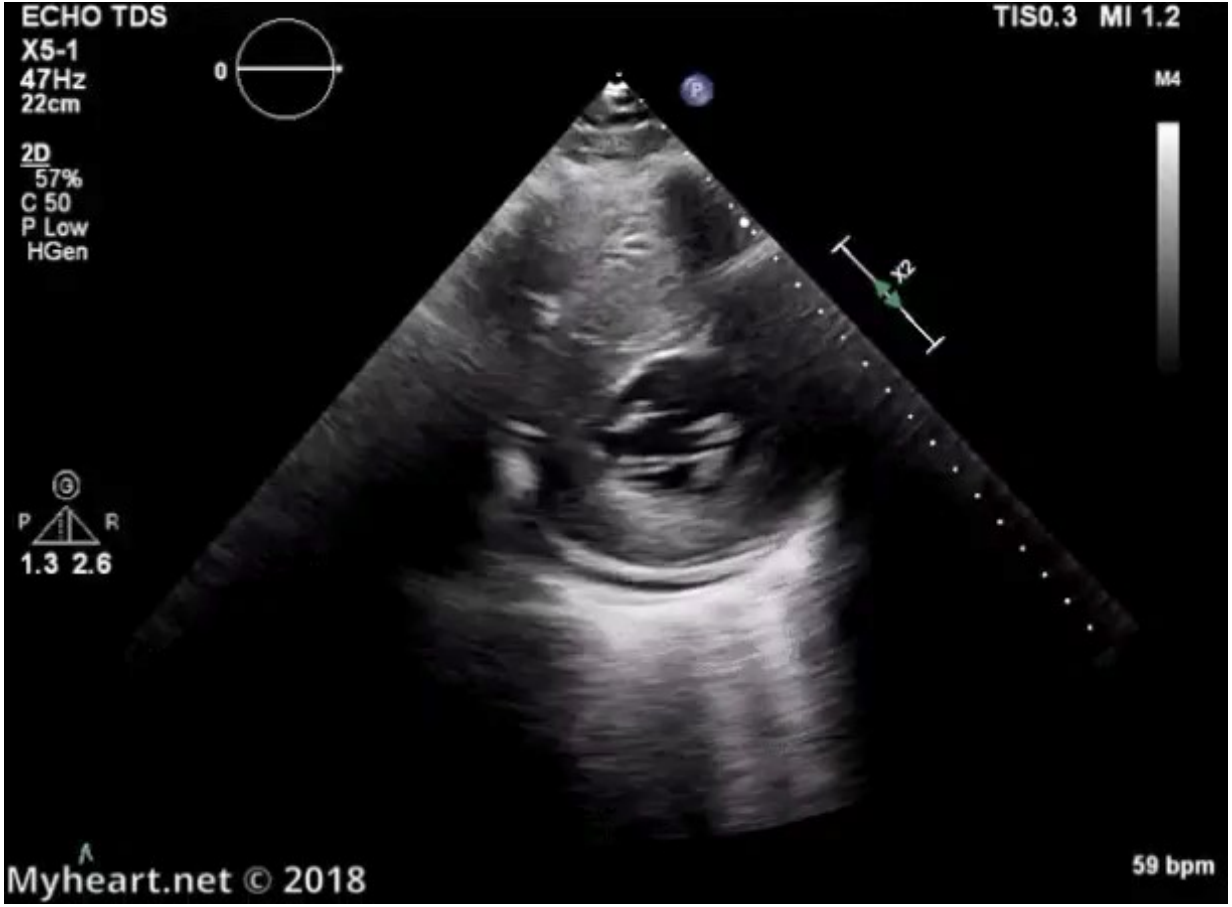
Left sided heart failure can be either Systolic HF (HFrEF , EF < 40%) or Diastolic HF (HFpEF , EF > 50%)

- **Systolic failure:** The left ventricle loses its ability to contract normally. The heart can't pump with enough force to push enough blood into circulation. This is also known as heart failure with reduced ejection, or HFrEF. When this occurs, the heart is pumping less than or equal to 40% EF. heart failure with mildly reduced ejection fraction (HFmrEF) is a newer concept. In this type of heart failure, the left ventricle pumps between 41% and 49% EF. They benefits to therapies similar than HFrEF.
- **Diastolic failure:** The left ventricle loses its ability to relax normally because the muscle has become stiff. The heart can't properly fill with blood during the resting period between each beat. This is also known as heart failure with preserved ejection, or HFpEF. When this occurs, the heart is pumping greater than or equal to 50%.


19 Sep 06
7:36:38 am
4V1c-S
65Hz
H4.25MHz
120mm
Cardiac
NTHI General /V
65dB T1/ 0/1/ 4
Gain= -2dB
Δ=4
Store in progress
1:38:16
HR= 60bpm


V
5
10
15
73
HR


imgflip.com
89 bpm


ECHO TDS
X5-1
47Hz
22cm
2D
57%
C 50
P Low
HGen
TIS0.3 MI 1.2
M4
X2
P R
1.3 2.6
Myheart.net © 2018
59 bpm

Compensation

How to elevate your cardiac output ?!!

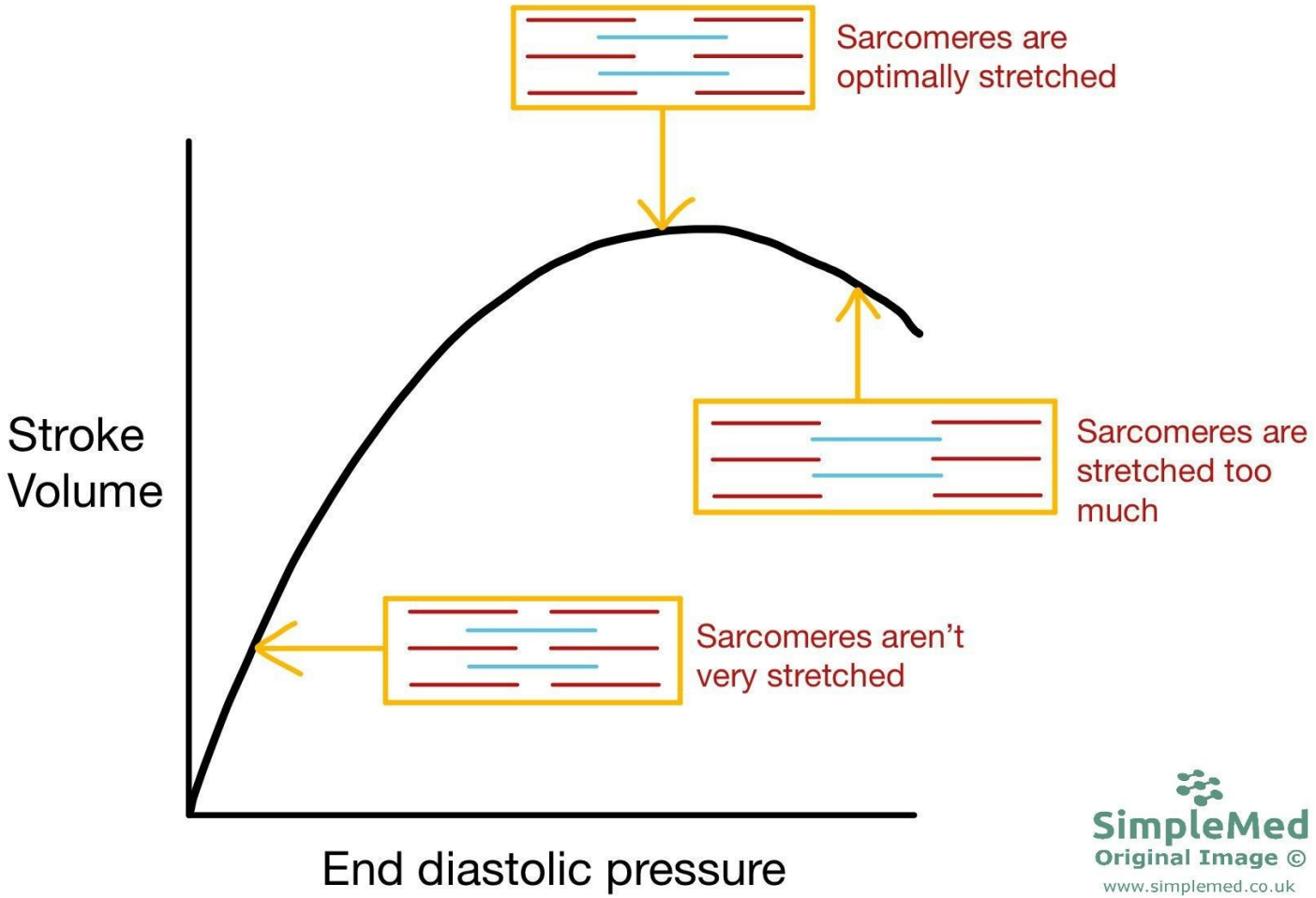
$$CO = SV \times HR$$

$$BP = CO \times TPR$$

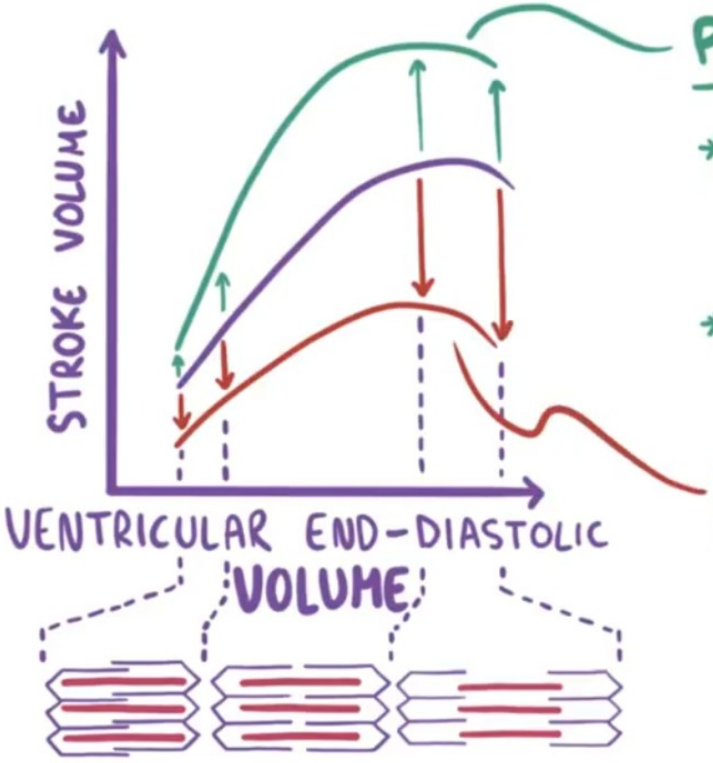
1. The Frank-Starling mechanism.

Increased end-diastolic filling volumes dilate the heart and cause increased cardiac myofiber stretching; these lengthened fibers contract more forcibly, thereby increasing cardiac output. If the dilated ventricle is able to maintain cardiac output by this means, the patient is said to be in compensated heart failure. However, ventricular dilation comes at the expense of increased wall tension and magnifies the oxygen requirements of an already-compromised myocardium. With time, the failing muscle is no longer able to propel sufficient blood to meet the needs of the body, and the patient develops decompensated heart failure.

Increase contractility with increase preload (end diastolic pressure) to some limit



FRANK STARLING RELATIONSHIP



POSITIVE INOTROPIC EFFECT

* ↑ STRENGTH of CONTRACTION & ↑ STROKE VOLUME
* e.g. — SYMPATHETIC NERVOUS SYSTEM
  — DIGOXIN

NEGATIVE INOTROPIC EFFECT

* ↓ STRENGTH of CONTRACTION & ↓ STROKE VOLUME
* e.g. β-BLOCKERS

2. Activation of neurohumoral systems:

- **sympathetic nervous system activation**

Release of the neurotransmitter norepinephrine by the autonomic nervous system increases heart rate and augments myocardial contractility and increase vascular resistance to elevate systemic blood pressure and improve body perfusion.

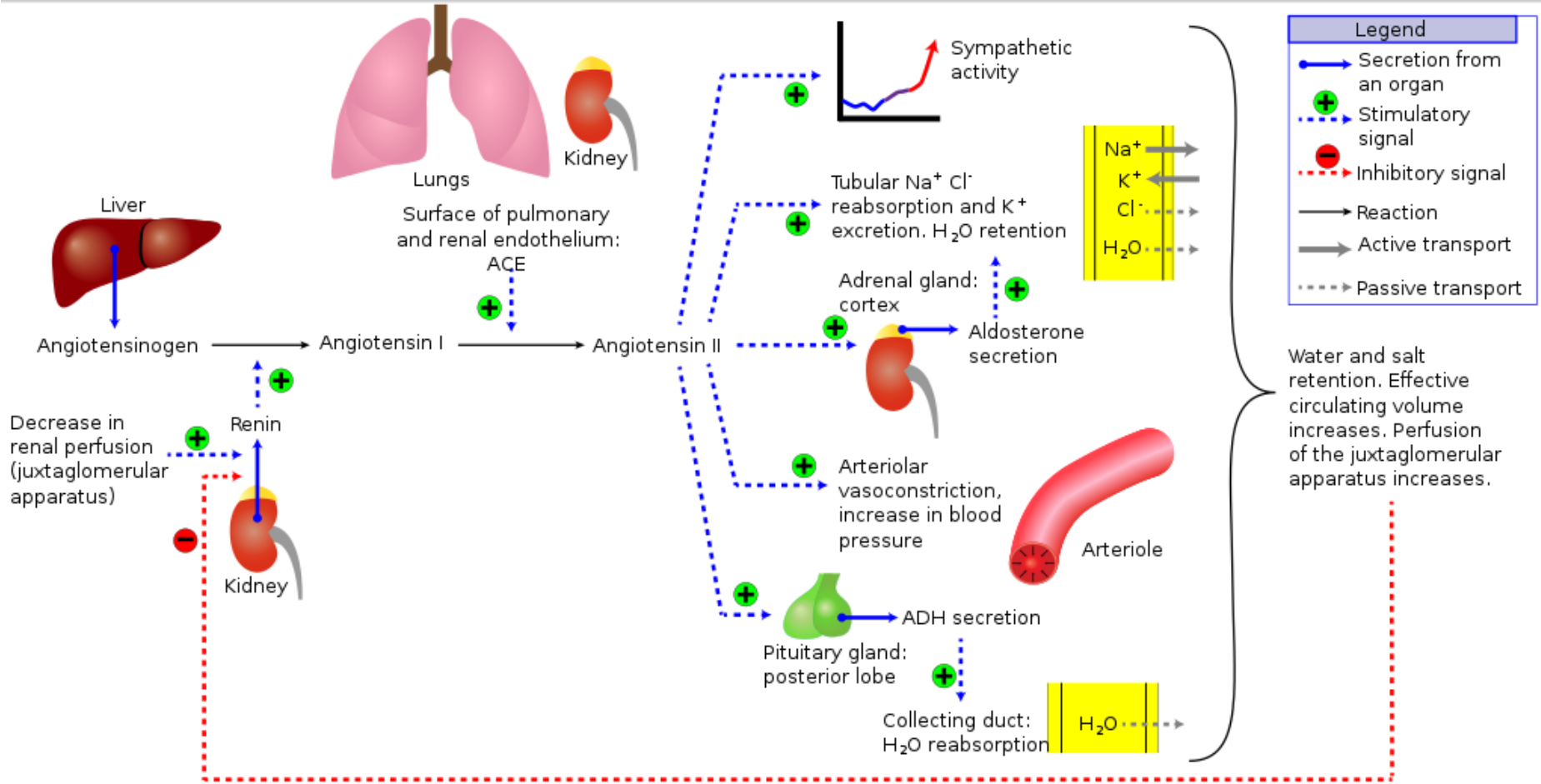
- **Activation of the renin-angiotensin-aldosterone system RAAS**

spurs water and salt retention (augmenting circulatory volume - preload) and increases vascular tone.

- **Release of atrial natriuretic peptide acts to balance**

the renin-angiotensin-aldosterone system through diuresis and vascular smooth muscle relaxation.

Renin–angiotensin–aldosterone system



Natriuretic peptides

- ANP is synthesized and secreted by cardiac muscle cells in the walls of the atria in the heart. These cells contain volume receptors which respond to increased stretching of the atrial wall due to increased atrial blood volume.

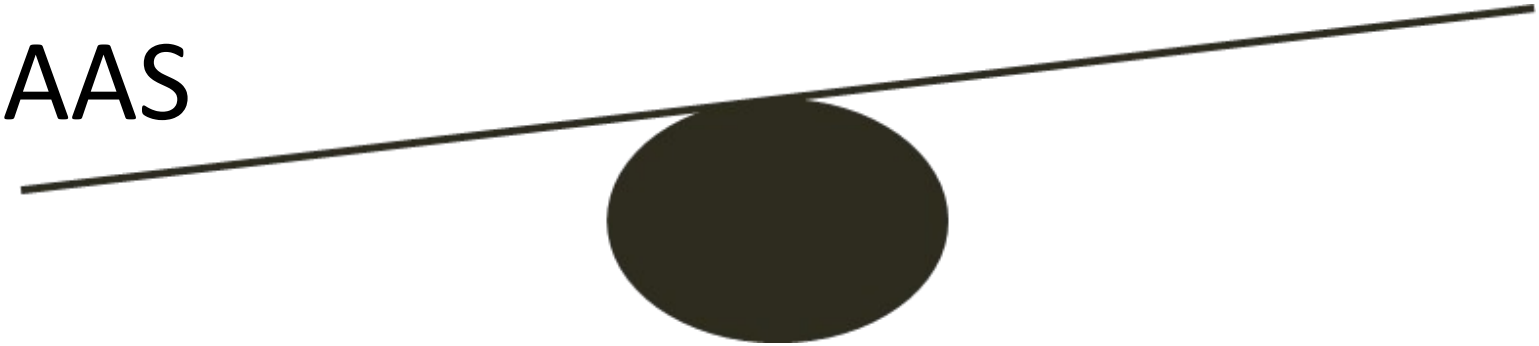
- Both rise with volume/pressure overload
- Both counter effects of RAAS system
  - ✓ increases renal sodium loss -> They decrease preload – natriuresis (decrease extracellular fluids)
  - ✓ Relaxes vascular smooth muscle in arterioles and venules -> decrease afterload
  - ✓ Reduces aldosterone secretion from adrenal cortex.

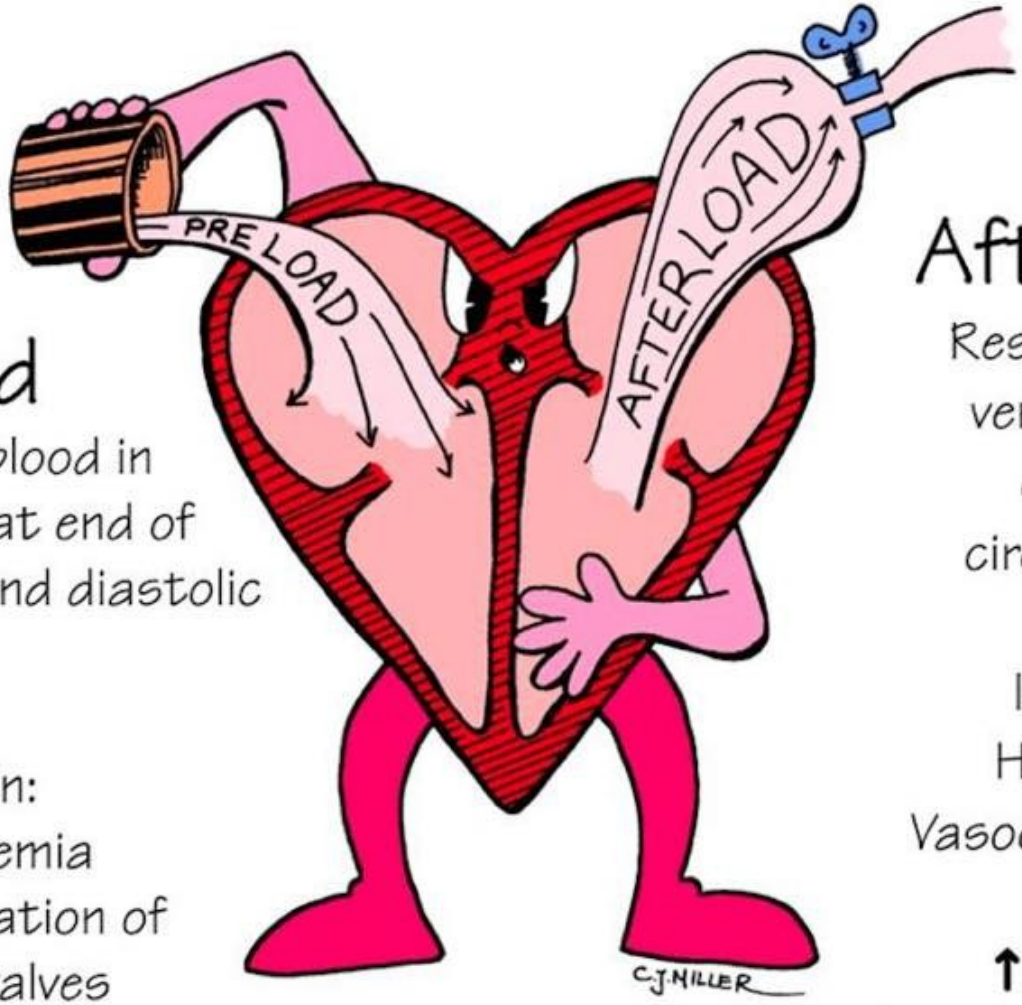
- Brain natriuretic peptide (BNP) – a misnomer; it is secreted by cardiac muscle cells in the heart ventricles – is similar to ANP in its effect. It acts via the same receptors as ANP does, but with 10-fold lower affinity than ANP. The biological half-life of BNP, however, is twice as long as that of ANP, and that of NT-proBNP is even longer, making these peptides better choices than ANP for diagnostic blood testing.

- Modulation of the effects of ANP is achieved through gradual degradation of the peptide by the enzyme neutral endopeptidase (NEP) – also called neprilysin . Recently, Neprilysin inhibitors have been developed, such as Sacubitril and Sacubitril/valsartan (Entresto). They may be clinically useful in treating patients in heart failure with reduced ejection fraction .

ANP/BNP

RAAS





Preload

Volume of blood in ventricles at end of diastole (end diastolic pressure)

Increased in:

- Hypervolemia
- Regurgitation of cardiac valves
- Heart Failure

Afterload

Resistance left ventricle must overcome to circulate blood

Increased in:

Hypertension

Vasoconstriction

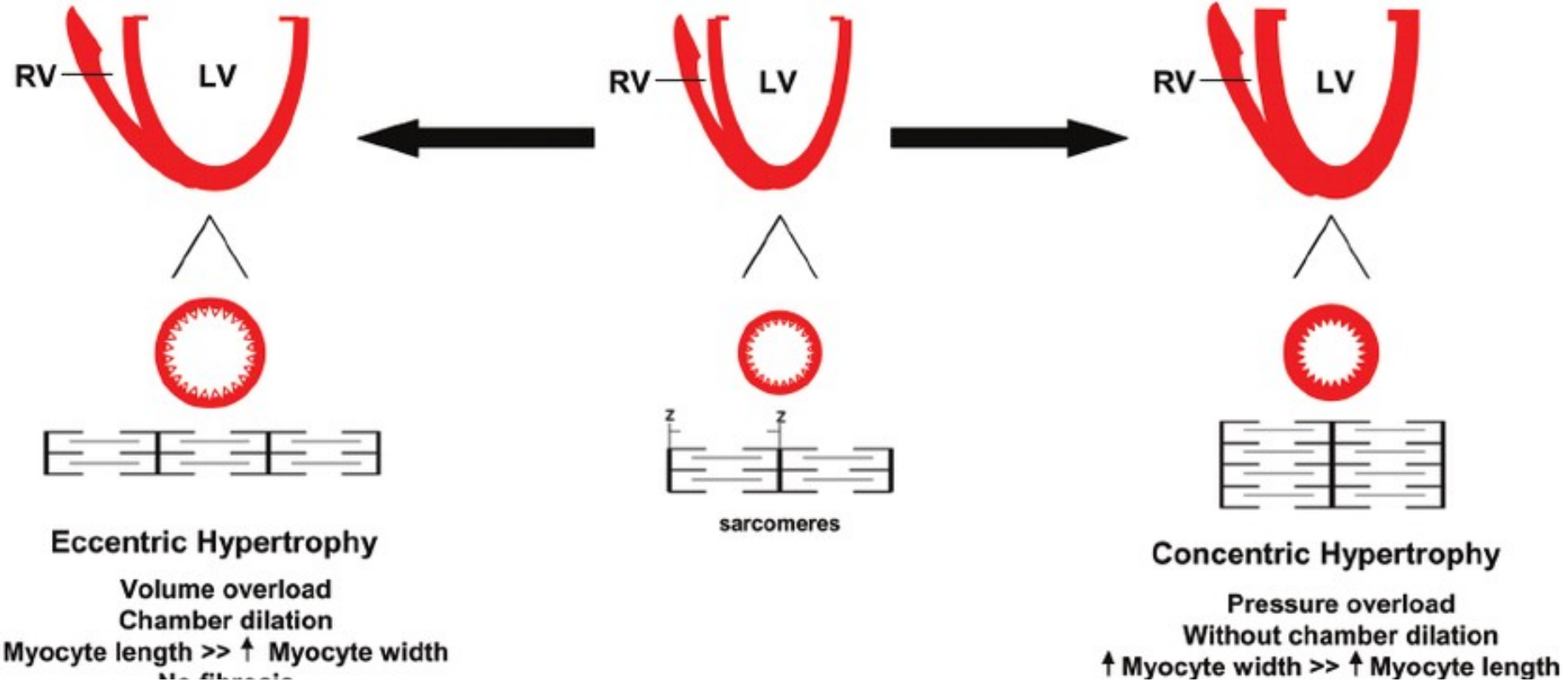
↑ Afterload = ↑ Cardiac workload

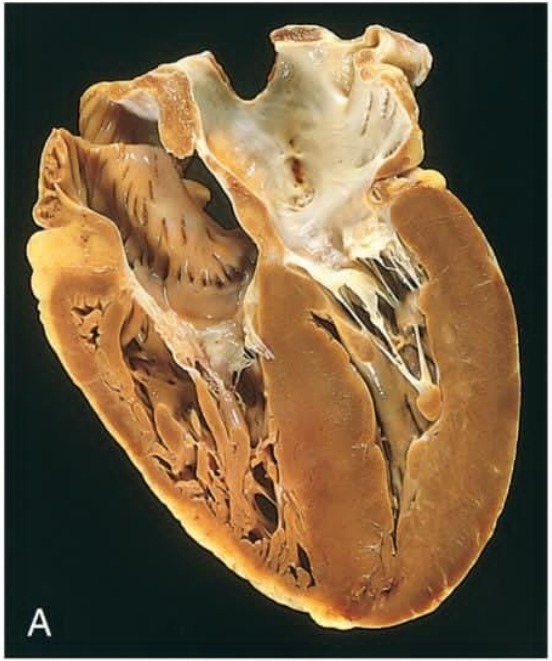
3. Myocardial structural changes

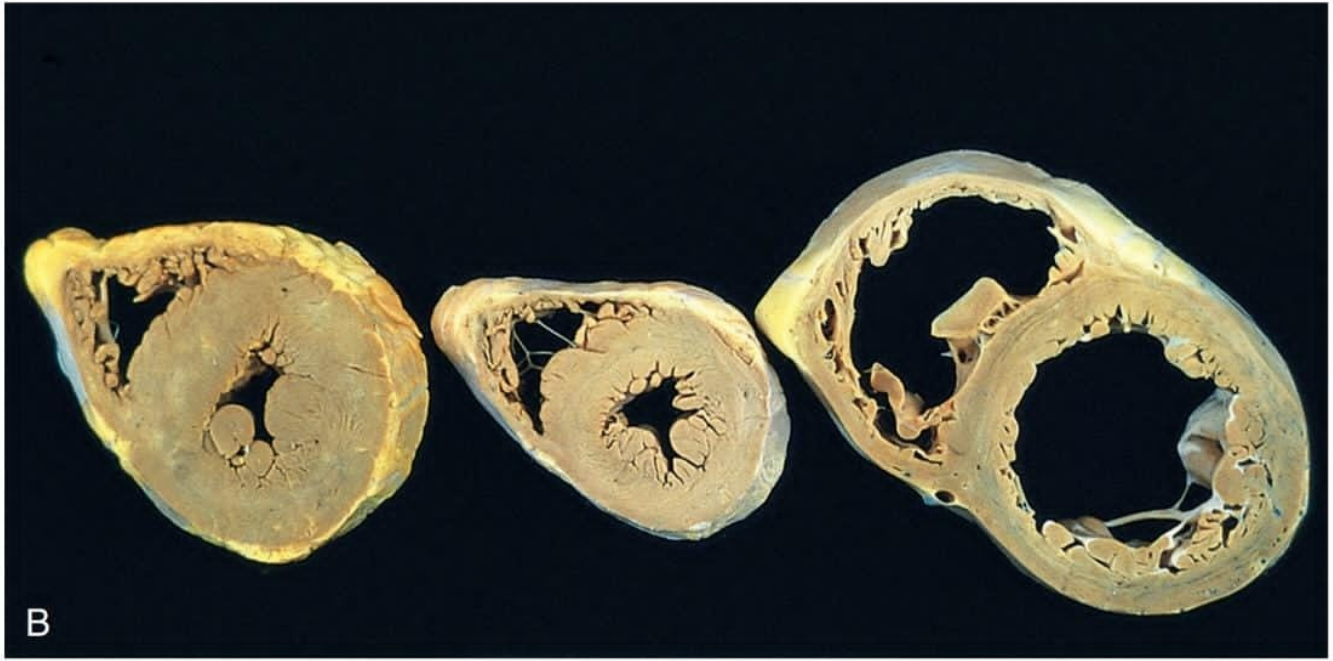
including augmented muscle mass. Cardiac myocytes adapt to increased work-load by assembling new sarcomeres, a change that is accompanied by myocyte enlargement (hypertrophy).

• In pressure overload states (e.g., hypertension or valvular stenosis), new sarcomeres tend to be added parallel to the long axis of the myocytes, adjacent to existing sarcomeres. The growing muscle fiber diameter thus results in **concentric hypertroph**y—the ventricular wall thickness increases without an increase in the size of the chamber.

• In volume overload states (e.g., valvular regurgitation or shunts), the new sarcomeres are added in series with existing sarcomeres, so that the muscle fiber length increases – **eccentric hypertrophy** .Consequently, the ventricle tends to dilate, and the resulting wall thickness can be increased, normal, or decreased; thus, heart weight —rather than wall thickness—is the best measure of hypertrophy in volume-overloaded hearts.

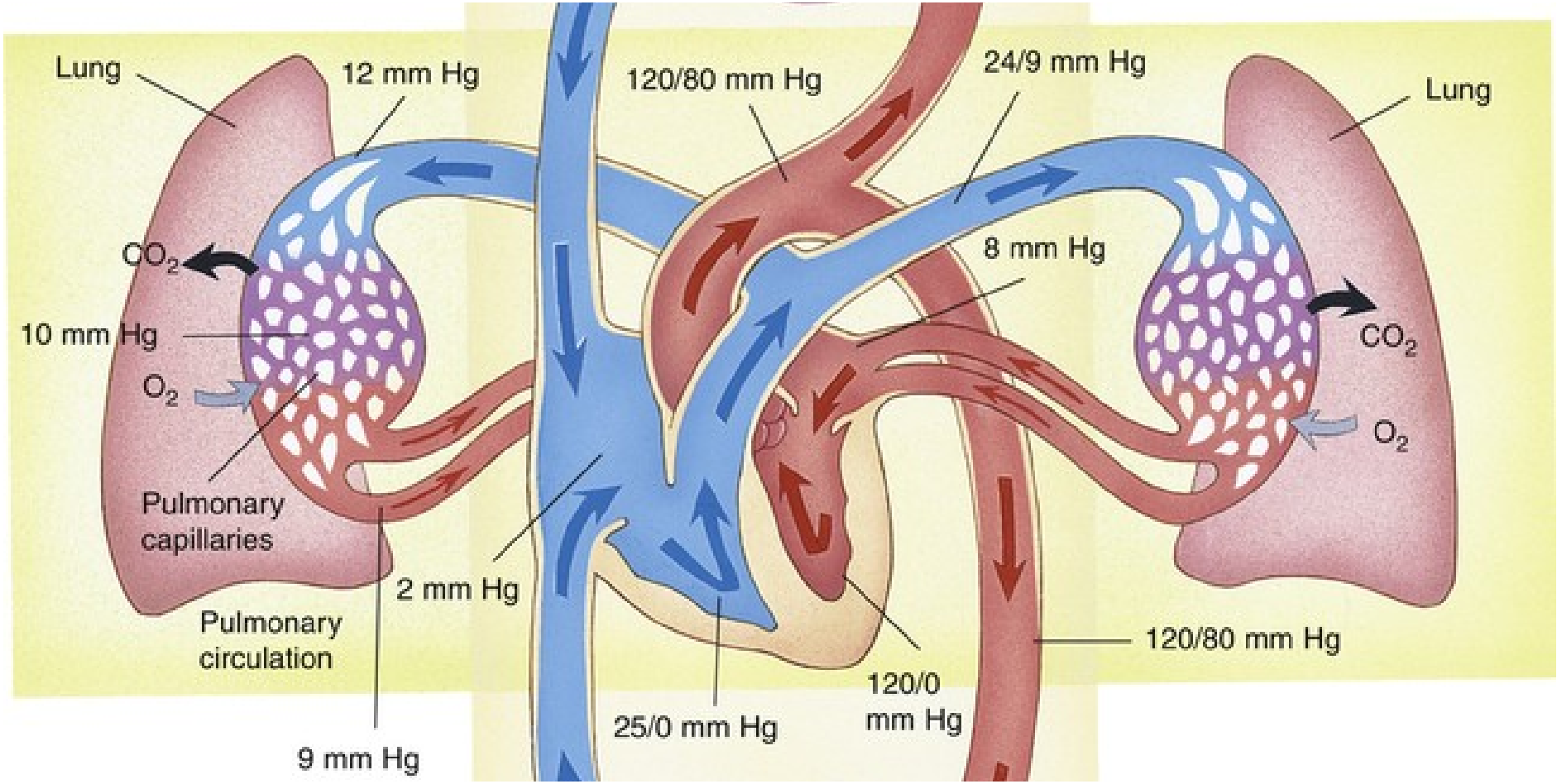

RV
LV
RV
LV
RV
LV
z
z
sarcomeres
Eccentric Hypertrophy
Volume overload
Chamber dilation
↑ Myocyte length >> ↑ Myocyte width
Concentric Hypertrophy
Pressure overload
Without chamber dilation
↑ Myocyte width >> ↑ Myocyte length





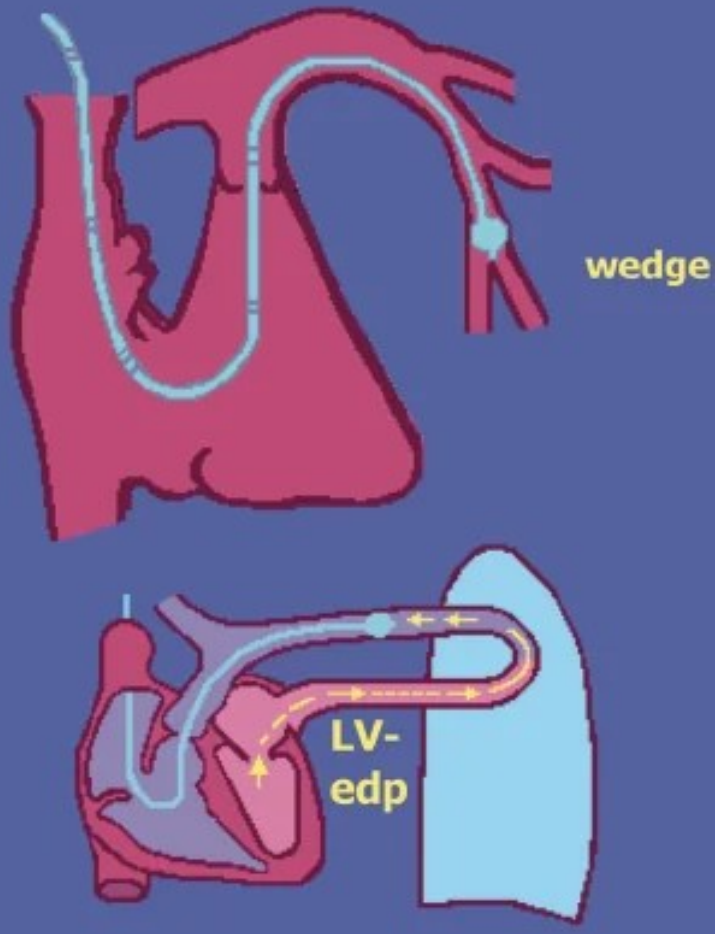
Compensatory hypertrophy comes at a cost. The oxygen requirements of hypertrophic myocardium are amplified owing to increased myocardial cell mass. Because the myocardial capillary bed does not expand in step with the increased myocardial oxygen demands, the myocardium becomes vulnerable to ischemic injury

Signs and Symptoms of HF


Lung
12 mm Hg
120/80 mm Hg
24/9 mm Hg
Lung
CO_2
8 mm Hg
10 mm Hg
CO_2
O_2
O_2
Pulmonary capillaries
2 mm Hg
Pulmonary circulation
120/80 mm Hg
120/0 mm Hg
25/0 mm Hg
9 mm Hg

Pulmonary Artery "Wedge" Pressure

- "PAW" or "PCW "pulmonary artery or capillary wedge pressure is measured by allowing a catheter to "wedge" in the lung bed
- The wedged catheter cuts off PA flow and the end hole lumen measures pressures through the capillary bed to the LA.
- PCW mean = LA mean = LVEDP



Signs and Symptoms of left sided HF

Breathlessness, a cardinal symptom of left ventricular (LV) failure, may manifest with progressively increasing severity as the following:

- **Exertional dyspnea**
- **Orthopnea**
- **Paroxysmal nocturnal dyspnea**
- **Dyspnea at rest**
- **Acute pulmonary edema**

Signs :

- **Bilateral basal crepitation**
- **Tachycardia**
- **Hypotension**
- **Gallop rhythm (S3 or S4)**

ORTHOPNEA

- Shortness of breath when lying down (recumbent position)
- Relieved by sitting up or elevation of head with pillows
- Occurs within 1-2 minutes after lying down
- Examples : Congestive cardiac failure (CCF), asthma, bilateral paralysis of diaphragm

MECHANISM OF ORTHOPNEA

Lying down / Horizontal position

↓

Redistribution of blood volume from lower extremities to the heart (increased venous return)

↓

In left ventricular failure, not able to pump out extra volume of blood

↓

Backflow of blood to the lung

↓

Pulmonary congestion

↓

Dyspnea

Diaphragm paralysis or lung collapse

↓

Elevated diaphragm

↓

↓ vital capacity → Dyspnea

PAROXYSMAL NOCTURNAL DYSPNEA

- Shortness of breath which occur at night and makes the patient wake up from sleep
  - Occur usually 1-2 hours after sleep
  - Shorter duration of dyspnea (10-30 min)
  - Example : Left sided failure / Cardiac asthma

MECHANISM OF PND

Due to gradual reabsorption of lower extremity interstitial edema into the circulation

↓

↑ intravascular blood volume

↓

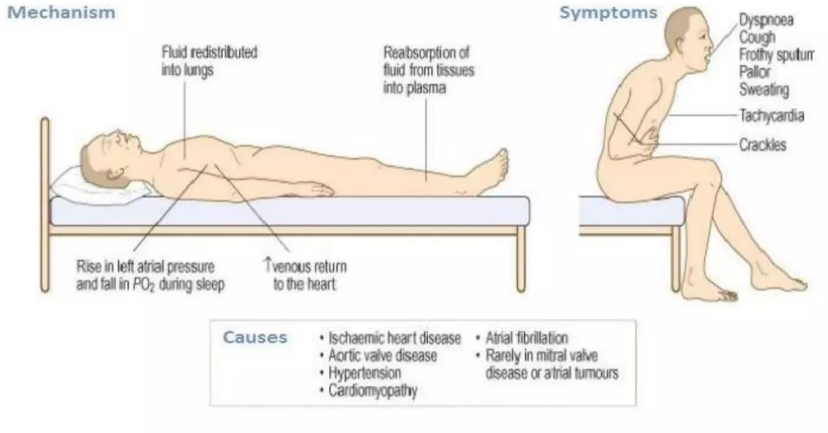
↑ venous return to the heart and lung

↓

Pulmonary congestion

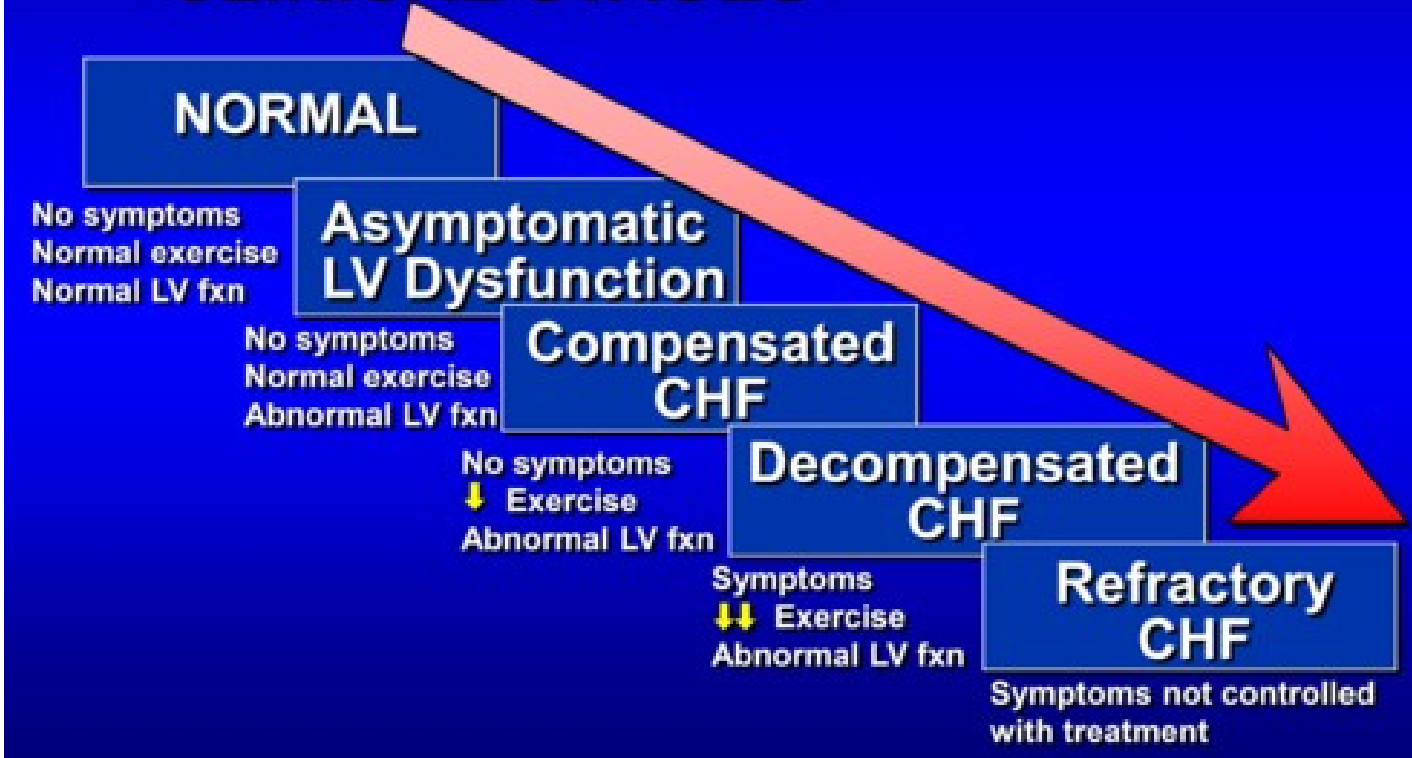
↓

Dyspnea



American Heart Association®
Fighting Heart Disease and Stroke

EVOLUTION OF CLINICAL STAGES

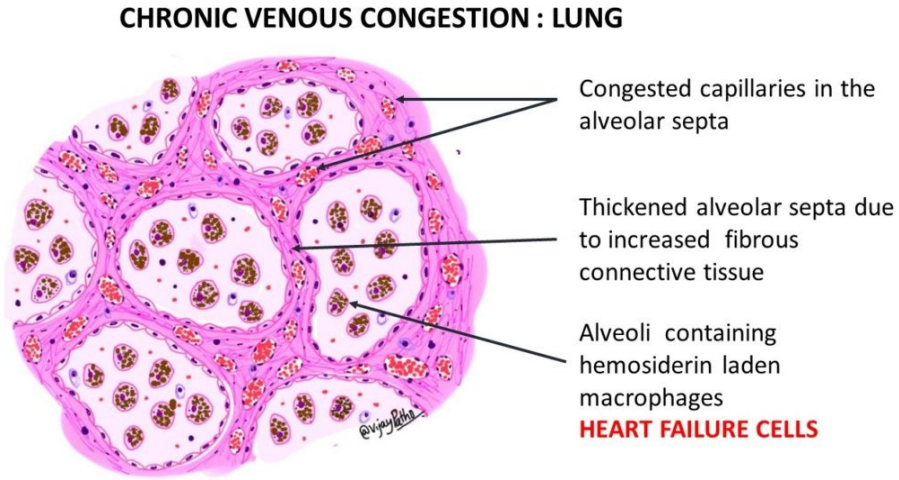


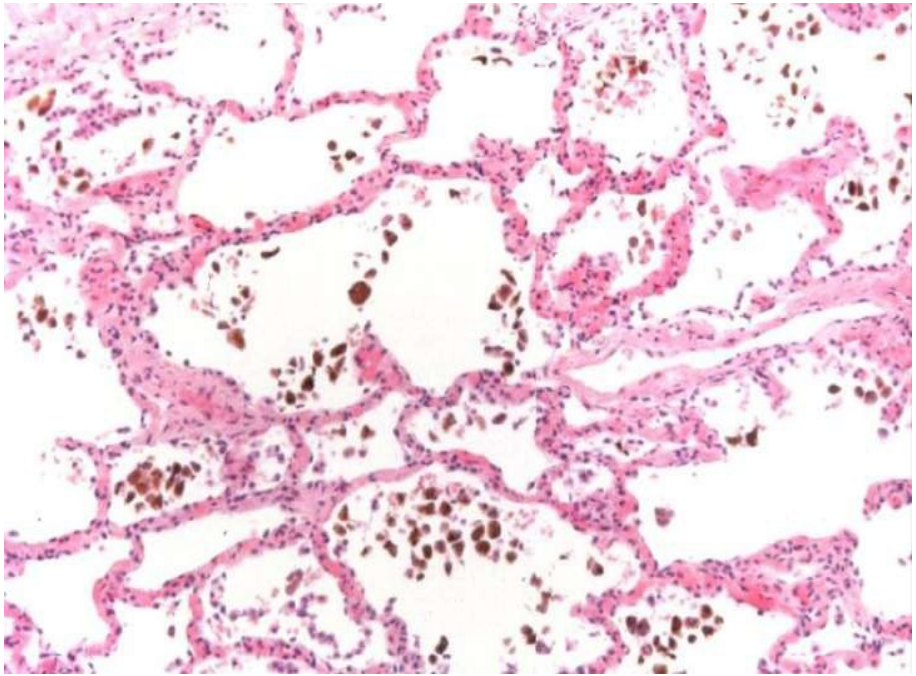
NYHA functional classification of HF

Class I (mild)	No limitation on physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea (shortness of breath)
Class II (mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea
Class III (moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnoea
Class IV (severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased

Lung Findings

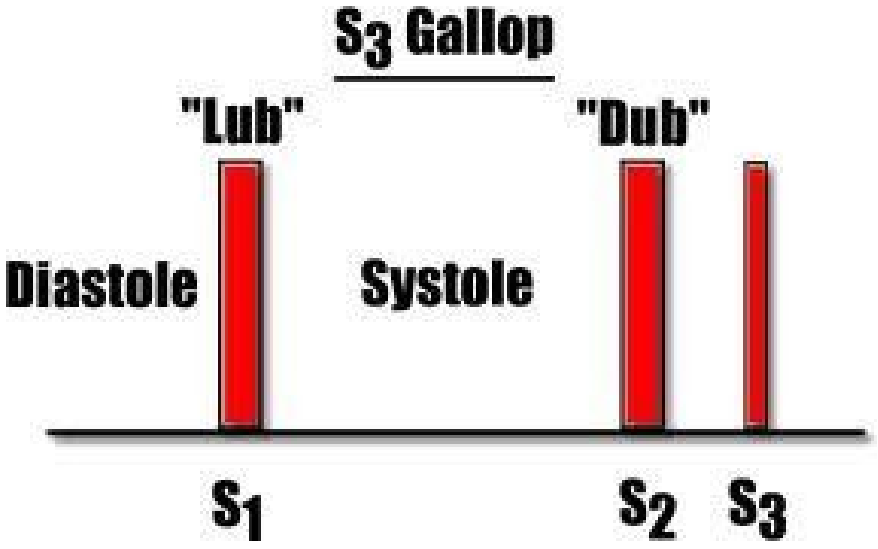
- Heart failure cells
- Hemosiderin (iron) laden macrophages
- Brown pigment in macrophages

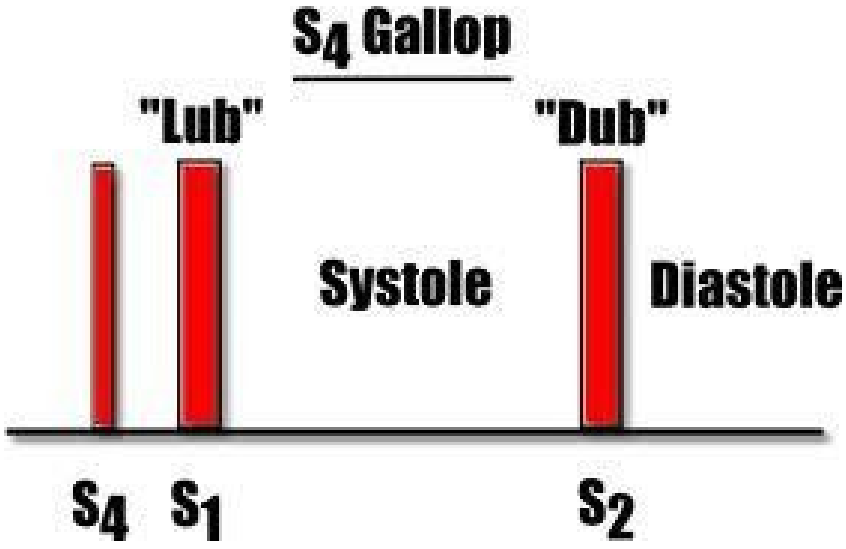




S3 vs. S4 heart sound(s):

S3-"ventricular gallop"	S4-"atrial gallop"
Occurs in early diastole	Occurs in late diastole
Occurs during passive LV filling	Occurs during active LV filling
May be physiologic at times	Almost always pathological
Requires a very compliant LV	Requires a non-compliant LV
Can be a sign of systolic CHF	Can be a sign of diastolic CHF
Associated with mitral & aortic regurgitation	Associated with aortic stenosis

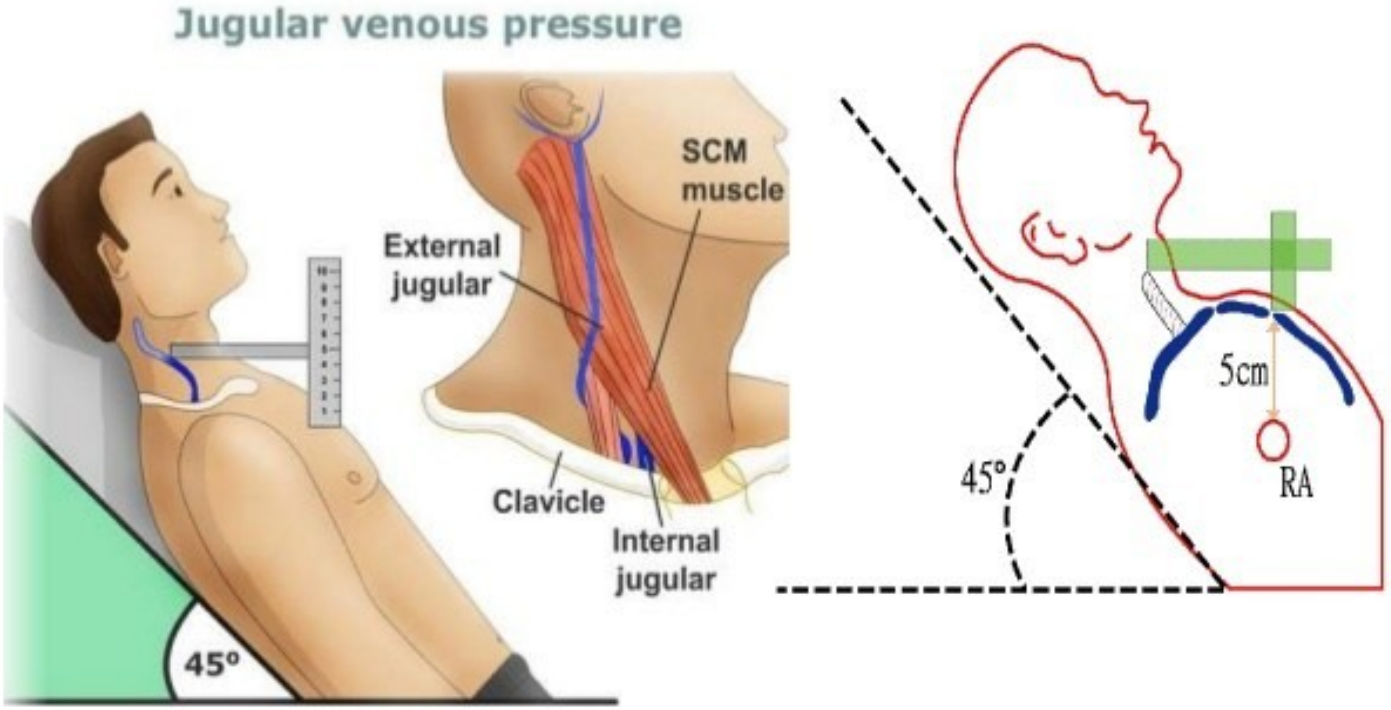

S3 Gallop
"Lub"
"Dub"
Diastole
Systole
S1
S2
S3

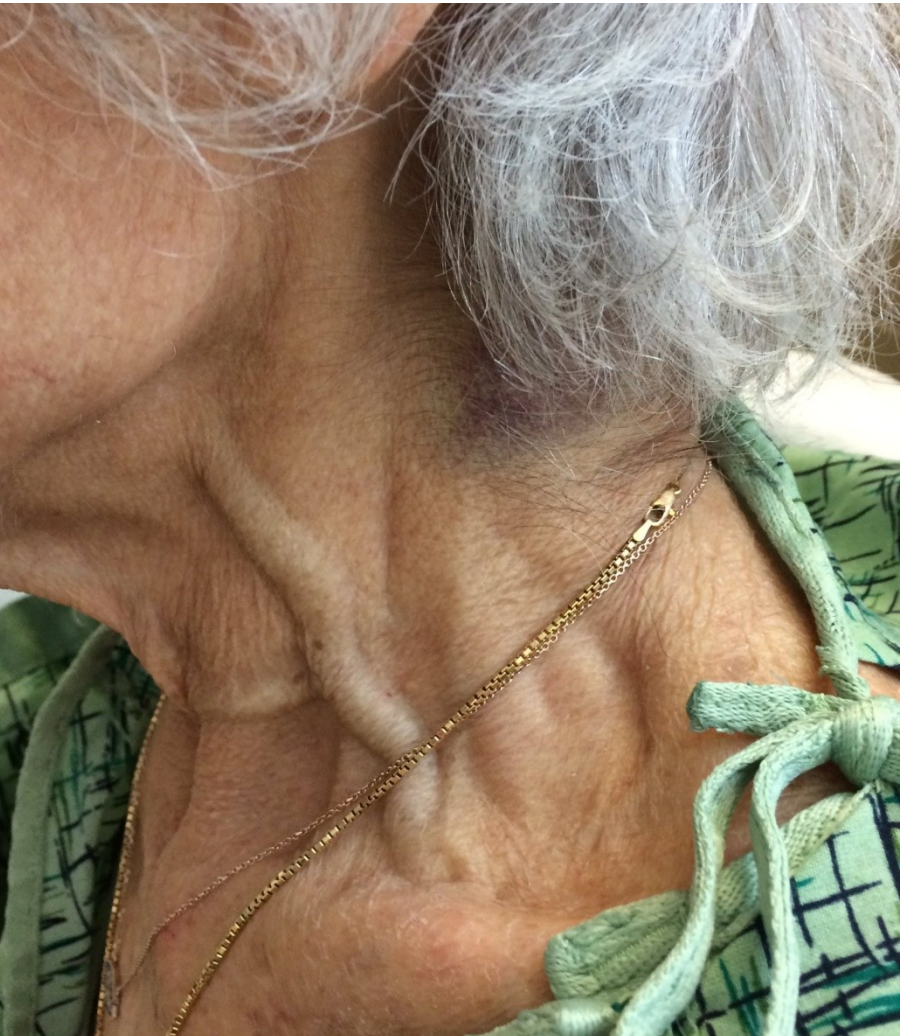

S4 Gallop
"Lub"
"Dub"
Systole
Diastole
S4
S1
S2

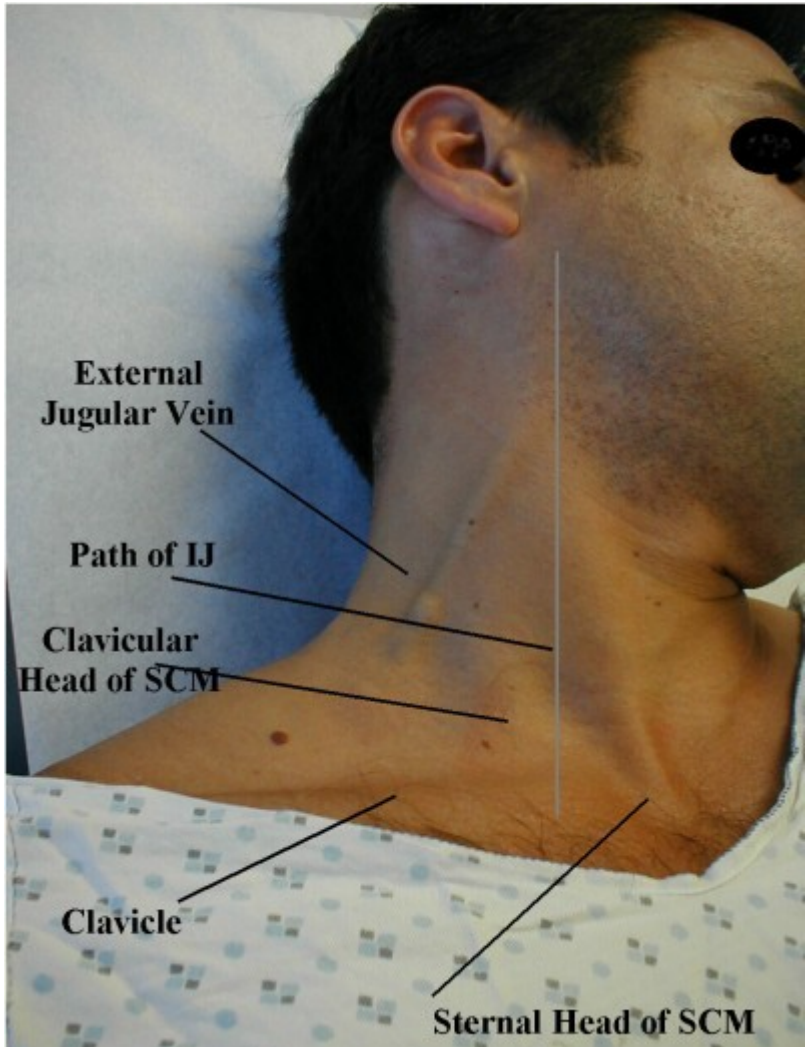
Signs and Symptoms of right sided HF

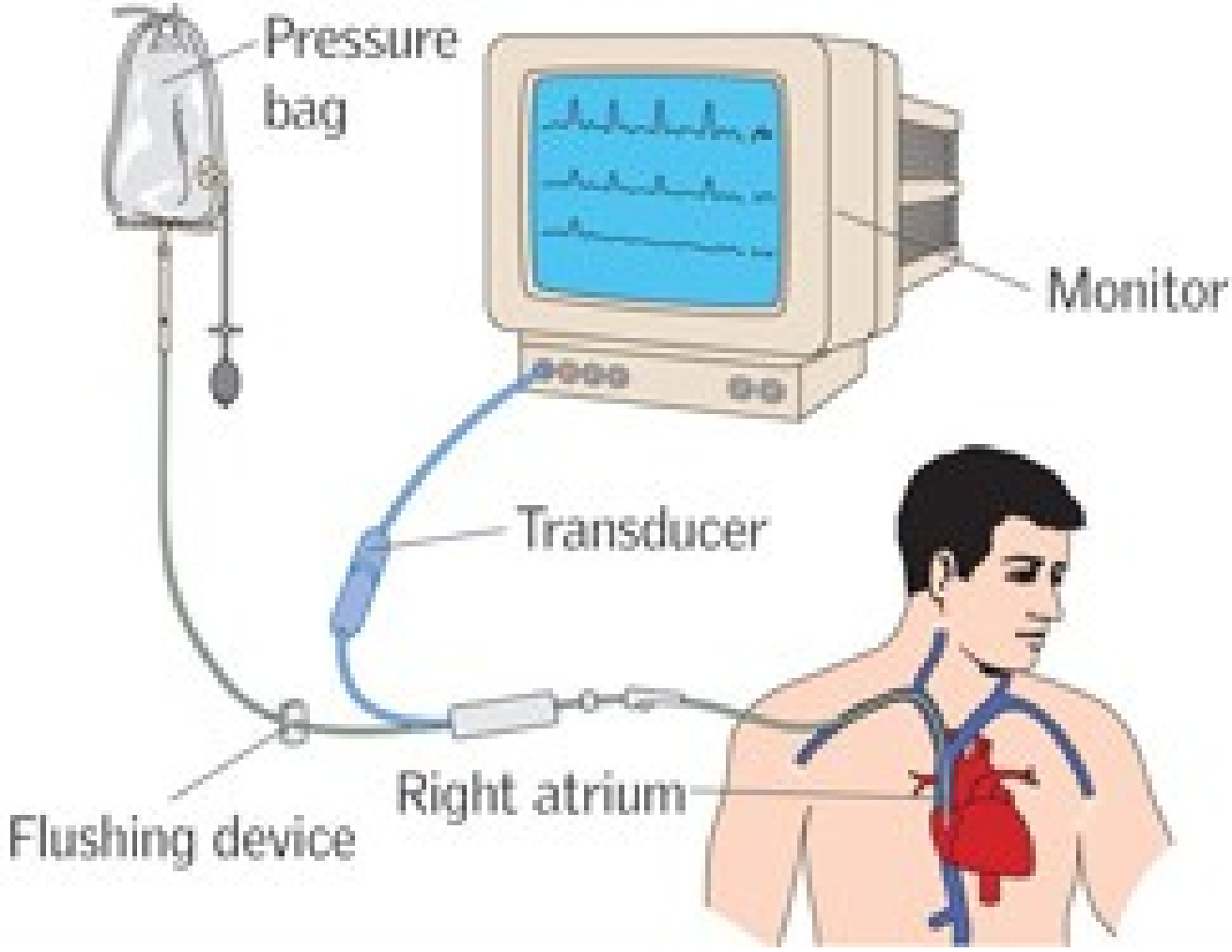
- Lower extremity pitting edema
- Elevated jugular venous pressure > 8 cm H2O (normal 6-8cmH2O)
- Liver congestion (rarely can cause cirrhosis)
  - Nutmeg liver
- Hepatojugular Reflux
  - Pressure on abdomen raises JVP 1-3cm normally
  - With failing RV, JVP increase greater than 3cm H2O

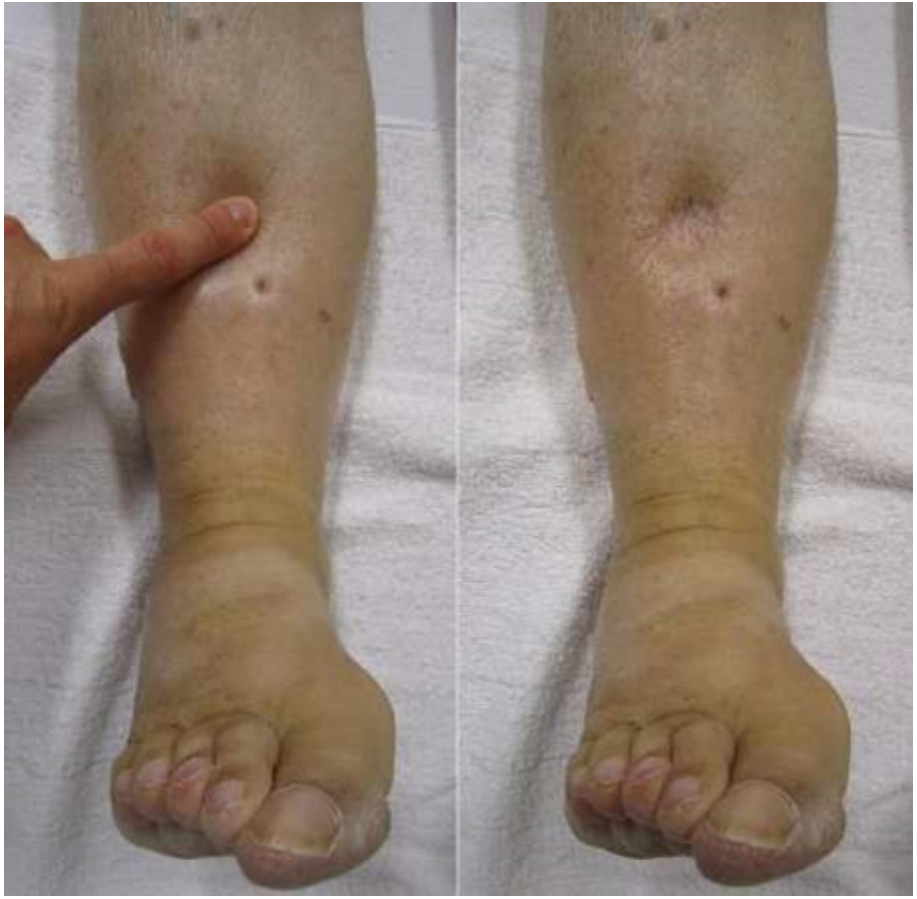
NON INVASIVE HAEMODYNAMIC ASSESSMENT

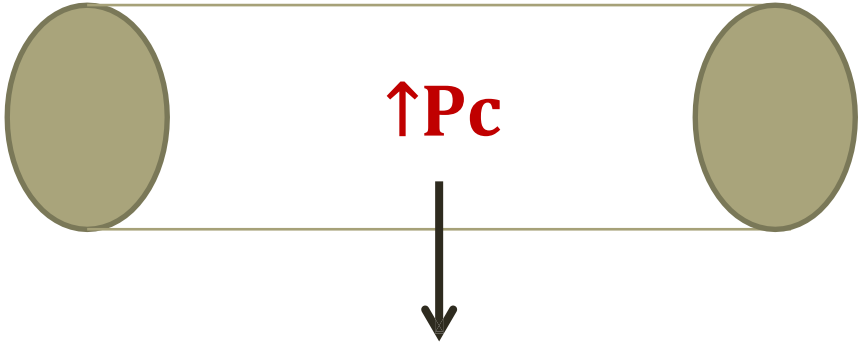


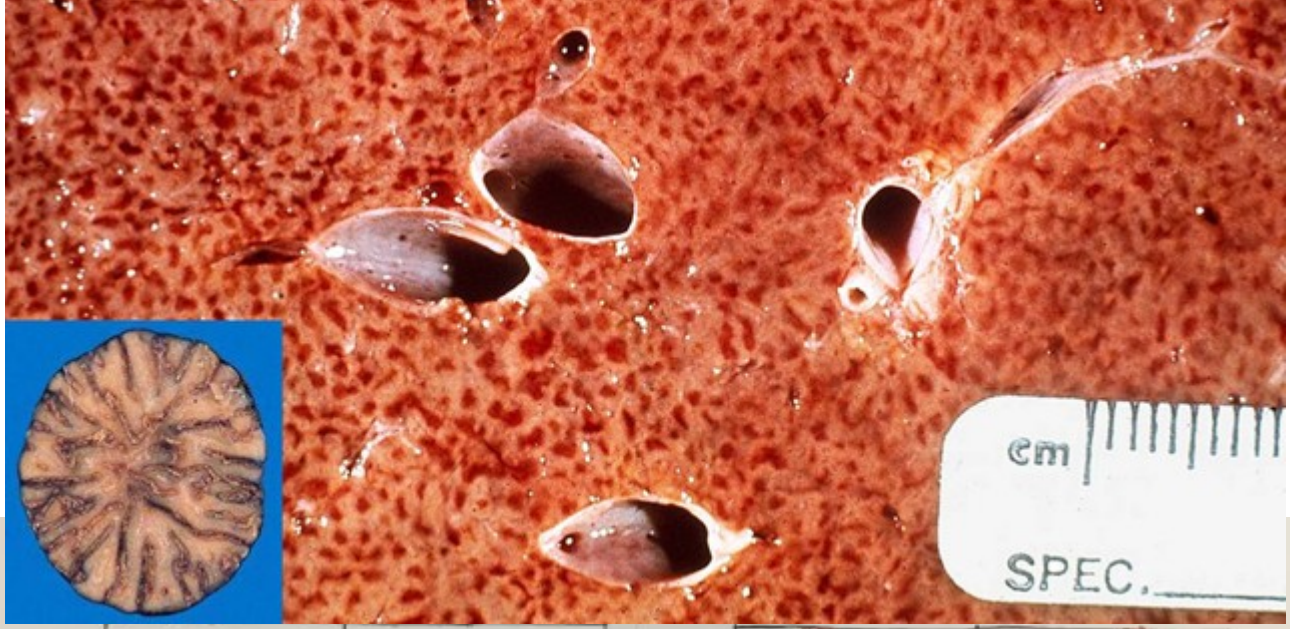


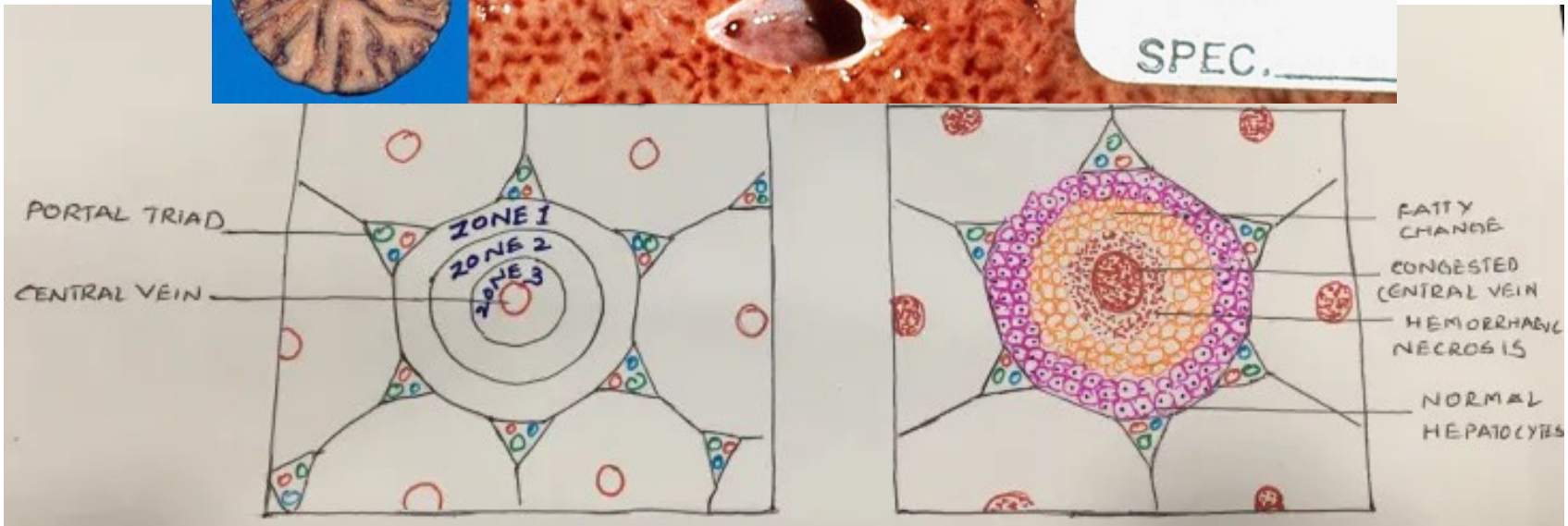

External
Jugular Vein
Path of IJ
Clavicular
Head of SCM
Clavicle
Sternal Head of SCM


Pressure bag
Monitor
Transducer
Right atrium
Flushing device



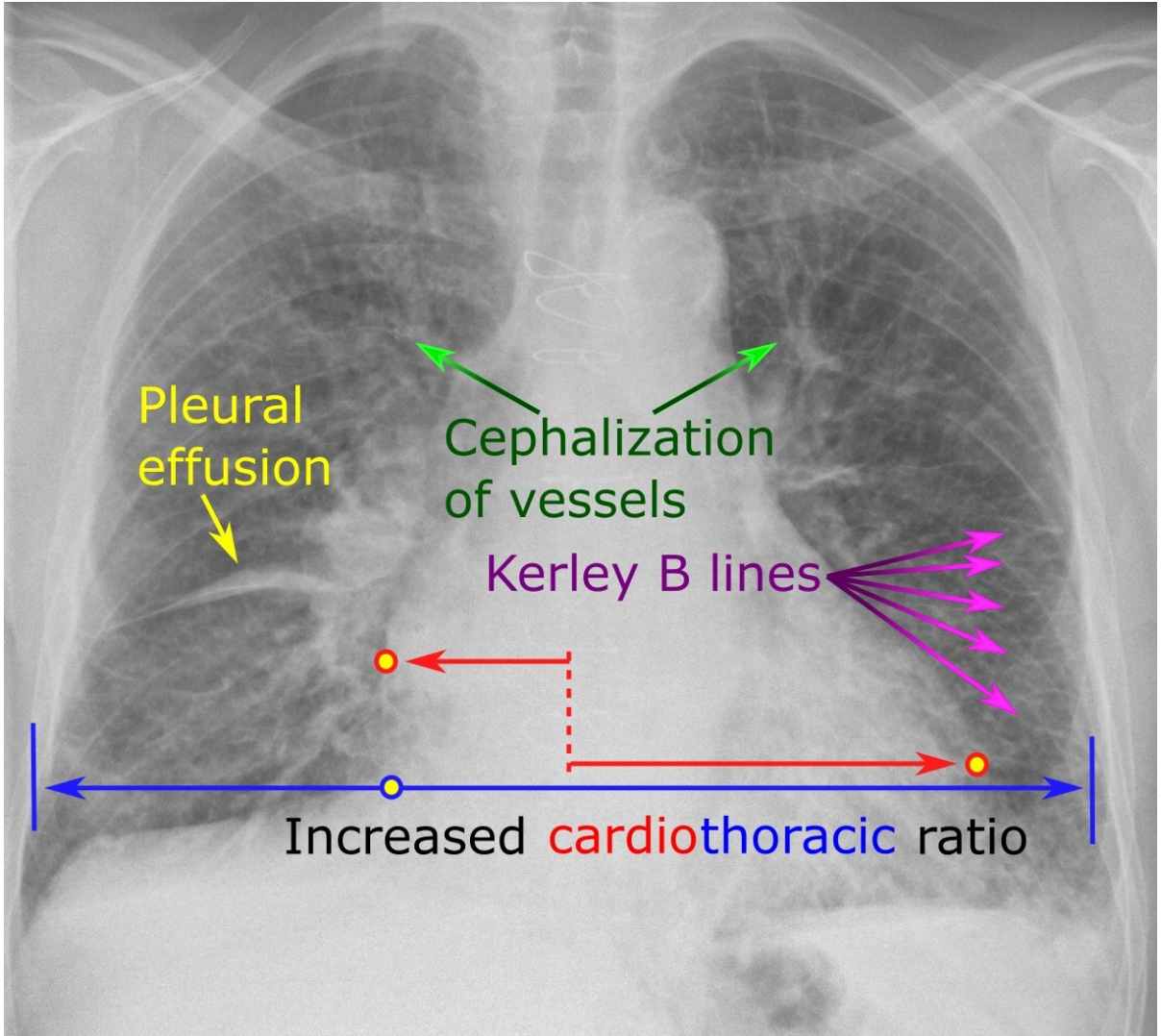

↑Pc


cm
SPEC.

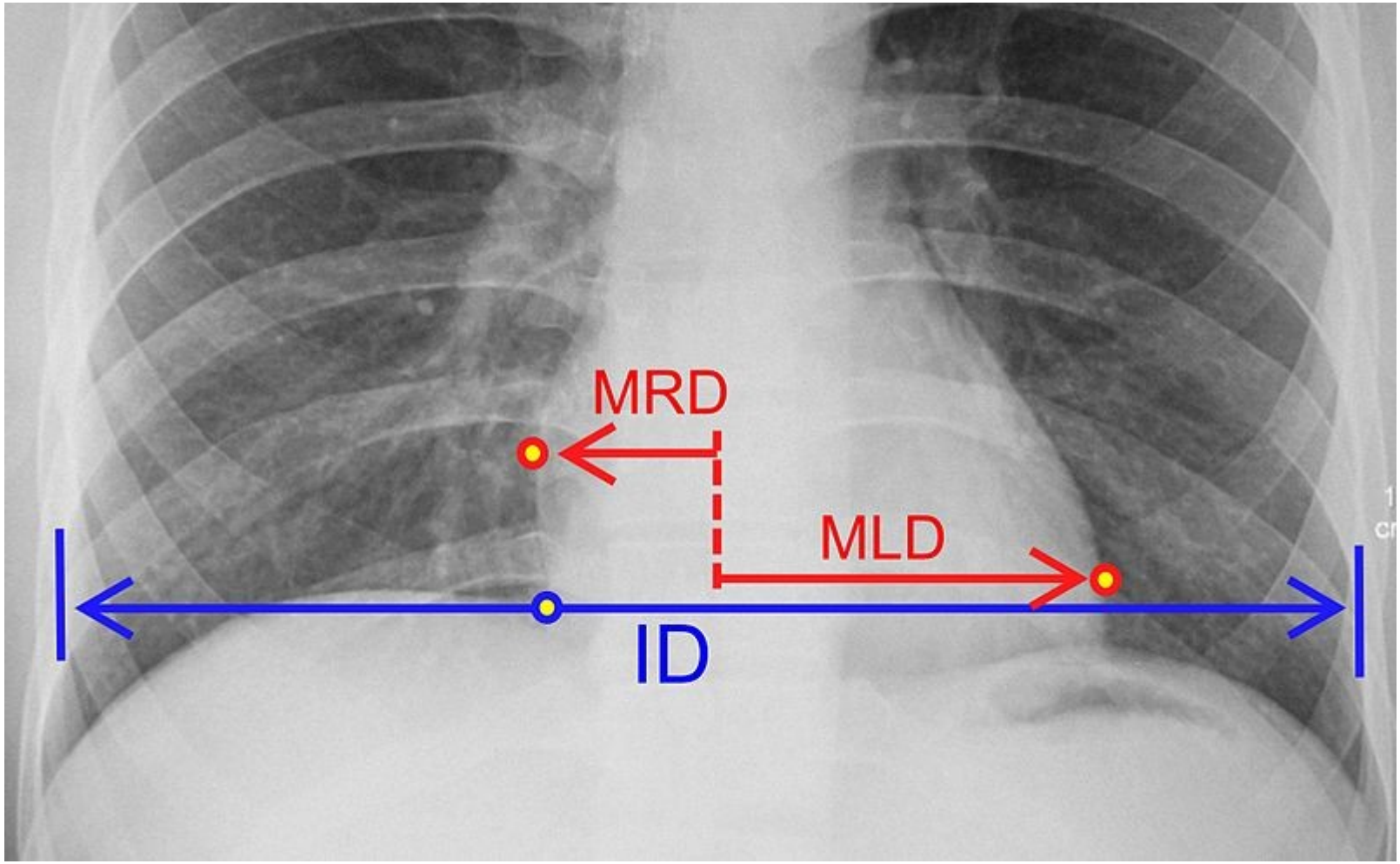

PORTAL TRIAD
CENTRAL VEIN
ZONE 1
ZONE 2
ZONE 3
FATTY CHANGE
CONGESTED CENTRAL VEIN
HEMORRHAGIC NECROSIS
NORMAL HEPATOCYTES

- **Plain radiograph**

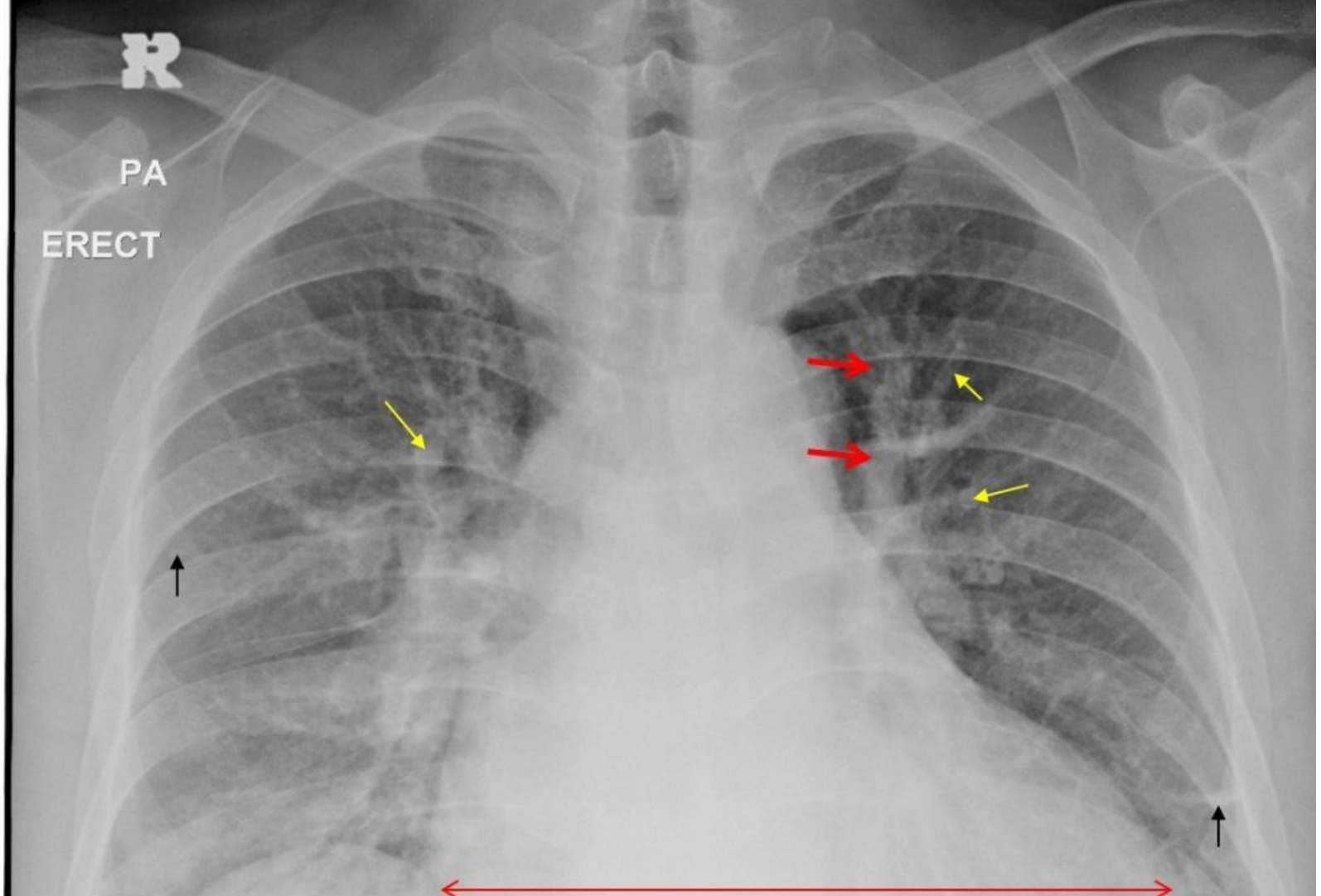
  - alveolar edema (bat wing opacities)
  - Kerley B lines
  - cardiomegaly
  - dilated upper lobe vessels
  - pleural effusion
  - Fluid in fissures

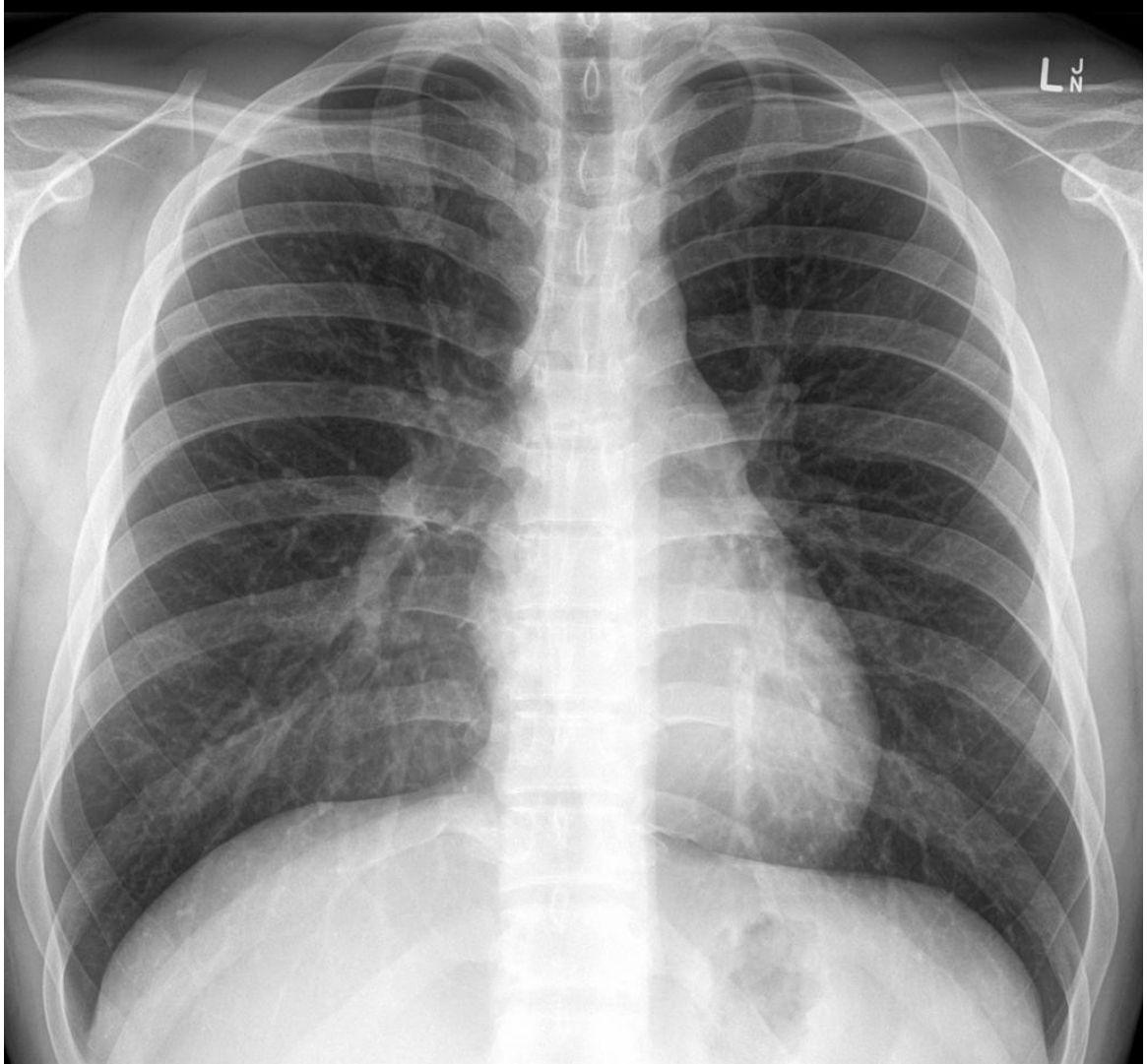

Pleural effusion
Cephalization of vessels
Kerley B lines
Increased cardiothoracic ratio

- the cardiothoracic ratio is measured on a PA chest x-ray, and is the ratio of maximal horizontal cardiac diameter to maximal horizontal thoracic diameter.
- A normal measurement in adults is <50%
- More than 50% - Cardiomegaly

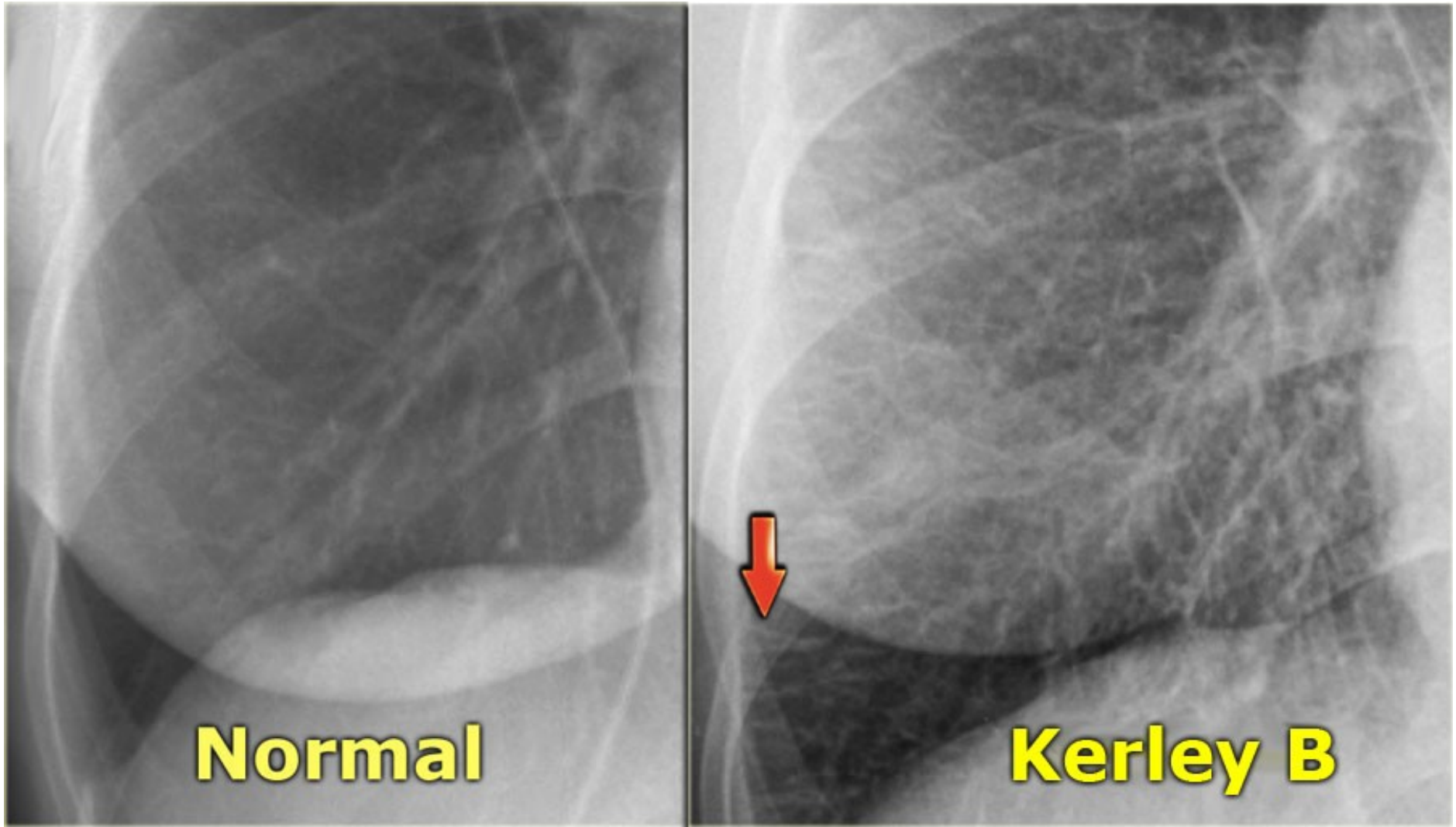

MRD
MLD
ID

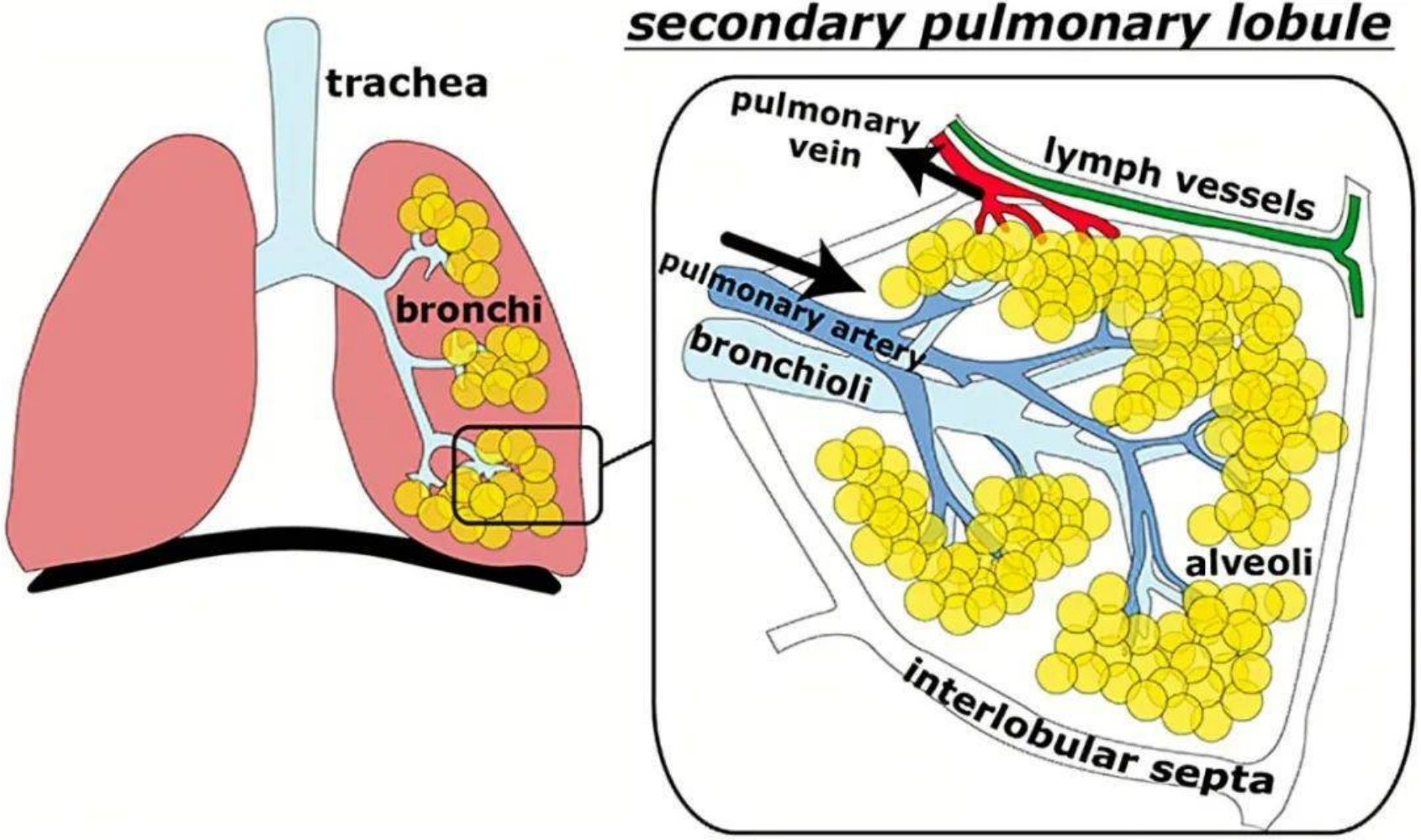
- Cephalization : the prominence of upper lobe vessels more than the lower zone vessels, which the inverse of normal. Redistribution (upper lobe diversion, upper zone redistribution) also indicates the redistribution of pulmonary flow to the upper lobes than the lower lobes, different from the normal situation.


R
PA
ERECT


L

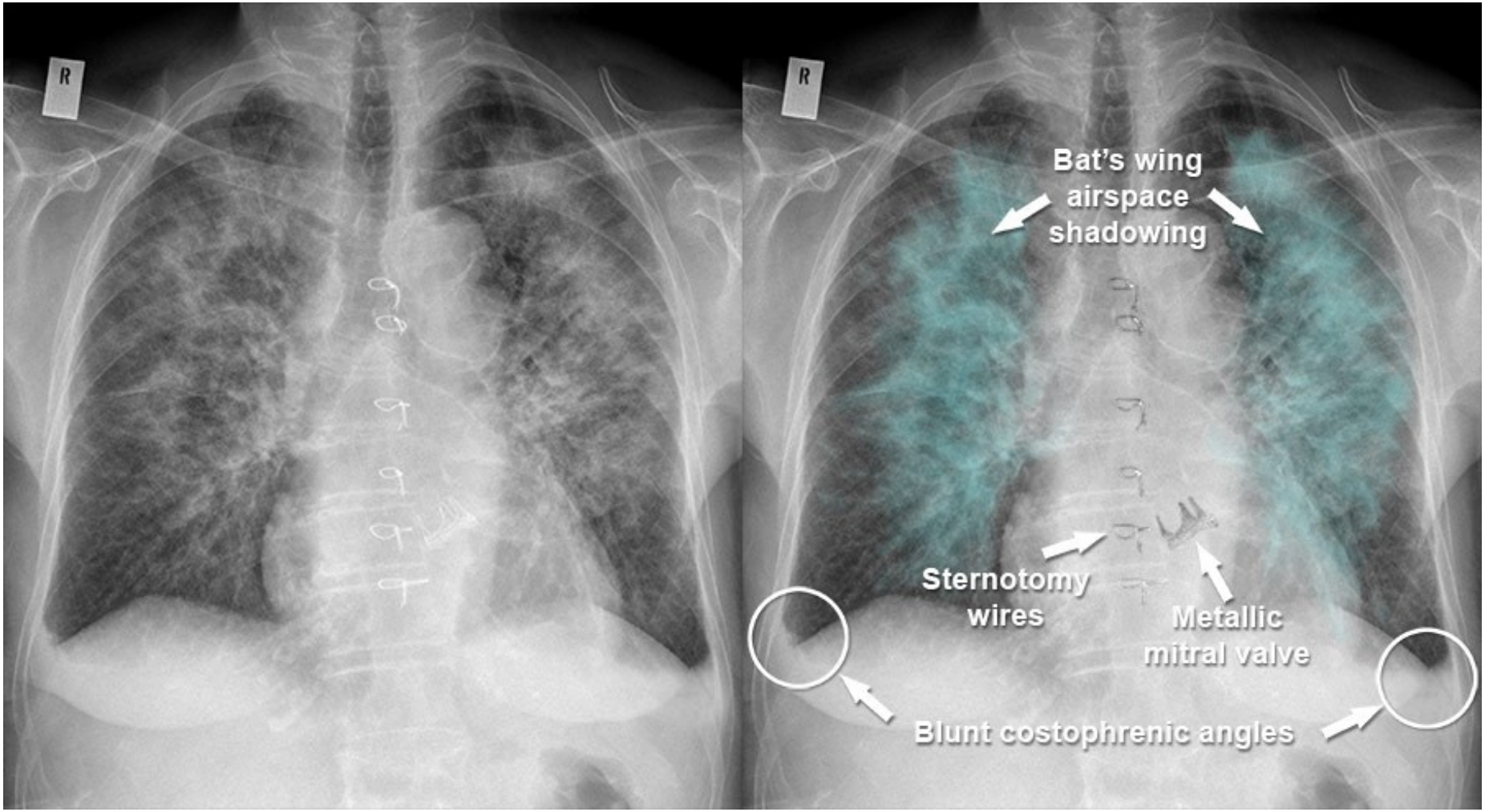
- fluid leakage into the interlobular and peribronchial interstitium as a result of the increased pressure in the capillaries.
  When fluid leaks into the peripheral interlobular septa it is seen as Kerley B or septal lines.
  Kerley-B lines are seen as peripheral short 1-2 cm horizontal lines near the costophrenic angles.
  These lines run perpendicular to the pleura.

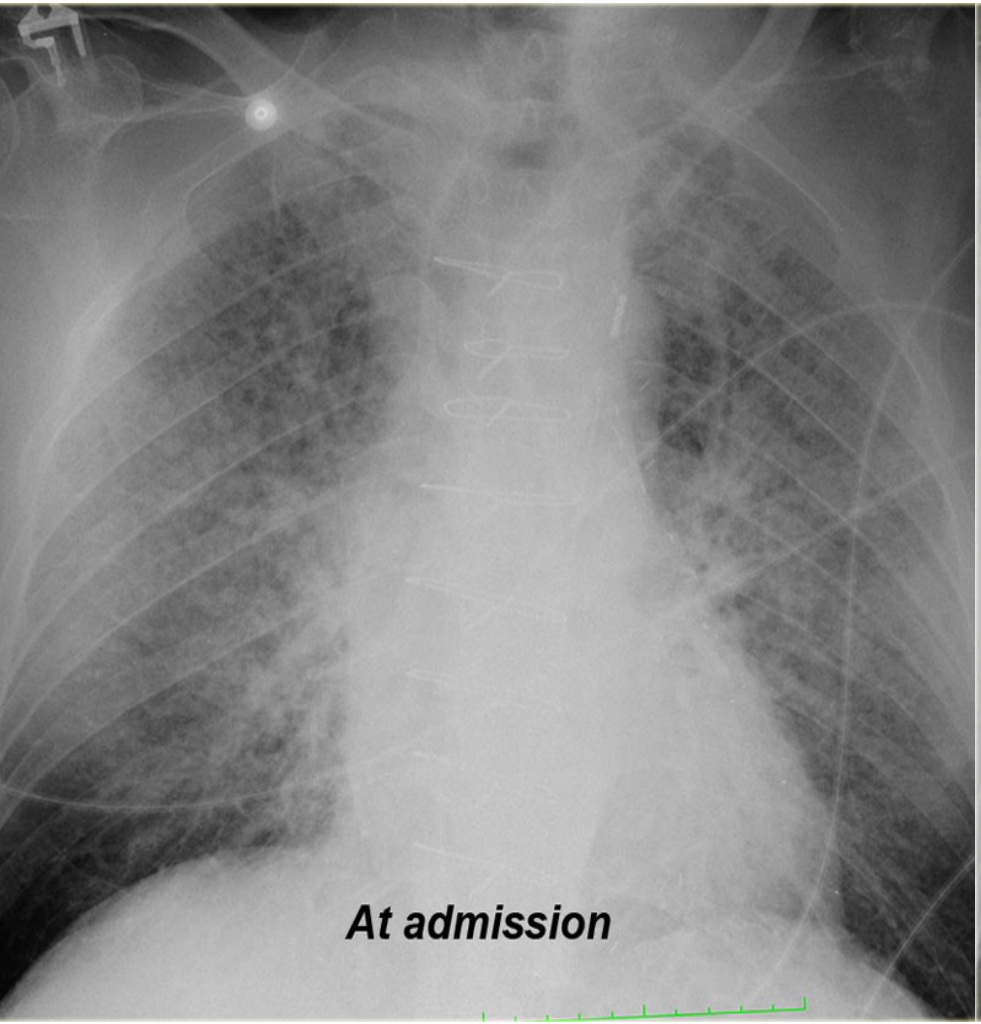

Normal
Kerley B

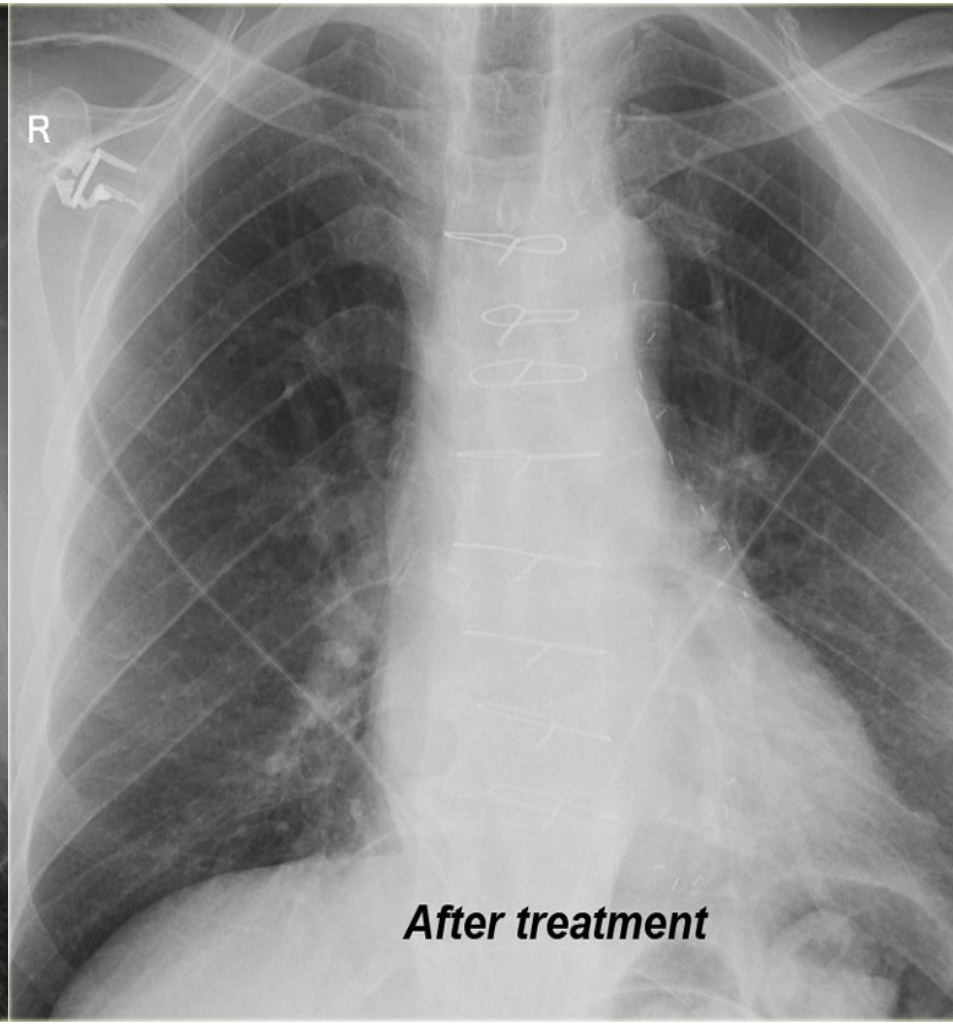

secondary pulmonary lobule
trachea
bronchi
pulmonary vein
lymph vessels
pulmonary artery
bronchioli
alveoli
interlobular septa

- Alveolar edema
- This stage is characterized by continued fluid leakage into the interstitium, which cannot be compensated by lymphatic drainage.
- This eventually leads to fluid leakage in the alveoli (alveolar edema) and to leakage into the pleural space (pleural effusion).

- **Bat wing appearance** is a radiologic sign referring to bilateral symmetrical perihilar lung opacities sparing cortical areas mainly caused by cardiogenic pulmonary edema


R
R
Bat's wing airspace shadowing
Sternotomy wires
Metallic mitral valve
Blunt costophrenic angles


At admission


R
After treatment

Cause	Examples of presentations
CAD	Myocardial infarction Angina or "angina-equivalent" Arrhythmias
Hypertension	Heart failure with preserved systolic function Malignant hypertension/acute pulmonary oedema
Valve disease	Primary valve disease e.g., aortic stenosis Secondary valve disease, e.g. functional regurgitation Congenital valve disease
Arrhythmias	Atrial tachyarrhythmias Ventricular arrhythmias
CMPs	All Dilated Hypertrophic Restrictive ARVC Peripartum Takotsubo syndrome Toxins: alcohol, cocaine, iron, copper

Congenital heart disease	Congenitally corrected/repaired transposition of great arteries Shunt lesions Repaired tetralogy of Fallot Ebstein's anomaly
Infective	Viral myocarditis Chagas disease HIV Lyme disease
Drug-induced	Anthracyclines Trastuzumab VEGF inhibitors Immune checkpoint inhibitors Proteasome inhibitors RAF+MEK inhibitors
Infiltrative	Amyloid Sarcoidosis Neoplastic
Storage disorders	Haemochromatosis Fabry disease Glycogen storage diseases

Endomyocardial disease	Radiotherapy Endomyocardial fibrosis/eosinophilia Carcinoid
Pericardial disease	Calcification Infiltrative
Metabolic	Endocrine disease Nutritional disease (thiamine, vitamin B1 and selenium deficiencies) Autoimmune disease

Right Heart Failure

- Most common cause R heart failure: Left heart failure
- Occasionally right heart failure occurs in isolation
- MI, arrhythmogenic right ventricular cardiomyopathy (ARVC), or rt sided valve disease
  - But usually secondary to a lung process
  - Normal left atrial pressure
  - High pulmonary artery, right ventricular, right atrial pressure
  - Pulmonary hypertension
  - COPD
  - This is often called “cor pulmonale”

Diagnostic tests

- **Electrocardiogram (ECG).**

A normal ECG makes the diagnosis of HF unlikely. The ECG may reveal abnormalities such as AF, Q waves, LV hypertrophy (LVH), and a widened QRS complex that increase the likelihood of a diagnosis of HF and also may guide therapy

- **Measurement of NPs.**

A normal plasma concentration of B-type natriuretic peptide (BNP) <35 pg/mL,N-terminal pro-B-type natriuretic peptide (NT-proBNP) <125 pg/ mL, or mid-regional pro-atrial natriuretic peptide (MR-proANP) <40 pmol/L68 make a diagnosis of HF unlikely

- **Basic investigations**

such as serum urea and electrolytes, creatinine,full blood count, liver and thyroid function tests are recommended to differentiate HF from other conditions, to provide prognostic information, and to guide potential therapy.

- **Echocardiography**

is recommended as the key investigation for the assessment of cardiac function. As well as the determination of the LVEF, echocardiography also provides information on other parameters such as chamber size, eccentric or concentric LVH, regional wall motion abnormalities , RV function, pulmonary hypertension, valvular function, and markers of diastolic function.

- **chest X-ray**

is recommended to investigate other potential causes of breathlessness (e.g. pulmonary disease). It may also provide supportive evidence of HF (e.g. pulmonary congestion or cardiomegaly)

- **Heart catheterization**

Increased LVEDP = left heart congestion/failure

Increased RA, RVEDP = right heart congestion/failure

prognosis

Death :

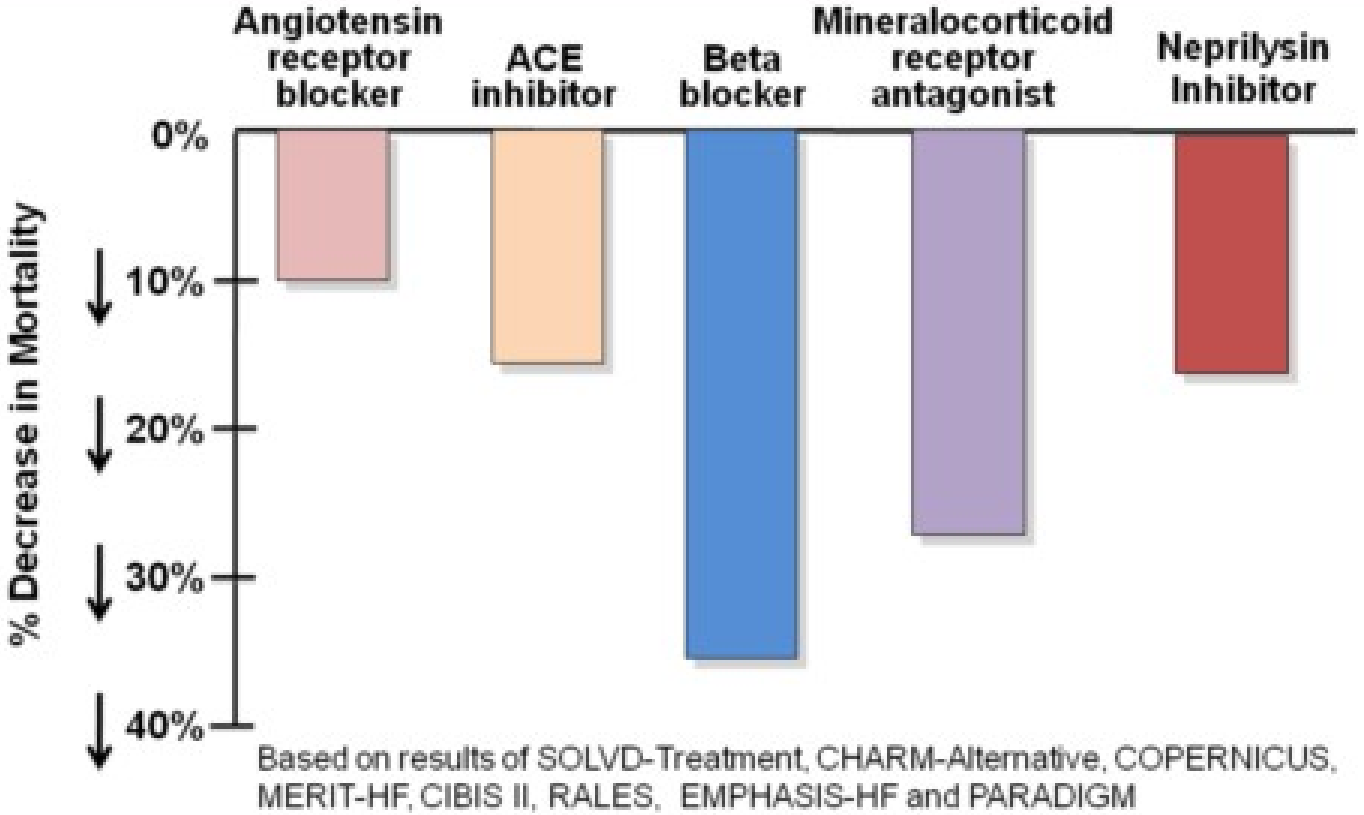
- 85% arrhythmia
- 10% thromboembolism
- 5% from HF itself

Management of heart failure

Acute vs chronic

- **Life style modification**
- **Drug therapy**
- **Devices**
- **Surgery**

Drugs That Reduce Mortality in Heart Failure With Reduced Ejection Fraction



Devices

1) Implantable cardioverter defibrillator (ICD)

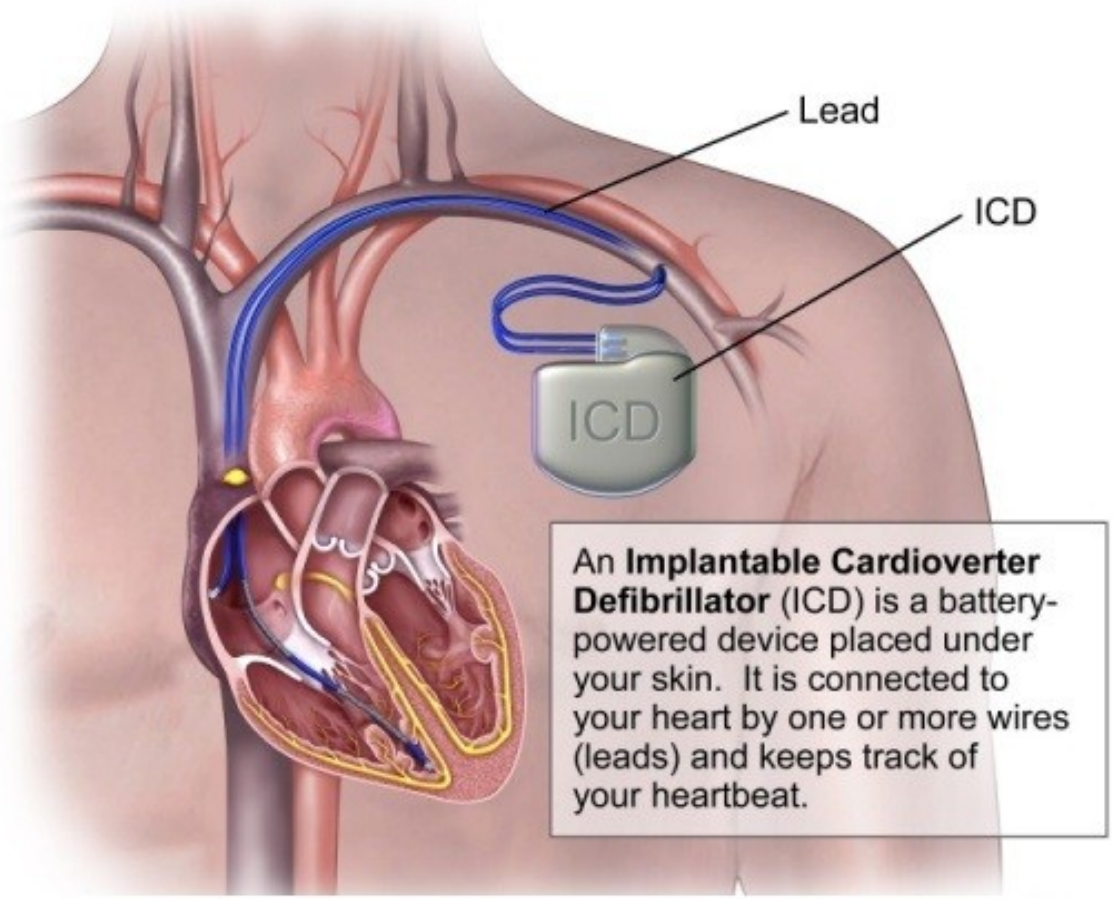
It recognizes ventricular tachycardia or fibrillation & automatically delivers shock to the heart to cause cardio version to sinus rhythm It is indicated in all survival pts who have experienced an episode of life-theatening ventricular tachyarrhythmia except:1st hours of MI / Hypo or hyperkalaemia (reversible cause)

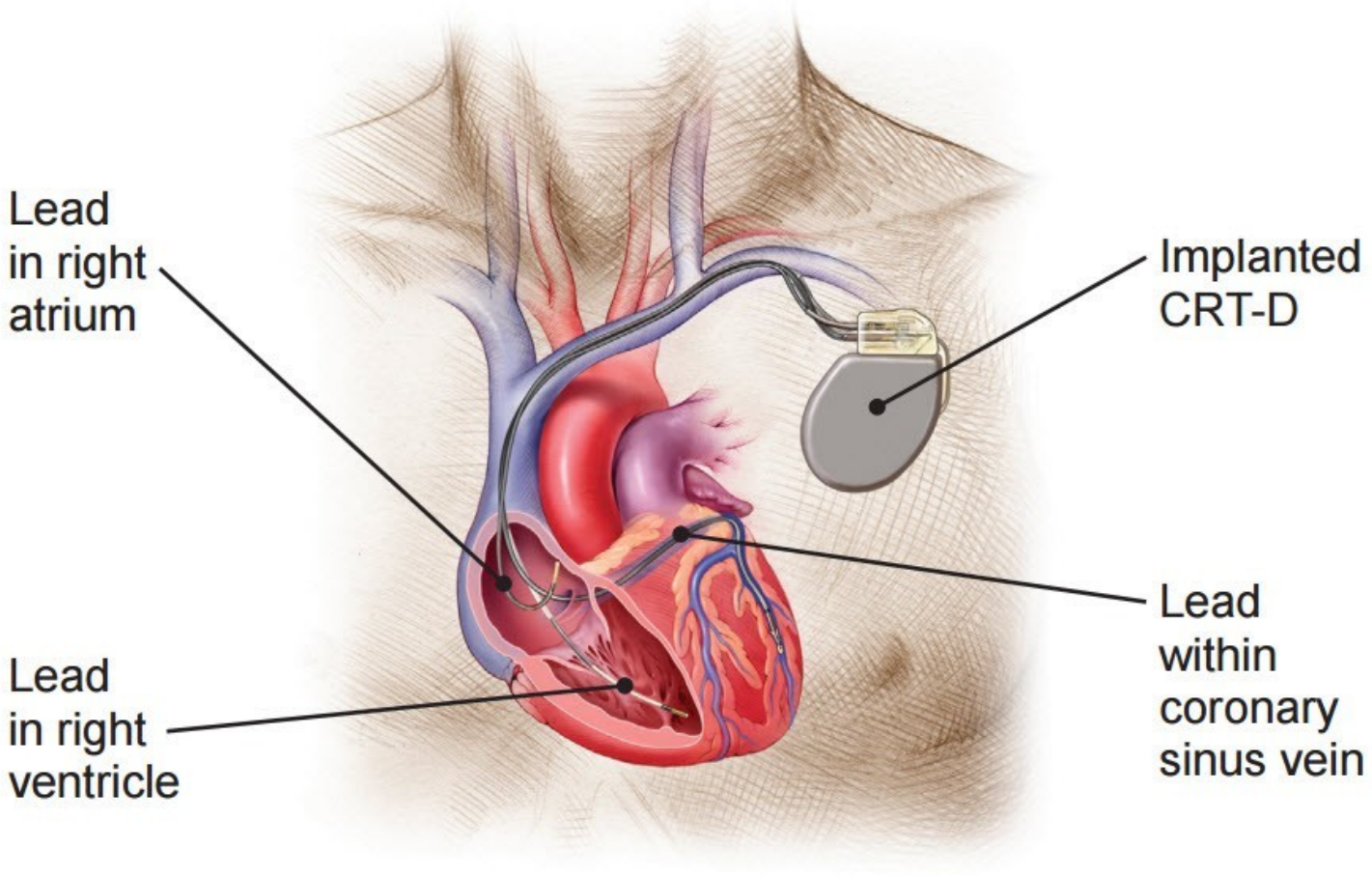
2) Cardiac resynchronization therapy (CRT)

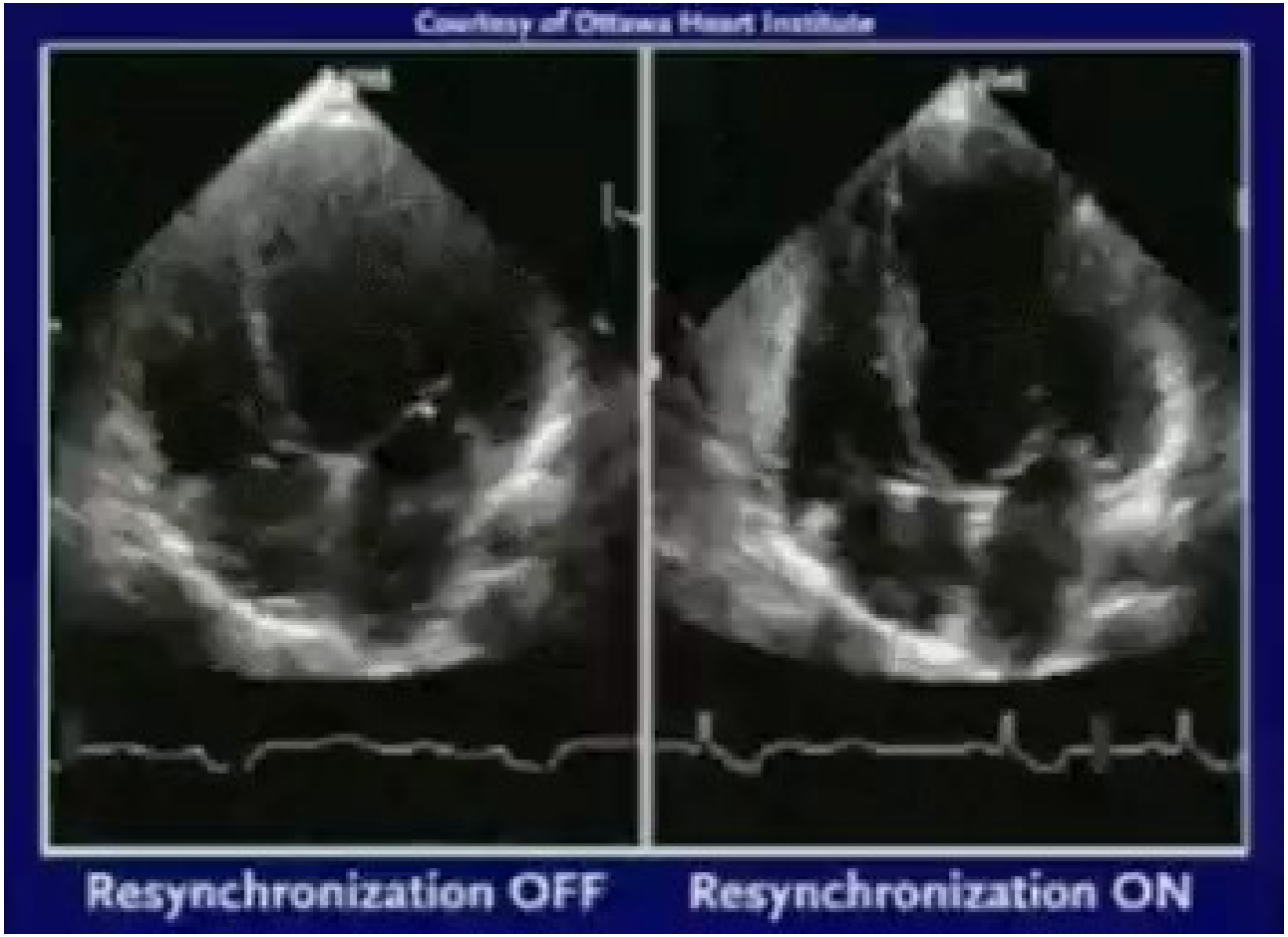
Biventricular pacemaker – makes all cardiac fibers work at the same time

3) Cardiac resynchronization therapy device(CRTD)

combined of previous 2 devices


Lead
ICD
ICD
An **Implantable Cardioverter Defibrillator** (ICD) is a battery-powered device placed under your skin. It is connected to your heart by one or more wires (leads) and keeps track of your heartbeat.


Lead
in right
atrium
Implanted
CRT-D
Lead
within
coronary
sinus vein
Lead
in right
ventricle


Courtesy of Ottawa Heart Institute
Resynchronization OFF
Resynchronization ON


thank
you