1. VALVULAR AND CONGENITAL HEART DISEASES.

2. ATHEROSCLEROSIS

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❑*ILOs*

After the lecture, students should be able to:

1. *Classify the **causes** of **valvular heart disease**.*
2. *Describe the **morphology** and **pathological** consequences of **stenosis** and **incompetence** of the different valves.*
3. *List causes and types of **congenital heart diseases.** Describe the effects of the common types of adult congenital heart disease including ASD, VSD, coarctation of the aorta and tetralogy of fallot.*

VALVULAR HEART DISEASE

- Valvular diseases are various forms of **congenital** and **acquired** diseases which cause **valvular deformities**.
- Many of them result in **cardiac failure**.
- **Rheumatic heart disease** is the most common form of acquired valvular disease.
- Valves of **the left side** of the heart are involved much more frequently than those of the right side of the heart.

- The valvular deformities may be of 2 types:
  - **stenosis** and **insufficiency**:

- ***Stenosis*** is the term used for failure of a valve to open completely during diastole resulting in obstruction to the forward flow of the blood.

- ***Insufficiency or incompetence or regurgitation*** is the failure of a valve to close completely during systole resulting in back flow or regurgitation of the blood.

CAUSES OF VALVULAR HEART DISEASE.

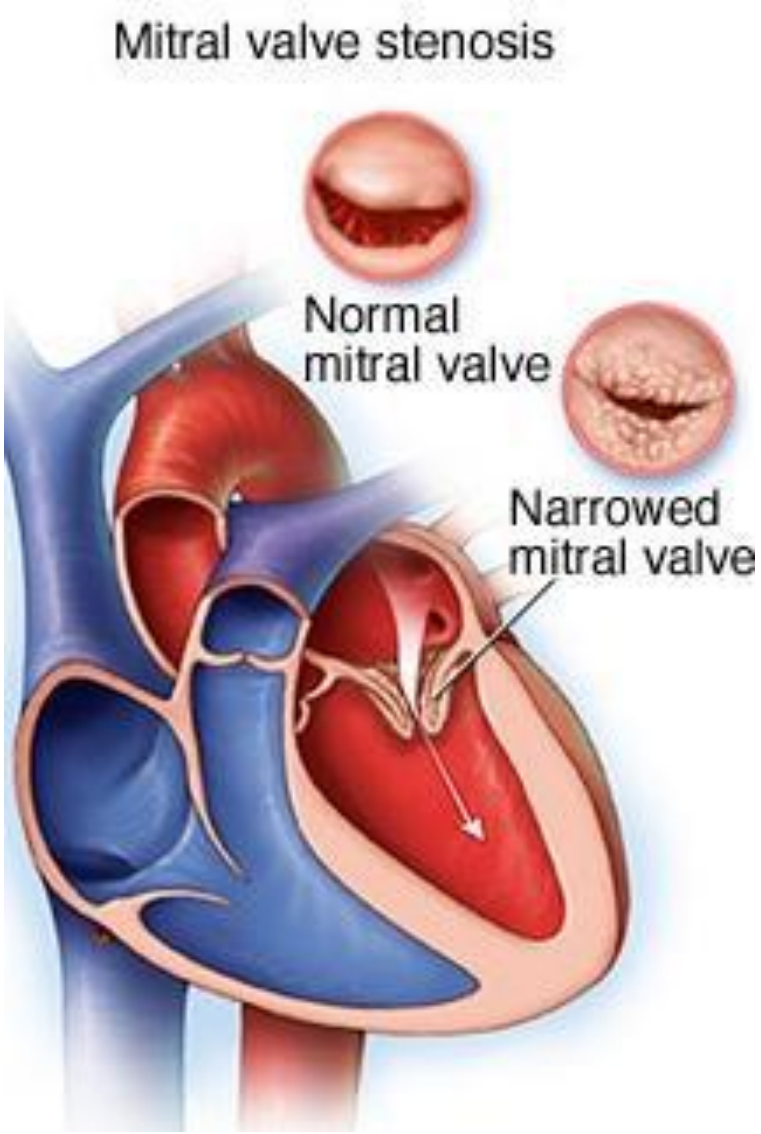
- ❖ **congenital or acquired.**

➢**Common acquired causes of heart valve disease include:**

1. Rheumatic fever, the commonest cause.
2. Infective endocarditis.
3. Syphilitic valvulitis
4. Calcific aortic valve stenosis
5. Calcification of mitral annulus
6. High blood pressure.

DISEASES OF MITRAL VALVE

Mitral stenosis:



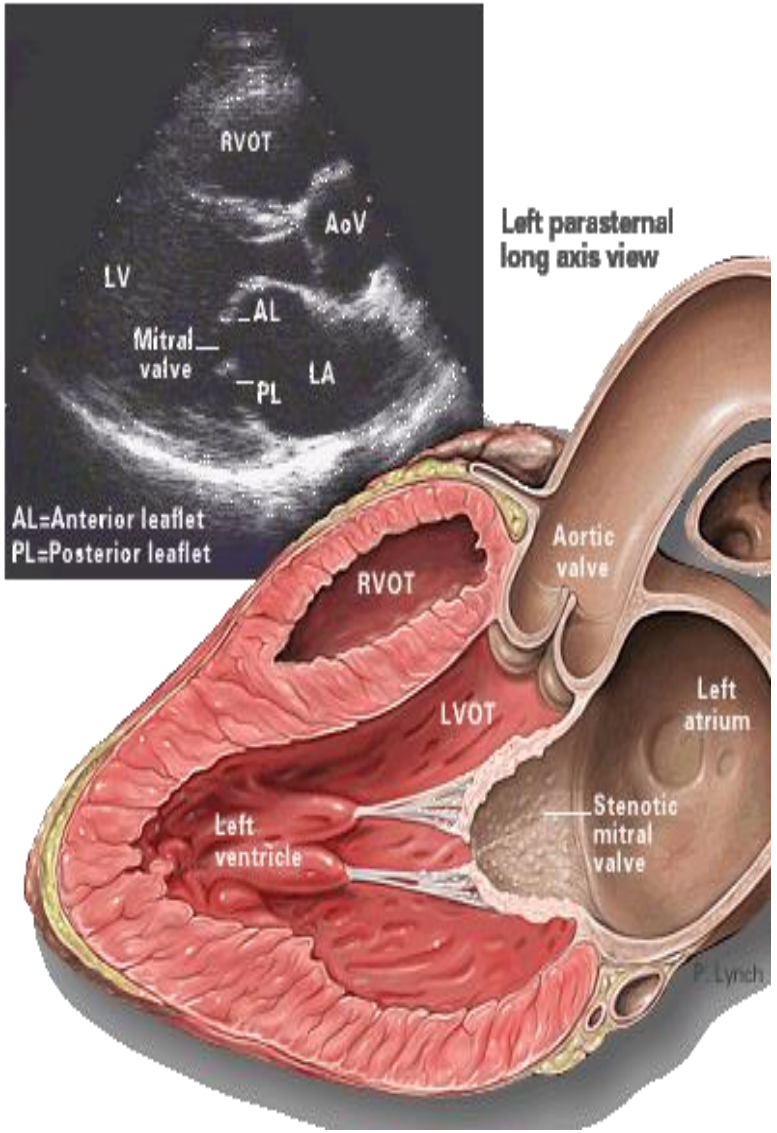
➢ **Etiology:**

Occurs in young and middle age due to:

- Healed rheumatic valvulitis is **the commonest cause**.
- Healed mild subacute infective endocarditis.
- Rare causes are SLE, rheumatoid arthritis.

➢Gross picture:

- **The cusps** are thickened, rigid and fused. Their surfaces are irregular due to fibrosis and calcification.
- **The mitral orifice** is narrowed and slit-like *"**Button hole**"*
- **The cordae tendinae** are fibrosed, thick and short.
- **The papillary muscles** show hypertrophy.



Microscopically:

- **The cusps** become thickened, distorted.
- It consists of dense fibrous tissue which may be infiltrated by lymphocytes and plasma cells.
- In some cases the cusps may be irregularly calcified.

Effects:

1. Hypertrophy and dilatation of left atrium
2. Lung congestion and pulmonary hypertension
3. **Right side heart failure** in long standing cases

MITRAL INCOMPETENCE

- Mitral incompetence is caused by RHD in about 50% of patients
- but in contrast to mitral stenosis, pure mitral incompetence
- ***Etiology:***
  - Rheumatic valvulitis is the commonest cause.
  - SlE.
  - Dilatation of the left ventricle as a result of anemia, hypertension, healed myocardial infarction and aortic incompetence causing stretching of the mitral ring and mitral incompetence.

Effects:

1. Dilatation and hypertrophy of the left ventricle.

2. Marked dilatation of the left atrium.

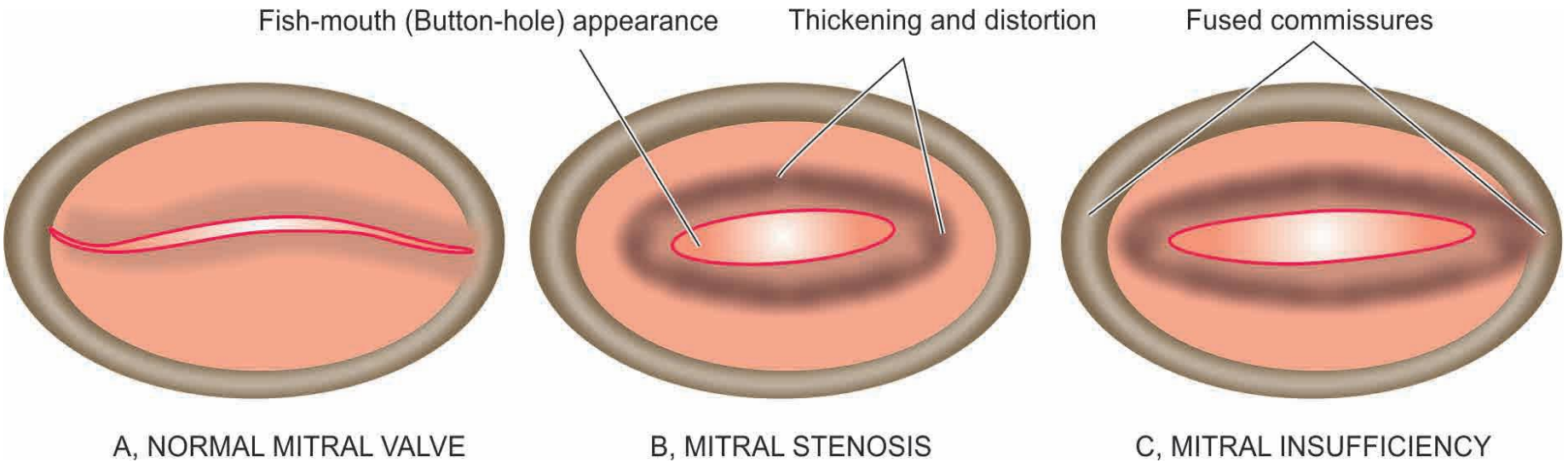
3. **left sided heart failure**

3. Features of pulmonary hypertension such as:

i) chronic passive congestion of the lungs;

ii) hypertrophy and dilatation of the right ventricle; and

iii) dilatation of the right atrium when right heart.



Mitral valve disease. Normal mitral valve (A) contrasted with mitral stenosis (B) and mitral insufficiency (C)

DISEASES OF AORTIC VALVE

Aortic stenosis:

Etiology:

A. Rheumatic valvulitis.

B. SIE.

C. Calcific aortic stenosis.

D. Congenital.

- In post-rheumatic aortic valve diseases, the cusps are thickened, vascularized, rigid and partly adherent.
- Stenosis is usually combined with incompetence.
- In 90% of cases the mitral valve is also affected.

Effects:

- Reduction of valve orifice by over 50% increase significantly the resistance to ejection of blood into the aorta.
- This results in **left ventricular hypertrophy** which is concentric.
- In most patients this maintains an adequate cardiac output for many years.
- There is severe increase in the left ventricular pressure to overcome the resistance of the stenotic valve.
- ventricular fibrillation (VF) and left sided heart failure may occur

Aortic incompetence:

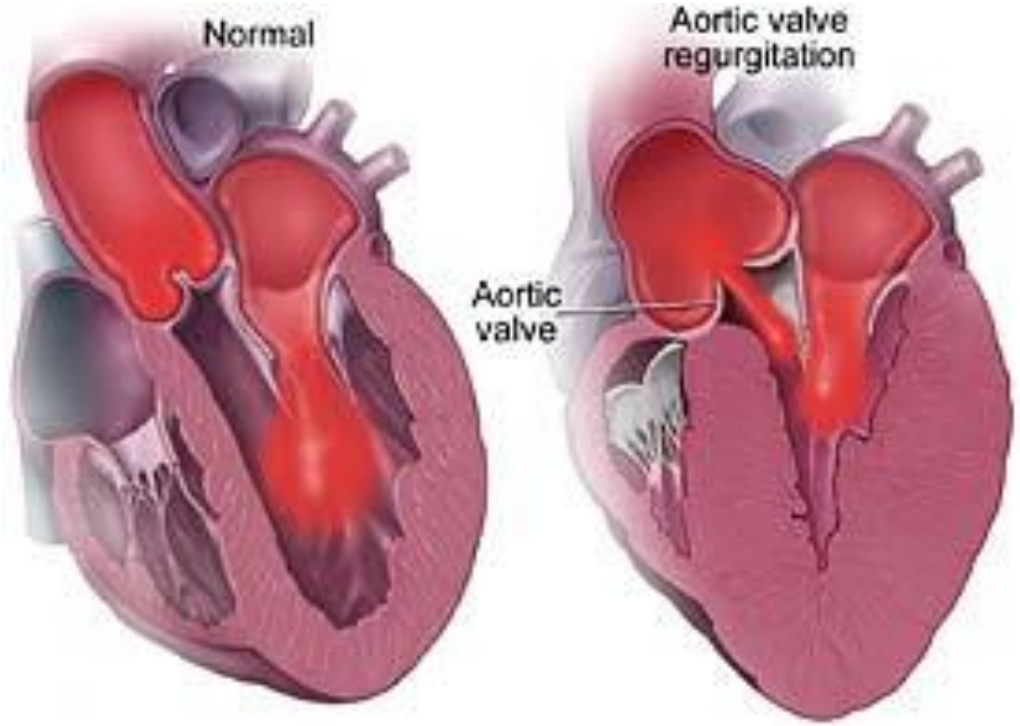
Etiology:

Rheumatic valvulitis.

Syphilitic aortitis and syphilitic valvulitis.

Effects:

- Left sided heart failure
- Arrythmias



DISEASES OF TRICUSPID VALVE

Tricuspid stenosis:

In 15% of cases of post-rheumatic valve diseases, the mitral, and aortic valves are affected.

Etiology:

1. Chronic rheumatic valvulitis.
2. Congenital.

Tricuspid incompetence:

Etiology:

1. Functional in cases of mitral stenosis; it is the most common cause.
2. Chronic rheumatic valvulitis.
3. Infective endocarditis; it is the most common cause of tricuspid incompetence due to intravenous drug abuse.

Effects:

Tricuspid stenosis, incompetence or a combination of the two have similar effects.

- Pressure rises in the right atrium, which dilates.
- The central venous pressure increase, and systemic venous congestion occurs with the development of *"cardiac edema"*.
- When associated with mitral stenosis or LVF, the tricuspid lesions tend to decrease the degree of pulmonary venous congestion and pulmonary hypertension by limiting the volume of blood reaching the lung and left side of the heart.

DISEASES OF PULMONARY VALVE

Pulmonary stenosis:

Causes:

- Congenital.
- Rheumatic valvulitis.
- Infective endocarditis.

Effects:

1. Right ventricular hypertrophy.
2. Right sided heart failure.

Pulmonary incompetence:

Causes:

A. Functional in cases of mitral stenosis.
B. Congenital.
C. Infective endocarditis.

More often it is due to pulmonary hypertension, with dilatation of the pulmonary artery and valve ring.

Effects:

The mechanical effects are not serious unless there is pulmonary hypertension and they are:

A. Right ventricular hypertrophy and dilatation.
B. Right sided heart failure.

CONGENITAL HEART DISEASES

- **Definition:** Abnormalities of the heart that usually presents at birth

- **The commonest** among all congenital birth defects
- Arise from abnormal embryogenesis during gestational weeks 3 through 8.

- Clinically: ranges from severe anomalies (incompatible with life) to mild lesions that induce minimal symptoms during life

Etiology:

The real cause is **unknown**, but the following factors are blamed:

1. Viral infection of the mother in the first 3 months by: German measles (rubella) or Coxsachie virus.
2. Certain medications or drugs; tertatogenic drugs such as thalidomide(for nausea,sedative), cortisone(corticosteroid).
3. Alcohol and/or tobacco.
4. Nutritional and vitamin deficiencies in pregnancy.
5. Maternal diabetes.
6. Down syndrome, Turner syndrome, and Marfan syndrome.
7. Syphilis. 8-exposure of pregnant to radiation

❑ *Classification of congenital heart disease:*

Three main categories

Malformations with left-to-right shunt (**Non-Cyanotic**)

1. Atrial septal defect (ASD)
2. Ventricular septal defect (VSD)
3. Patent ductus arteriosus PDA

Malformations with right-to-left shunt (**Cyanotic**)

1. Fallot`s tetralogy
2. Transposition of great vessels

Malformations that interfere with blood flow(non cyanotic with no shunt

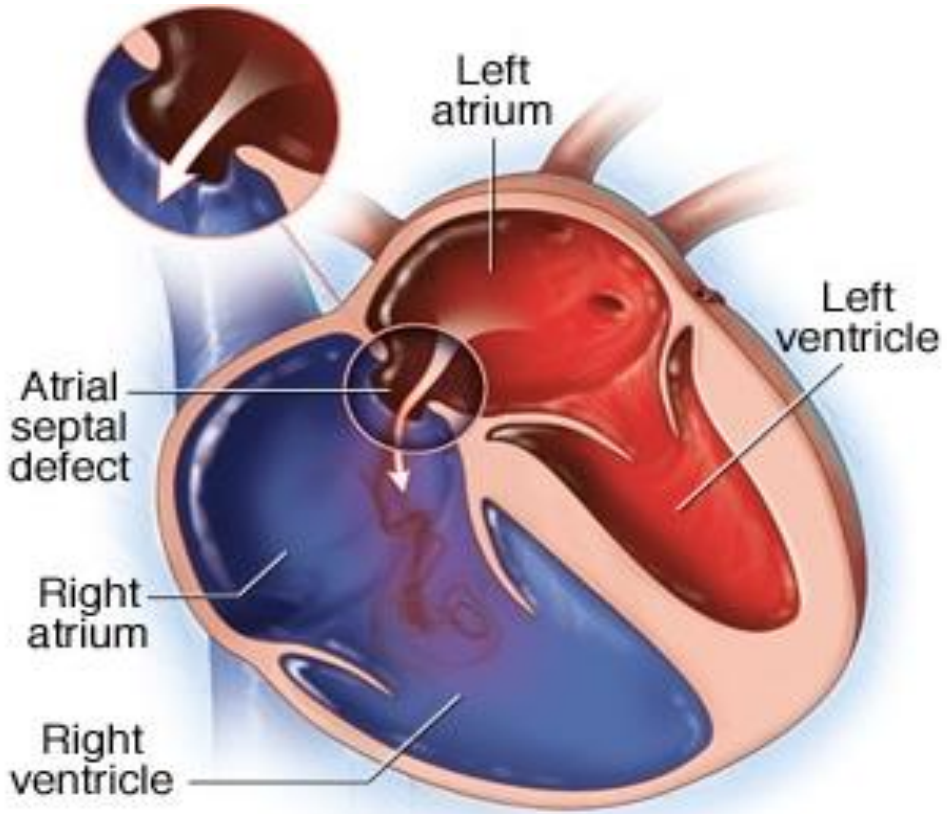
1. Coarctation of aorta
2. Aortic stenosis & incompetence
3. Mitral stenosis & incompetence
4. Pulmonary stenosis

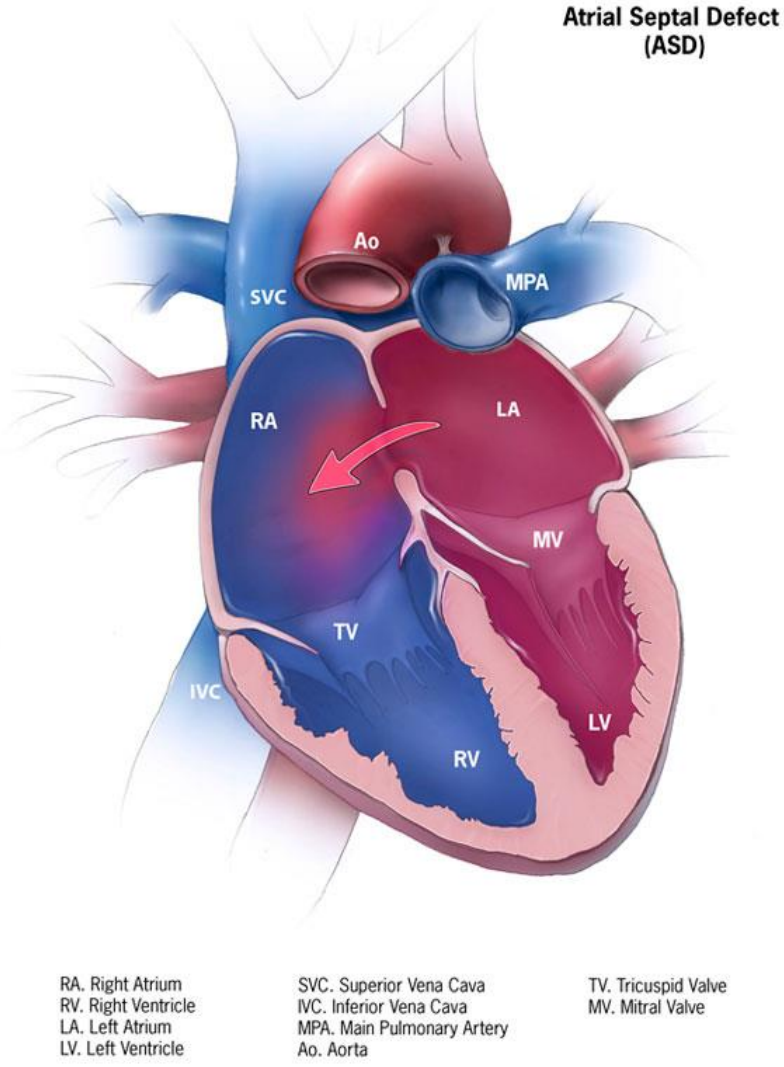
ATRIAL SEPTAL DEFECT (ASD)

Definition: defect in inter-atrial septum. Even when the defect is large, it appears to have little effect on the circulation. **The blood that comes out of the heart is oxygenated**

Effects:

- The blood flows from the left to the right atrium.
- The right atrium undergoes hypertrophy and dilatation.
- Hypertrophy and dilatation of the right ventricle which may result in pulmonary congestion and pulmonary hypertension.
- Chronic pressure overload may induce damage of cardiac endothelium which raises risk of infective endocarditis.





RA. Right Atrium
RV. Right Ventricle
LA. Left Atrium
LV. Left Ventricle

SVC. Superior Vena Cava
IVC. Inferior Vena Cava
MPA. Main Pulmonary Artery
Ao. Aorta

TV. Tricuspid Valve
MV. Mitral Valve

VENTRICULAR SEPTAL DEFECT (VSD)

Definition: defect in inter-ventricular septum. **The most common congenital anomaly** of the heart (about 30% of all congenital heart diseases). frequently part of other congenital anomaly such as Fallot's tetralogy.

Types:

Small defect: Rare and occurs in the muscular part of the septum represent 10%. Cardiac hypertrophy does not occur.

Big defect: More common (90%) and occurs in the membranous septum just below the aortic valve.

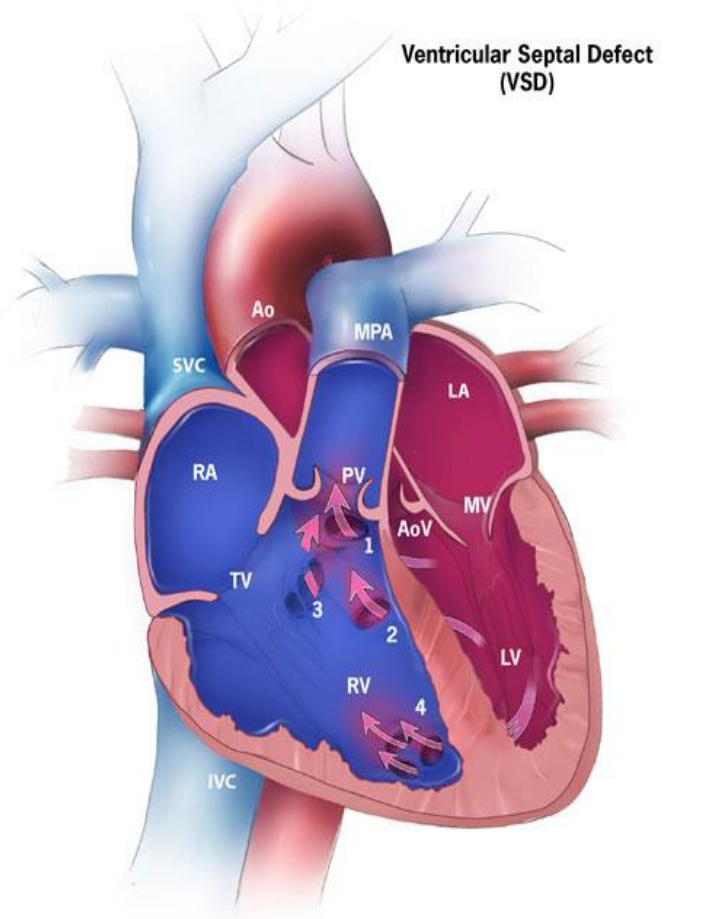
Effects:

Blood is shunted from the left ventricle to the right ventricle to the pulmonary artery causing slight enlargement.

Hypertrophy of right ventricle.

Dilatation of pulmonary artery, lung congestion and pulmonary hypertension.

Progressive pulmonary hypertension induce **reversal** of the shunt; so blood passes from right to left that causes **cyanosis.**



RA. Right Atrium
RV. Right Ventricle
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SVC. Superior Vena Cava
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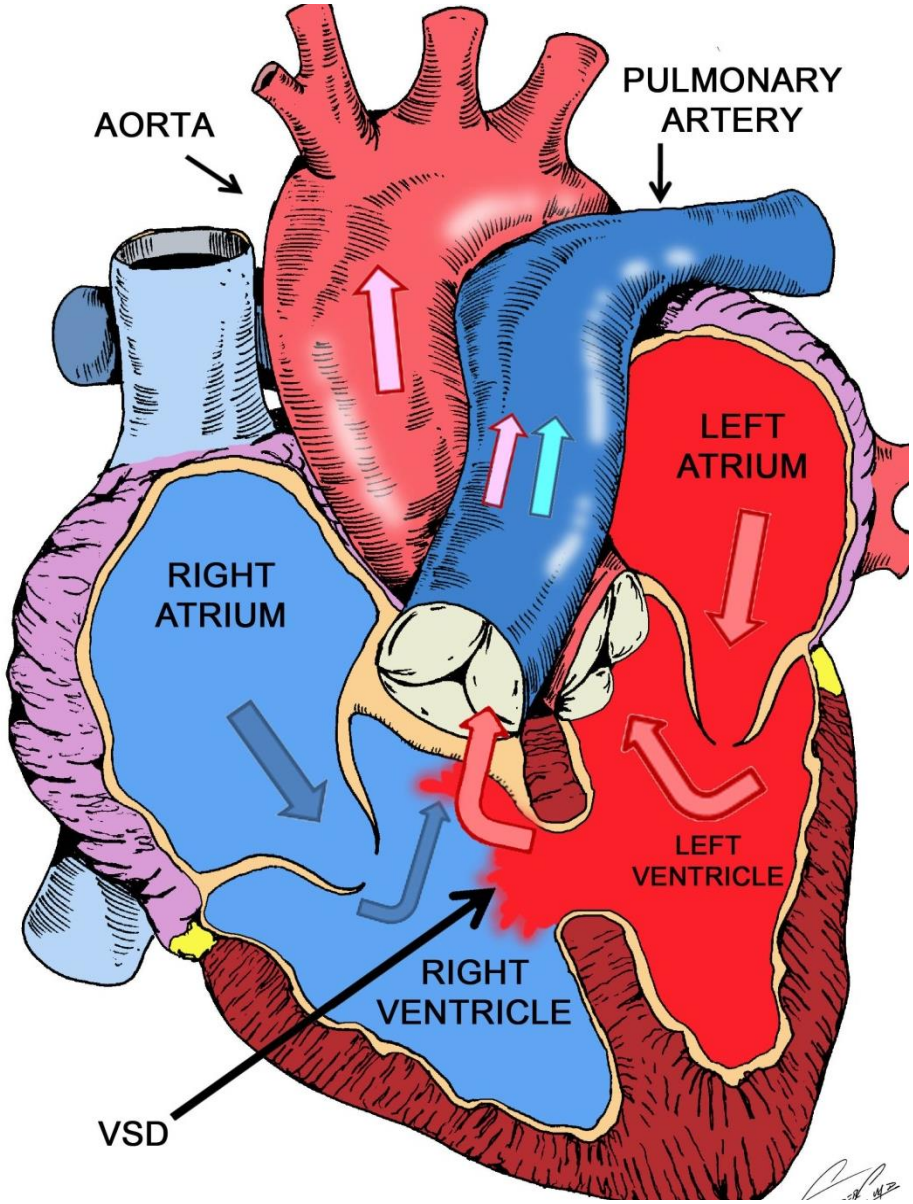
Ao. Aorta

TV. Tricuspid Valve
MV. Mitral Valve
PV. Pulmonary Valve
AoV. Aortic Valve

1. Conoventricular, malaligned
2. perimembranous
3. inlet
4. muscular



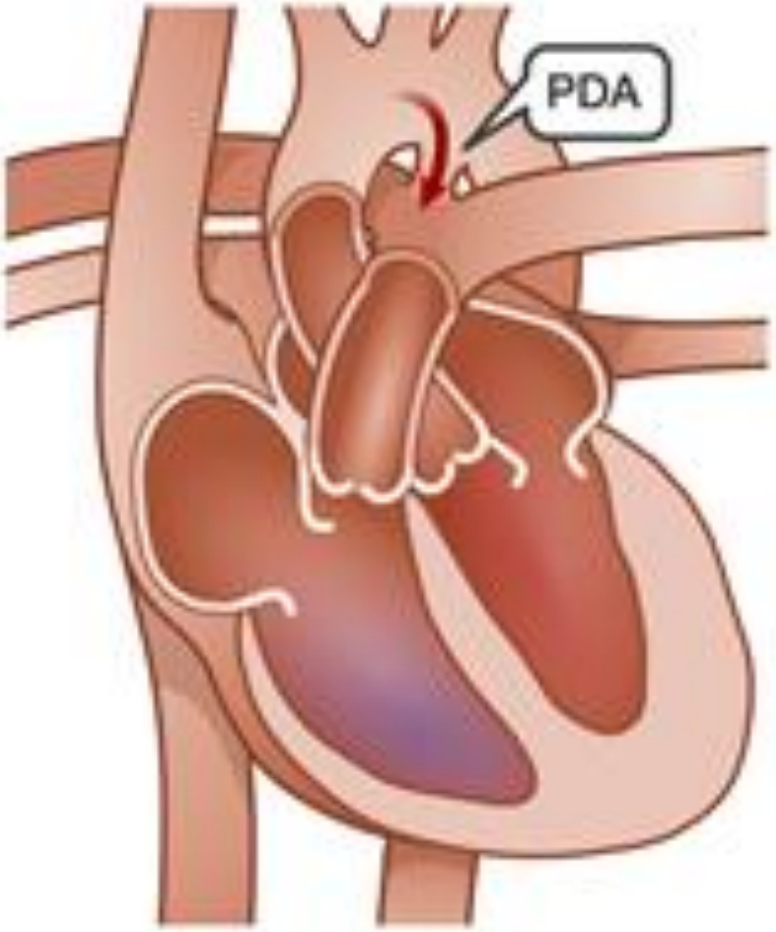
PATENT DUCTUS ARTERIOSUS (PDA)

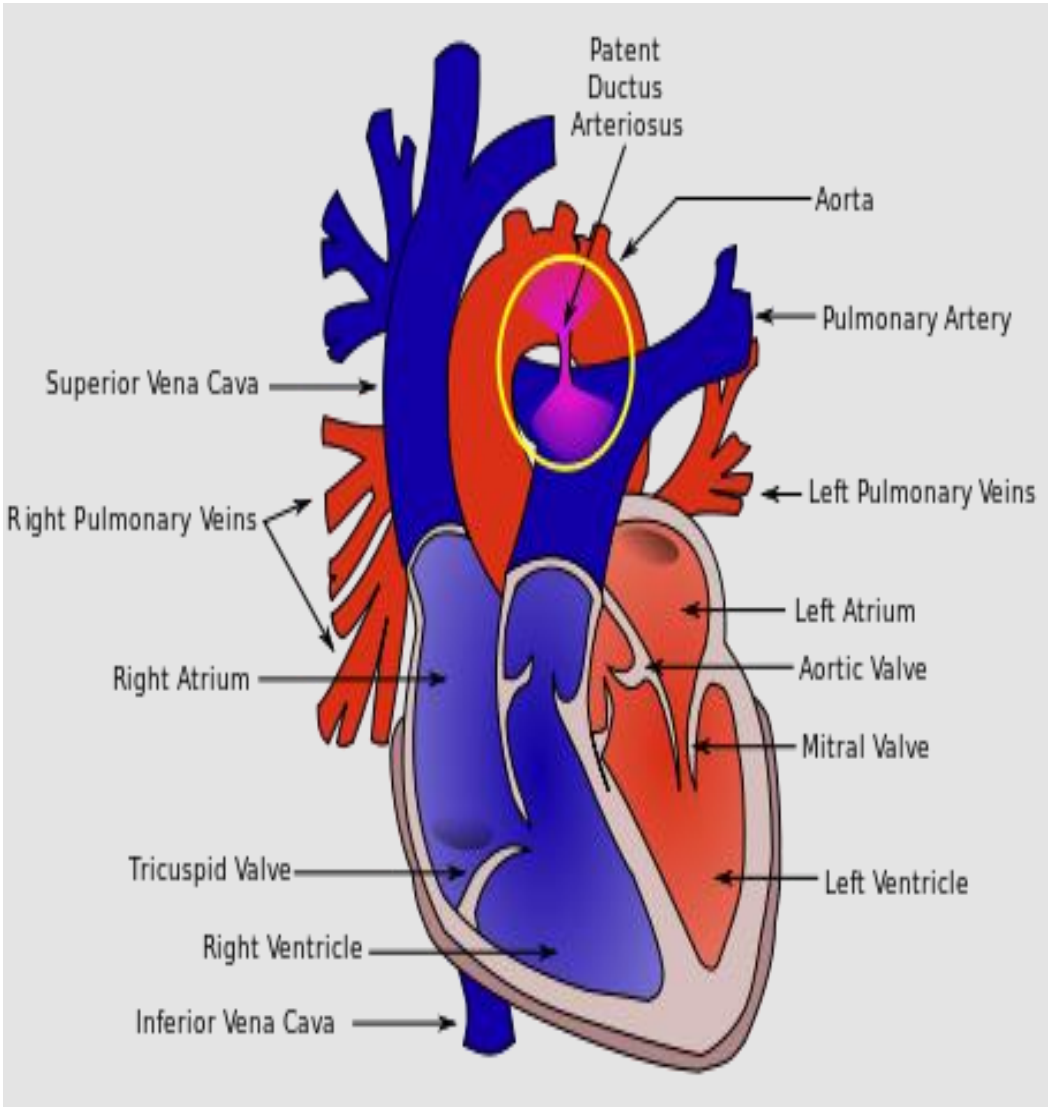
Definition: means persistent opened ducts between pulmonary artery and aorta. The blood pass from aorta to pulmonary artery.

- ductus arteriosus arises from left pulmonary artery and joins aorta just distal to origin of left subclavian artery.
- During intrauterine life, it permits blood flow from pulmonary artery to aorta. Shortly after birth, ductus constricts is closed within 1 to 2 days and changes to a fibrous ligament (ligamentum arteriosum).

Effects:

- *Blood pass from the aorta to pulmonary artery*
- The left ventricle increase its output to compensate for the shunted blood so it undergoes hypertrophy and dilatation.
- The increased strain on the right venricle causes its hypertrophy and dilatation.
- Volume overload on the lung ⇒ lung congestion and pulmonary hypertension in chronic cases.
- Failure to close the ducts leads to heart failure.


PDA


Patent
Ductus
Arteriosus
Aorta
Pulmonary Artery
Superior Vena Cava
Left Pulmonary Veins
Right Pulmonary Veins
Left Atrium
Aortic Valve
Right Atrium
Mitral Valve
Tricuspid Valve
Left Ventricle
Right Ventricle
Inferior Vena Cava

FALLOT'S TETRALOGY

The commonest anomaly of the cyanotic group is the tetralogy of Fallot.

It is composed of:

1. **Ventricular septal defect (VSD).**
2. **Displacement of aorta to override the VSD.**
3. **Pulmonary stenosis (obstruction).**
4. **Right ventricular hypertrophy.**

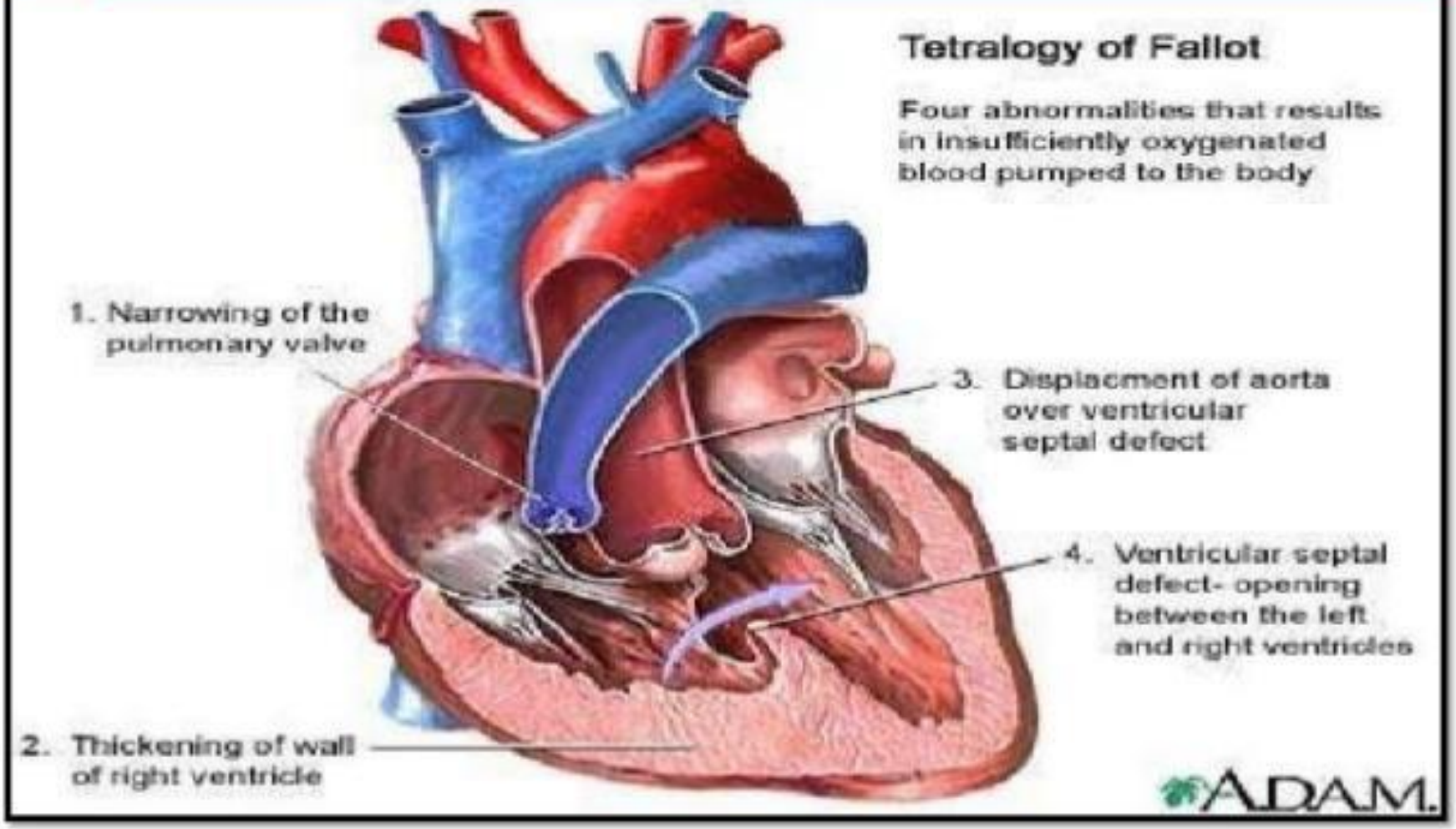
a. Obstruction of the outflow tract of the right ventricle, usually from *stenosis of the pulmonary valve*, or obstruction of the infandibular part of the right venricle.

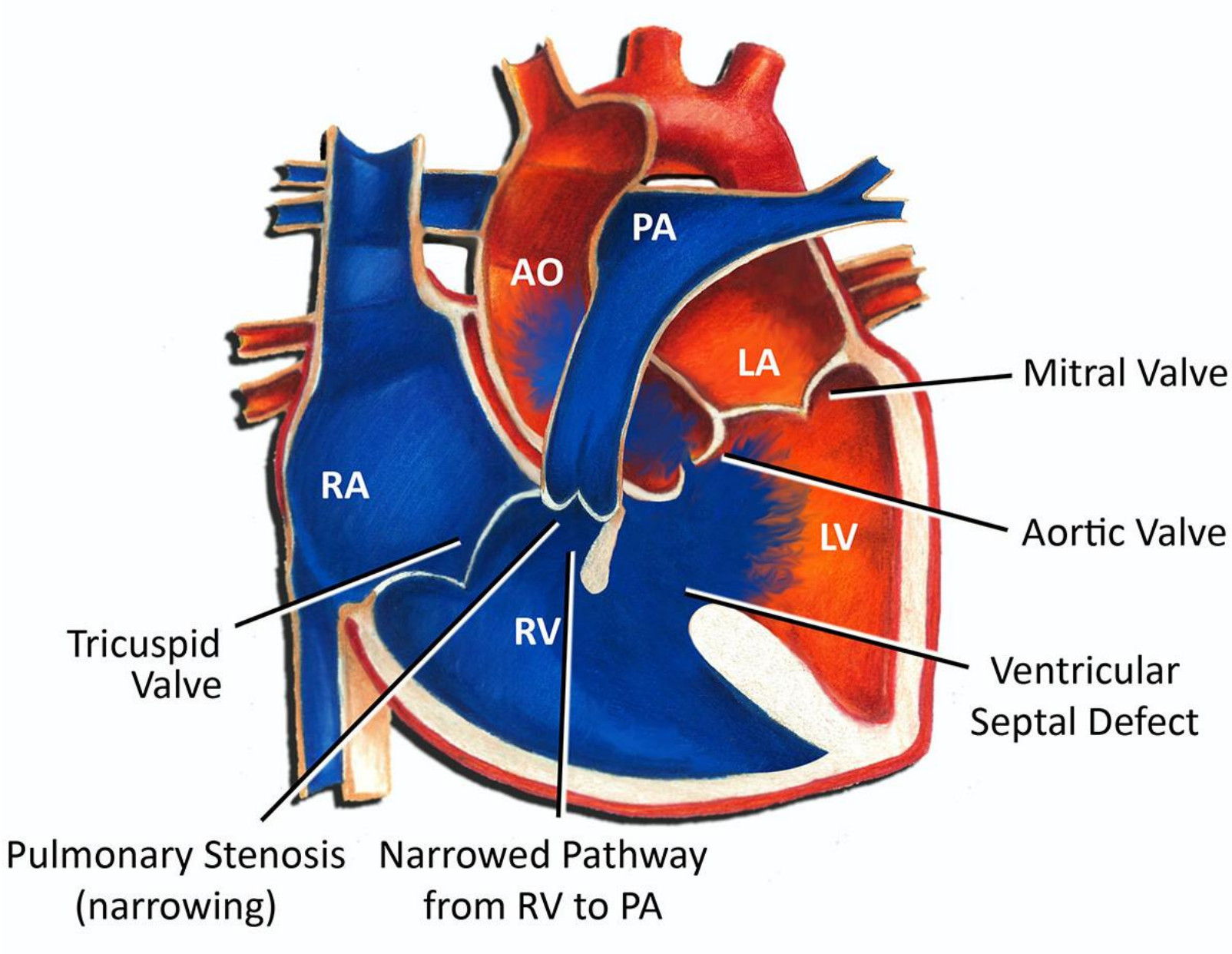
b. This results in *right ventricular hypertrophy* and the pressure in this chamber is raised.

c. Some of the un-oxygenated blood in the chamber is shunted into the aorta through a *high interventricular septal defect*.

d. The *aorta partially overrides the septal defect*, and so in addition to receiving oxygenated blood from the LV, it also receives venous blood from the right ventricle.

1.TETRALOGY OF FALLOT




PA
AO
LA
Mitral Valve
RA
LV
Aortic Valve
Tricuspid Valve
RV
Ventricular Septal Defect
Pulmonary Stenosis (narrowing)
Narrowed Pathway from RV to PA

Effects:

- Right to left shunting of blood, decreased pulmonary blood flow, and increased aortic blood volume.

- Aorta obtains mixed oxygenated and non oxygenated blood; resulting in cyanosis. Cyanosis leads to polycythaemia (due to hypoxia) with blood hyper-viscosity and susceptibility to thrombosis

- The clinical severity depends on the degree of pulmonary stenosis.

- Increased risk of infective endocarditis, and systemic embolization.

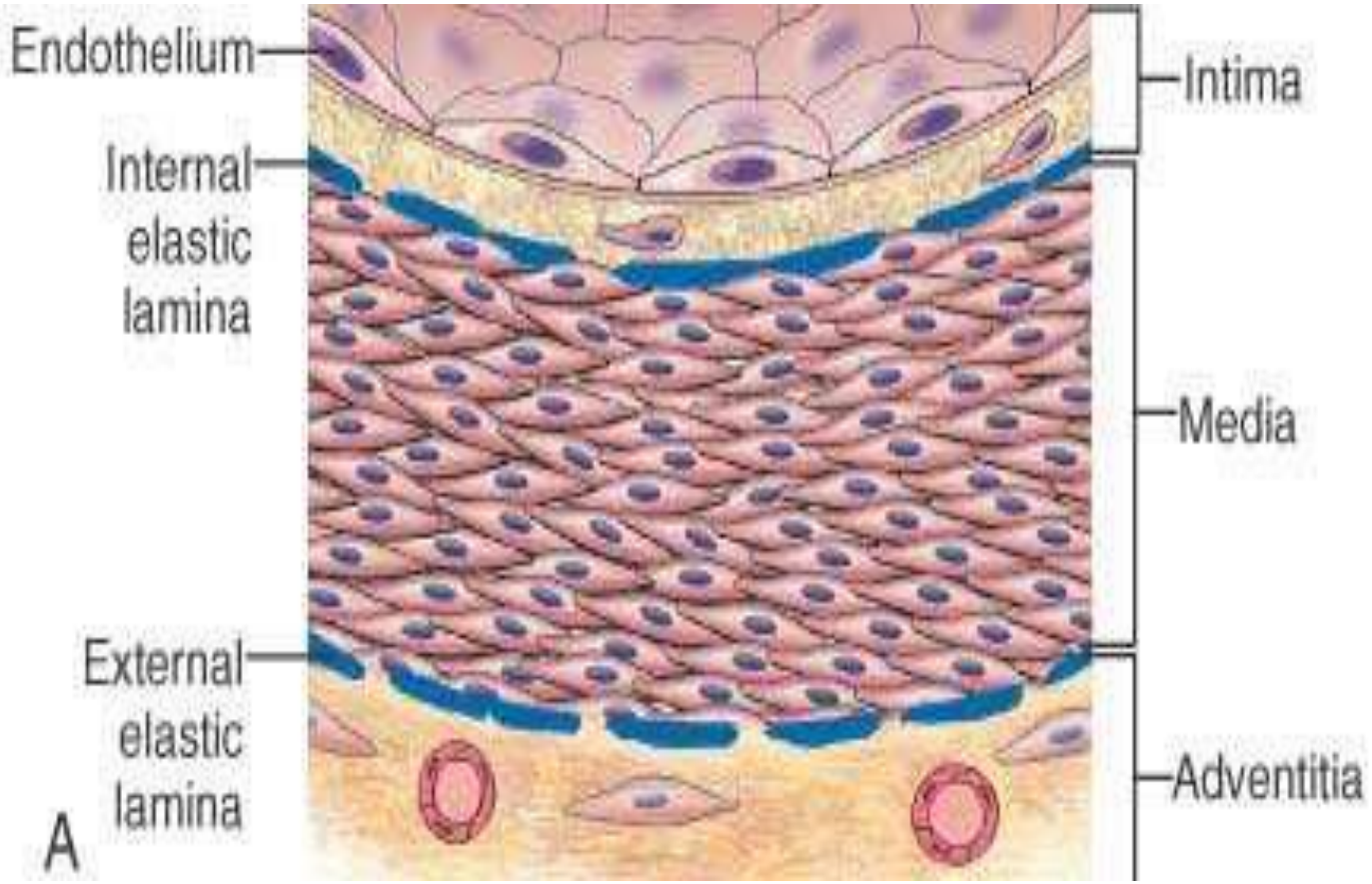
ATHEROSCLEROSIS

ILOs

After the lecture, students should be able to:

1. Define the term **atherosclerosis** and list the **risk factors** for its development and mention its **pathogenesis**.
2. Describe the **morphological changes** that occur in vessel wall in the various stages of development of **atheroma**.
3. Outline the **common complications** of atheroma.

Normal blood vessel



ATHEROSCLEROSIS

❑ Definition:

- Atherosclerosis is a common ***degenerative disease*** in which patchy deposits of fatty material develop in the walls of medium-sized and large arteries, followed by fibrosis, leading to reduced blood flow.

- Thickening and hardening of large and medium-sized muscular arteries, primarily due to involvement of tunica intima and is characterised by fibrofatty plaques or atheromas.

➢It is a slow complex process in which fatty substances, cholesterol, cellular waste products, and calcium build up in the inner lining of an artery. This buildup is called ***plaque*****.**

➢The term atherosclerosis is derived from *athero-* (meaning porridge) referring to the soft lipid-rich material in the centre of atheroma, and *sclerosis* (scarring) referring to connective tissue in the plaques.

❑ Major Risk Factors for Atherosclerosis

❑Non-modifiable (Constitutional)

Genetic abnormalities

Family history

Increasing age

Male gender

❑Modifiable

Hyperlipidemia

Hypertension

Cigarette smoking

Diabetes

Inflammation

❑ Pathogenesis:

Respons to injury theory:

This theory suppose that atherosclerosis is a response to endothelial injury. It was the most accepted theory till recently.

Injury may be:

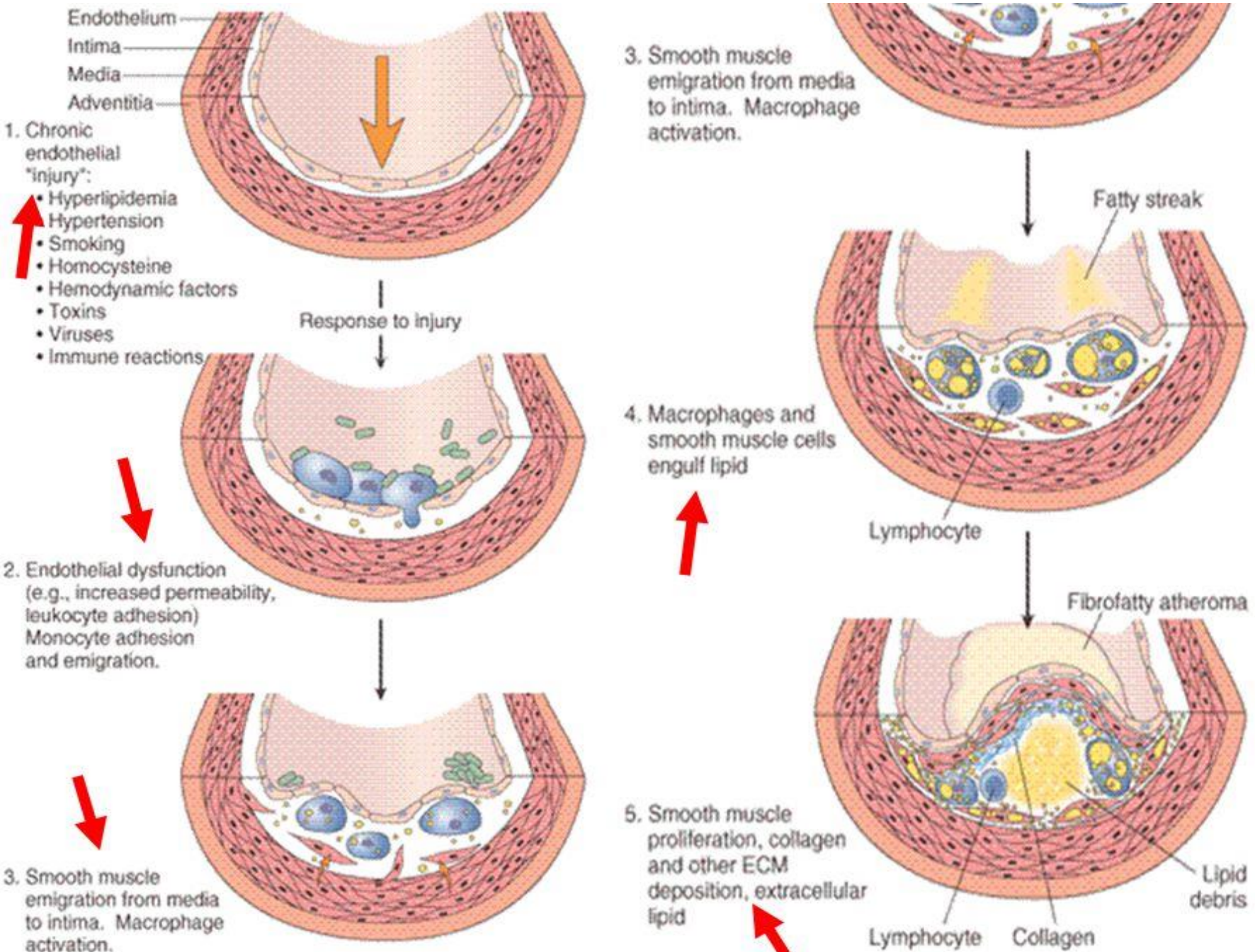
- Gross e.g. physical, chemical traumas.
- Subtle e.g. hypertension, diabetes, hyperlipidemia, cigarette smoking.

1. *Endothelial injury and dysfunction*, causing increased vascular permeability, leukocyte adhesion, and thrombosis
2. *Accumulation of lipoproteins* (mainly LDL and its oxidized forms) in the vessel wall
3. *Monocyte adhesion to the endothelium*, followed by migration into the intima and transformation into *macrophages* and *foam cells*
4. *Platelet adhesion*

5. *Factor release* from activated platelets, macrophages, and vascular wall cells, inducing *smooth muscle cell recruitment*, either from the media or from circulating precursors

6. *Smooth muscle cell proliferation*, *extracellular matrix production*, and *recruitment of T cells.*

7. *Lipid accumulation* both extracellularly and within cells (macrophages and smooth muscle cell)


Endothelium
Intima
Media
Adventitia
1. Chronic endothelial "injury":
• Hyperlipidemia
• Hypertension
• Smoking
• Homocysteine
• Hemodynamic factors
• Toxins
• Viruses
• Immune reactions
Response to injury
2. Endothelial dysfunction (e.g., increased permeability, leukocyte adhesion) Monocyte adhesion and emigration.
3. Smooth muscle emigration from media to intima. Macrophage activation.
3. Smooth muscle emigration from media to intima. Macrophage activation.
Fatty streak
4. Macrophages and smooth muscle cells engulf lipid
Lymphocyte
Fibrofatty atheroma
5. Smooth muscle proliferation, collagen and other ECM deposition, extracellular lipid
Lipid debris
Lymphocyte
Collagen

❑ Gross Picture:

1. Yellow slightly raised yellow streaks and round patches on the intimal surface caused by deposition of cholesterol in the subintimal connective tissue.
2. Raised large **white plaques or nodules** due to fibrosis around the deposited lipids.
3. Superficial **atheromatous ulcers** due to necrosis of the endothelium covering the lesions. The ulcers have irregular outlines, sharp edges and rough floors.

4. Atheromatous nodules and ulcers may show **calcification** and appear chalky white.

5. Thrombi over the ulcers and the rough surface.

6. The media opposite the lesion is t**hin and atrophic**.

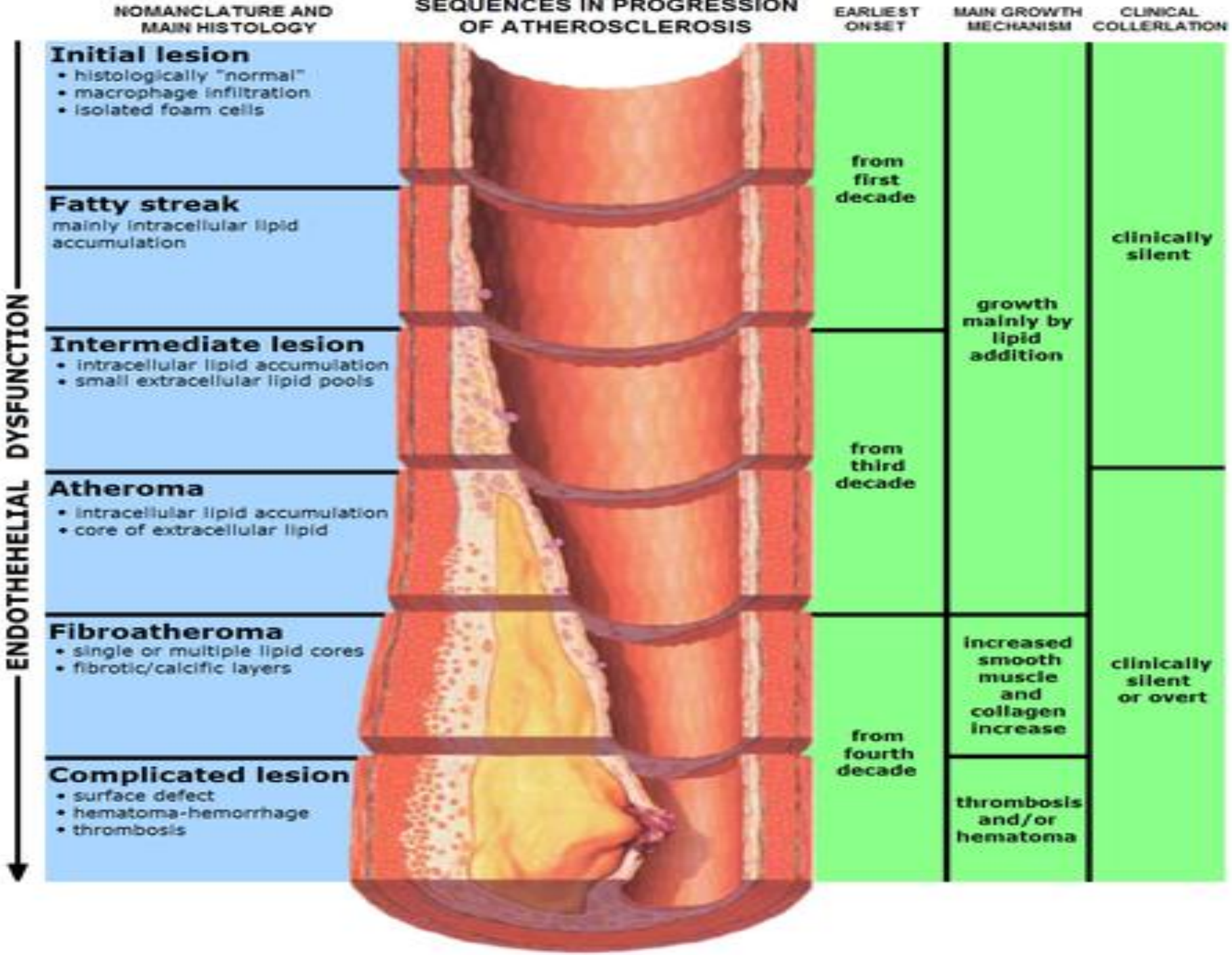
Atherosclerotic plaques have three principal components:

(1) smooth muscle cells, macrophages, and T cells

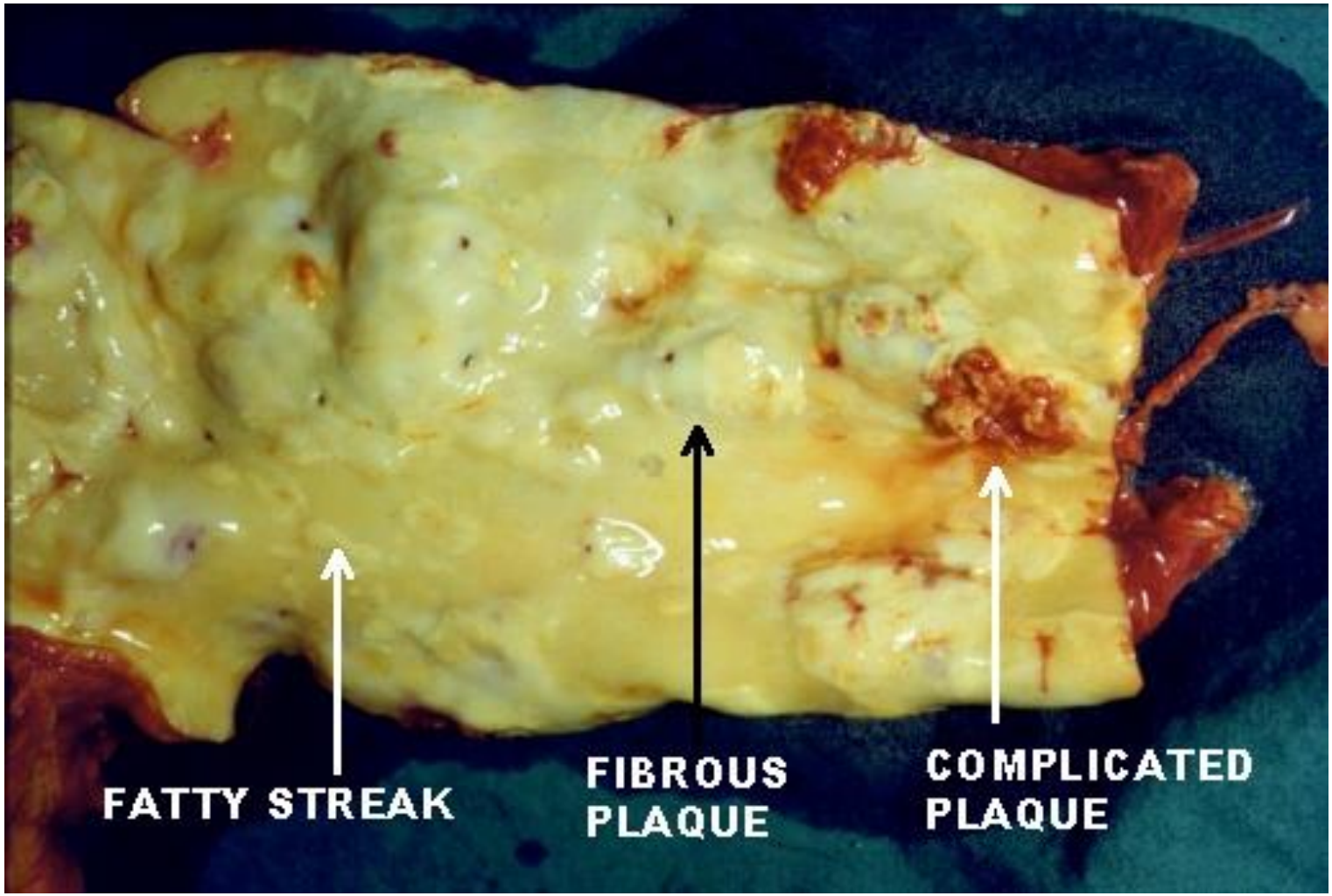
(2) extracellular matrix, including collagen, elastic fibers, and proteoglycans; and

(3) intracellular and extracellular lipid.

These components occur in varying proportions and configurations in different lesions.


NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly intracellular lipid accumulation
Intermediate lesion
• intracellular lipid accumulation
• small extracellular lipid pools
Atheroma
• intracellular lipid accumulation
• core of extracellular lipid
Fibroatheroma
• single or multiple lipid cores
• fibrotic/calcific layers
Complicated lesion
• surface defect
• hematoma-hemorrhage
• thrombosis
from first decade
from third decade
from fourth decade
growth mainly by lipid addition
increased smooth muscle and collagen increase
thrombosis and/or hematoma
clinically silent
clinically silent or overt

PLAQUE MORPHOLOGY



❑ Microscopic picture:

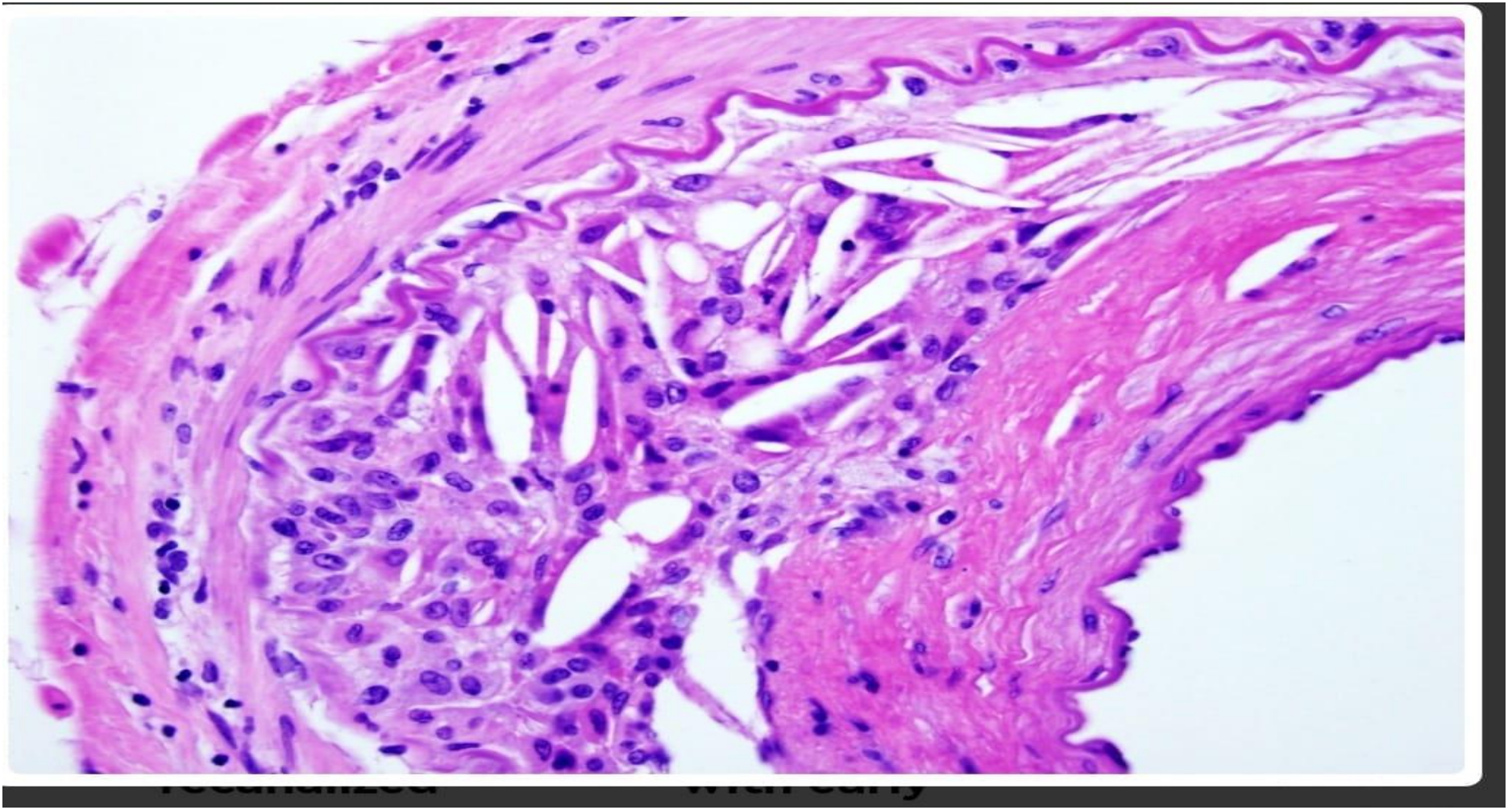
1. Cholesterol are deposited in the subintimal connective tissue. They are found free, inside smooth muscle cells derived from the media and inside macrophages (foam cells).

2. In paraffin sections the free cholesterol crystals appear as needle-shaped or rhombic-shaped empty spaces (dissolved).

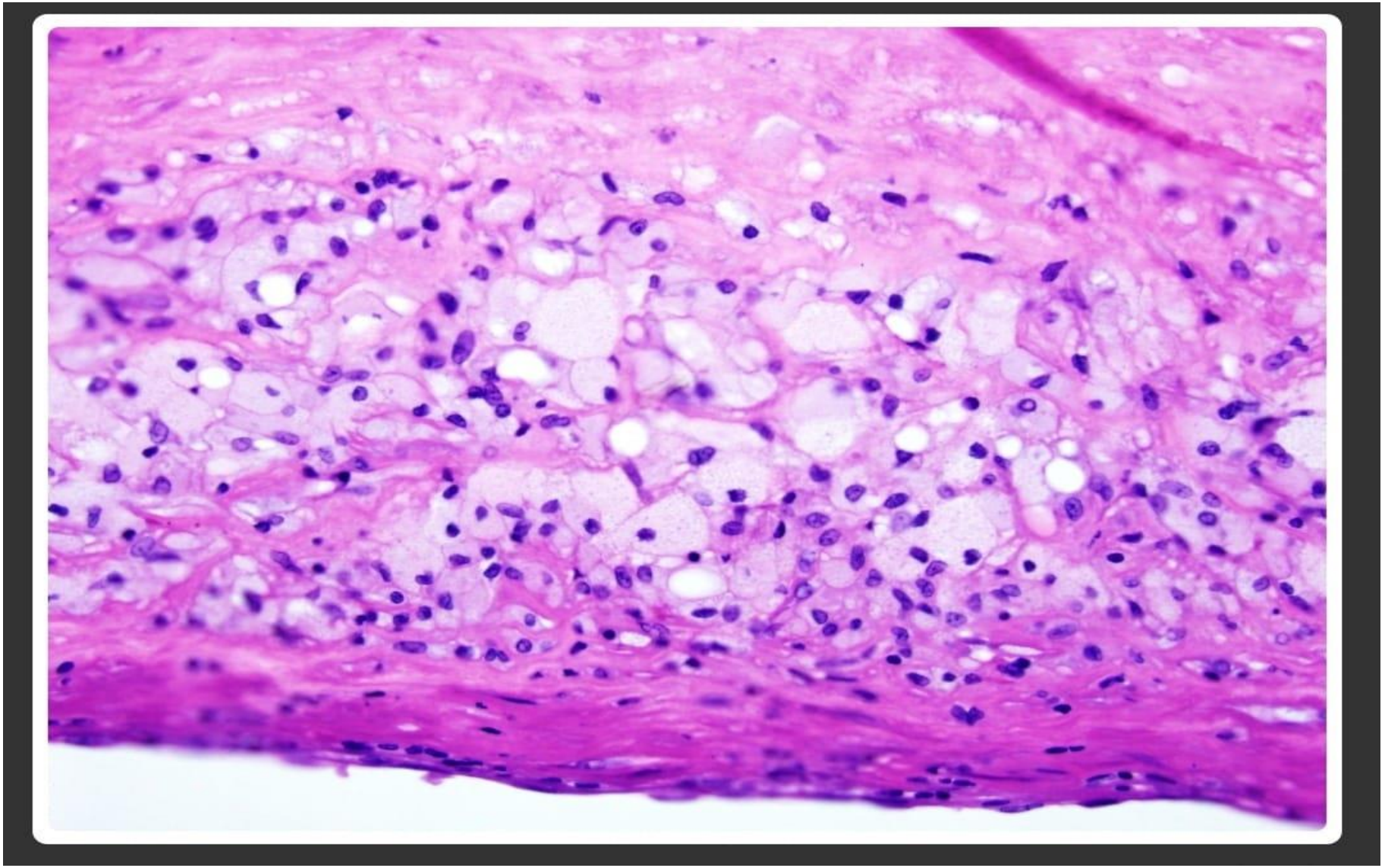
3. Fibrosis and hyalinosis of the subintimal connective tissue around the deposited lipids.

4. Dark blue stained calcium granules may be deposited in old lesions.

5. Fragmentation of the internal elastic lamina and atrophy of the media opposite the atheroma.



Appearance of fat in the subintimal layer both free and inside macrophage. Hypertrophy and upward migration of smooth muscle fibers to intima. Central part of fat undergo necrosis. Appearance of surface fibrous cap. Spread of the process to underlying media. Surface ulceration with thrombus formation. Appearance of cholesterol deposits in the central lesion



Foam cells within lipid rich core of atheromatous plaque

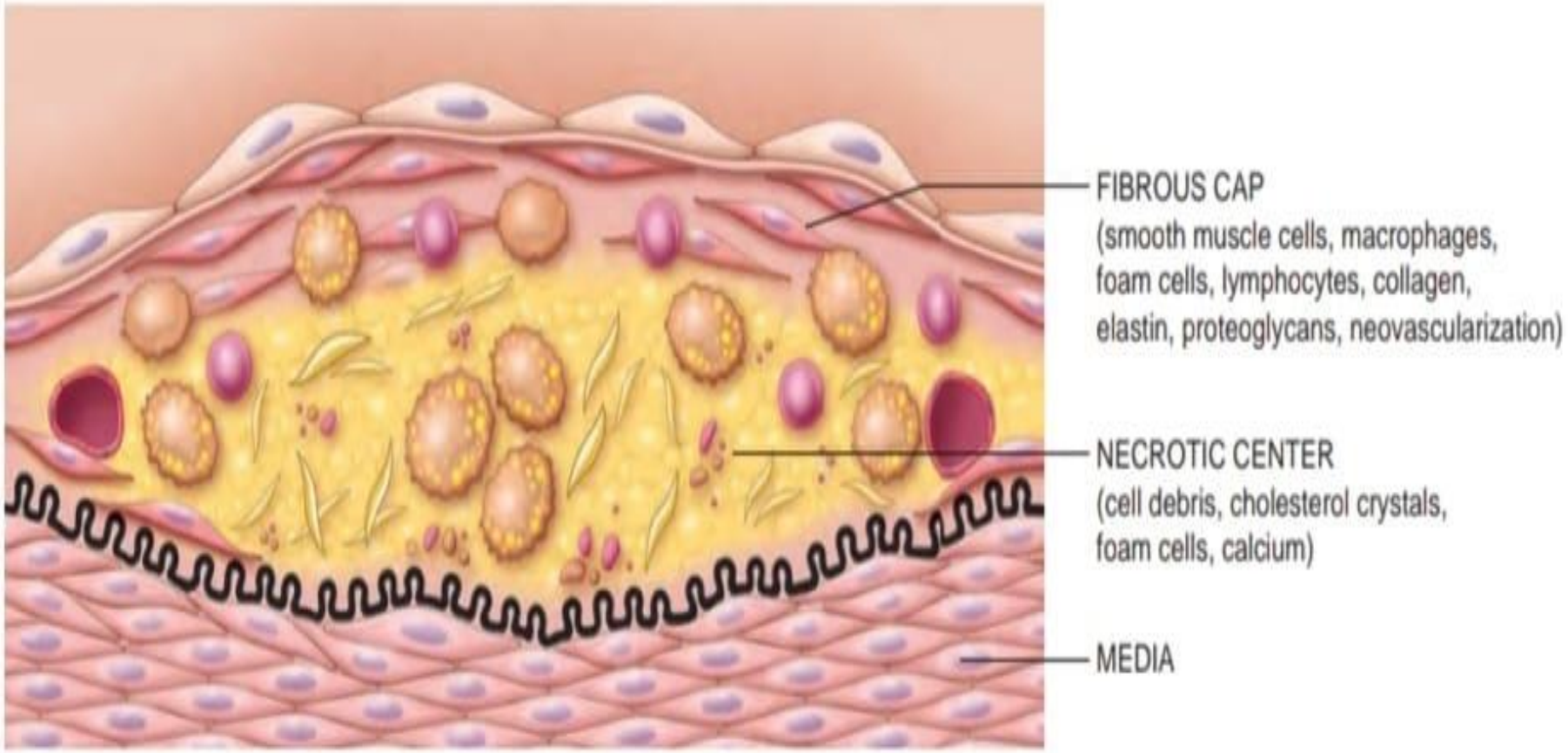
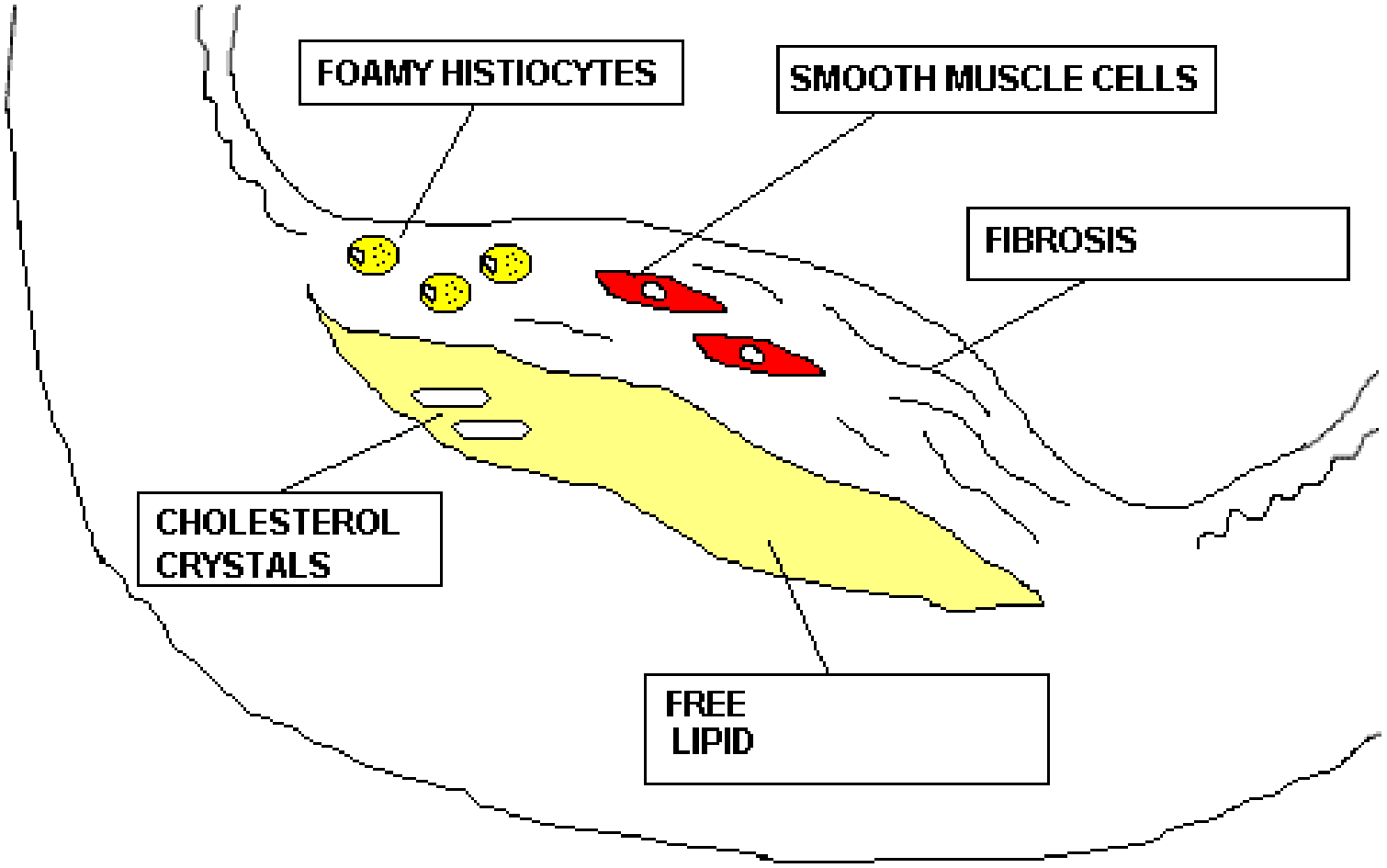
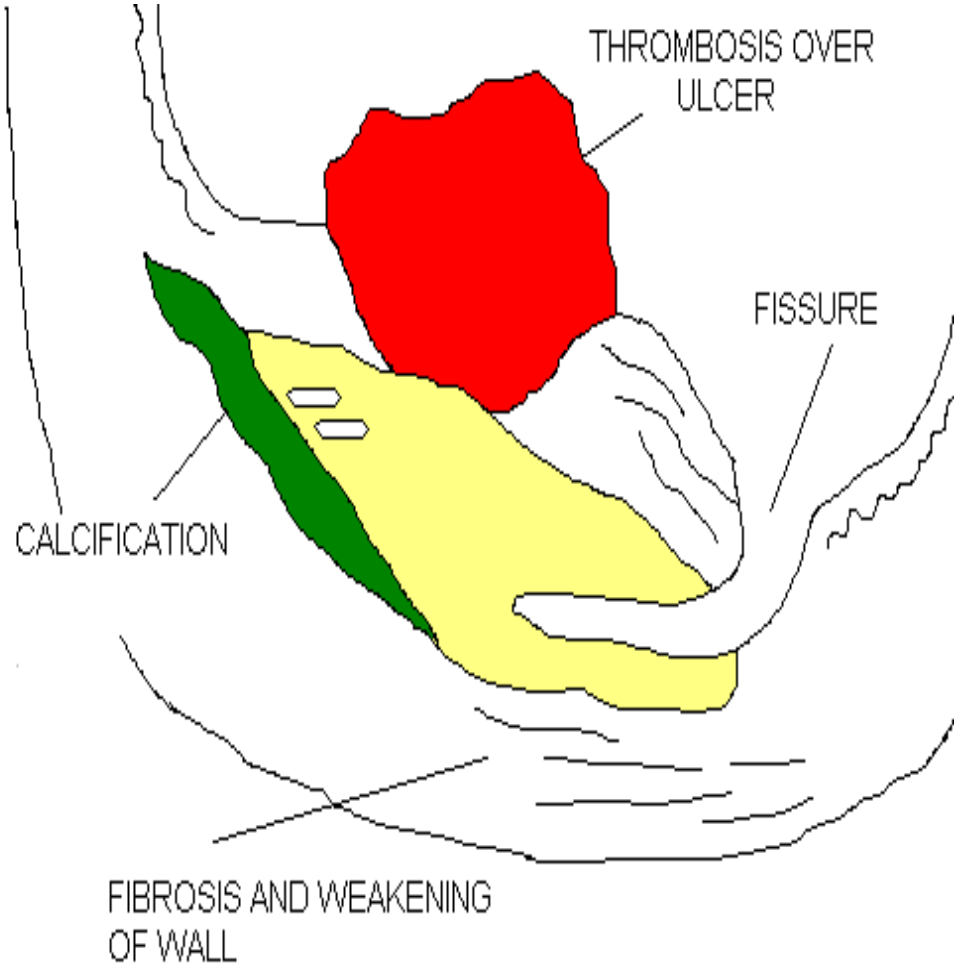


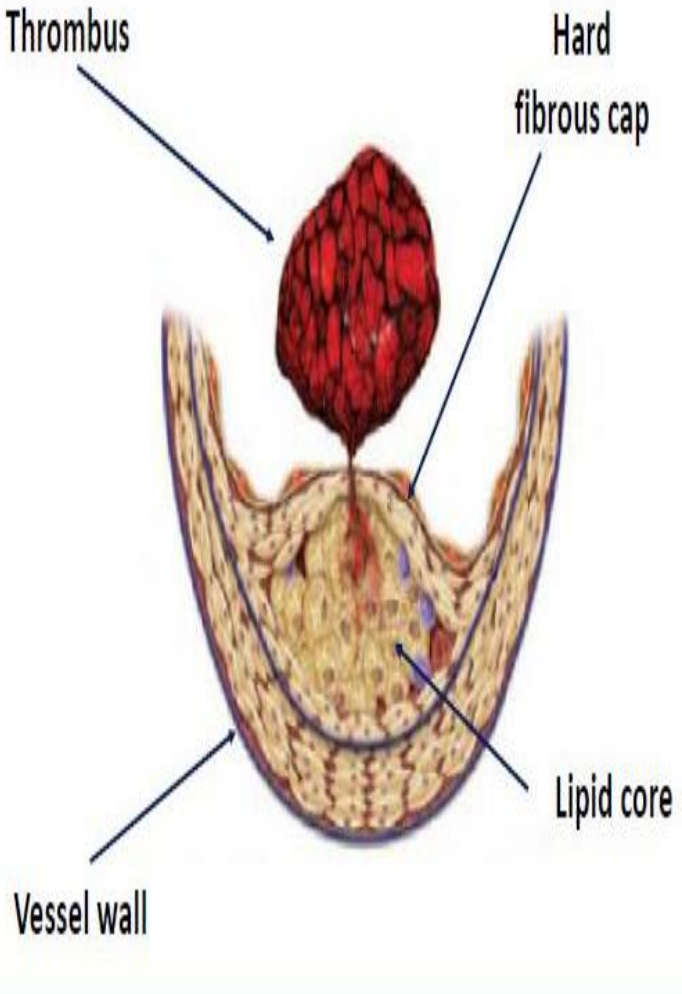
Figure 11.7 Basic structure of an atherosclerotic plaque. Note that atherosclerosis is an intimal-based process with a complex interplay of cells and extracellular materials. Plaques can have secondary effects on the underlying media including a reduction in smooth muscle cells.

THE FIBROUS PLAQUE



THE COMPLICATED PLAQUE





❑ Clinical effects

They vary depending on the size of the artery involved:

1. Uncomplicated atheroma of large arteries usually has no clinical effects because it doesn't reduce the lumen significantly or seriously thicken the wall.

2. In advanced cases an aneurysm may form.

3. Fragments of thrombi and athermanous debris from ulcerated plaques may form emboli which lodge in arteries of the legs and abdominal organs such as the gut, kidneys and spleen.

4. The most important effect of atheroma is due to involvement of smaller arteries.

5. The lumen may be progressively narrowed by an atheromatous plaque causing *chronic ischemia* or suddenly occluded by thrombosis which often causes *infarction*.

6. The most dangerous effect is the *coronary artery thrombosis*.

7. If ischemia is severe *gangrene* may develops which starts in the toes and spreads proximally.


Many thanks