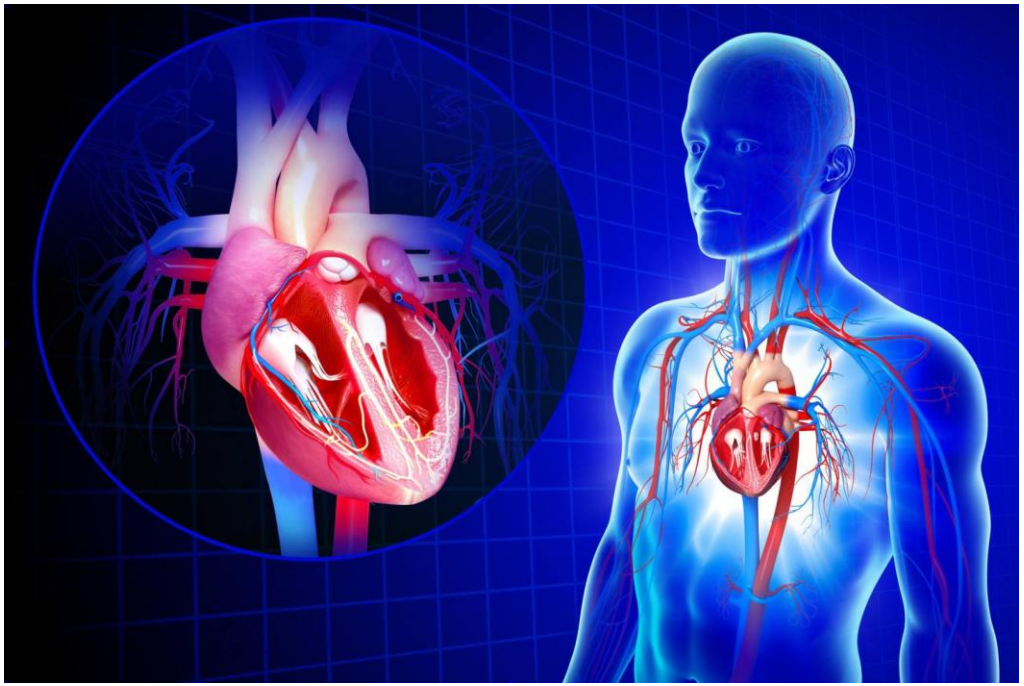
DISORDERS of Cardiovascular System



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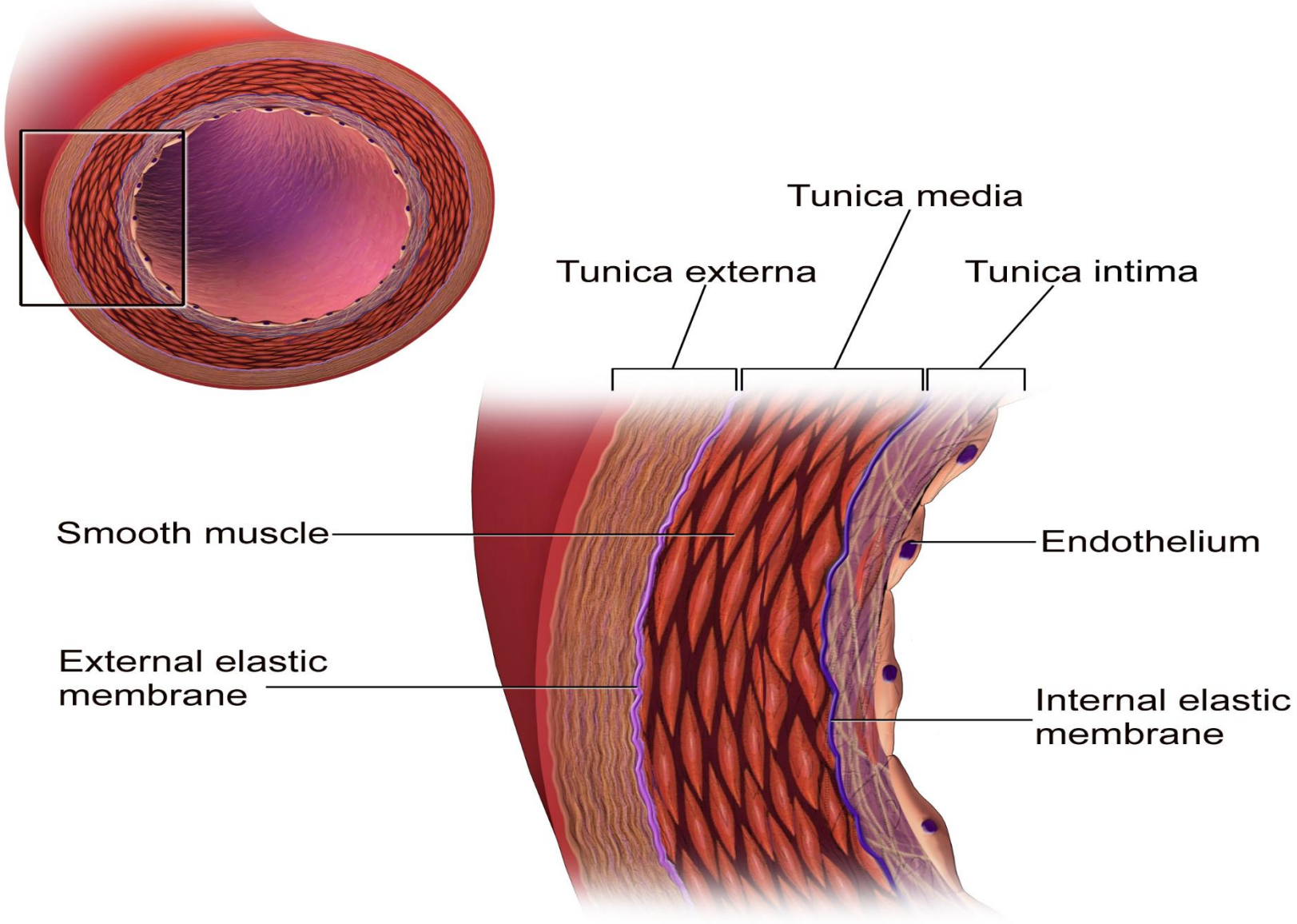
Ph.D in Pharmacy

Atherosclerosis

- Atherosclerosis is a disease of large elastic arteries and medium sized muscular arteries. Its basic lesion is the atheroma (fibro-fatty plaque) which is a raised patch within the intima having a core of lipid (mainly cholesterol) and a cup of fibrous tissue.

The Structure of an Artery Wall



Risk factors for atherosclerosis:

Modified risk factors:

- Diet and hyperlipidemia, high carbohydrate intake
- Hypertension
- Cigarette smoking
- Diabetes mellitus
- Obesity
- Physical inactivity
- stress

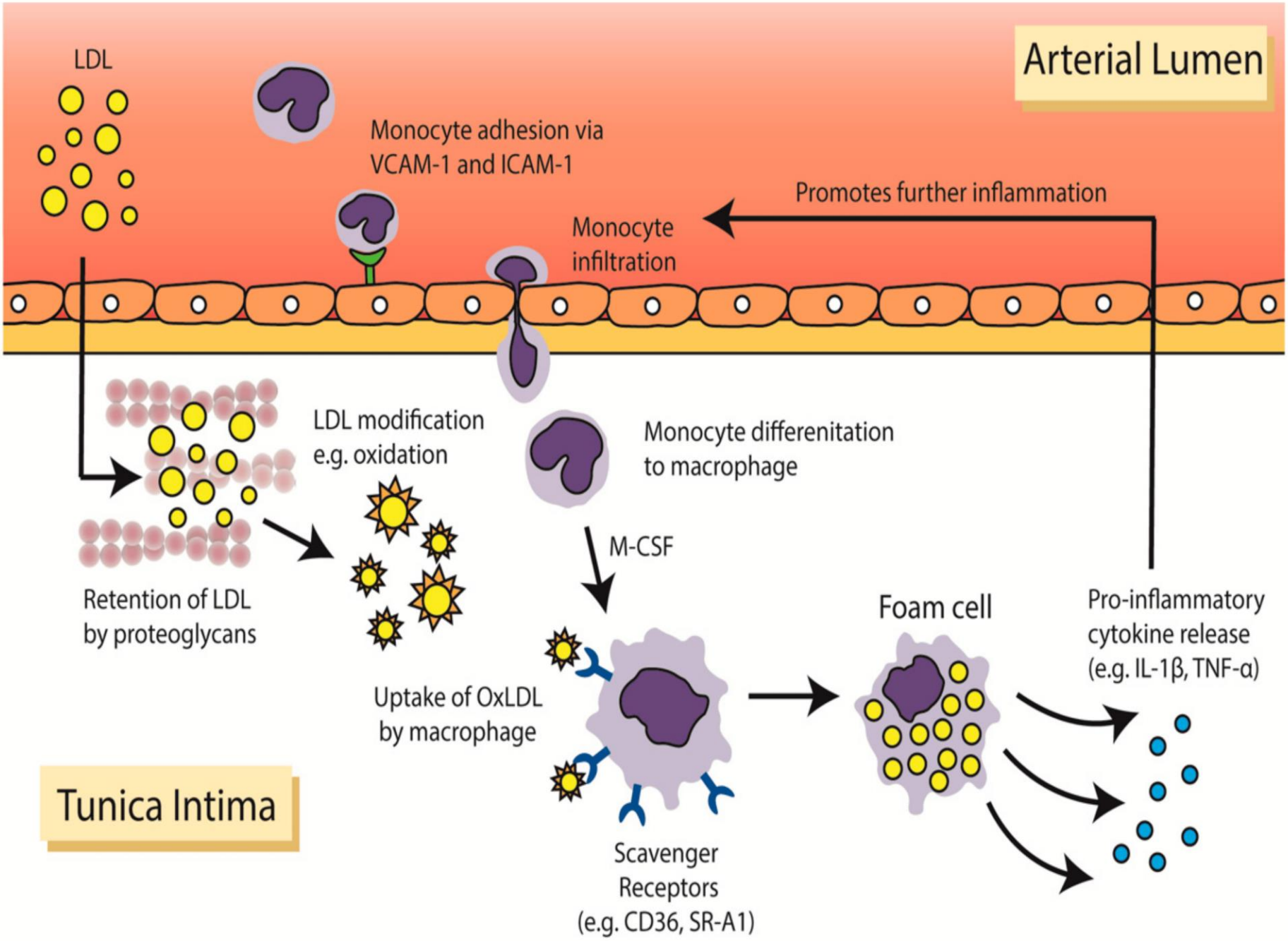
Non-modified risk factors:

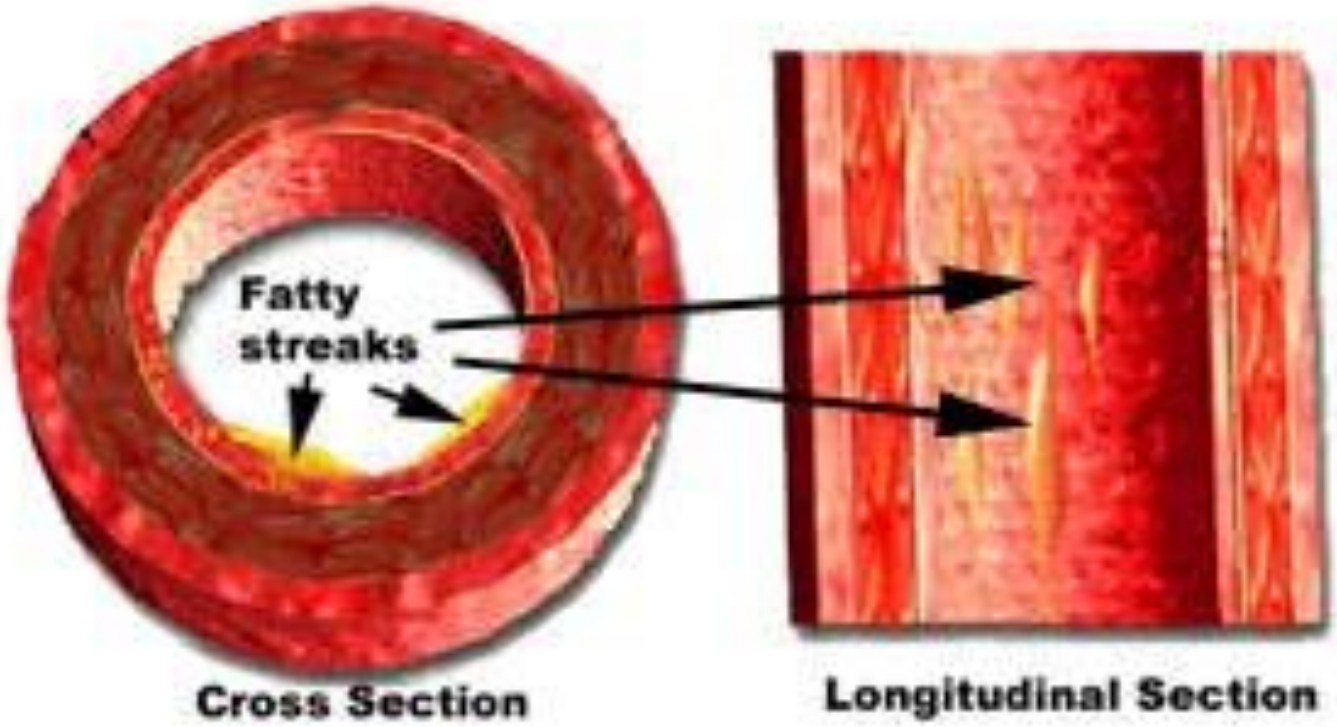
- Increase age
- Male gender
- Family history
- Genetic abnormality

Pathology and pathogenesis of atherosclerosis:

The most widely accepted theory of pathogenesis is called "**the response to injury hypothesis**" it includes the following stages:

1.Fatty streak stage: Earliest visible lesions that appear as areas of yellow discoloration on artery's inner surface, this stage start as endothelial dysfunction caused by any of predisposing factors, this lead to Increased endothelial permeability allows for entry of LDL into the vessel intima, then monocyte infiltration which differentiate to macrophage and engulf the fat globules and transformed to foam cells


Arterial Lumen
LDL
Monocyte adhesion via
VCAM-1 and ICAM-1
Promotes further inflammation
Monocyte
infiltration
LDL modification
e.g. oxidation
Monocyte differenitation
to macrophage
M-CSF
Retention of LDL
by proteoglycans
Foam cell
Pro-inflammatory
cytokine release
(e.g. IL-1β, TNF-α)
Uptake of OxLDL
by macrophage
Tunica Intima
Scavenger
Receptors
(e.g. CD36, SR-A1)

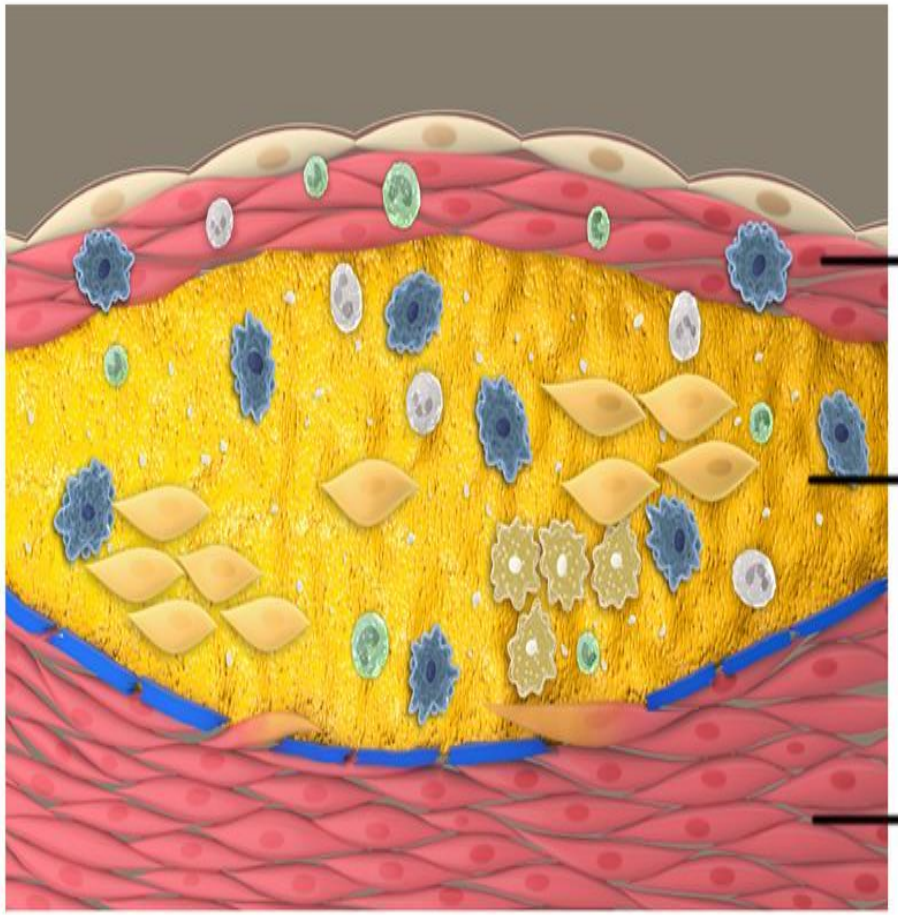

Fatty
streaks
Cross Section
Longitudinal Section

2.Progression stage: foam and platelet cells release mediators that cause migration of smooth muscle cell from media to intima with fibrous deposition covering the lipid plaque forming fibrin cap. Macrophages produces oxygen free radicles that oxidize lipid (LDL) , this oxidized LDL becomes more atherogenic as it:

- Chemotactic to blood monocytes
- Inhibits macrophages motility preventing them from leaving the atheroma
- Cytotoxic to endothelial cells increasing their permeability

The plaque may enlarge causing narrowing or occlusion of the artery

Atherosclerotic Plaque Anatomy



Fibrous Cap

- Smooth muscle cells
- Macrophages
- Lymphocytes
- Collagen

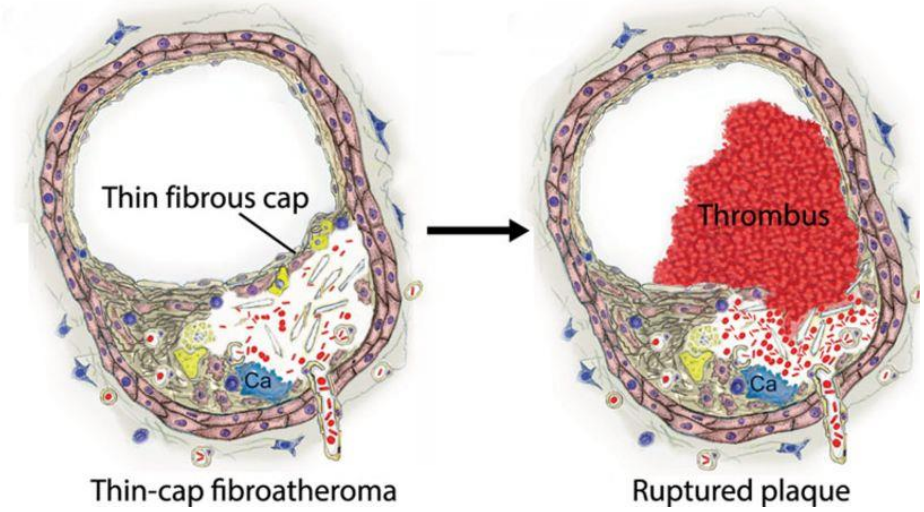
Necrotic Center

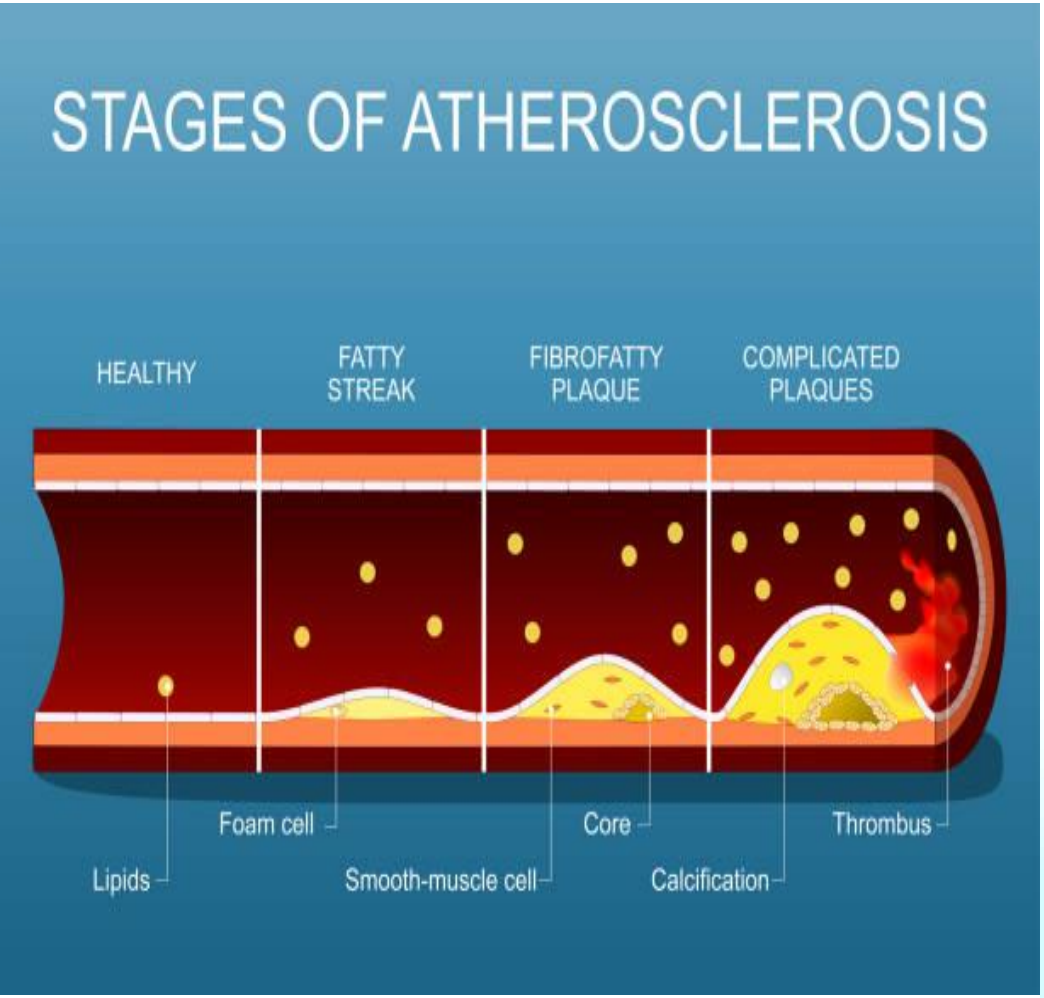
- Smooth muscle cells
- Macrophages
- Foam cells
- Lymphocytes
- Cholesterol crystals
- Calcium
- Cell debris

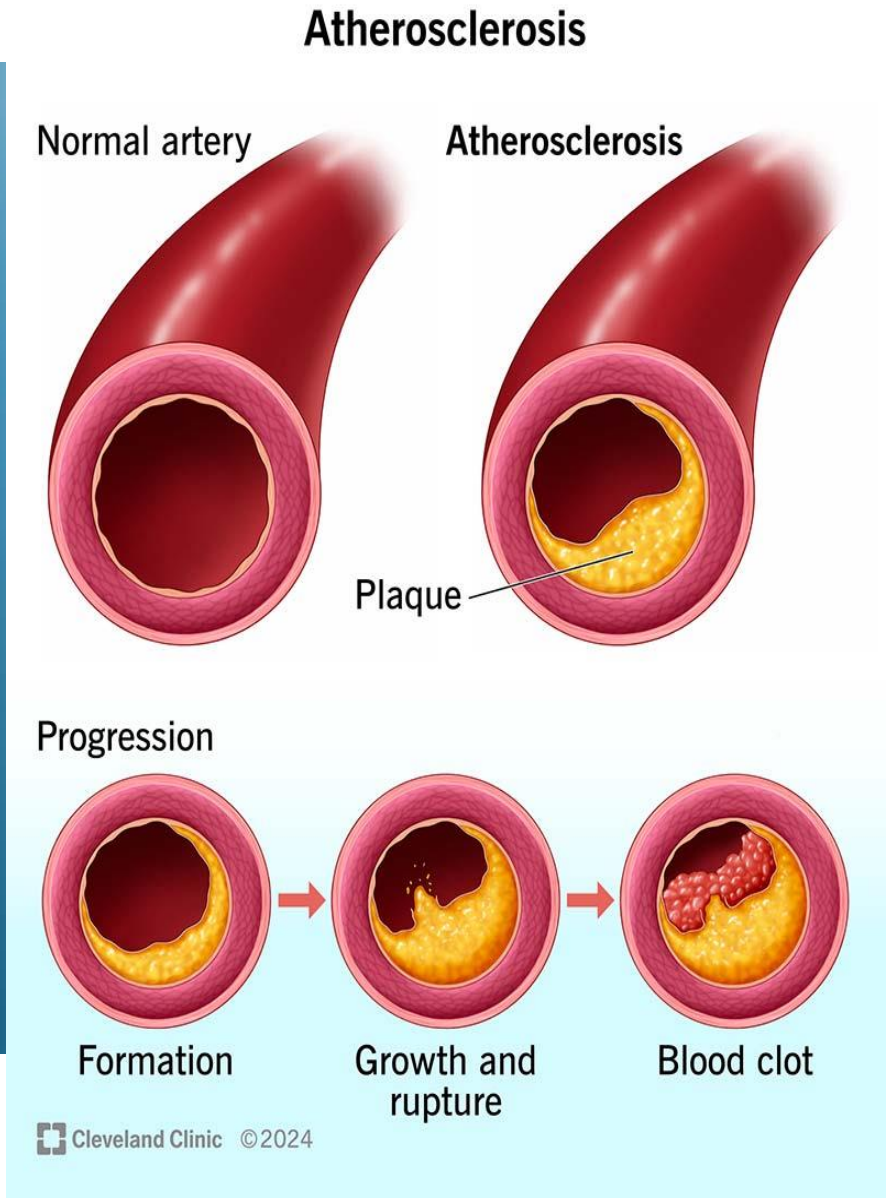
Media

- Smooth muscle cells

3. Plaque rupture: atheroma can be ruptured leading to sever endothelial injury and thrombus formation.




STAGES OF ATHEROSCLEROSIS
HEALTHY
FATTY STREAK
FIBROFATTY PLAQUE
COMPLICATED PLAQUES
Lipids
Foam cell
Smooth-muscle cell
Core
Calcification
Thrombus

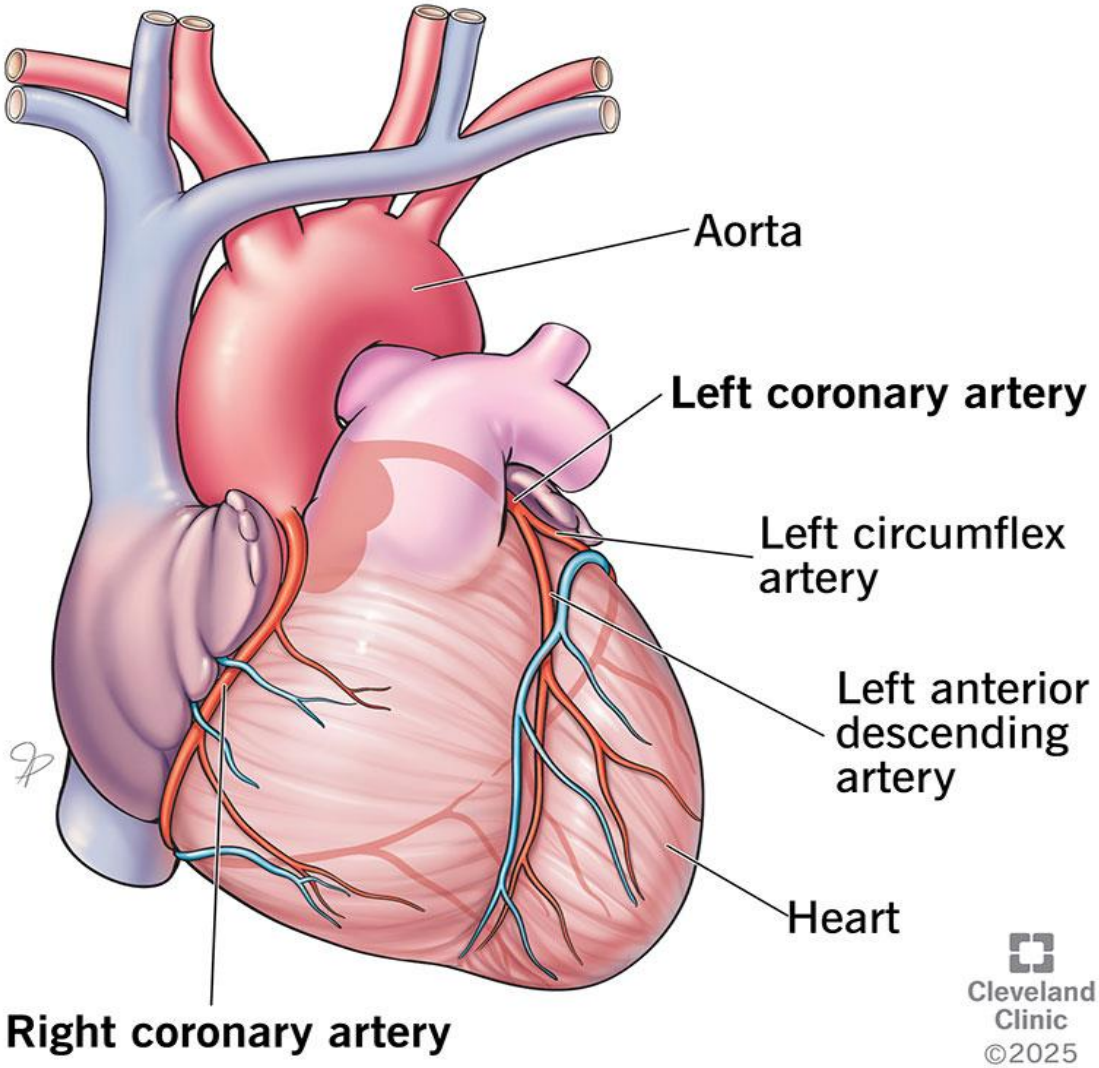

Atherosclerosis
Normal artery
Atherosclerosis
Plaque
Progression
Formation
Growth and rupture
Blood clot
Cleveland Clinic ©2024

Ischemic heart disease IHD

IHD: an imbalance between myocardial oxygen supply and demand results in myocardial hypoxia and accumulation of waste metabolites. IHD include the followings:

- Angina pectoris
- Myocardial infarction
- Sudden death

Coronary arteries



Pathogenesis:

1.Reduction in coronary artery blood flow (90% of the cases)

a) Atherosclerosis (the main cause)
b) Coronary artery spasm
c) Hemodynamic disorders (circulatory disorders)
d) Non atherosclerotic coronary diseases (arteritis)

2.Increase cardiac demand

a) Tachycardia
b) Ventricular hypertrophy

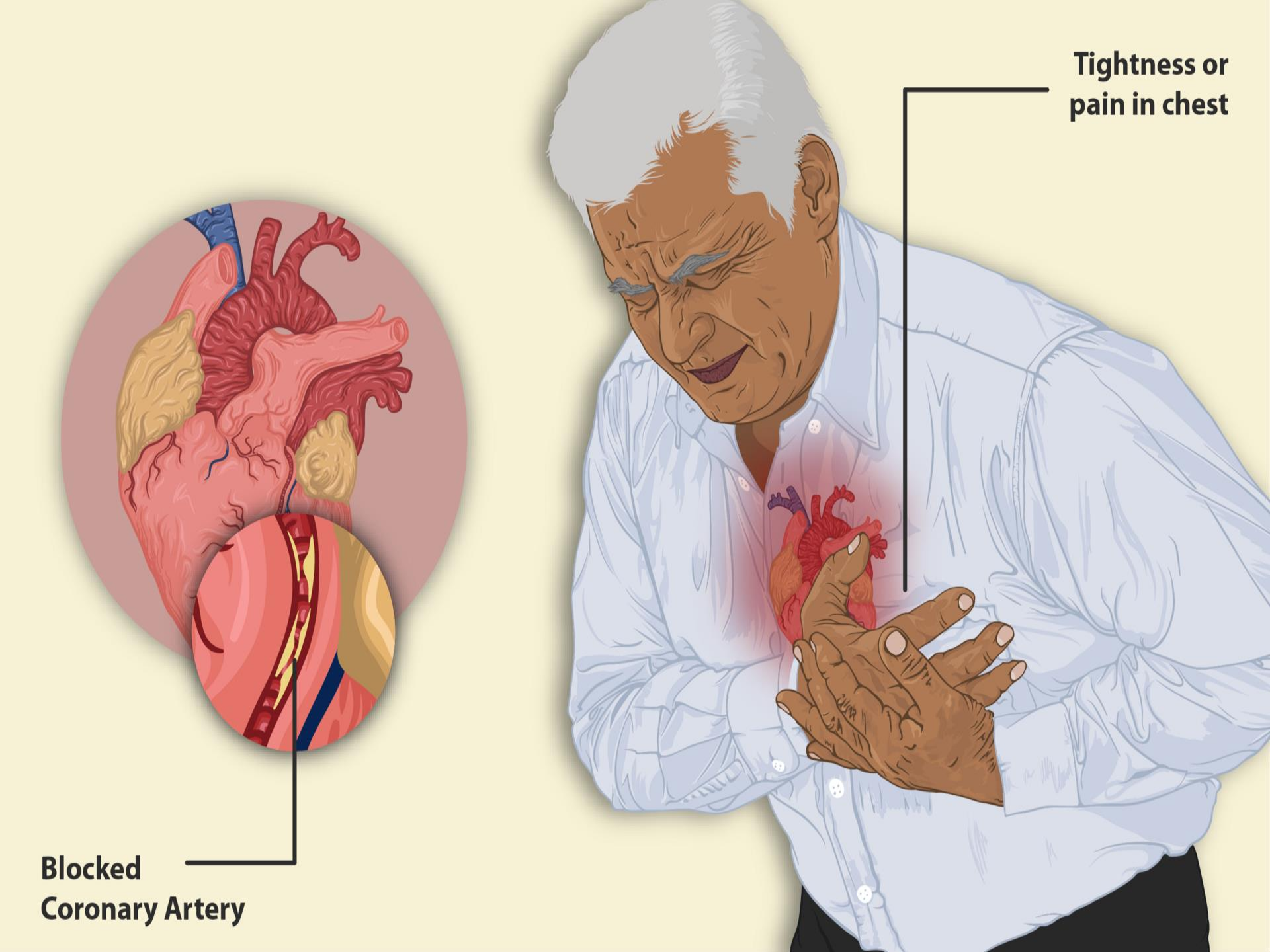
3.Reduced oxygen carrying capacity of the blood

a) Anemia
b) Cigarette smoking
c) Advanced lung diseases
d) Cyanotic congenital heart diseases
e) Carbon monoxide poisoning

Angina pectoris

Angina pectoris: recurrent retrosternal chest discomfort or pain caused by transient myocardial ischemia. This ischemia is not sufficient to induce infarction. There are three overlapping pattern of angina:

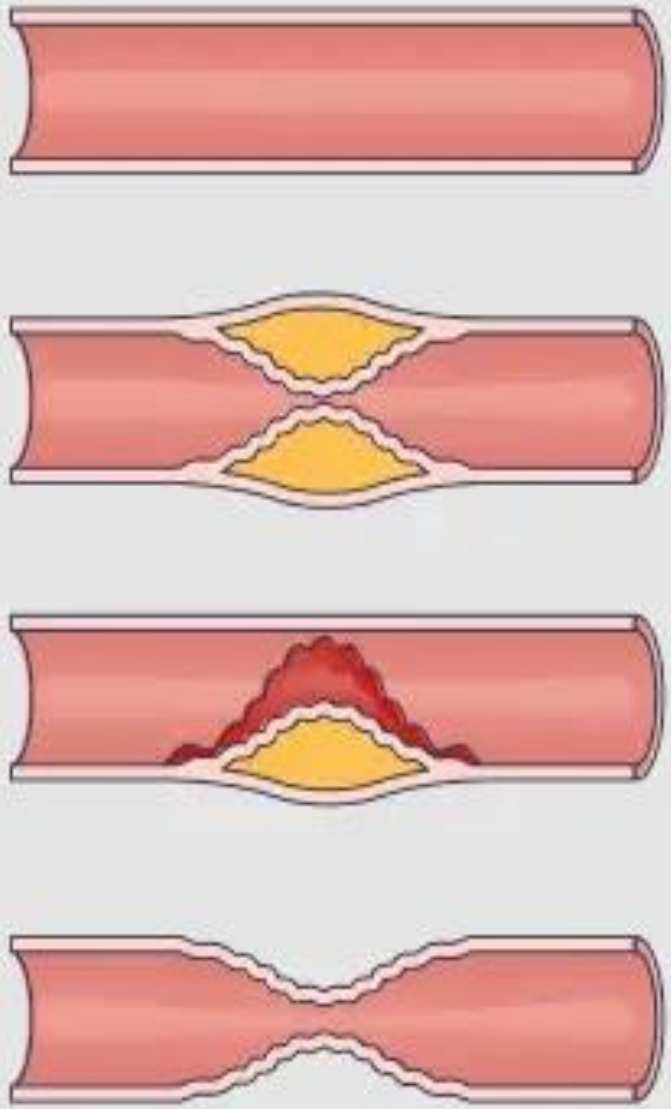
1. Stable angina: chronic transient angina pectoris, precipitated by physical activity or emotional upset, relieved by rest or nitroglycerin within a few minutes. Usually occurs when about 75% of coronary artery lumen stenosed by atheroma (chronic cause).


Tightness or
pain in chest
Blocked
Coronary Artery

2. Prinzmetal (variant) angina: Atypical anginal discomfort, usually at rest, which develops because of coronary artery spasm, rather than an increase of myocardial oxygen demand.

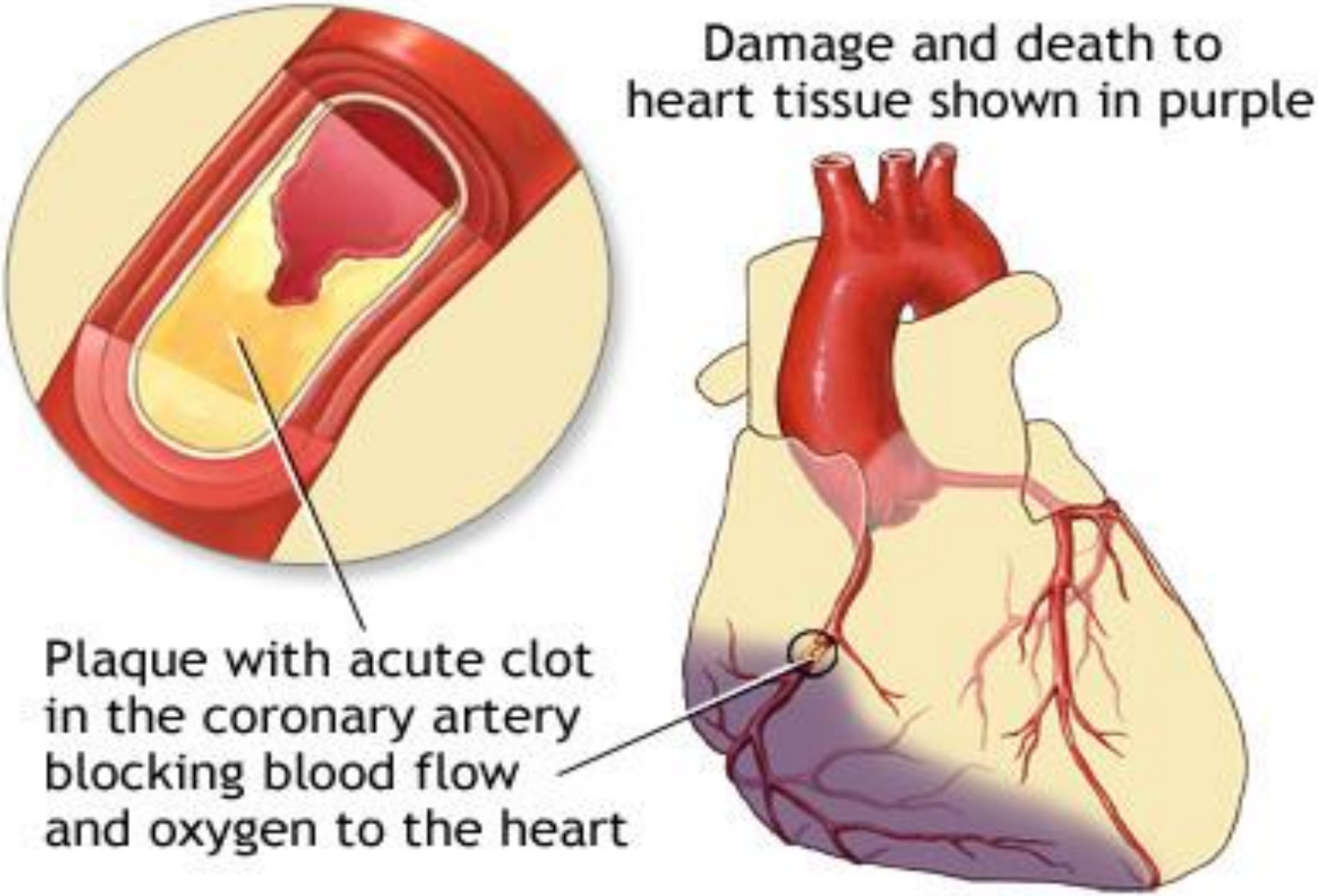
3. Unstable angina: acute coronary syndrome characterized by progressively increased frequency and more prolonged attack of angina. It usually occurs due to disrupted atherosclerotic plaque with superimposed thrombosis. It has high frequency of progression to myocardial infarction if untreated

TYPES OF ANGINA



Myocardial infarction (MI):

- Region of **myocardial necrosis** usually due to complete cessation of blood supply; most often results from acute thrombus at site of coronary atherosclerotic stenosis. It may be the first clinical manifestation of ischemic heart disease, or there may be a history of angina pectoris.


Damage and death to heart tissue shown in purple
Plaque with acute clot in the coronary artery blocking blood flow and oxygen to the heart

- The MI could be

1. Transmural MI: (full wall thikness) which is most common type about 90% of the cases. There is complete occlusion to the blood supply of the area by thrombus formation due to ruptured atheroma.

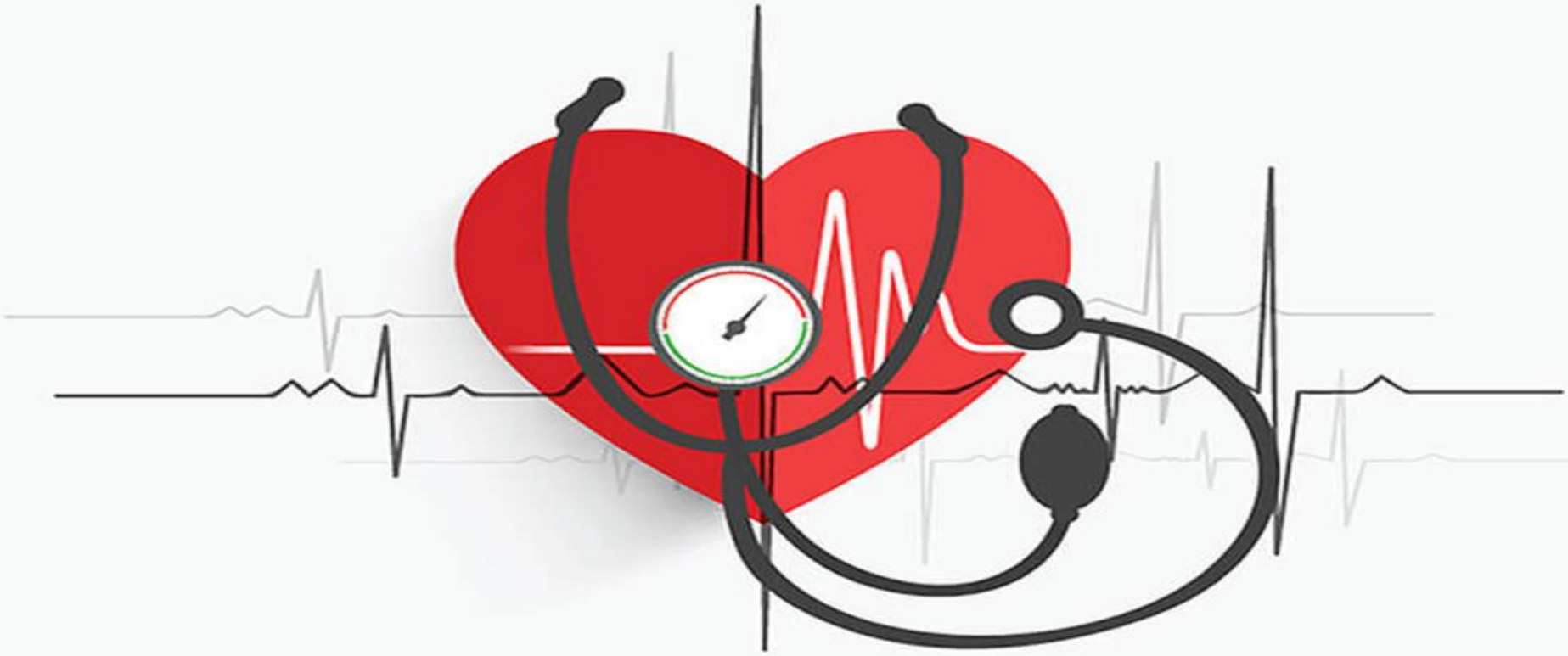
2. Subendothelial MI: the subendothelium is the most vulnerable region to any reduction in blood flow.In this type there is advanced but not sever coronary atherosclerosis lead to subendothelial infarction only.

Sudden death

- It is unexpected death from cardiac causes early after symptom onset (usually within hour) or without onset of symptoms (a symptomatic). Usually it is the first clinical manifestation of IHD. In young patient it could be due to:

1. Congenital coronary abnormalities
2. Aortic artery stenosis
3. Mitral valve prolapse
4. Myocarditis and cardiomyopathy
5. Arrhythmia

Medbury Medical Services



HYPERTENSION

A SILENT KILLER

Hypertension

- Hypertension: defined as increase in blood pressure
- Blood pressure depends on cardiac output (CO) and systemic vascular resistance (SVR)
- BP = CO x SVR*
  SVR= systemic vascular resistance
- Cardiac output depends on heart rate (HR) and stroke volume (SV)
- CO = HR x SV** SV= stroke volume

- Systolic blood pressure = left ventricle contraction = stroke volume
- Diastolic blood pressure = left ventricle relaxation = filling time = SVR

Mechanism of BP regulation:

Short term regulation:

1) Mediated by the sympathetic nervous system – it increases both HR and SVR.

2) Baroreceptor reflex - senses pressure changes in aortic and carotid arteries. It is responsible for regulation of short term blood pressure fall and correct it. It Accommodates changes in posture, exercise, fear and anxiety, fever, etc.. by increase HR and SVR.

Long term regulation:

1) Major contributor is the renin-angiotensin-aldosterone system (Na+ and water retention)

2) Atrial natriuretic peptide material (ANP): it is Natural diuretic, causes kidneys to increase Na and water excretion

3) Antidiuretic hormone ADH: influence the kidney to reabsorb water and electrolyte

4) Endothelial and inflammatory cell mediators: initiating vasodilatation or vasospasm response

Pathogenesis of hypertension

First: increase cardiac output (increase cardiac preload): causes

- Increase fluid volume from excess sodium intake or renal sodium retention
- Excess stimulation of the renin-angiotensin-aldosterone system (RAAS)
- Sympathetic nervous system (SNS) over activity (increase venous return)

Second: increase systemic vascular resistance (after load hypertension)

- Systemic vessels contraction (increase in sympathetic nervous system stimulation).
- Narrowing of blood vessels e.g by atheroma

Stages of hypertention:

Stage I (moderate) systolic 140-159 mmHg OR diastolic 90-99 mmHg

Stage II (severe) systolic >160 mmHg OR diastolic >100 mmHg

Types of hypertension:

- Primary (essential) hypertension: 90% of the cases. The cause is unknown.
- Secondary hypertension: causes:

Steroids, renal vascular disease, renal parenchymal disease, pregnancy related, pheochromocytoma, Cushing's syndrome, coarctation of the aorta or primary hyperaldosteronism.

- Malignant hypertension: hypertension with multiple organ dysfunction.