Pathophysiology I

Chapter (4A): Cardiovascular disorders

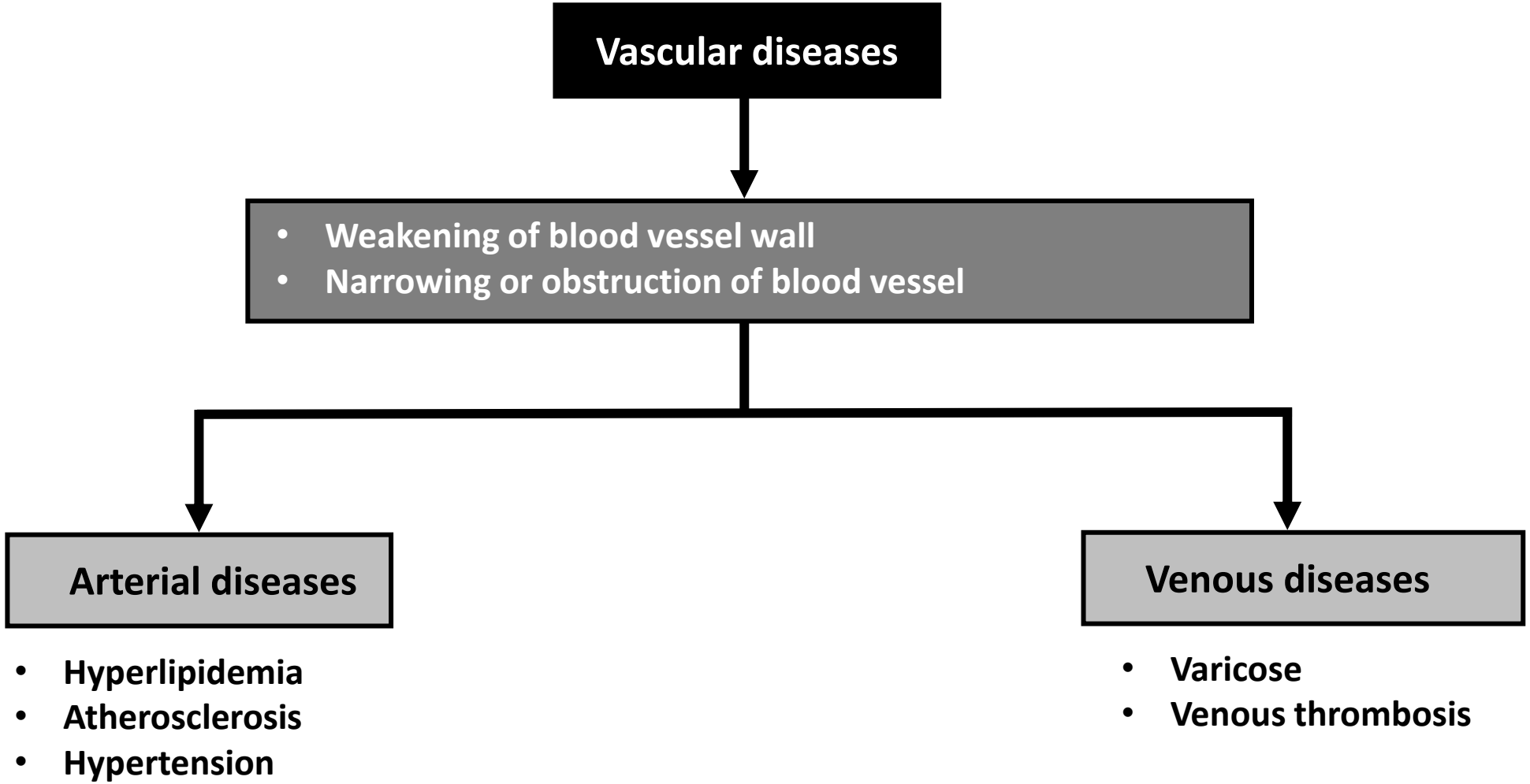
- **Blood vessels disorders**

  A. Arterial disorders
  B. Veins disorders

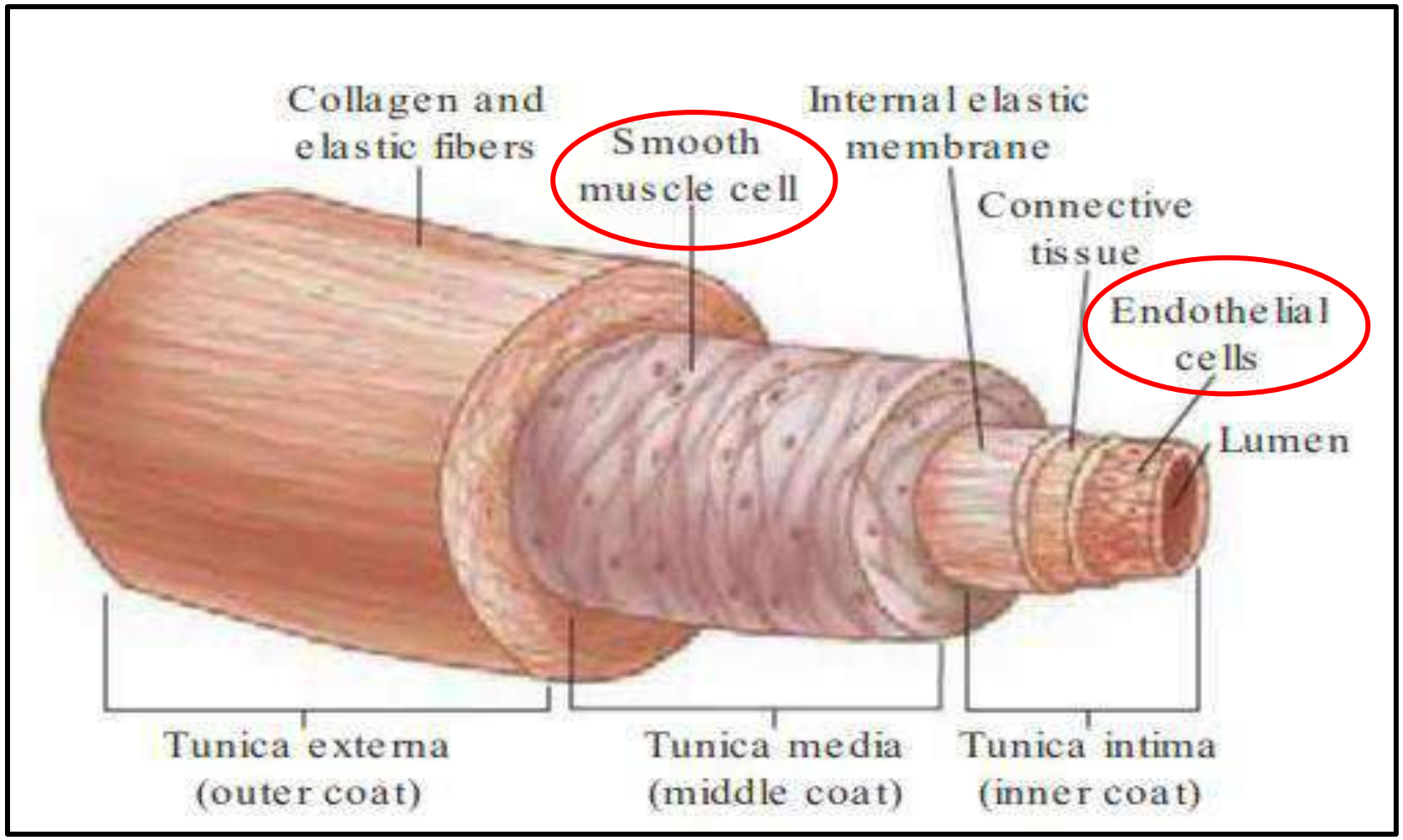
- **Heart disorders**

Blood vessels disorders

- **Disorders affecting blood vessels are called vascular diseases**

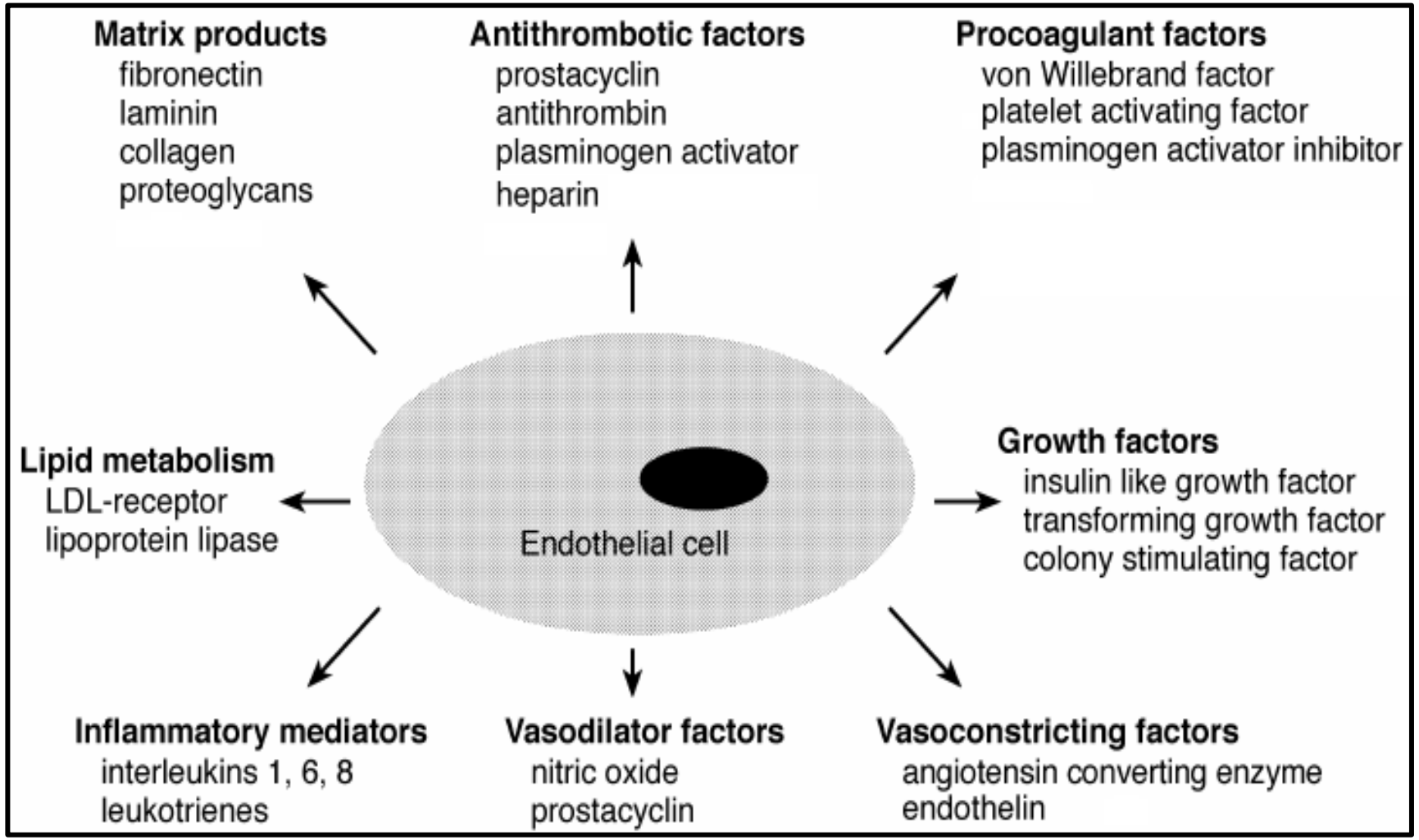


Blood vessels disorders



Blood vessels disorders

- **Endothelial cells functions**



Endothelial dysfunction

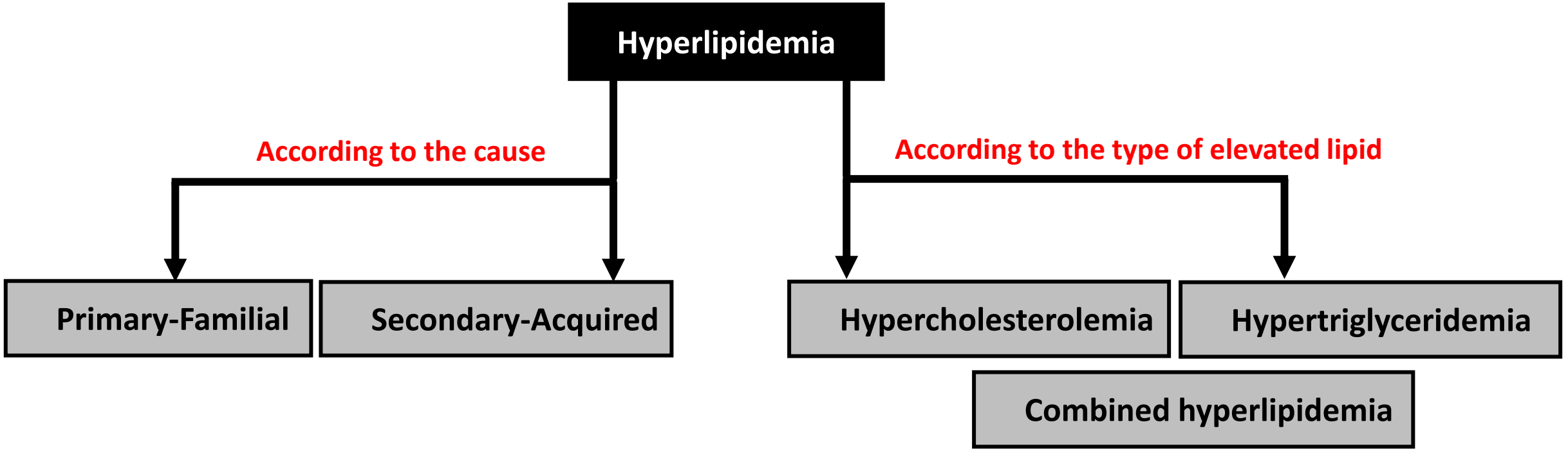
risk factors

- Smoking
- Hyperlipidemia
- Diabetes
- Aging
- Hypertension

Blood vessels disorders

Arterial disorders

- **Hyperlipidemia is abnormal increase in the levels of any or all lipid profiles in the blood.**



Blood vessels disorders

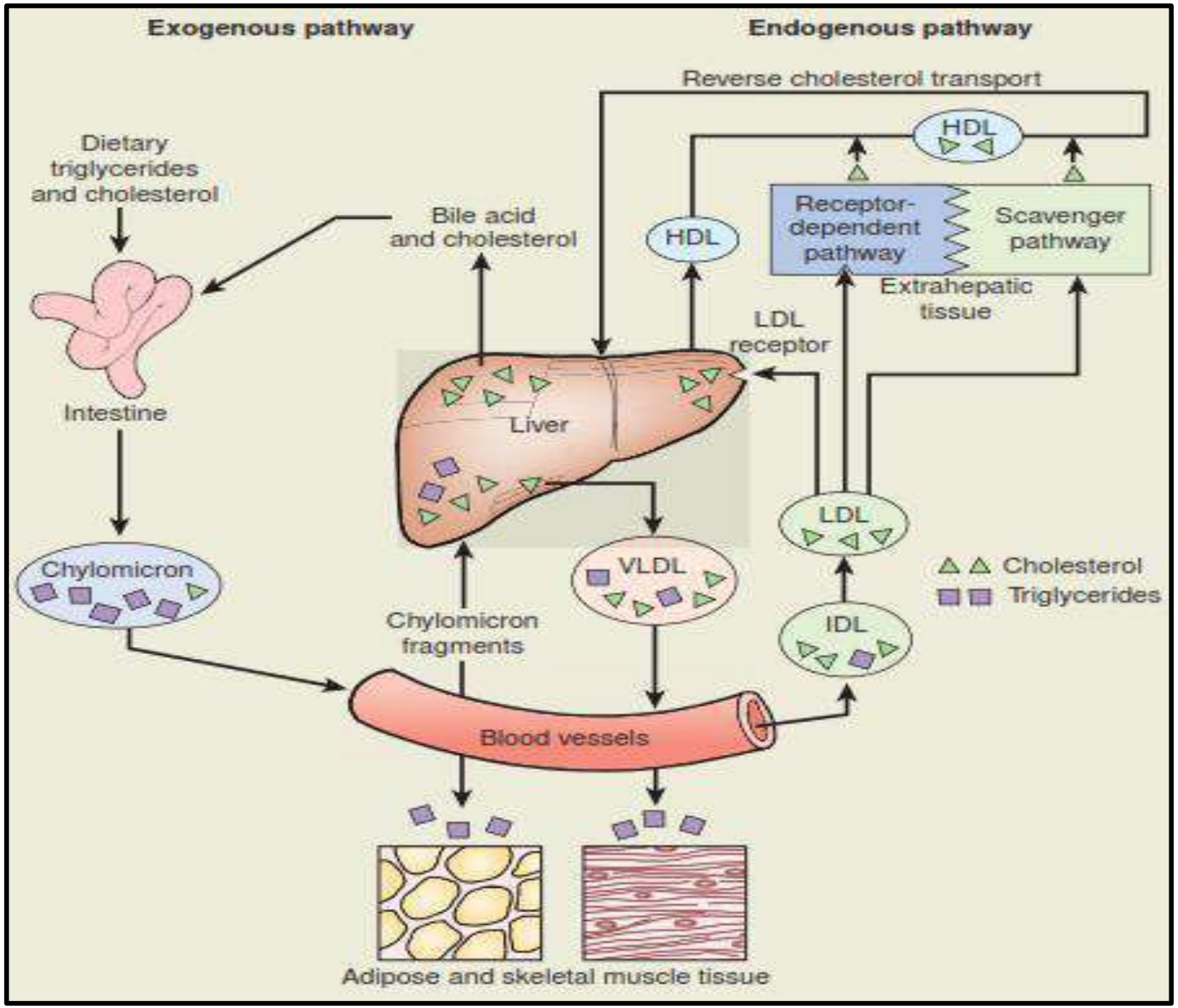
- **Classification of hyperlipidemia**

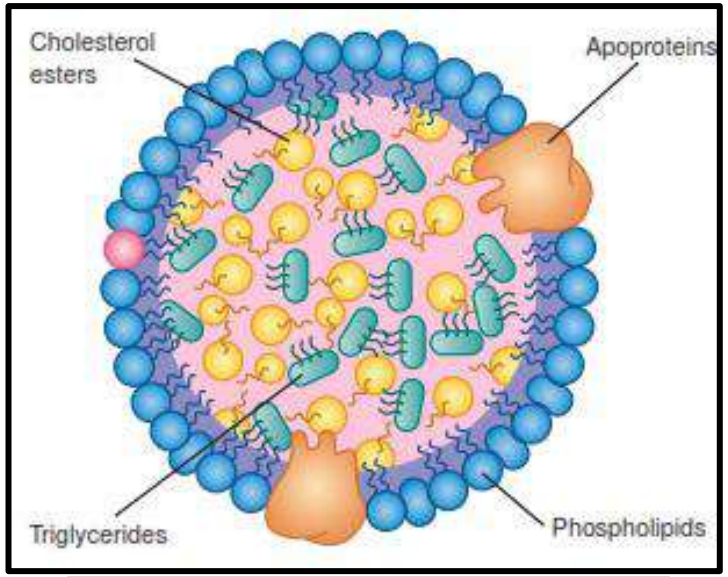
1. Primary (Familial) hyperlipidemia: Genetically based

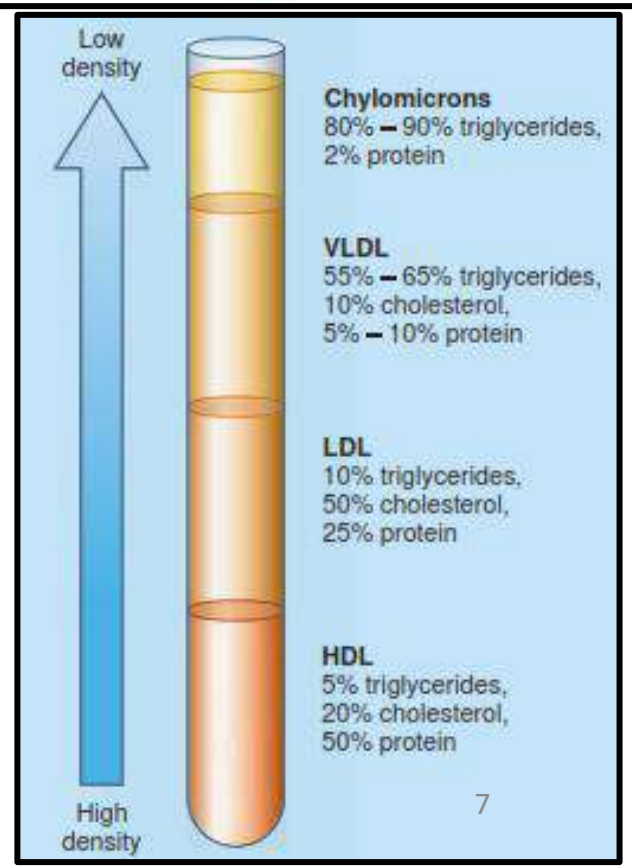
Class	Increased lipoprotein	Synonym	
Type I	↑ chylomicrons	Familial chylomicronemia	**Deficiency of lipoprotein lipase (LPL)**
Type IIa	↑ LDL	Familial hypercholesterolemia	**Mutation either in the LDL receptor gene or the ApoB100 gene**
IIb	↑ LDL and VLDL	Familial combined hyperlipidemia	
Type III	↑ IDL	Familial dysbetalipoproteinemia	**Mutation in ApoE gene**
Type IV	↑ VLDL	Familial hypertriglyceridemia	**Increased VLDL production and LPL deficiency**

2. Secondary (Acquired) hyperlipidemia: Other diseases based

Lipids transport

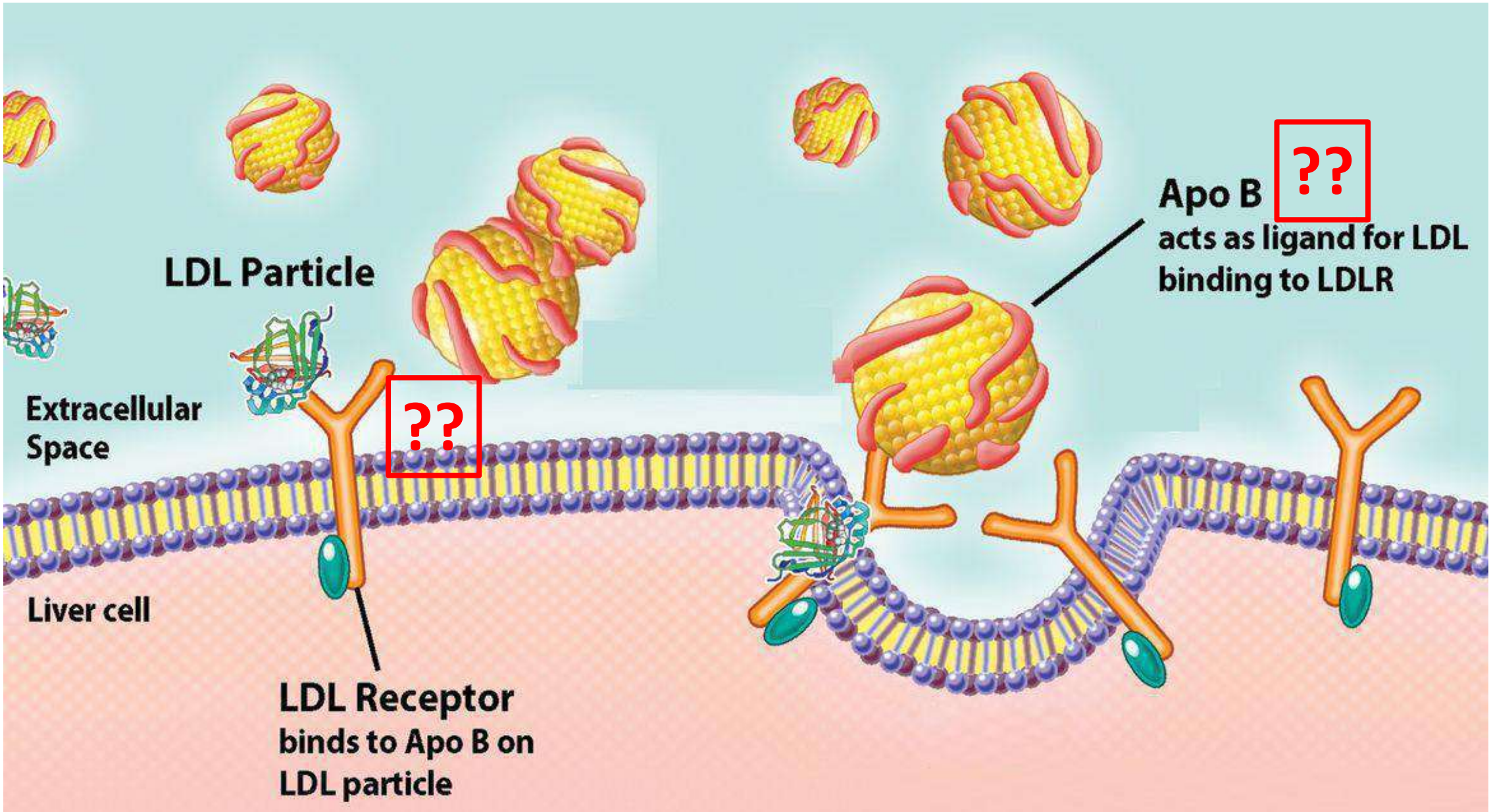






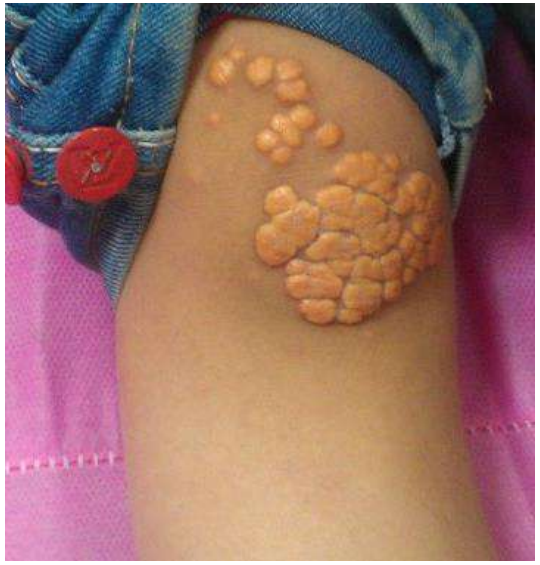
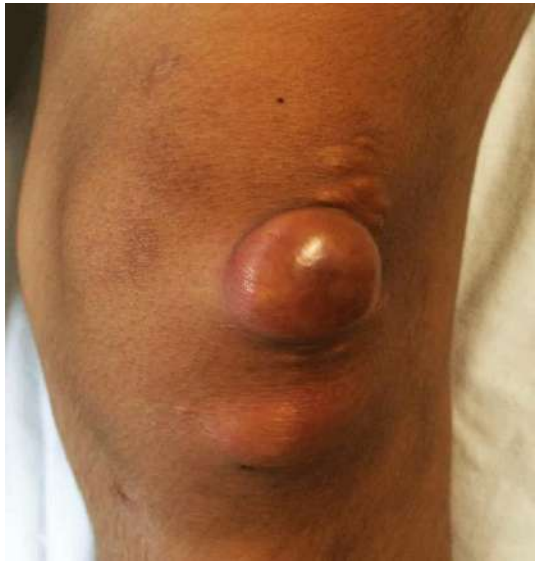
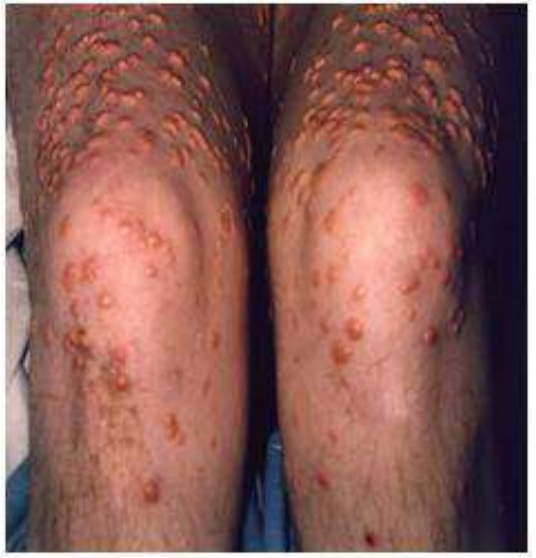
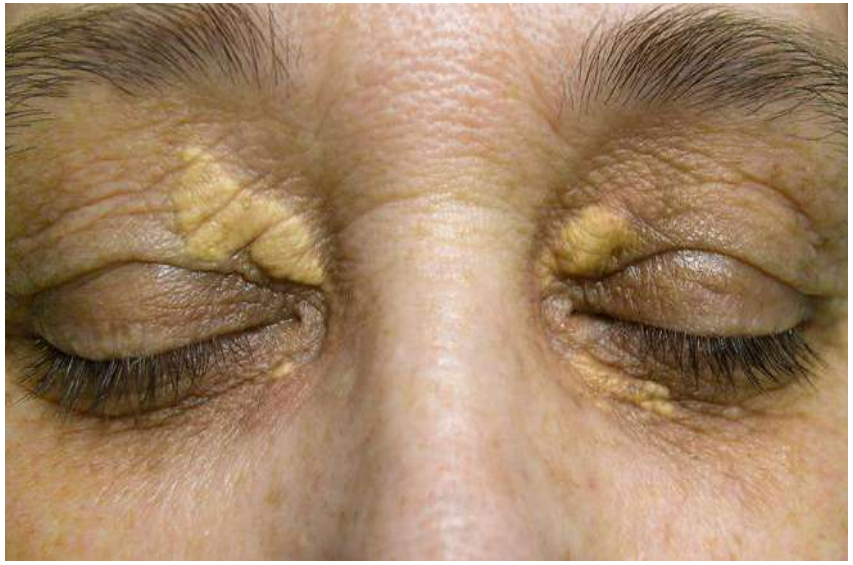
Blood vessels disorders

Pathogenesis of Familial Hypercholesterolemia



Blood vessels disorders

- **Symptoms:**
  - **Xanthomas**

  - **Cardiovascular diseases: atherosclerosis, myocardial infraction**

Blood vessels disorders

- **Diagnosis: Lipid profiles after overnight fasting**

TABLE 18-2 NCEP Adult Treatment Panel III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol	
<100	Optimal
100–129	Near optimal/above optimal
130–159	Borderline high
160–189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200–239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

Triglyceride levels

Classification	Triglyceride level*
Normal	Less than 150
Borderline high	150–199
High	200–499
Very high	500 or higher

*Values in milligrams per deciliter (mg/dL)

National Cholesterol Education Program [NCEP]

Blood vessels disorders

- **Management of hypercholesterinemia**

A. Non-pharmacological therapy

- Decrease calorie intake
- Decrease saturated fatty acids intake
- Decrease cholesterol intake
- Exercise

B. Pharmacological therapy

- Inhibitors of HMG-CoA reductase, a key enzyme in the cholesterol biosynthetic pathway: **Statins**
- Cholestrol absorption inhibitor agents: **Ezetimibe**
- Bile acids binding resins: **Cholestyramine**

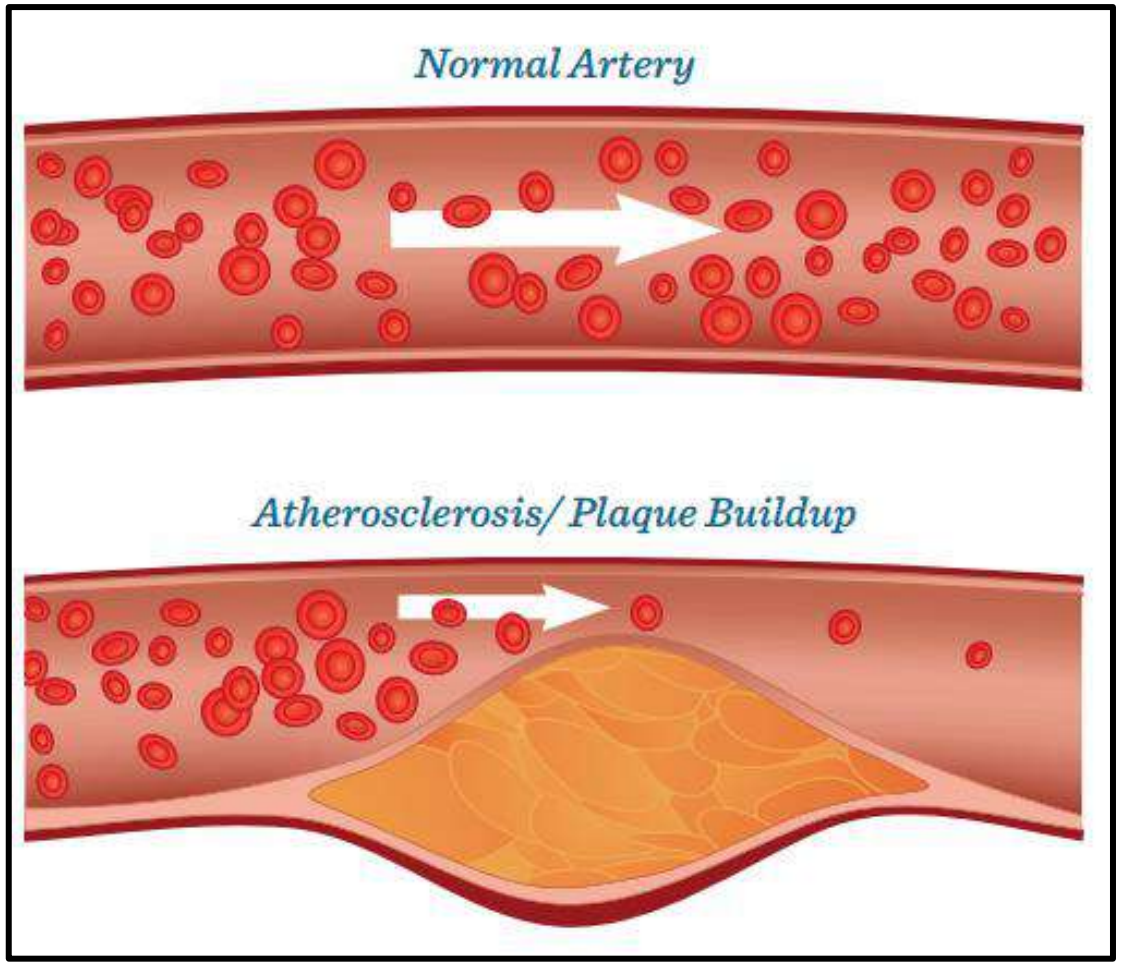
Blood vessels disorders

Arterial disorders

2. Atherosclerosis

- **Atherosclerosis is a disease characterized by narrowing the artery as a result of the accumulation of lipids and other materials.**

- **Formation of fibrofatty plaque in the intimal layer of an artery.**



Blood vessels disorders

Arterial disorders

2. Atherosclerosis

- **Causes and risk factors**

CHART 18-1 Risk Factors for Atherosclerosis

Nonmodifiable

- Increasing age
- Male gender
- Genetic disorders of lipid metabolism
- Family history of premature coronary artery disease

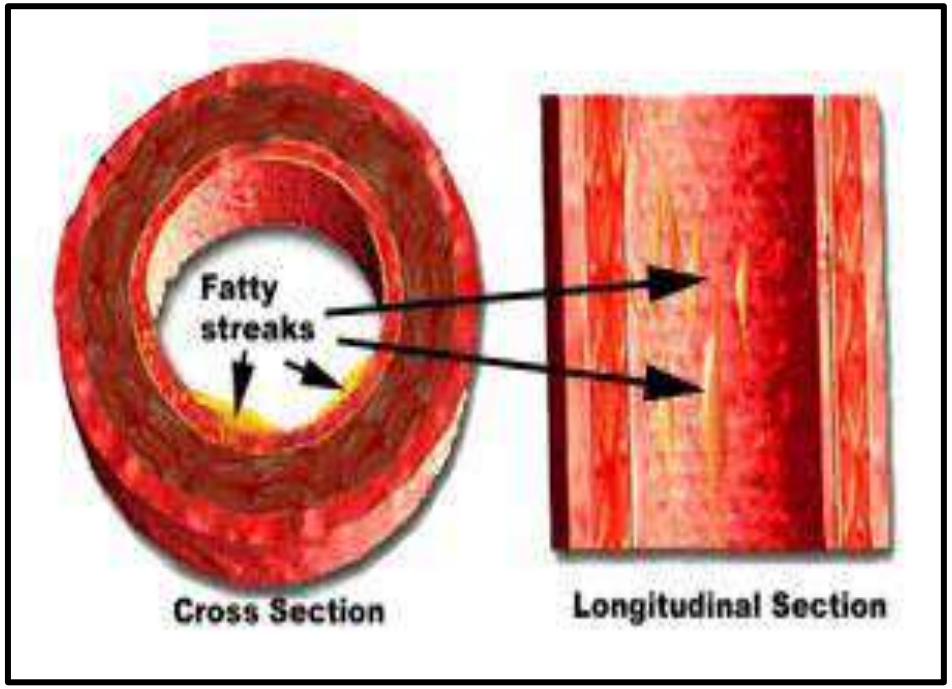
Potentially Modifiable

- Cigarette smoking
- Obesity
- Hypertension
- Hyperlipidemia with elevated low-density lipoprotein and low high-density lipoprotein cholesterol
- Diabetes mellitus

Additional Nontraditional

- Inflammation marked by elevated C-reactive protein levels
- Hyperhomocysteinemia
- Increased lipoprotein (a) levels

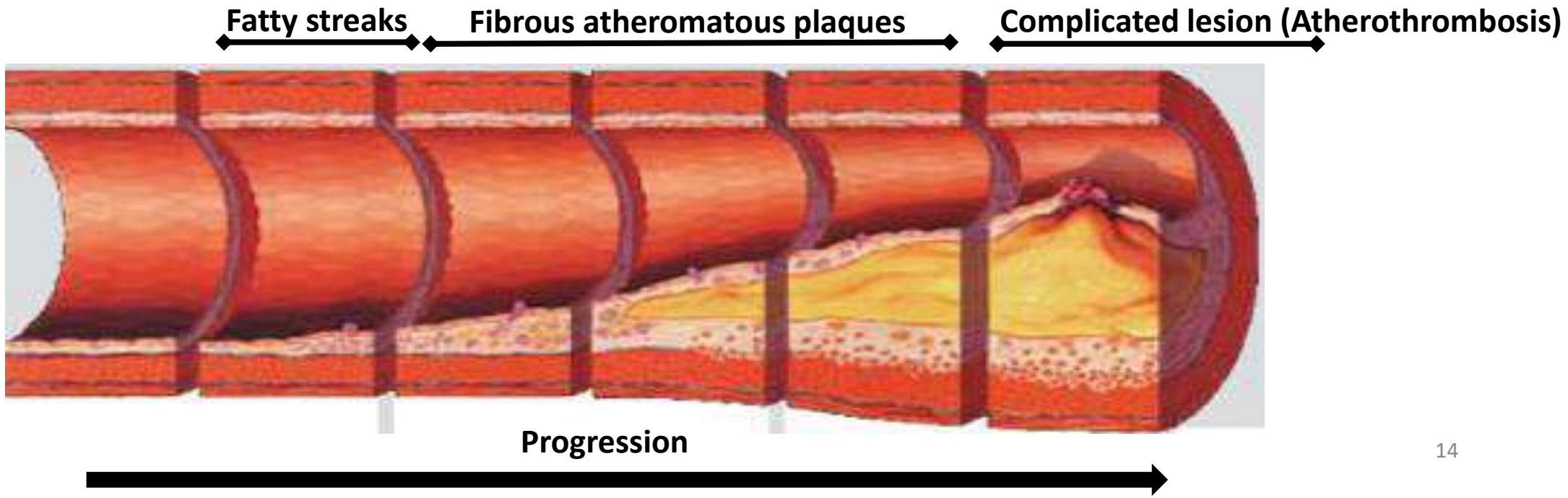
Blood vessels disorders



Arterial disorders

2. Atherosclerosis

- **Pathogenesis**



Blood vessels disorders

Arterial disorders

2. Atherosclerosis

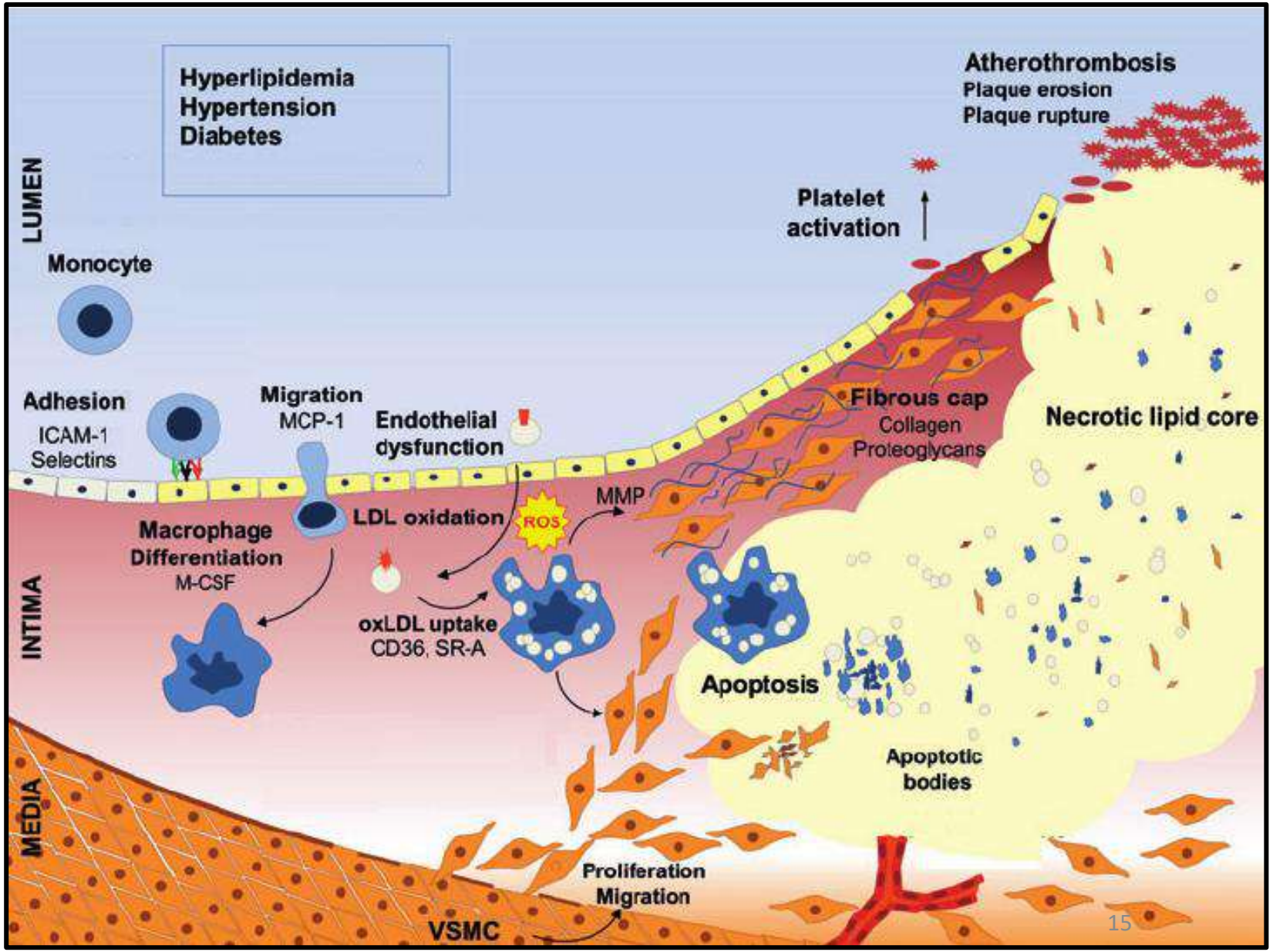
- **Pathogenesis**

a. Endothelial cell injury

b. Migration of inflammatory cells

c. Lipid accumulation and smooth muscle cell proliferation

d. Fibrous plaque formation



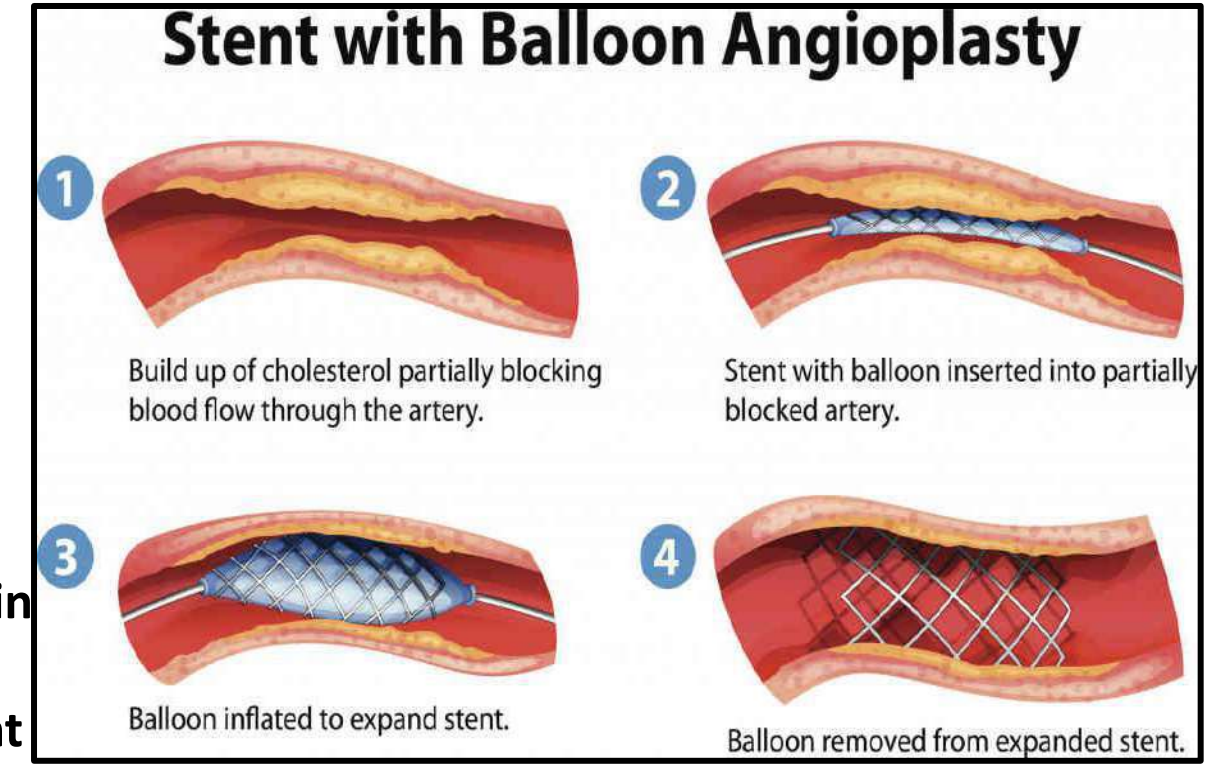
Blood vessels disorders

Arterial disorders

2. Atherosclerosis

Treatment

- Drugs to lower cholesterol such as statins, Ezetimibe
- Drugs that decrease thrombosis process, such as aspirin
- Angioplasty (balloon angioplasty) with or without stent



Blood vessels disorders

Arterial disorders

3. Vasculitides (Vasculitis)

TABLE 30.2 CLASSIFICATION OF THE VASCULITIDES

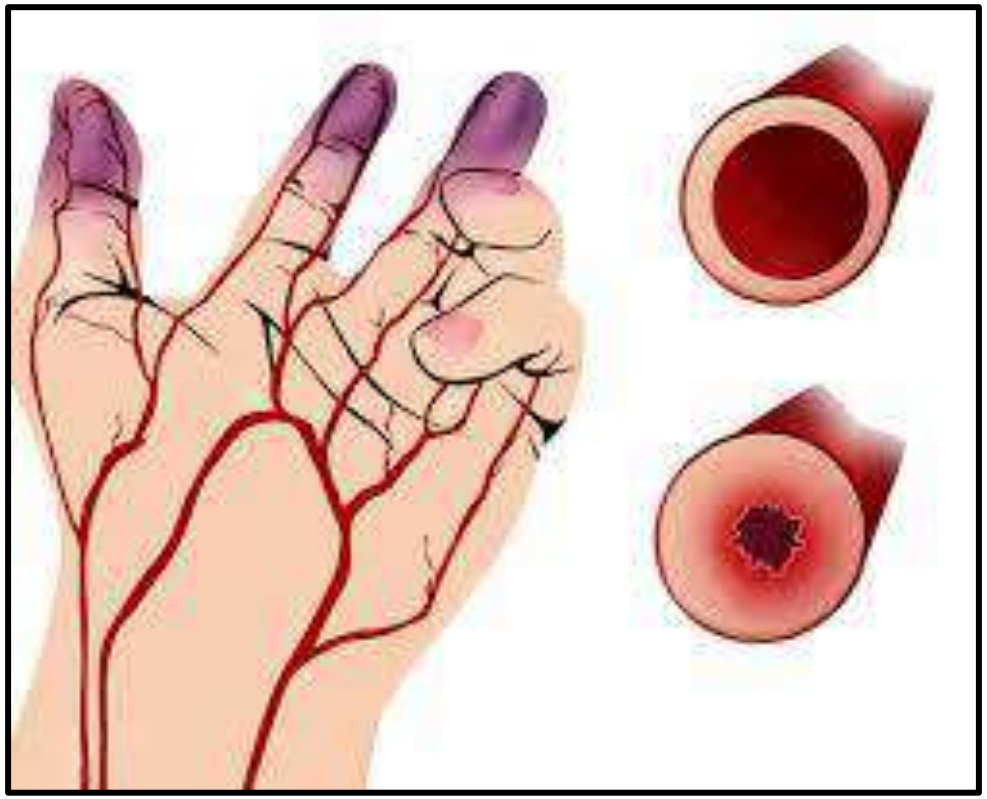
GROUP	EXAMPLES	CHARACTERISTICS
Small vessel vasculitis	Microscopic polyangiitis	Necrotizing vasculitis with few or no immune deposits affecting medium and small blood vessels, including capillaries, venules, and arterioles; necrotizing glomerulonephritis and involvement of the pulmonary capillaries are common
	Wegener granulomatosis	Granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting capillaries, venules, arterioles, and arteries; necrotizing glomerulonephritis is common
Medium-sized vessel vasculitis	Polyarteritis nodosa	Necrotizing inflammation of medium-sized or small arteries without vasculitis in arteries, capillaries, or venules; usually associated with underlying disease or environmental agents
	Kawasaki disease	Involves large, medium-sized, and small arteries (frequently the coronaries) and is associated with mucocutaneous lymph node syndrome; usually occurs in small children
	Thromboangiitis obliterans	Segmental, thrombosing, acute and chronic inflammation of the medium-sized and small arteries, principally the tibial and radial arteries but sometimes extending to the veins and nerves of the extremities; occurs almost exclusively in men who are heavy smokers
Large vessel vasculitis	Giant cell (temporal) arteritis	Granulomatous inflammation of the aorta and its major branches with predilection for extracranial vessels of the carotid artery; infiltration of vessel wall with giant cells and mononuclear cells; usually occurs in people older than 50 years of age and is often associated with polymyalgia rheumatica
	Takayasu arteritis	Granulomatous inflammation of the aorta and its branches; usually occurs in people younger than 50 years of age

Blood vessels disorders

Arterial disorders

Thromboangiitis obliterans (Buerger's disease)

- It is an inflammation (vasculitis) of the medium-sized arteries of the extremities (feet and hands).
- Young and middle-aged heavy smokers: 25-35 years
- Causes: Smoking or chewing tobacco



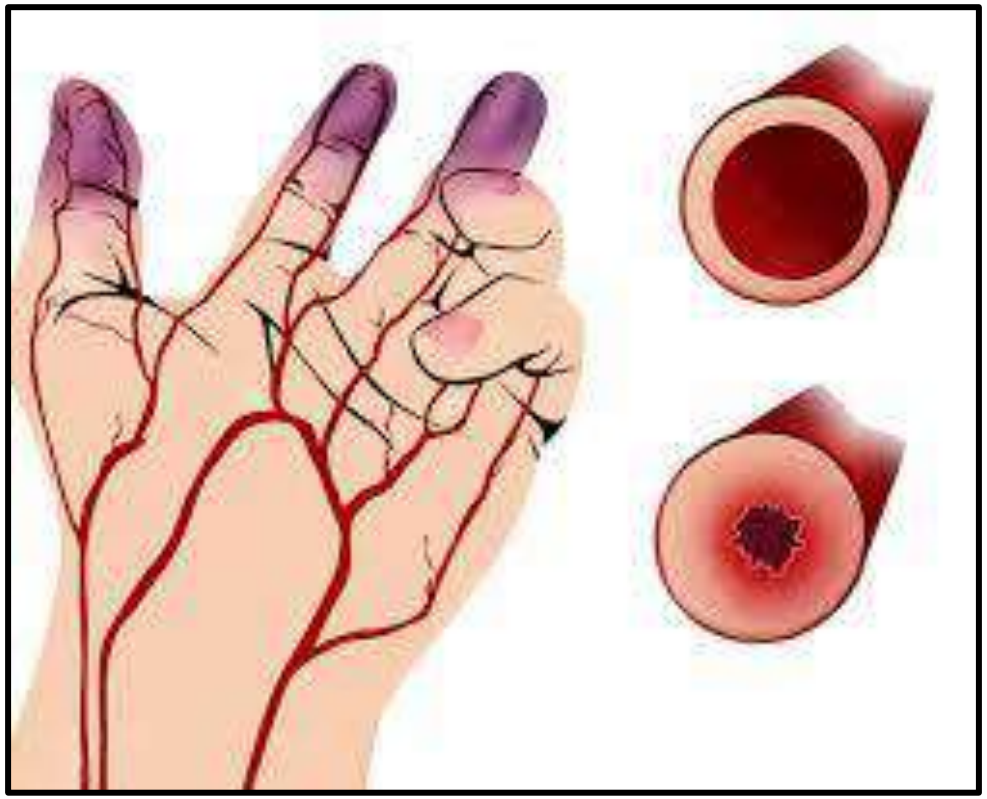
Blood vessels disorders

Arterial disorders

Thromboangiitis obliterans (Buerger's disease)

Pathogenesis

- ROS, interaction between NO and superoxide results in nitrite ⟶ lipid peroxidation (endothelial injury)
- Adhesion molecules expression
- Macrophages, CD4+, CD8+ in intimal layer
- Vasospasm and activation of coagulation process



Blood vessels disorders

Arterial disorders

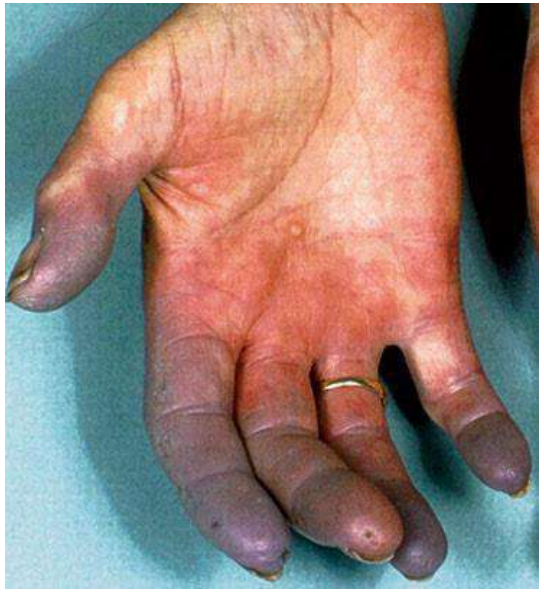
Thromboangiitis obliterans (Buerger's disease)

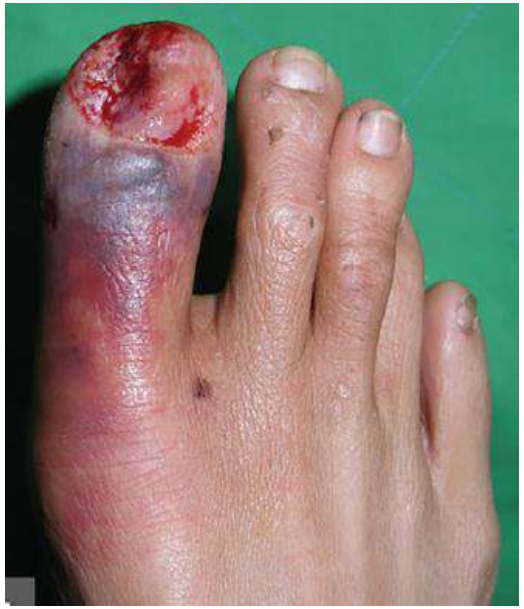
Symptoms

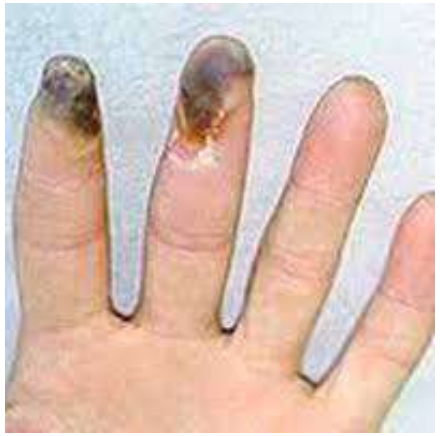
- Pain even at rest
- Cold sensation
- Color change in toes and fingers: reddish blue
- Malformed nails
- Ulceration, gangrene

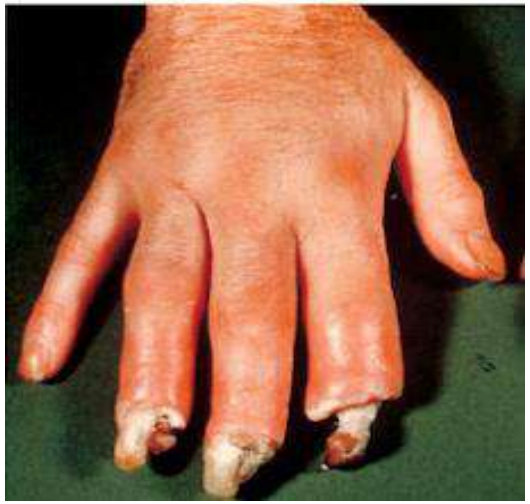
Treatment

- Stop smoking
- Vasodilators
- Sympathoectomy









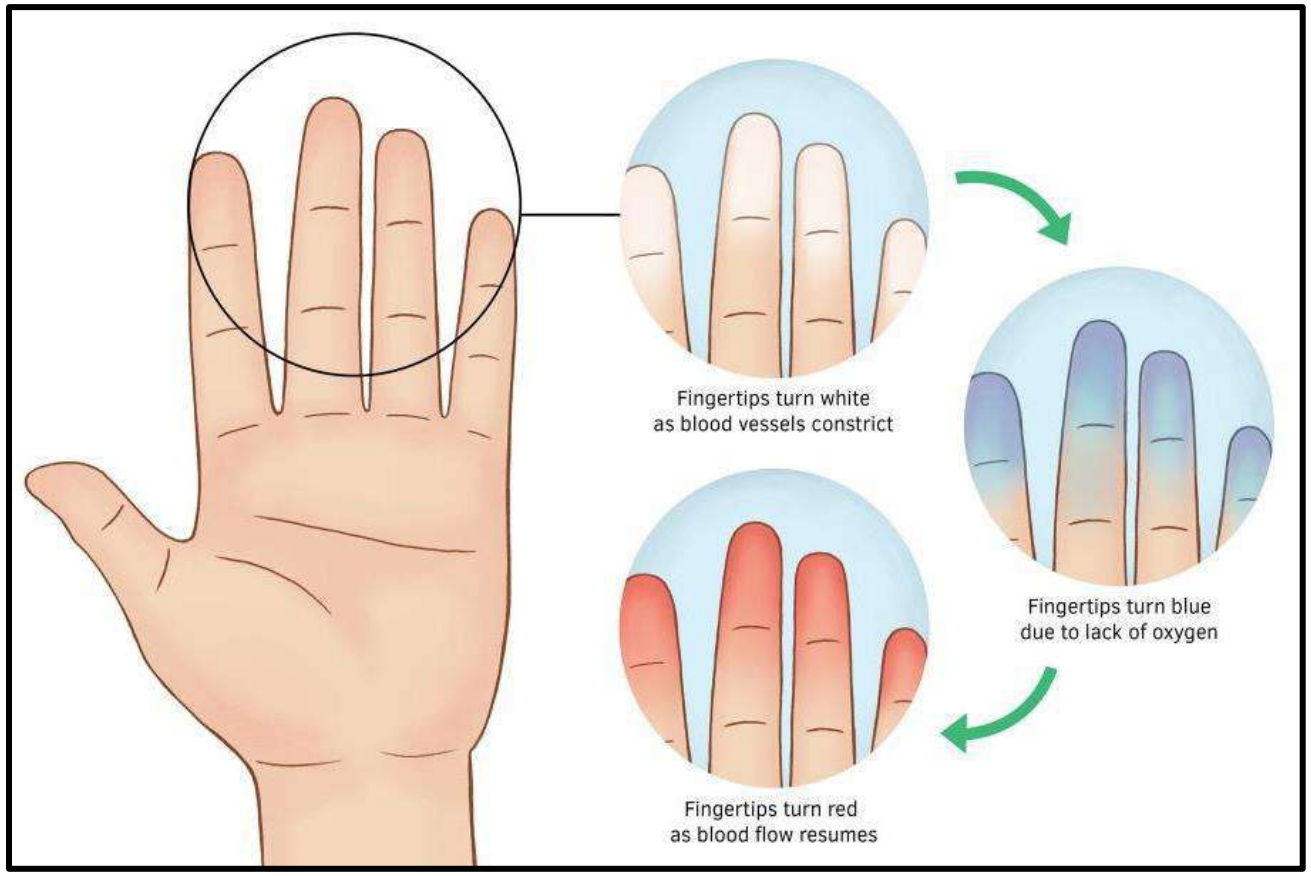
Blood vessels disorders

Arterial disorders

4. Raynaud disease (phenomenon)

- It is a functional disorder caused by intense vasospasm of the arteries and arterioles in the fingers (rarely toes).

- Primary Raynaud: healthy young women
- Secondary Raynaud: trauma, frostbite, neurologic disorders, collagen disease, drugs.
- Causes: idiopathic



Blood vessels disorders

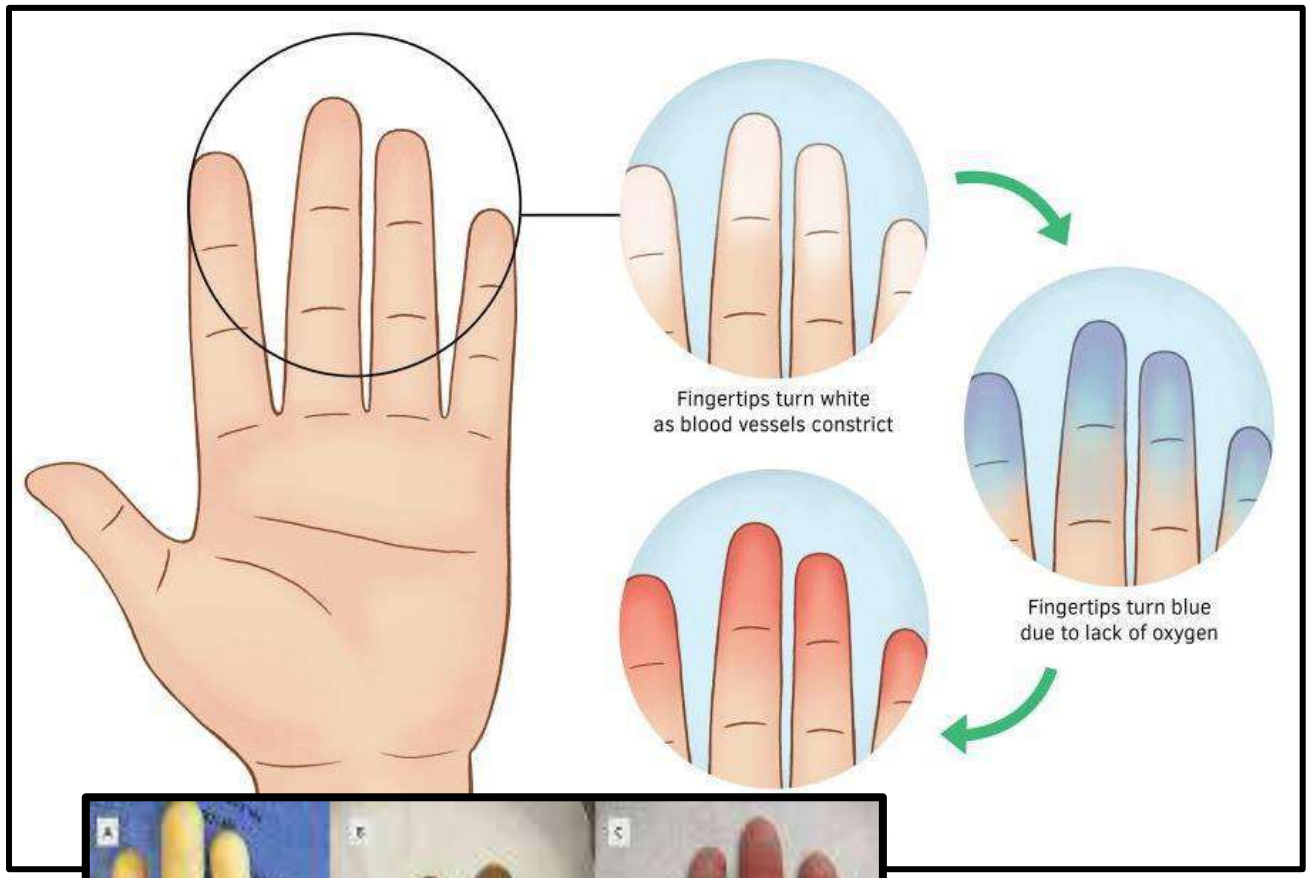
Arterial disorders

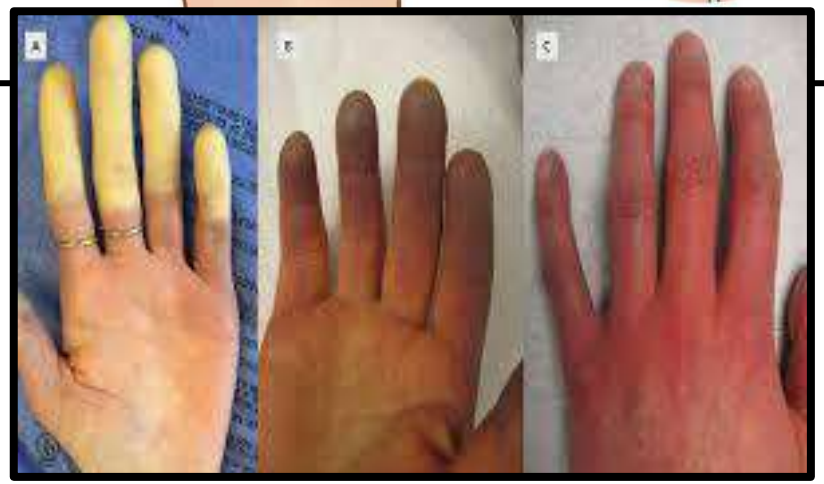
4. Raynaud disorder

- **Pathogenesis**

Hyperactivity of the sympathetic nervous system causing extreme vasoconstriction of peripheral blood vessels, leading to tissue hypoxia.

- **Symptoms: color change, numbness, tingling, cold sensation, ulceration, gangrene (severe case)**
- **Treatment**



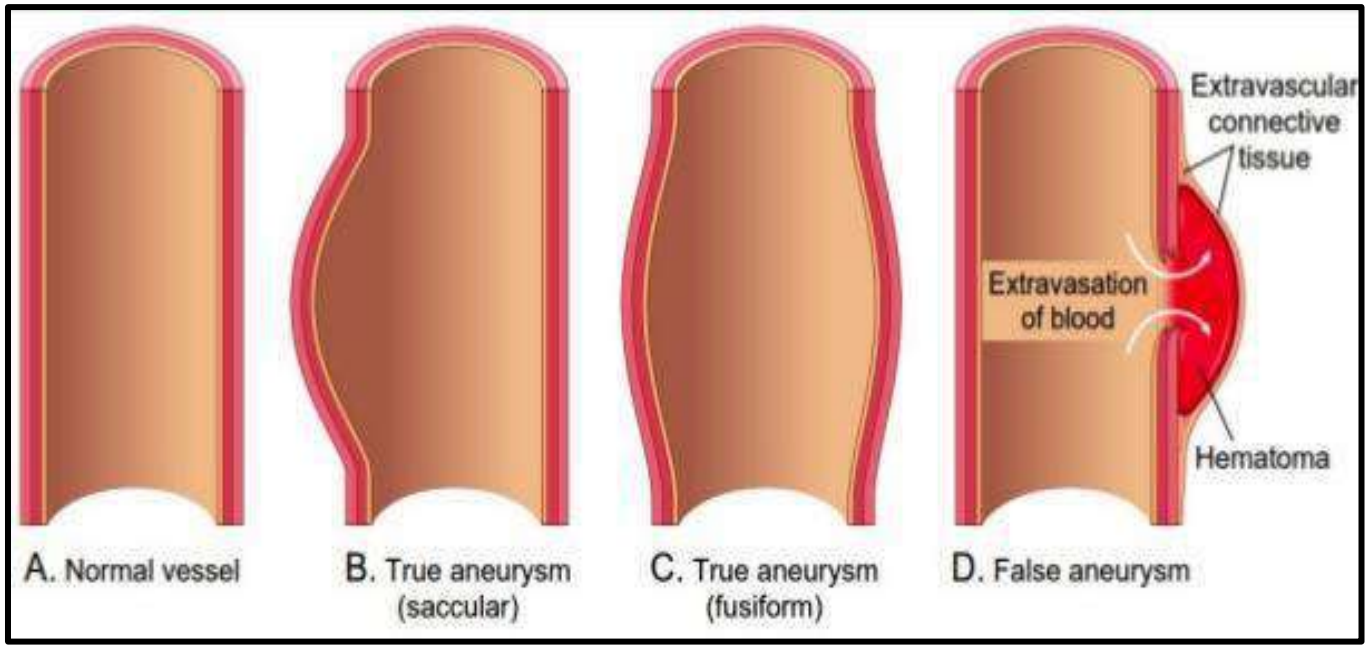


Blood vessels disorders

Arterial disorders

5. Aortic aneurysms

- Aneurysms is an abnormal localized dilation of a blood vessel.
- Types
  - True
  - False
- Causes

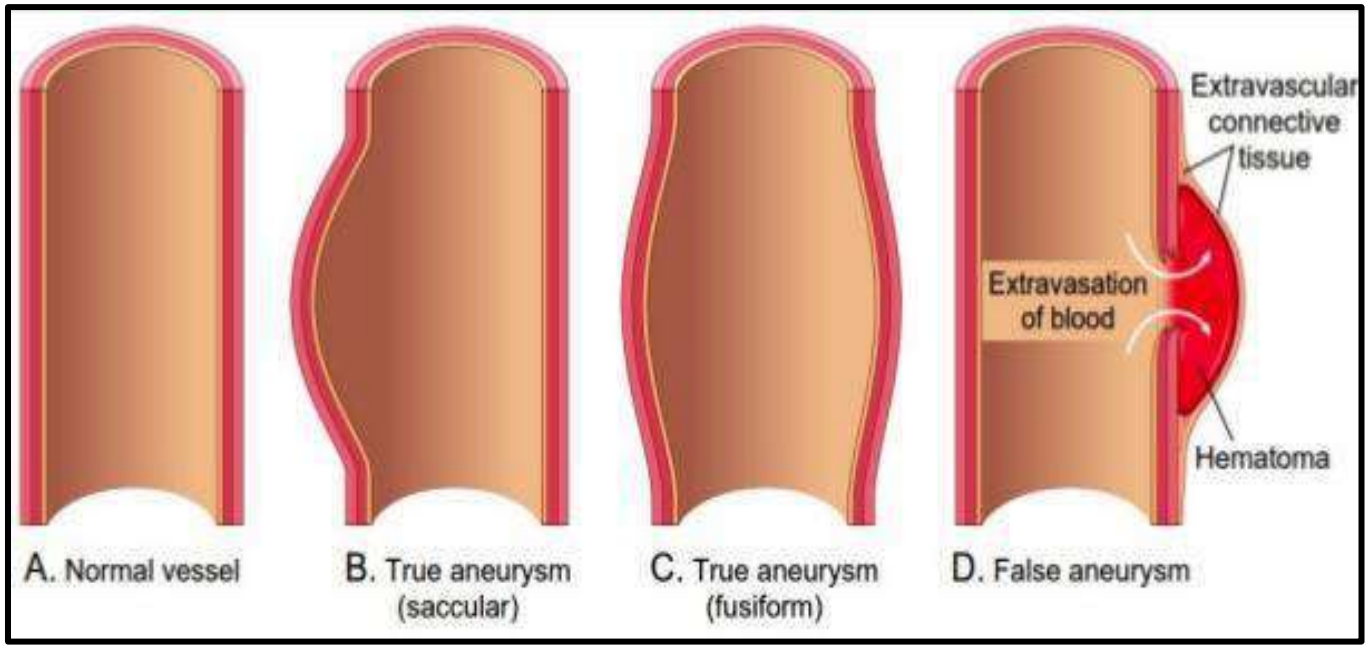


Blood vessels disorders

Arterial disorders

5. Aortic aneurysms

- **Pathogenesis**
- **Diagnosis**
- **Treatment**

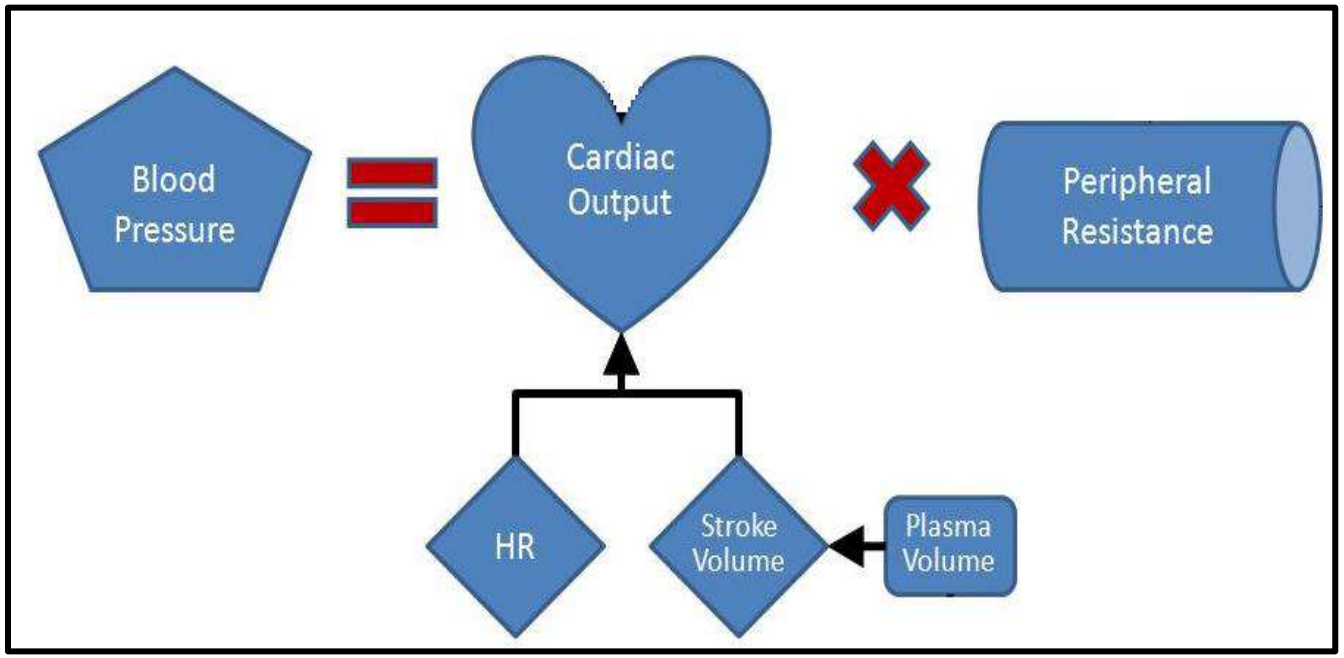


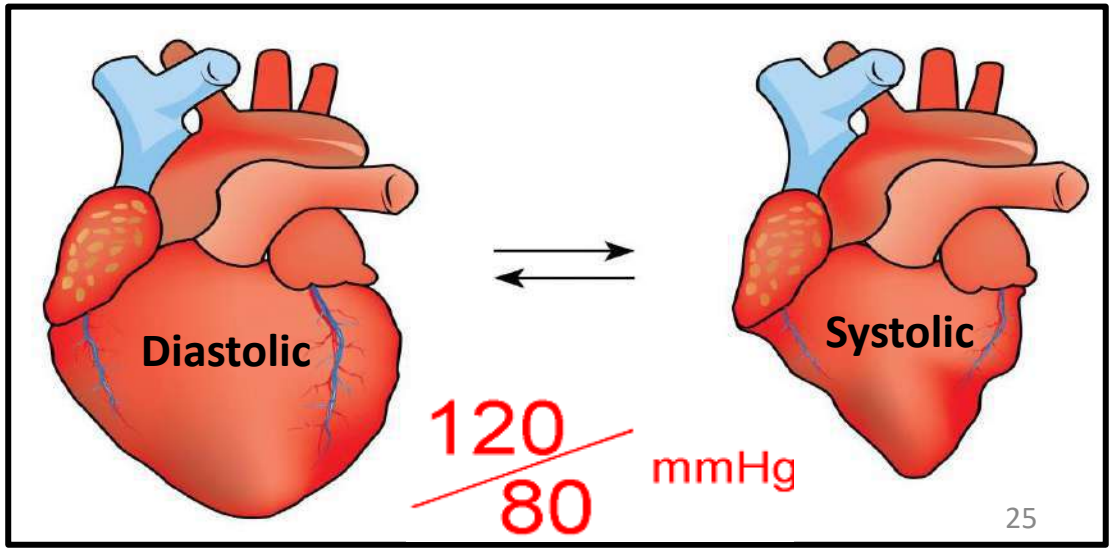
Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

- **Blood pressure (BP) is the pressure of circulating blood on the walls of blood vessels (arteries).**





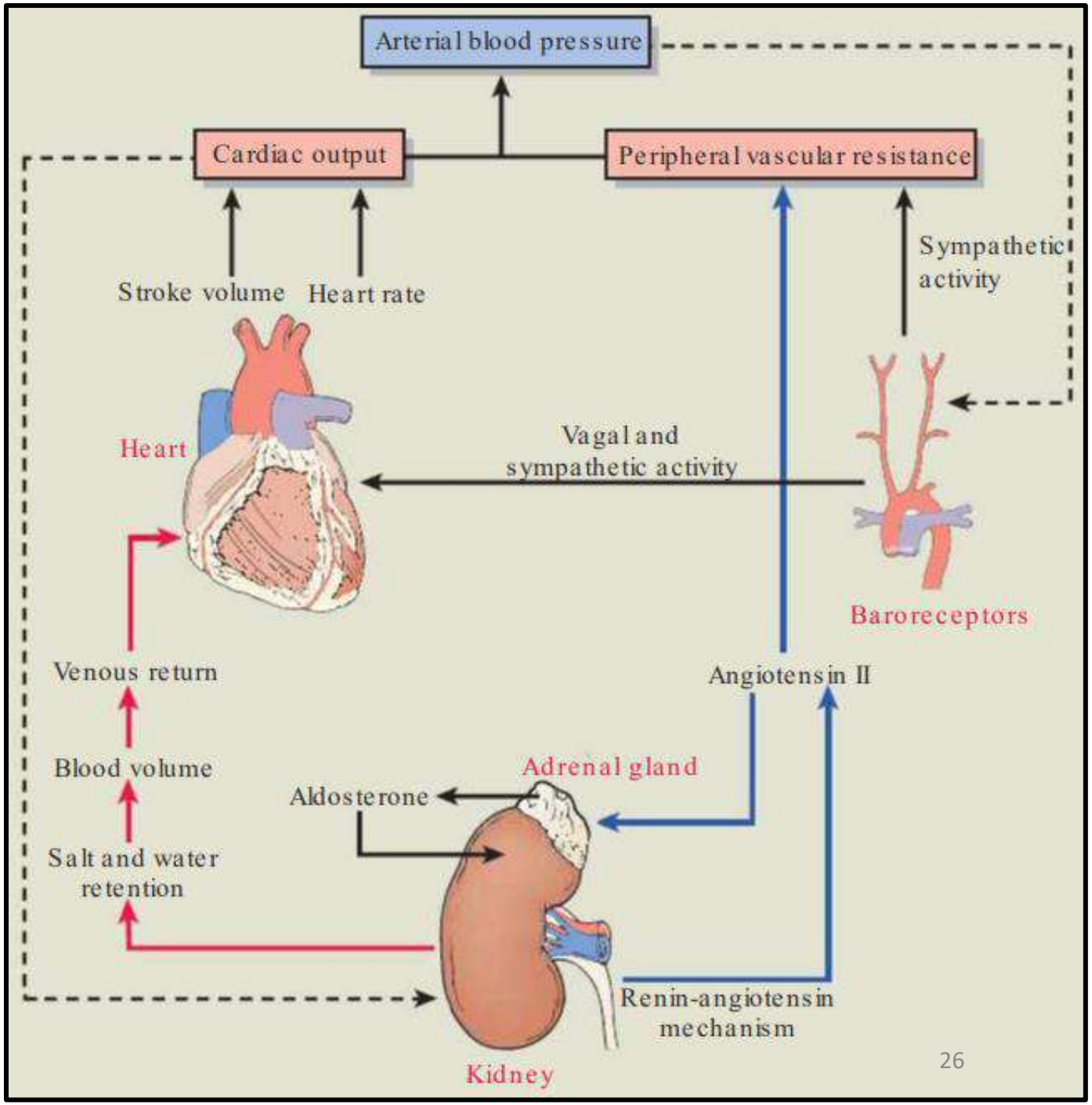
Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

Mechanisms of Blood Pressure Regulation

- **Neural Mechanisms**
- **Humoral Mechanisms**



Blood vessels disorders

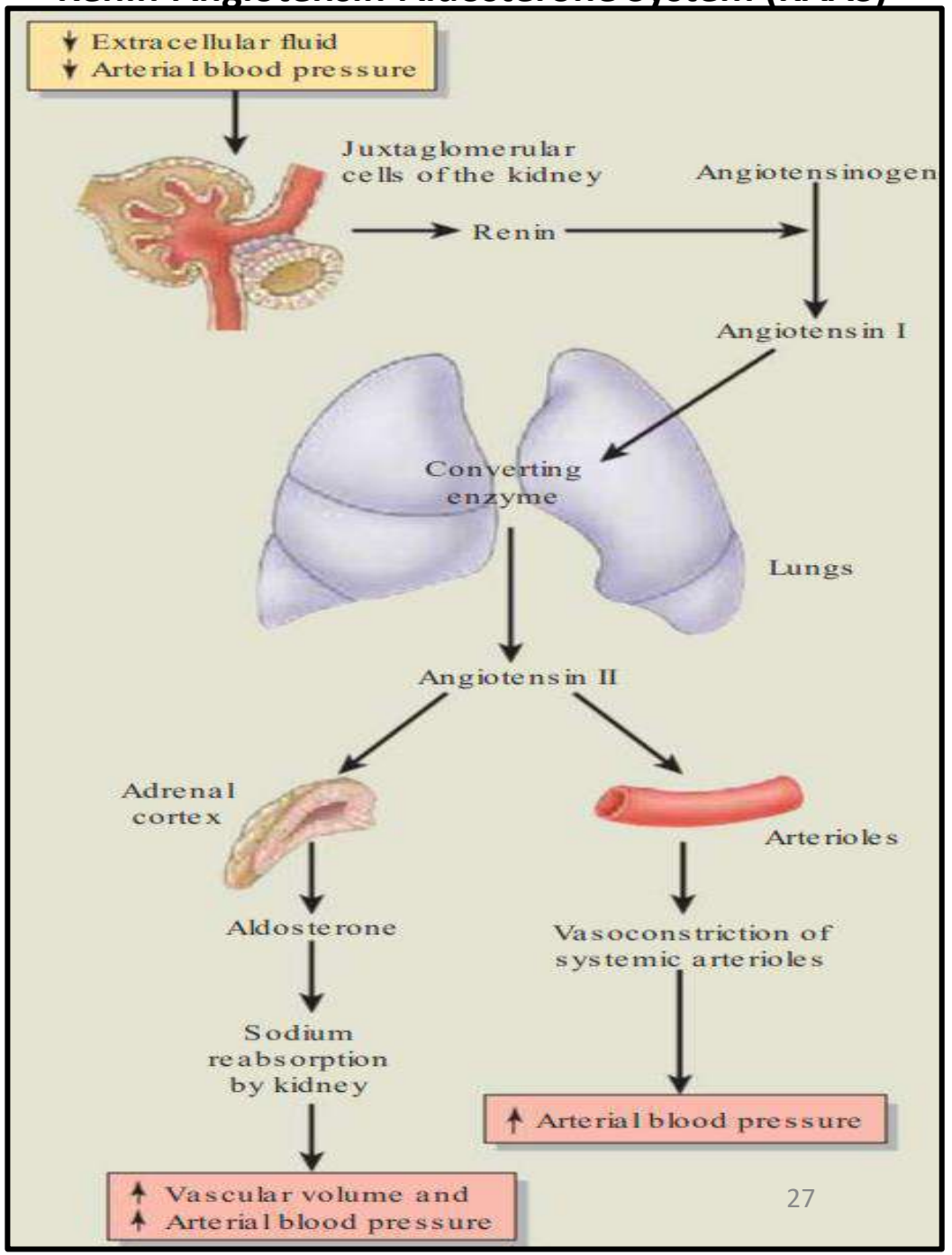
Arterial disorders

5. Arterial Hypertension

Mechanisms of Blood Pressure Regulation

- Neural Mechanisms
- Humoral Mechanisms
  - RAAS

Renin-Angiotensin-Aldosterone System (RAAS)

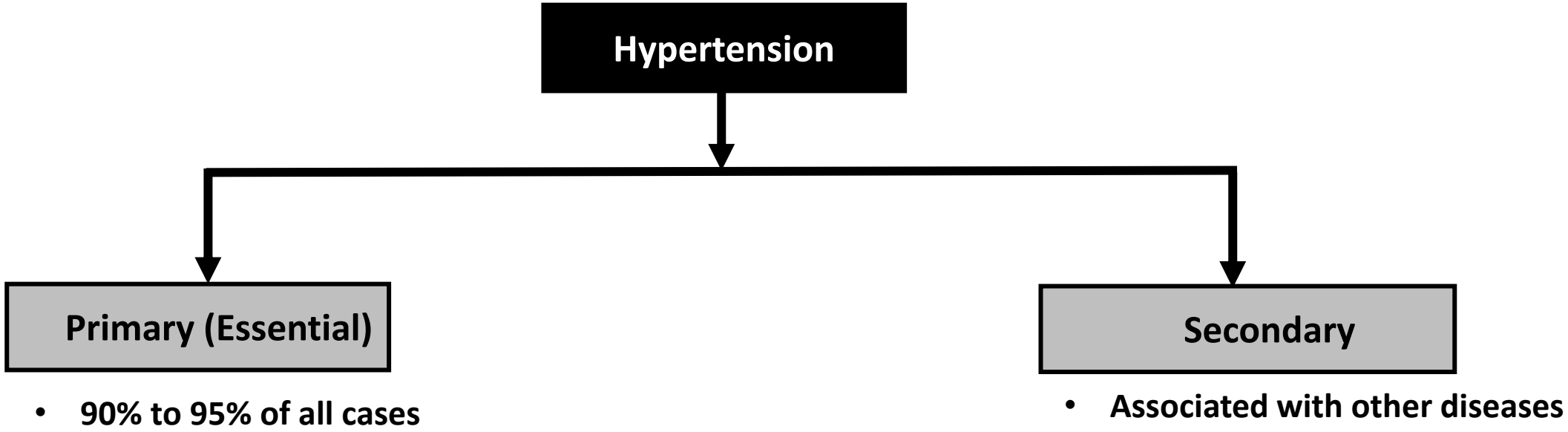


Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

- **Hypertension (HTN), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated.**



Blood vessels disorders

Arterial disorders

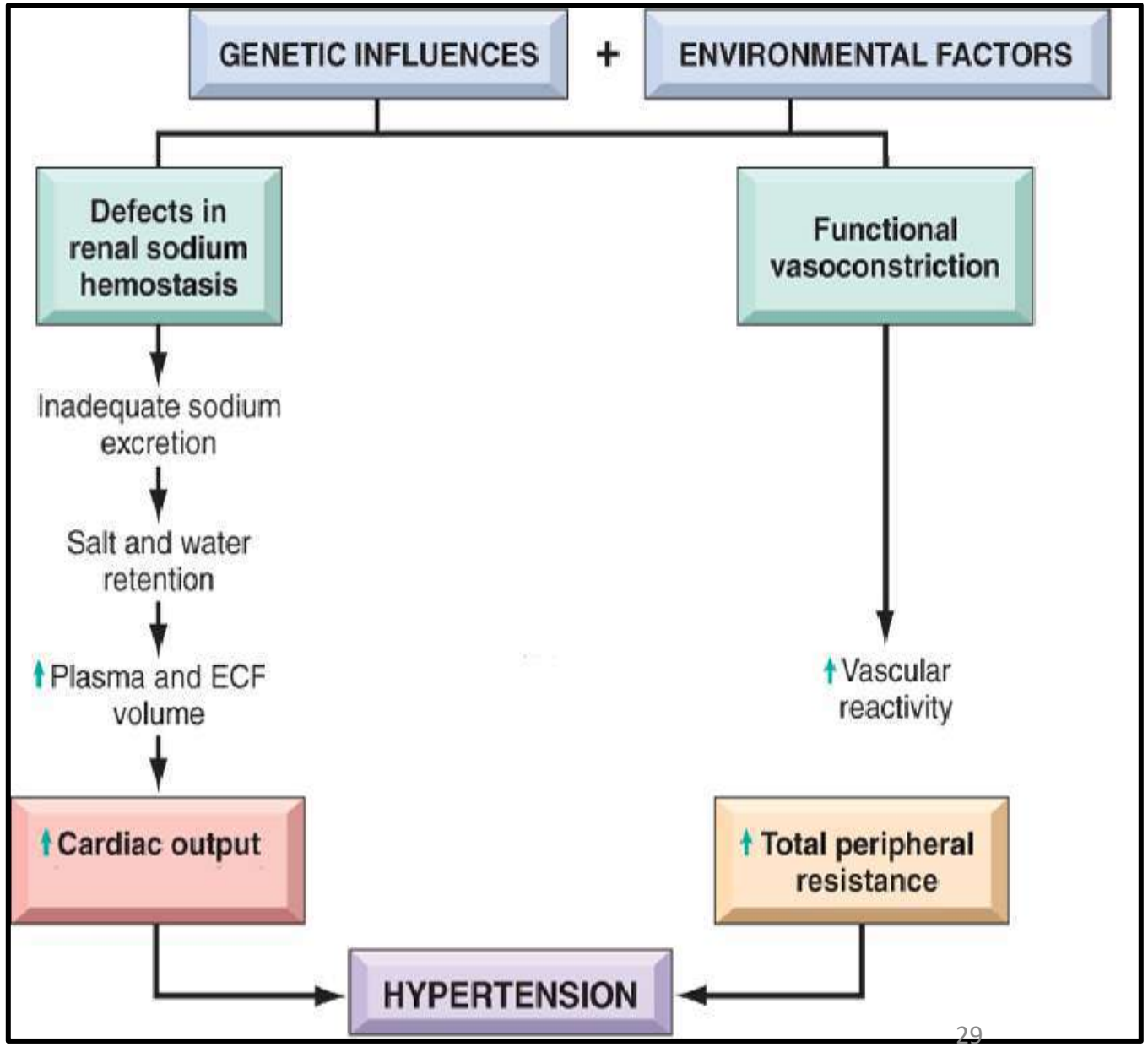
5. Arterial Hypertension

- **Classification of Hypertension (HTN)**

1. Primary (Essential) Hypertension

- **No cause can be identified.**
  - **Risk factors: age, race, family history**
  - **Lifestyle factors: stress, high salt intake, excessive calorie intake and obesity, smoking, and high saturated fats and cholesterol intake**

Pathogenesis



Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

- **Classification of Hypertension (HTN)**

1. Secondary Hypertension

- **Secondary hypertension, which describes an elevation in blood pressure due to another disease, and accounts for 5% to 10% of hypertension cases.**

- **Causes**

  - **Renal disease (main cause): Renovascular hypertension**
  - **Disorders of Adrenocortical Hormones: hyperaldosteronism and Cushing syndrome**
  - **Diabetes mellitus**
  - **Pheochromocytoma: catecholamine-secreting tumors of chromaffin cells**
  - **Coarctation of the aorta: a congenital condition in which a narrowing of the lumen of the aorta**
  - **Drugs: oral contraceptives**

Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

Diagnosis

- **Sphygmomanometer**

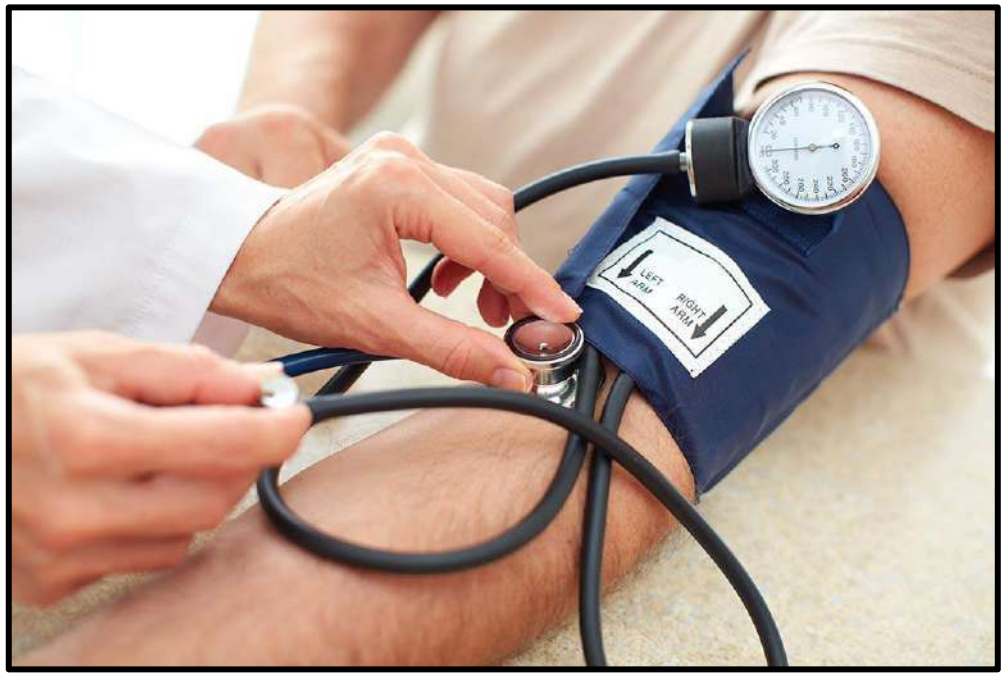


TABLE 18-4 Classification of Blood Pressure for Adults

Blood Pressure Classification	Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)
Normal	<120	And <80
Prehypertensive	120–139	or 80–89
Stage 1 hypertension	140–159	or 90–99
Stage 2 hypertension	≥160	or ≥100

Blood vessels disorders

Arterial disorders

5. Arterial Hypertension

Treatment

- **The main objective for treatment of hypertension is to achieve and maintain arterial blood pressure below 140/90 mm Hg.**
- **In persons with hypertension and diabetes or renal disease, the goal is blood pressure below 130/80 mm Hg.**
- **Treatment methods include:**
  - **Lifestyle modifications**
  - **Pharmacological agents: Drug selection is based on the stage of hypertension.**
    - ✓ Diuretics
    - ✓ ß-adrenergic receptor inhibitors
    - ✓ ACE inhibitors
    - ✓ Angiotensin II receptor blockers
    - ✓ Calcium channel blockers
    - ✓ Central α2-adrenergic agonists
    - ✓ α1-adrenergic receptor blockers
    - ✓ Vasodilators

Blood vessels disorders

Arterial disorders

5. Arterial Hypertension: Hypertensive Crisis

- It is a severe form of hypertension, defined as a systolic pressure greater than 180 or a diastolic pressure greater than 120 mmHg.
- It is classified as hypertensive urgency or emergency.
- Hypertensive urgency: No rapid progression of target-organ damage.
- Hypertensive emergency: Characterized by end-organ damage.
- Immediate treatment, **BUT** the goal of initial treatment should be to obtain a reduction in BP to a safer, less critical level, rather than to normotensive levels.

Blood vessels disorders

Arterial disorders

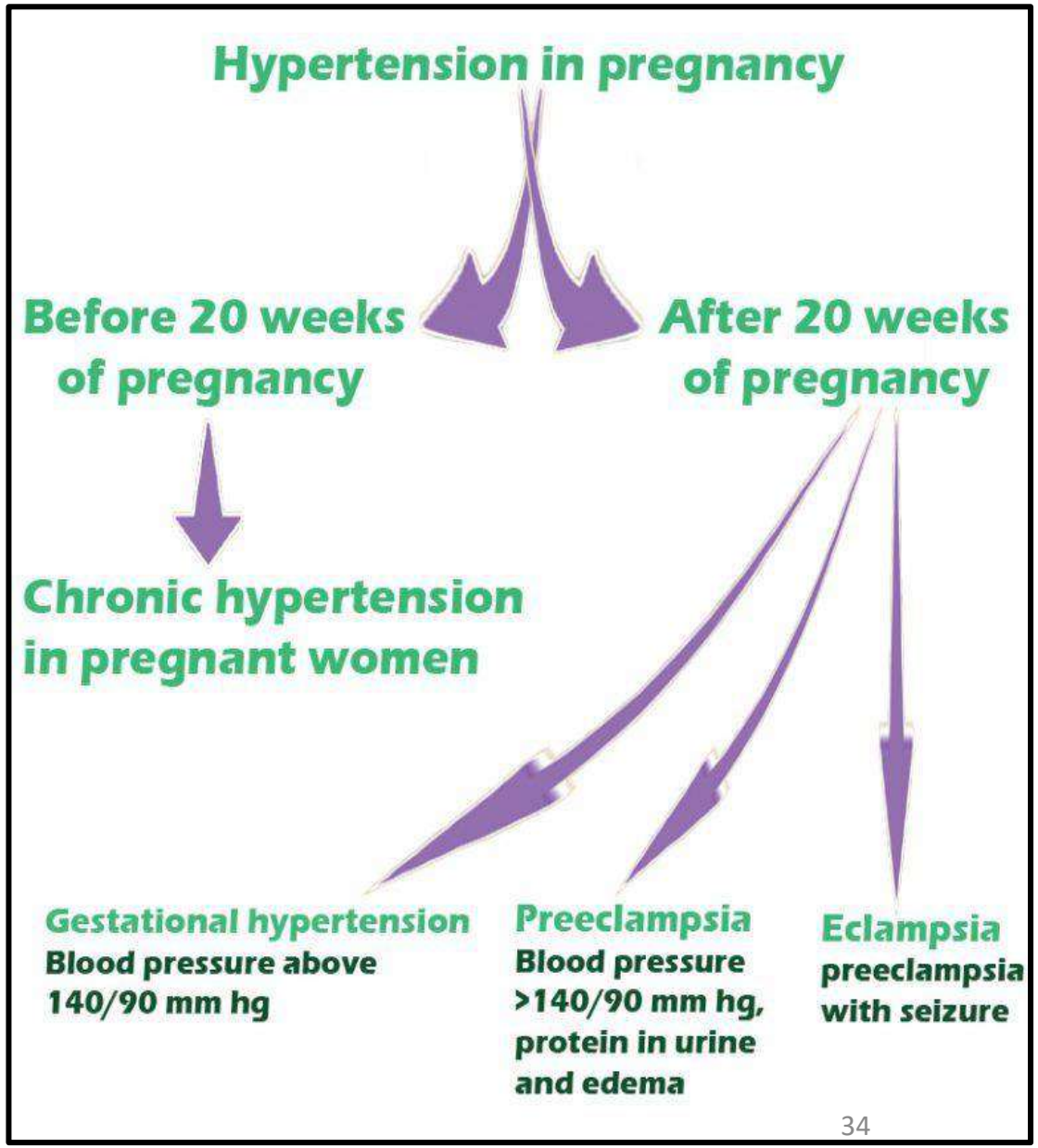
5. Arterial Hypertension: Hypertension in pregnancy

- Hypertensive disorders complicate 5% to 10% of pregnancies.

Preeclampsia Superimposed on Chronic Hypertension

Treatment

- Bed rest is a traditional therapy.
- Antihypertensive medications must be carefully chosen:
  - Methyldopa, drug of choice
  - Labetalol
  - Calcium channel blockers

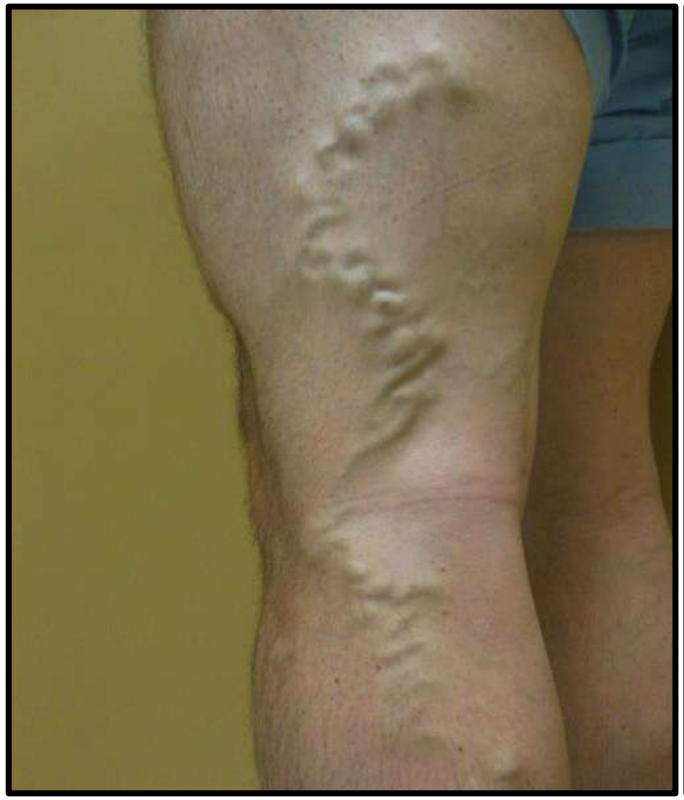


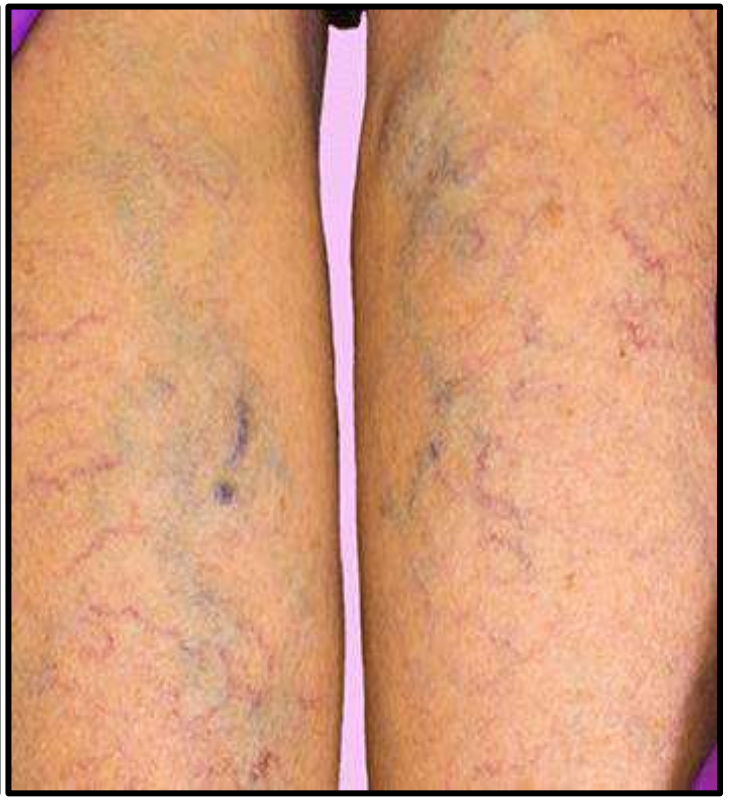
Blood vessels disorders

Venous disorders

1. Varicose Veins

- Varicose veins is a condition that often occurs in the lower extremities, in which veins become dilated, twisted and swollen.
- Venous circulation disorder
- It is more common after 50 years of age, and it occurs more often in women.



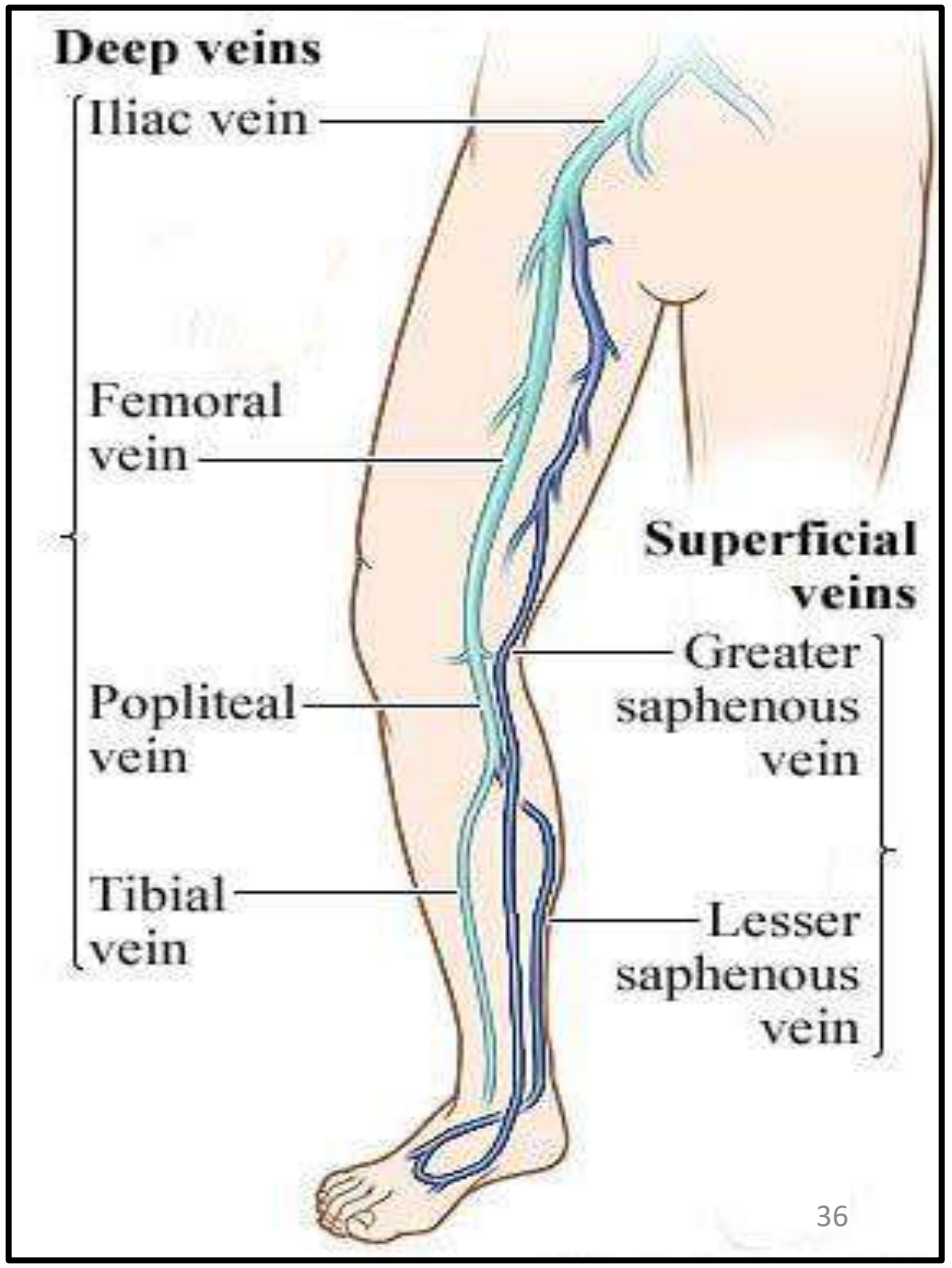


Blood vessels disorders

Venous disorders

1. Varicose Veins

- Varicose veins are classified into primary or secondary.
- Primary varicose veins originate in the superficial saphenous veins: Prolonged standing, increased intraabdominal pressure and pregnancy.
- Secondary varicose veins result from impaired blood flow in the deep veins: deep vein thrombosis, congenital venous malformations, and pressure on the abdominal veins caused by pregnancy or a tumor.

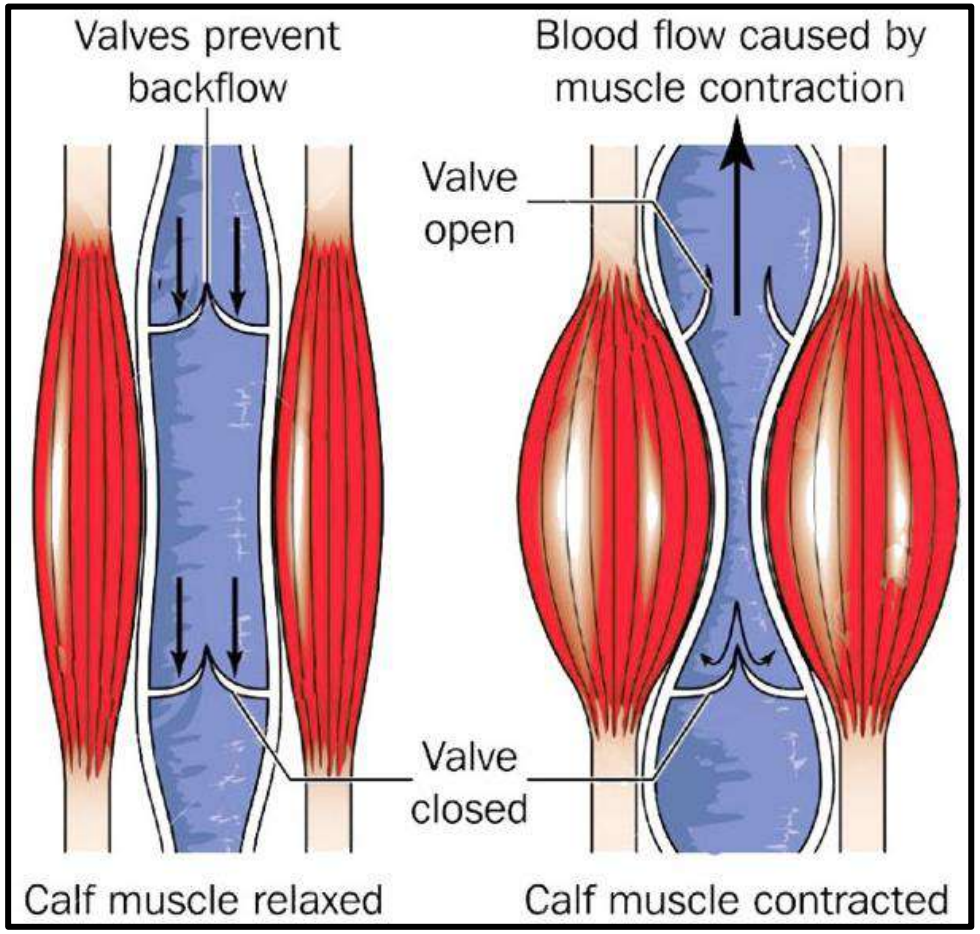


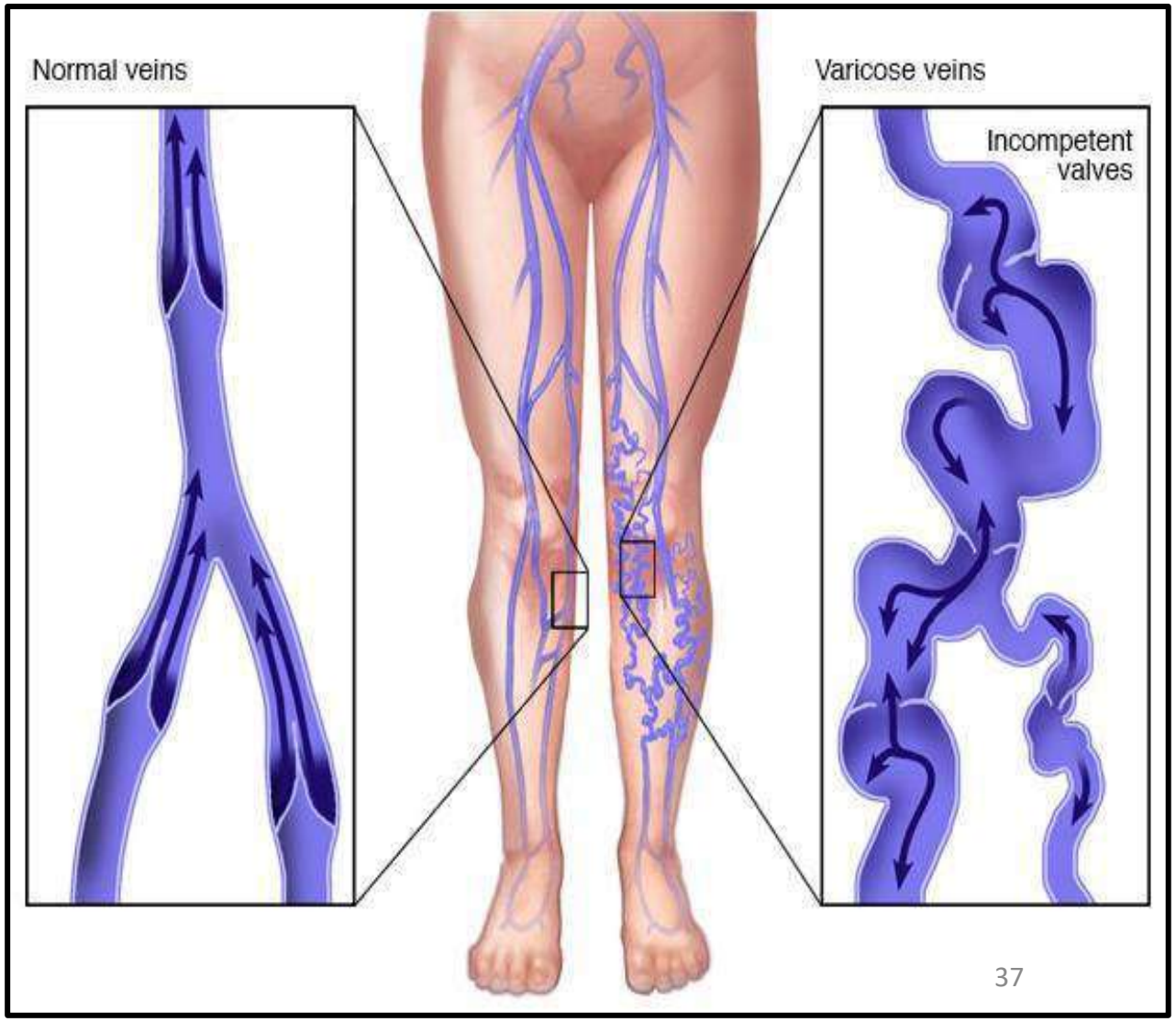
Blood vessels disorders

Venous disorders

1. Varicose Veins

- **Pathogenesis: venous reflux**





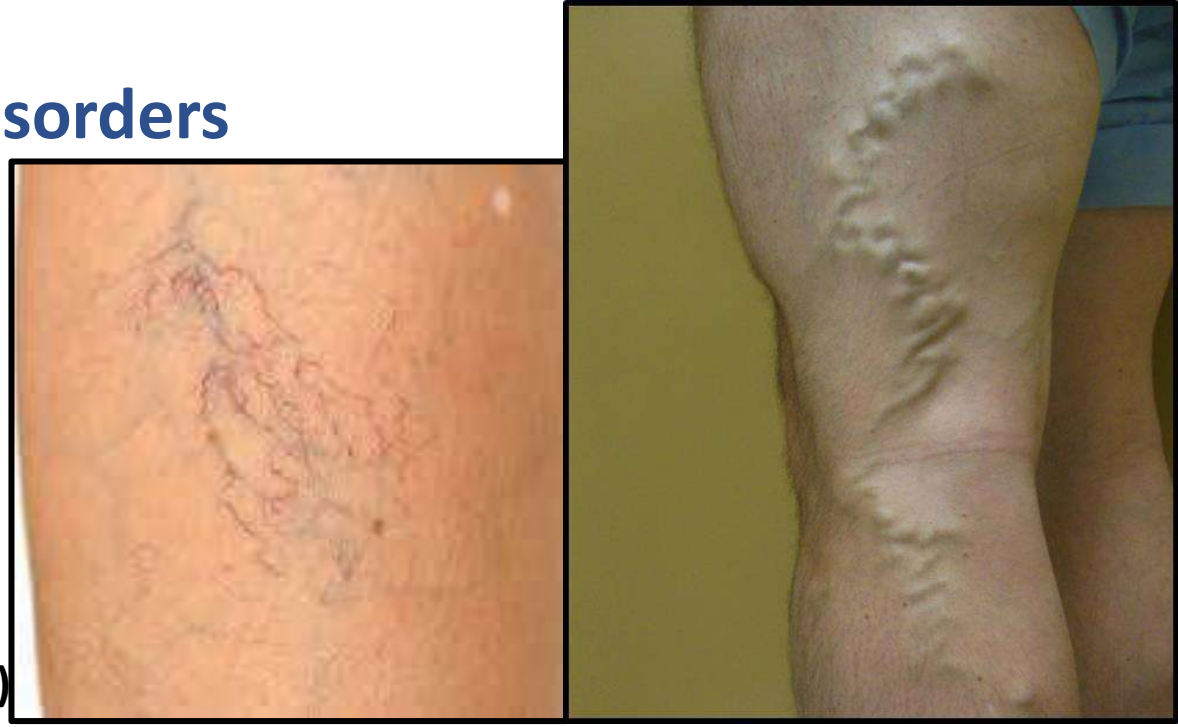
Blood vessels disorders

Venous disorders

1. Varicose Veins

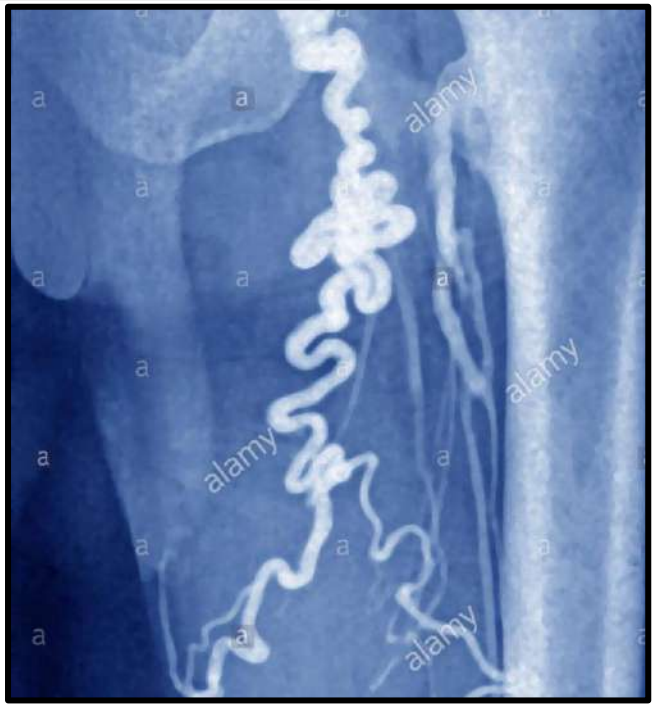
Symptoms

- Pain, heavy legs (often worse at night and after exercise).
- Unsightly appearance: twisted and spider veins (Telangiectasia)
- Bluish red color
- Edema in the leg



Diagnosis

- Physical inspection
- Doppler ultrasound
- Angiography by injecting radio-contrast agent



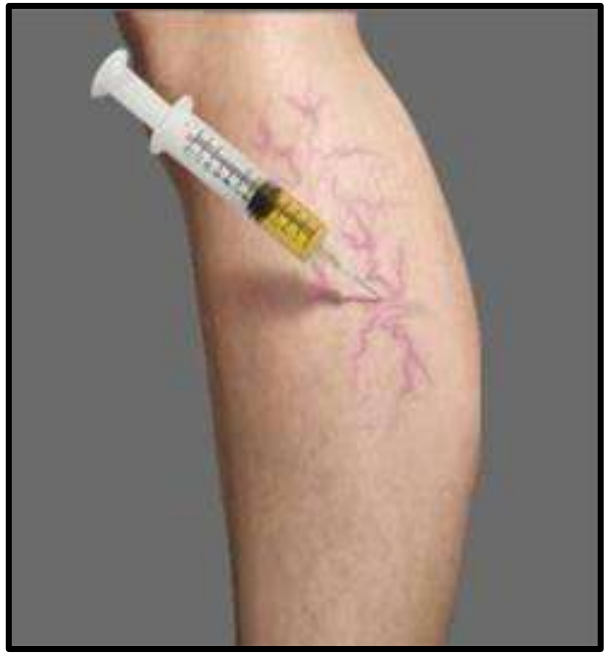
Blood vessels disorders

Venous disorders

1. Varicose Veins

Treatment: Improving venous flow and preventing tissue injury

- Elastic support stockings
- Sclerotherapy: sodium tetradecyl sulphate, glycerin
- Surgery



Heart disorders

1. Coronary Artery Disease (CAD)

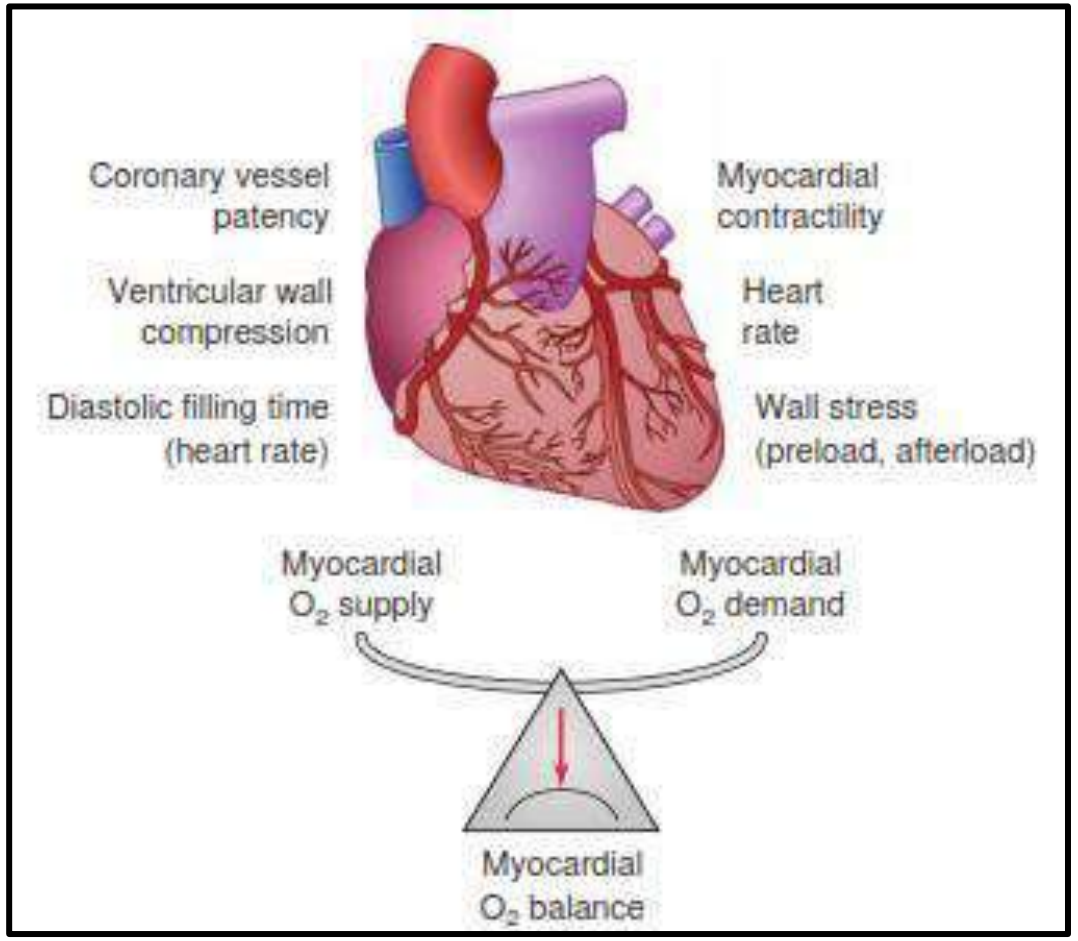
Coronary blood flow

Metabolic activity

- **O2 demand**
- **Adenosine**

Endothelial cells

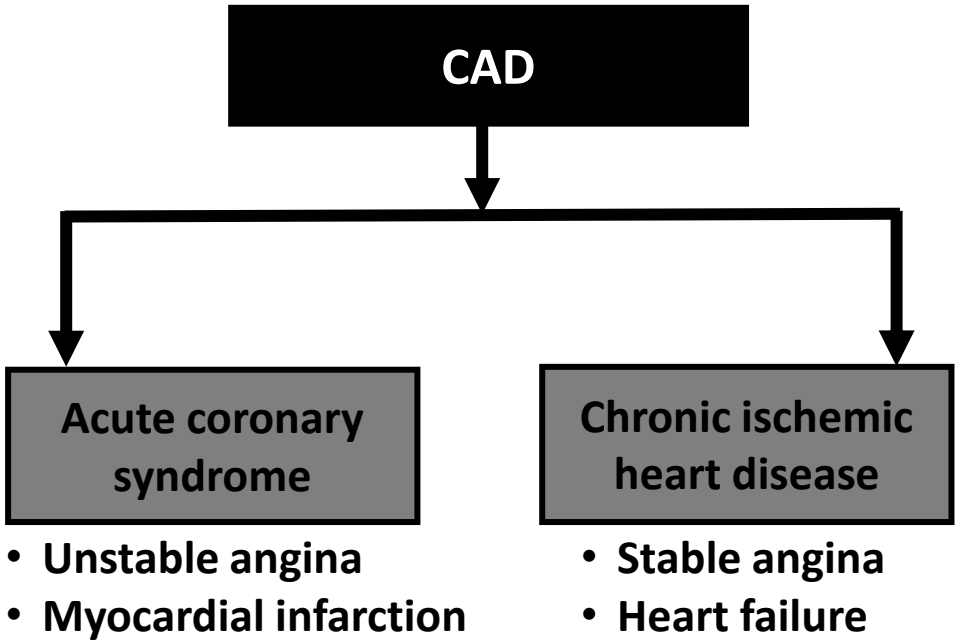
- **Vasodilators**
- **Vasoconstrictors**



Heart disorders

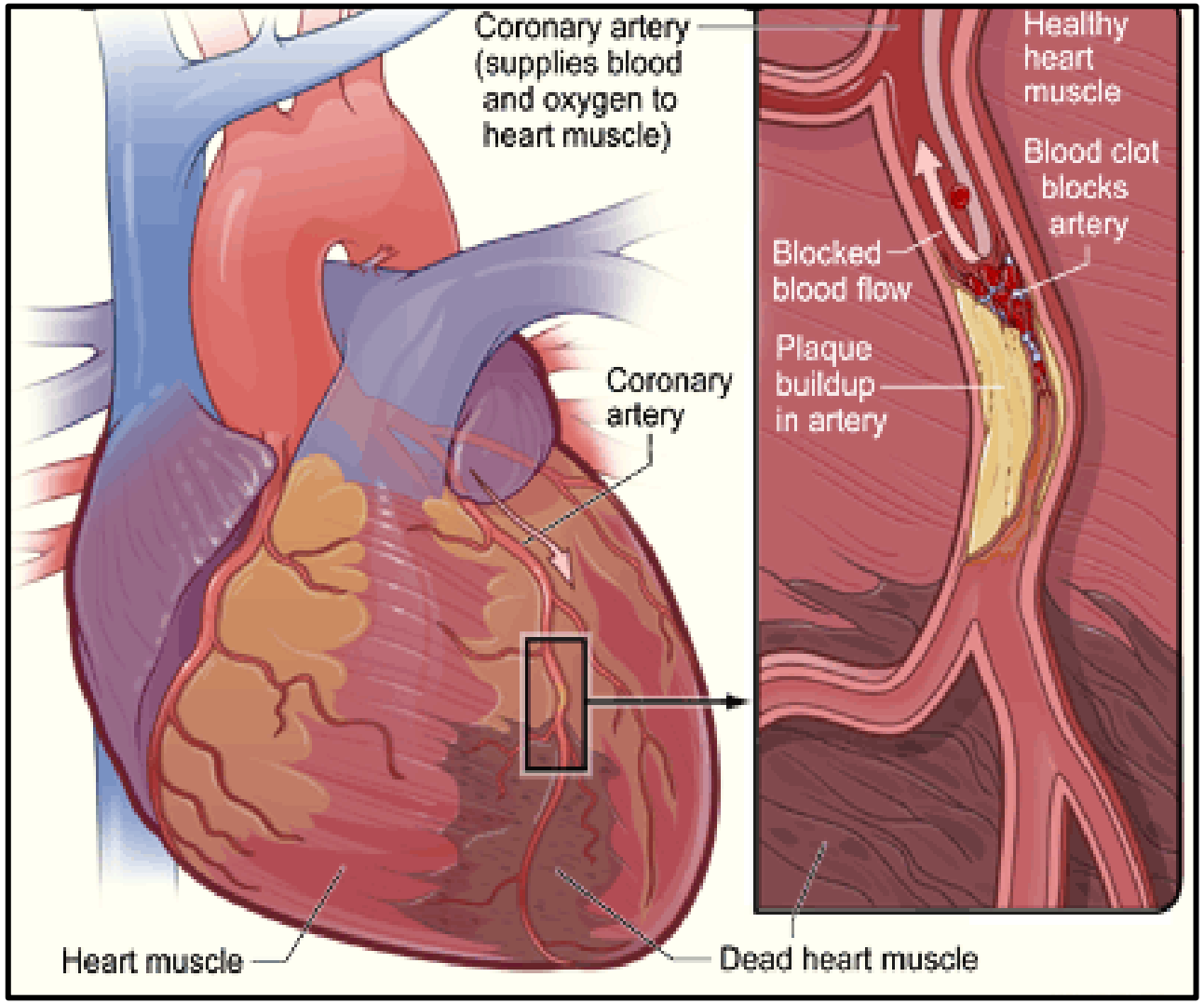
1. Coronary Artery Disease (CAD)

- **Coronary artery disease is a heart disease caused by impaired coronary blood flow.**



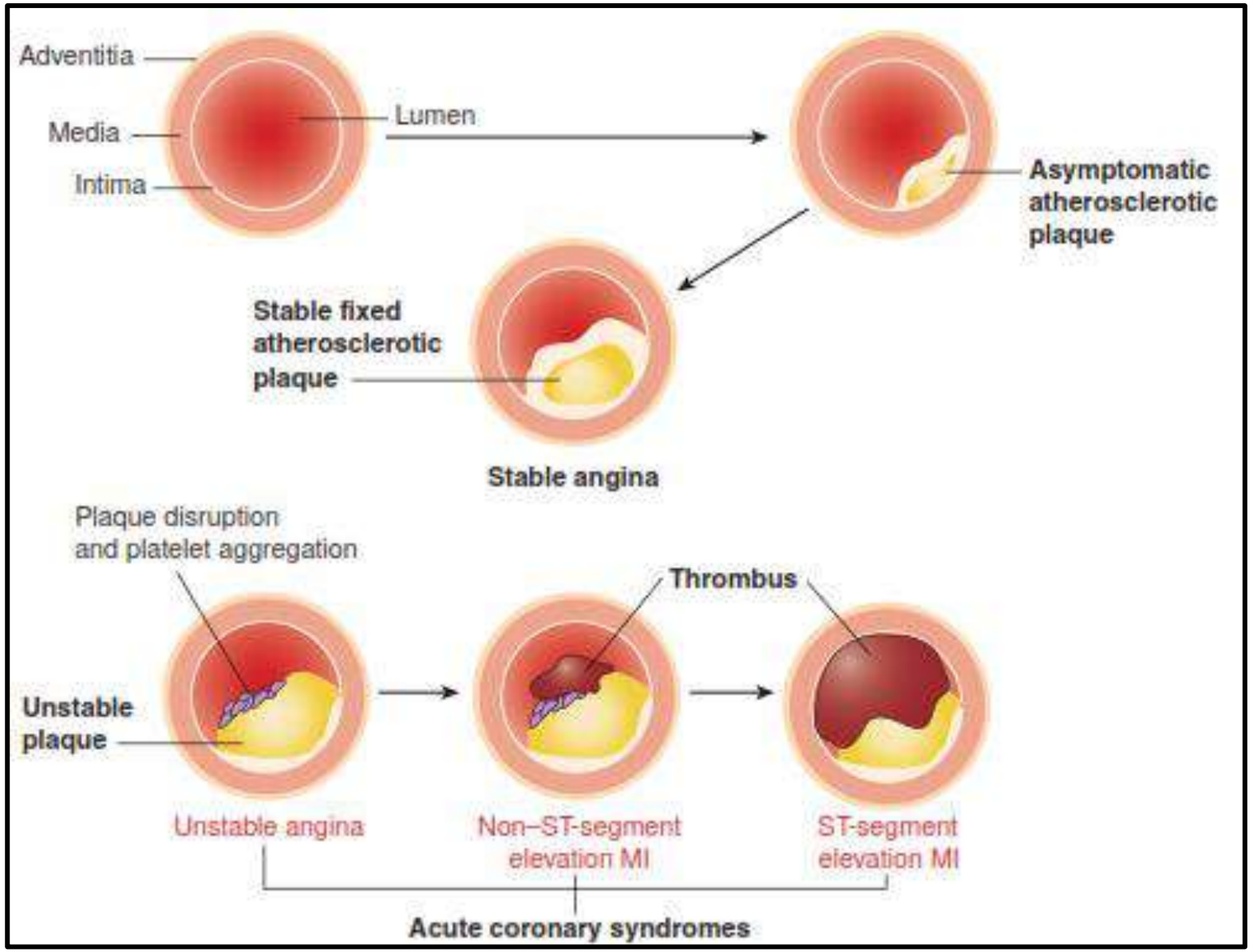
- **Unstable angina**
- **Myocardial infarction**

- **Stable angina**
- **Heart failure**



Heart disorders

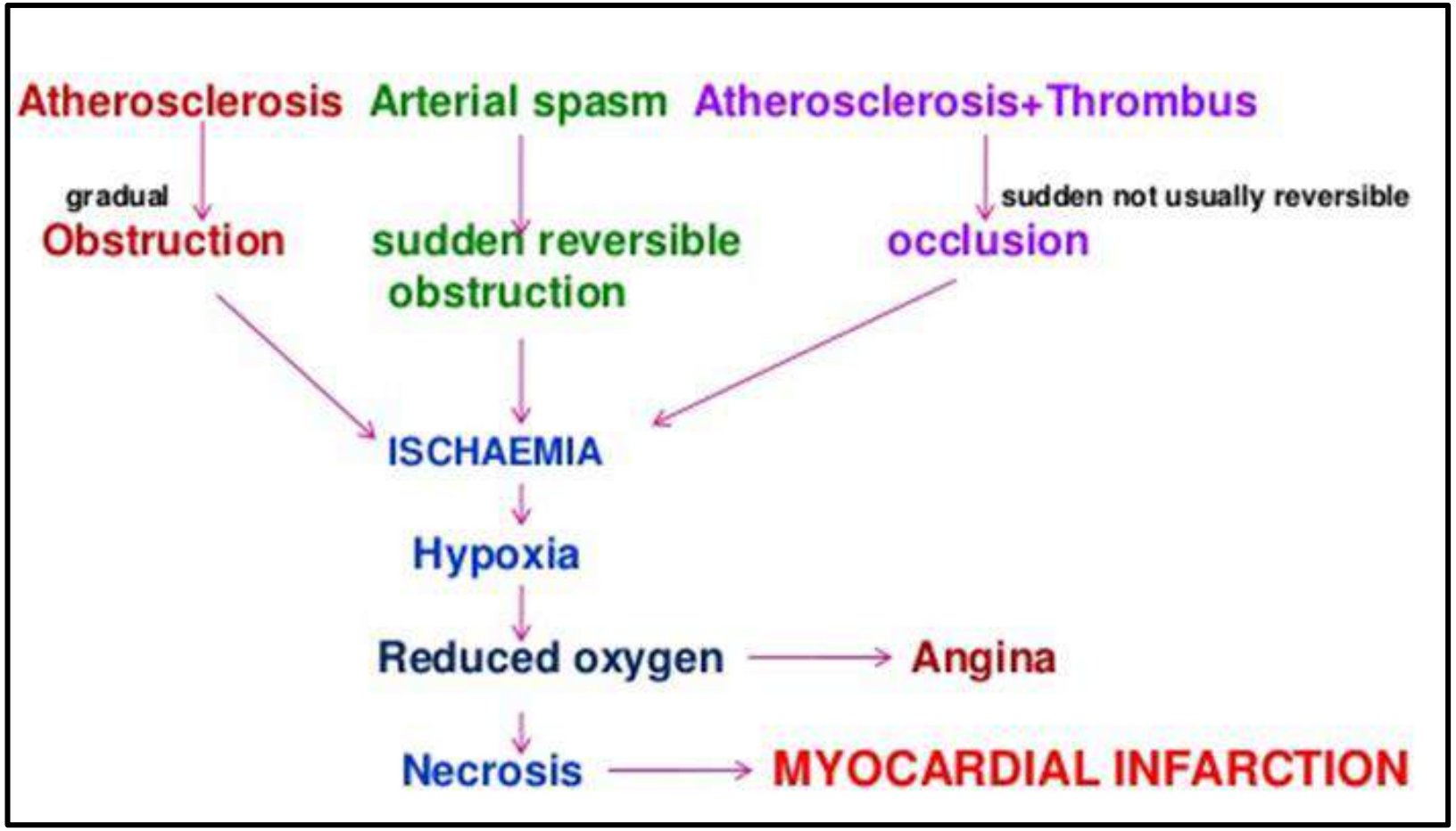
1. Coronary artery disease (CAD)



Heart disorders

1. Coronary artery disease (CAD)

Pathogenesis

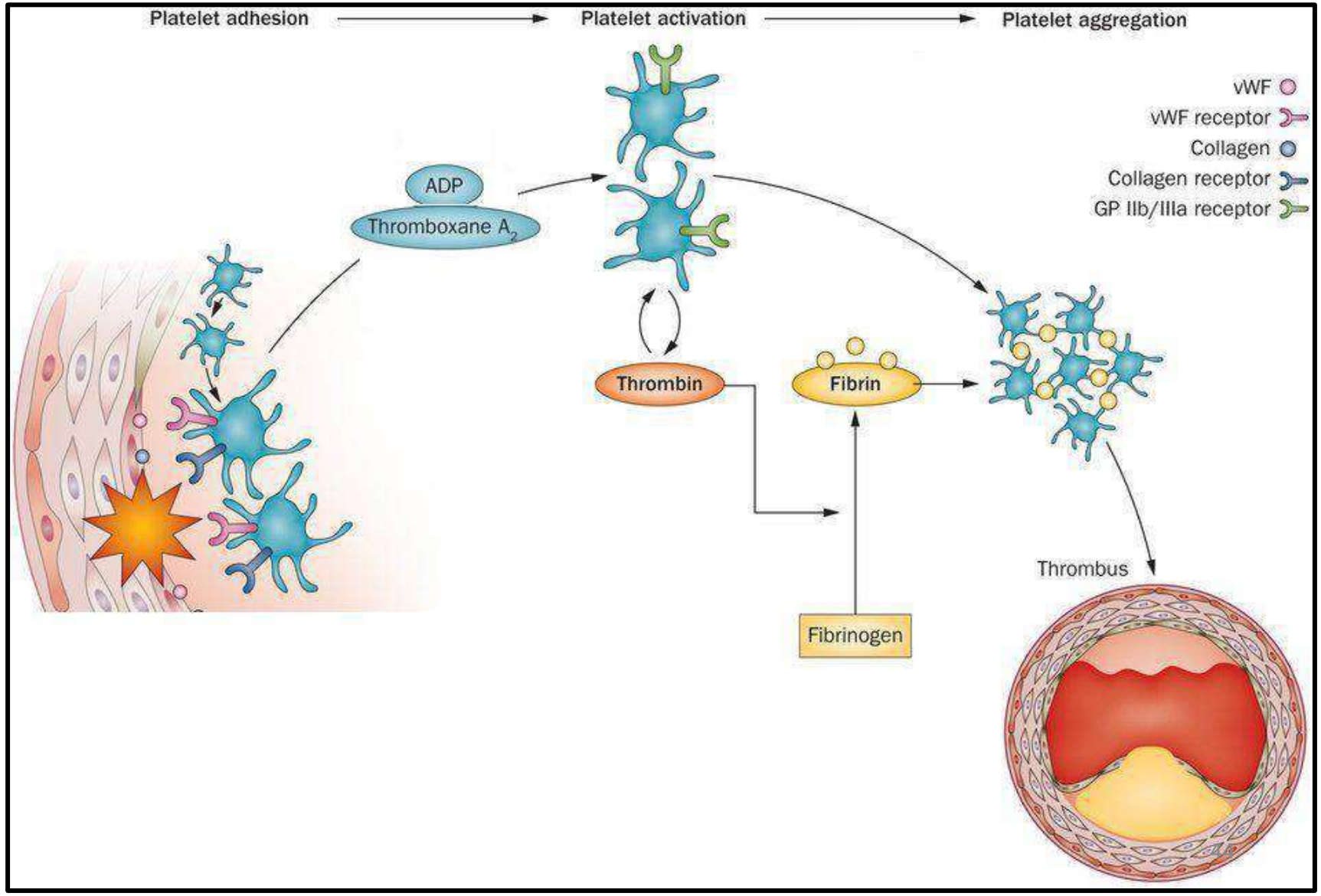


Heart disorders

1. Coronary artery disease (CAD)

Pathogenesis

- **Thrombus formation**



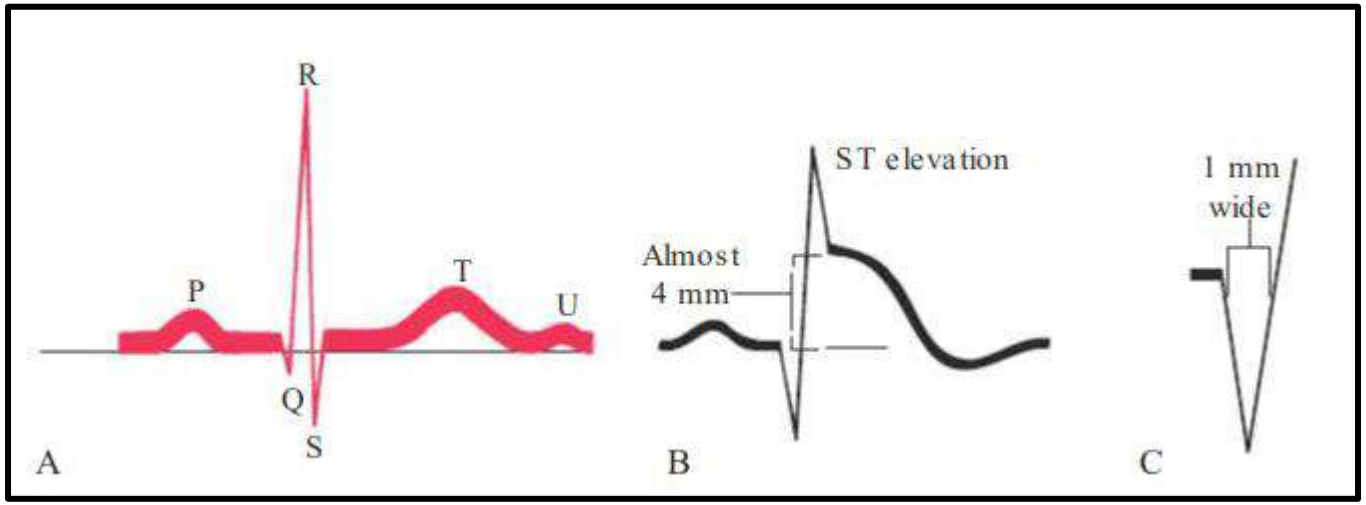
Heart disorders

1. Coronary artery disease (CAD)

Acute Coronary Syndrome (ACS)

- **It is acute ischemic heart diseases ranging from:**

  - **Unstable Angina**
  - **Non ST elevation MI**
  - **ST elevation MI**



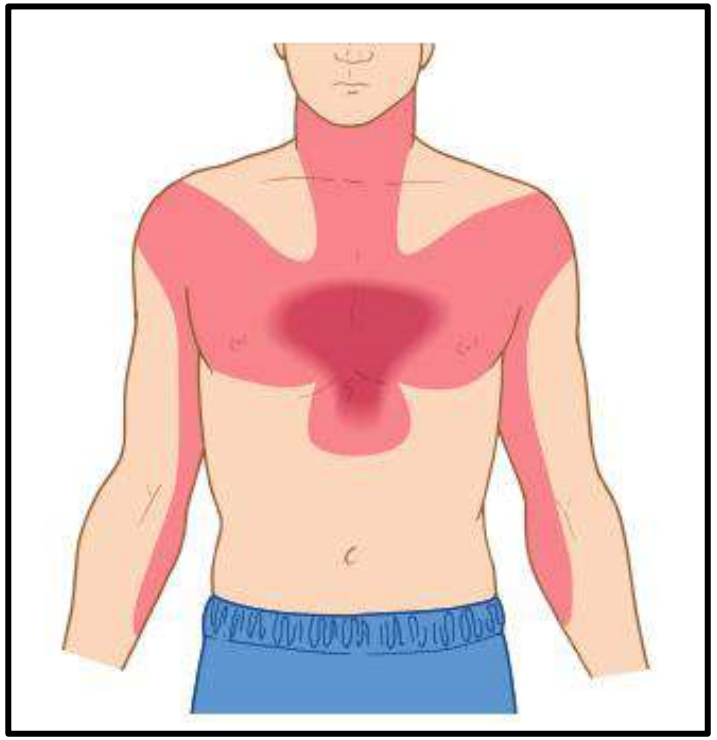
Heart disorders

1. Coronary artery disease (CAD)

Chronic ischemic heart disease

- It is the inability of the coronary arteries to supply blood to meet the metabolic demands of the heart.
- Atherosclerosis (fixed plaque) is the main cause, but vasospasm may serve as a contributing factor.
  - Stable angina pectoris (effort angina)
  - Silent myocardial ischemia (silent angina)
  - Vasospastic angina (variant, Prinzmetal angina)

Heart disorders

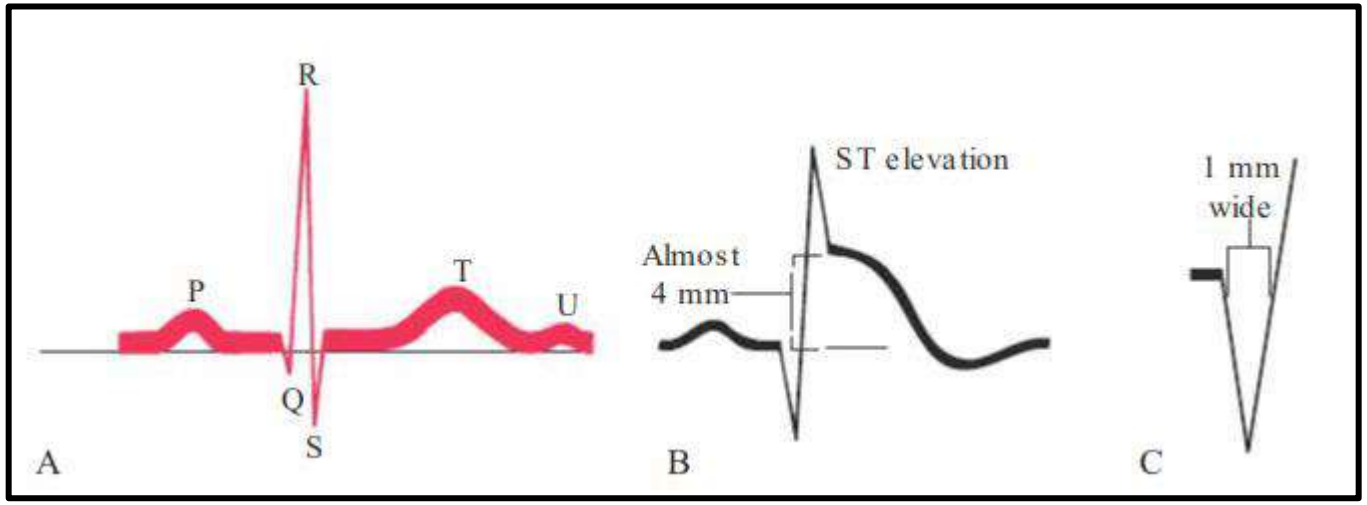


1. Coronary artery disease (CAD)

Diagnosis

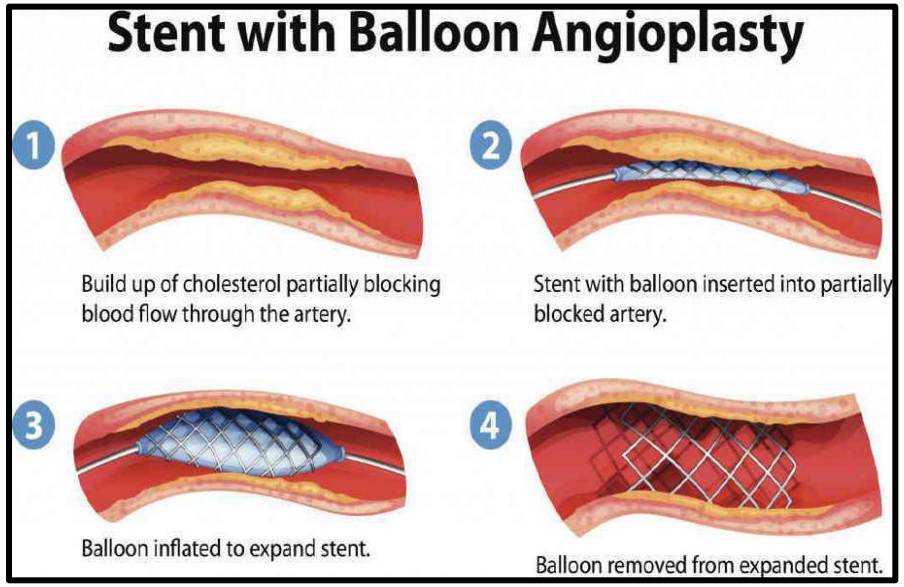
- Pain: Paroxysmal chest pain
- Exercise stress test, rest test
- ECG: ST segment, T wave
- Computed tomography (CT)

- Serum biomarkers:
  - Troponin I, T (Troponin assay): 3hr-7Days
  - Creatine kinase MB: 4hr-3Days



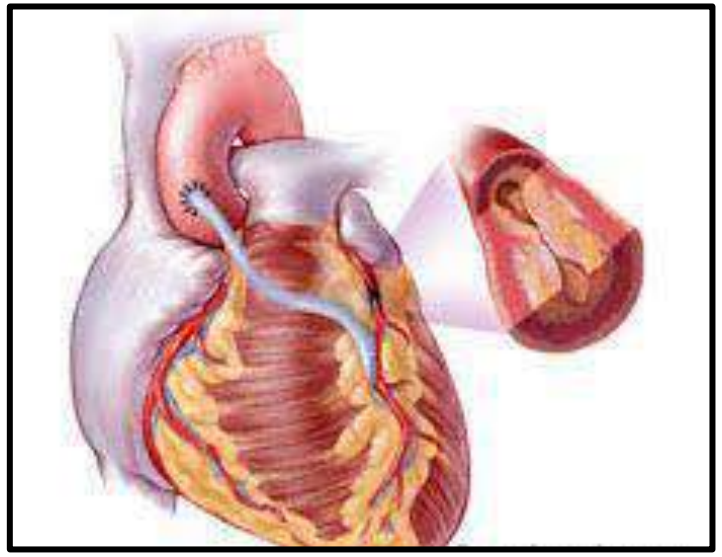
Heart disorders

1. Coronary artery disease (CAD)



Treatment

- Administration of oxygen
- Antiplatelet aggregation: aspirin
- Fibrinolytic: plasminogen activator
- Vasodilators: nitrates
- ß-adrenergic blockers
- ACE inhibitors
- Strong analgesics: morphine
- Percutaneous coronary intervention (PCI): angioplasty with/without stent
- Coronary artery bypass graft (CABG)



Heart disorders

2. Heart Failure (Congestive Heart Failure)

- It is a chronic heart disease.
- It is the inability of the heart to pump sufficiently.

- Impairment of the ventricles to contract and eject blood (systolic failure)
- Impairment of the ventricles to relax to refill with blood (diastolic failure)

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Pathogenesis

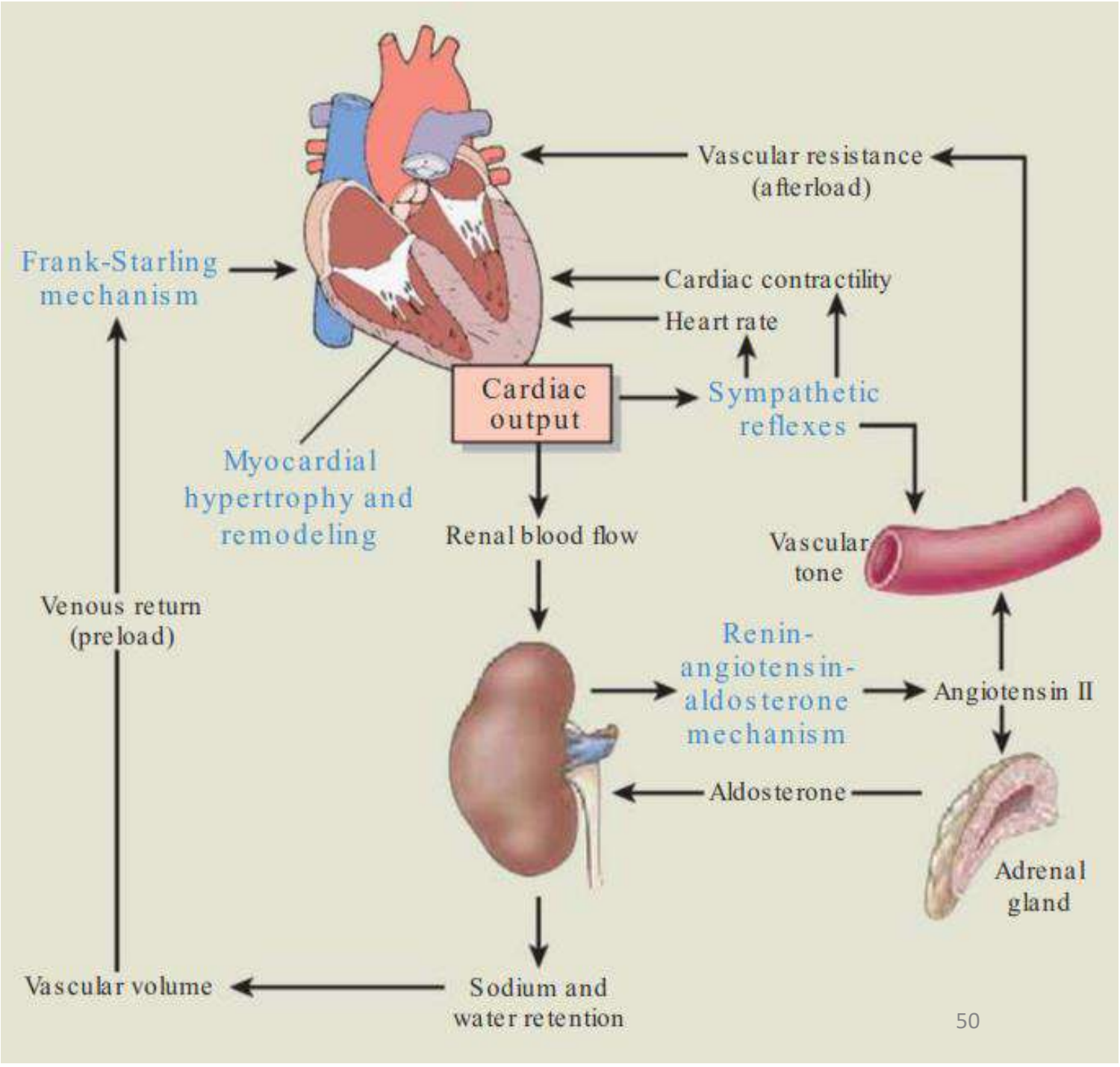
Causes

- The most common causes of heart failure are:
  - Coronary artery disease
  - Hypertension
  - Cardiomyopathy
  - Valvular heart disease

Heart disorders

2. Heart Failure

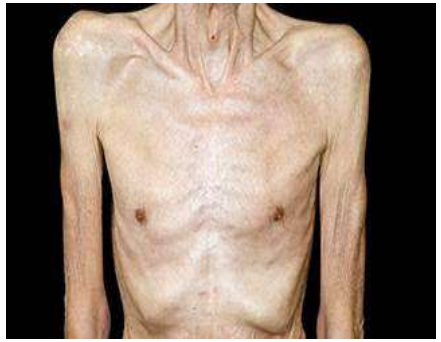
Compensatory mechanisms of Heart Failure

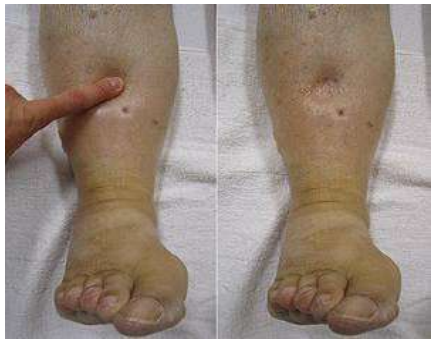


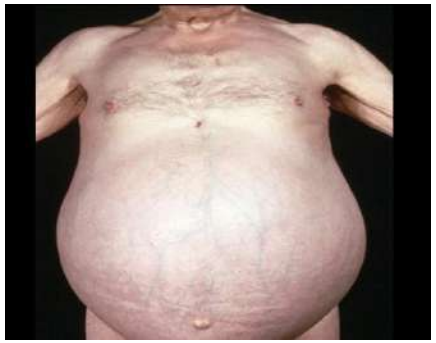
Heart disorders

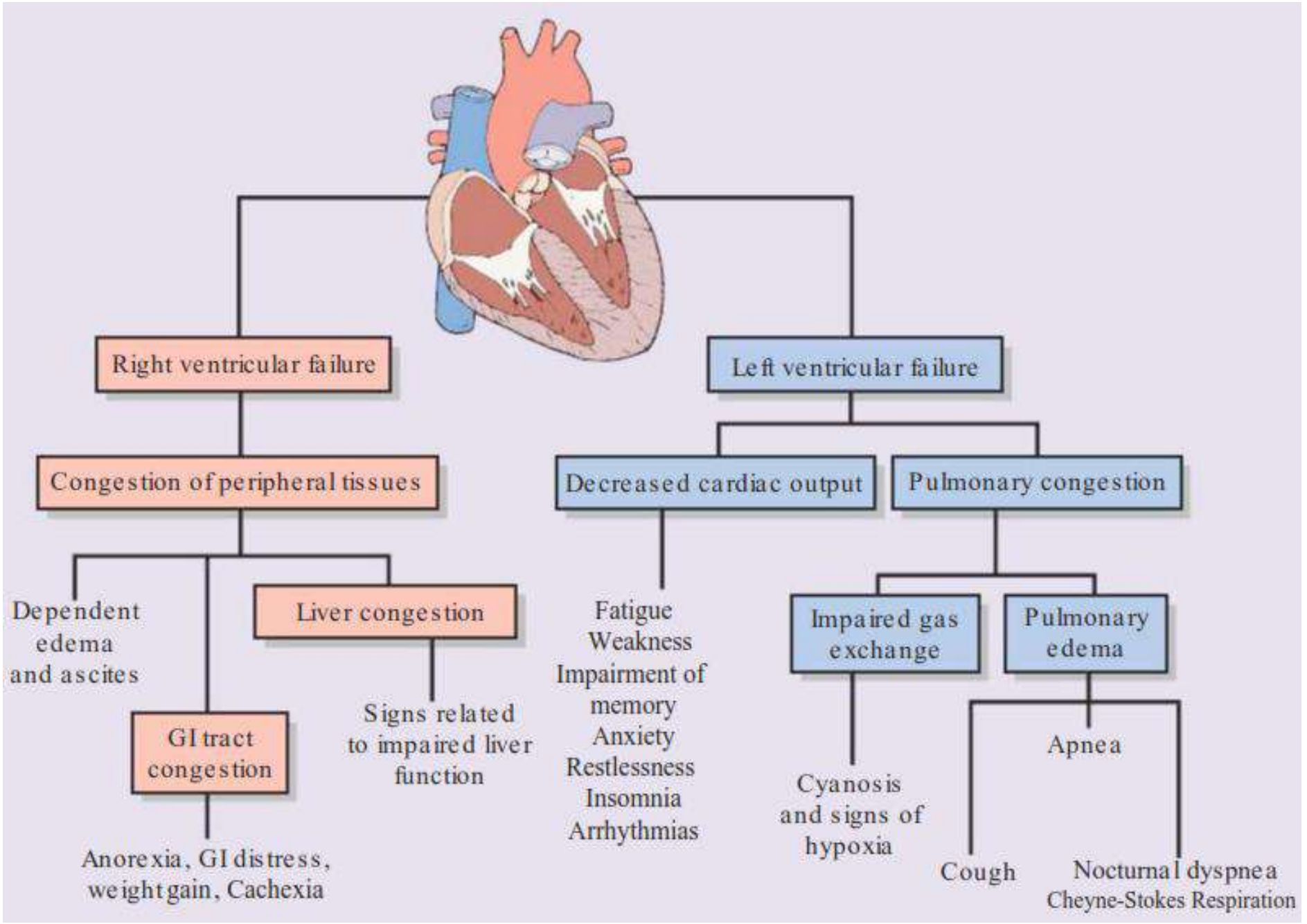
2. Heart Failure

- **Manifestations**



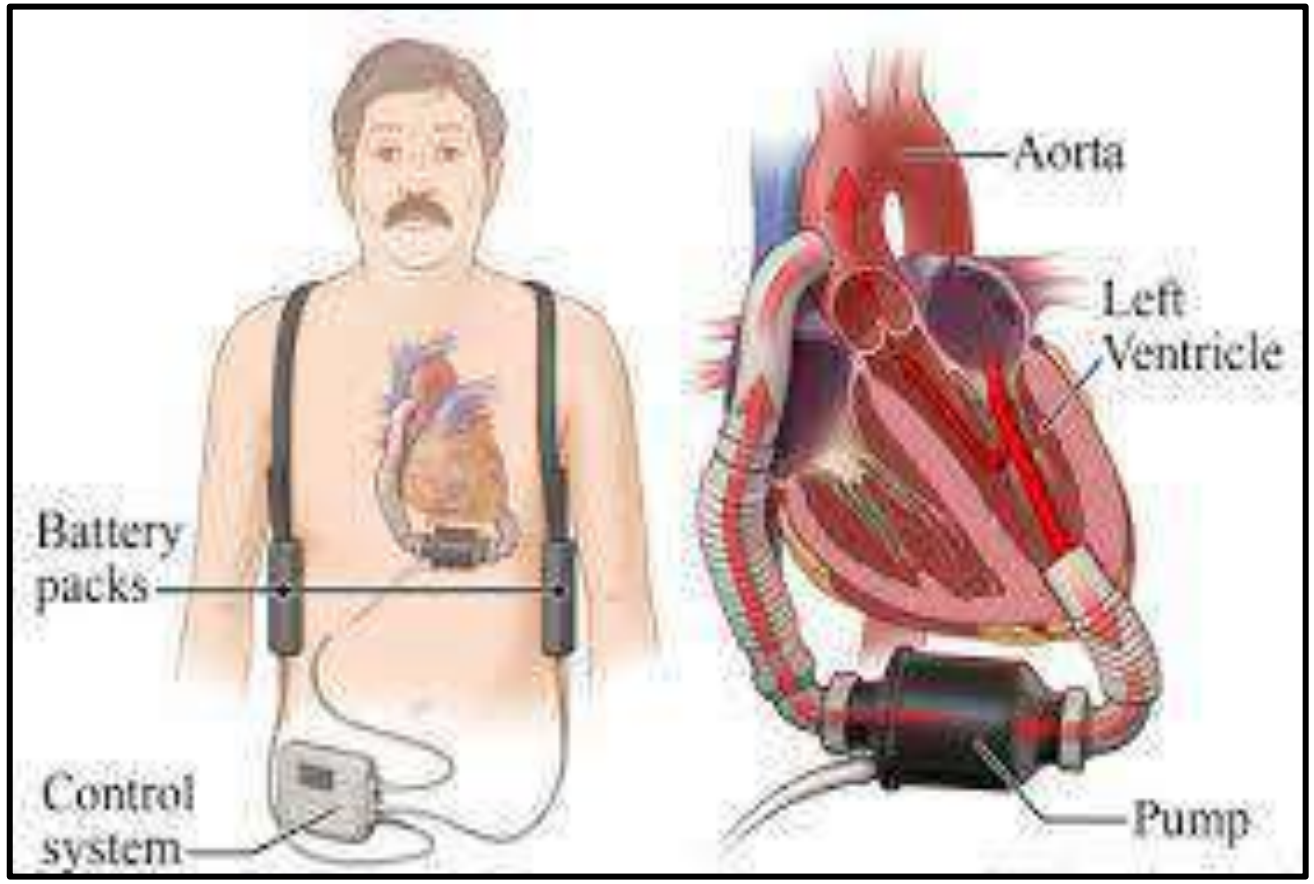






Heart disorders

2. Heart Failure



Treatment

- ACE inhibitors
- ß-adrenergic blockers
- Angiotensin II receptor blockers
- Aldosterone antagonists
- Digitalis (Digoxin)
- Diuretics
- Vasodilators: nitrates
- Mechanical support devices as ventricular assist device (VAD). NOT artificial cardiac pacemakers
- Heart transplant