Diseases of The Cardiovascular System:
Diseases of Blood Vessels:

The diameter of blood vessels usually controls the blood pressure within narrow limits, especially of arterioles because they are responsive to different types of stimuli resulting in vasodilatation or vasoconstriction. All blood vessels are lined by endothelial cells that have a critical function:

1. Maintenance of Permeability Barrier
2. Elaboration of Anticoagulant, Antithrombotic, Fibrinolytic regulators
- Prostacyclin
- Thrombomodulin
- Heparin-like molecules
- Plasminogen activator

3. Elaboration of Prothrombotic Molecules
- Von Willebrand factor
- Tissue factor
- Plasminogen activator inhibitor

4. Extracellular Matrix Production (collagen, proteoglycans)
5. Modulation of Blood Flow and Vascular Reactivity
- Vasconstrictors: endothelin, ACE
- Vasodilators: NO, prostacyclin

6. Regulation of Inflammation and Immunity
- IL-1, IL-6, chemokines
- Adhesion molecules: VCAM-1, ICAM, E-selectin P-selectin
- Histocompatibility antigens

7. Regulation of Cell Growth
- Growth stimulators: PDGF, CSF, FGF
- Growth inhibitors: heparin, TGF-β

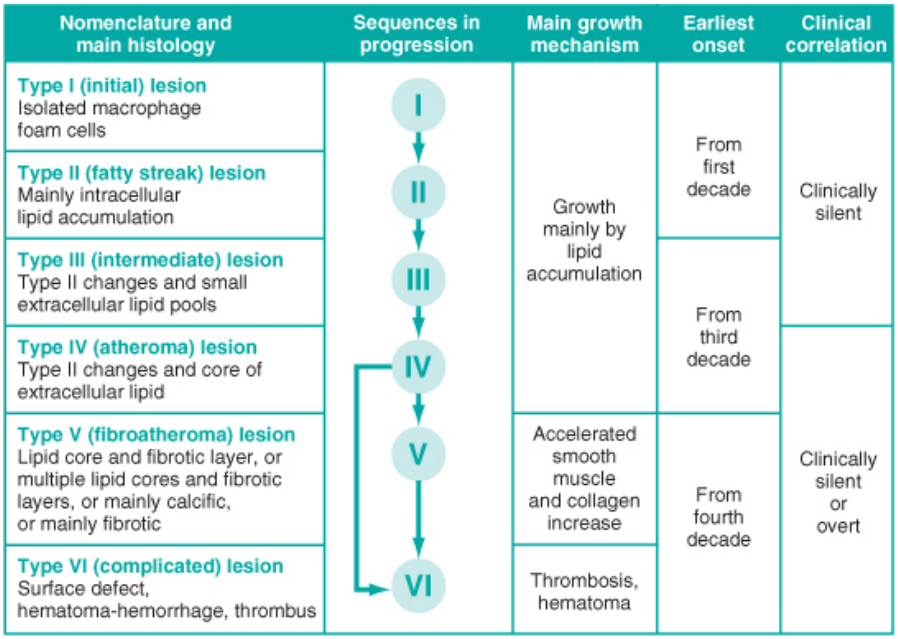
8. Oxidation of LDL

Endothelial cells can be activated by cytokines and bacterial products, which cause inflammation and septic shock; hemodynamic stresses and lipid products, critical to the pathogenesis of atherosclerosis; advanced glycosylation end products (important in diabetes), as well as viruses, complement components, and hypoxia.

Vascular smooth muscle cells are responsible for vasoconstriction and dilation in response to normal or pharmacologic stimuli. They also synthesize collagen, elastin, and proteoglycans; and elaborate growth factors and cytokines. They migrate to the intima and proliferate following vascular injury.

Atherosclerosis:

Is characterized by intimal lesions called atheromas, or atheromatous or fibrofatty plaques, which protrude into and obstruct vascular lumens and weaken the underlying media. It is the cause of ischæmic heart disease, forming the major cause of death world-wide. The American Heart Association classification divides atherosclerotic lesions into six types:



Fatty streaks are the earliest lesion of atherosclerosis, composed of subendothelial lipid-filled foamy cells, with few T lymphocytes and extracellular lipid, appear in the aorta in all children above the age of 10. Some fatty streaks may progress to atheromatous plaques, developing primarily in elastic arteries (e.g., aorta, carotid, and iliac arteries) and large and medium-sized muscular arteries (e.g., coronary and popliteal arteries), resulting in partial or complete obstruction. In small arteries plaques can undergo disruption and precipitate thrombi that further obstruct blood flow.

Atherosclerotic plaques have three principal components: 1. cells, including SMCs, macrophages, and other leukocytes; 2. ECM, including collagen, elastic fibers, and proteoglycans; and 3. intracellular and extracellular lipid (cholesterol and cholesterol esters).

Complications:

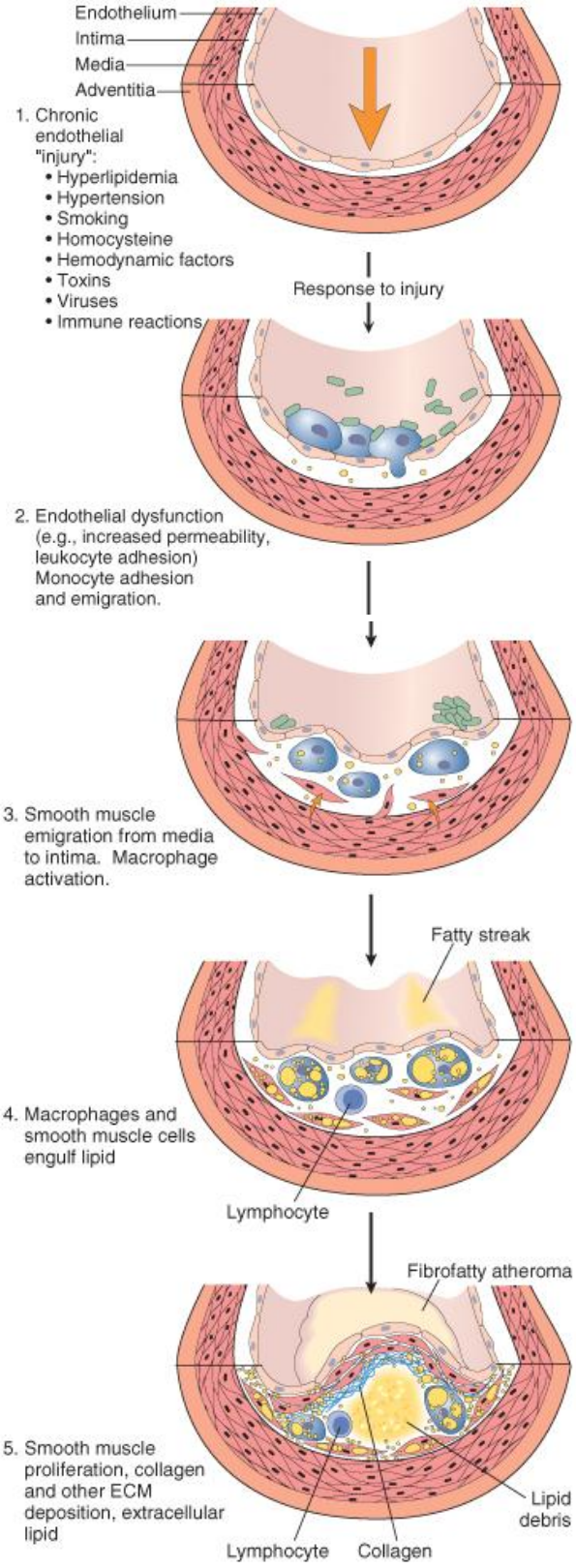
1. Rupture, ulceration and erosion.
2. Hæmorrhage into the plaque.
3. Thromosis.
4. Aneurysmal dilatation.

Risk factors of IHD:

Major	**Minor**
Nonmodifiable	
Increasing age Male gender Family history Genetic abnormalities	Obesity Physical inactivity Stress ("type A" personality) Postmenopausal estrogen deficiency High carbohydrate intake
Potentially Controllable	
Hyperlipidemia (cholesterol) Hypertension Cigarette smoking Diabetes	Alcohol Lipoprotein Lp(a) Hardened (trans)unsaturated fat intake *Chlamydia pneumoniæ*

Pathogenesis:

- Chronic endothelial cell injury.
- Accumulation of lipoproteins mainly LDL.
- Oxidation of lipoproteins.
- Migration of monocytes to the intima, phagocytosing lipids (foam cells).
- Adhesion of platelets.
- Smooth muscle cell migration to the intima and proliferation.
- Enhanced accumulation of lipids



Hypertension:

Hypertension is one of the most important risk factors for both coronary artery disease and cerebrovascular accidents; it can lead to cardiac hypertrophy and, potentially, heart failure (hypertensive heart disease), aortic dissection, and renal failure. The pathogenesis is multifactorial depending on genetic and environmental

causes, but the main cause of hypertension remains unknown in most of the cases. Hypertension is defined as a sustained diastolic pressure greater than 90 mm Hg or a sustained systolic pressure in excess of 140 mm Hg. It is estimated that 25% of the population are hypertensive.

Types And Causes:

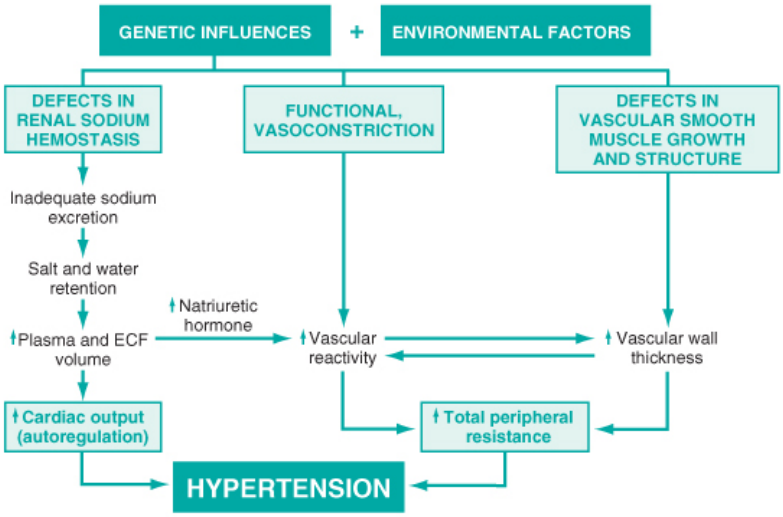
I. Essential Hypertension.

II. Secondary Hypertension:

1. Renal
    - Acute glomerulonephritis
    - Chronic renal disease
    - Polycystic disease
    - Renal artery stenosis
    - Renal artery fibromuscular dysplasia
    - Renal vasculitis
    - Renin-producing tumors
2. Endocrine
    - Adrenocortical hyperfunction (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, licorice ingestion)
    - Exogenous hormones (glucocorticoids, estrogen [including pregnancy-induced and oral contraceptives], sympathomimetics and tyramine-containing foods, monoamine oxidase inhibitors)
    - Pheochromocytoma
    - Acromegaly
    - Hypothyroidism (myxœdema)
    - Hyperthyroidism (thyrotoxicosis)
3. Pregnancy-induced
4. Cardiovascular
    - Coarctation of aorta
    - Polyarteritis nodosa (or other vasculitis)
    - Increased intravascular volume
    - Increased cardiac output
    - Rigidity of the aorta
5. Neurologic
    Psychogenic
    Increased intracranial pressure
6. Sleep apnea
7. Acute stress, including surgery

The kidneys play an important role in regulation of blood pressure through:

1. Renin-angiotensin system: Angiotensin II raises blood pressure by increasing both peripheral resistance (direct action on vascular SMCs) and blood volume (stimulation of aldosterone secretion, increase in distal tubular reabsorption of sodium).
2. Production of prostaglandins and NO, resulting in reduction of blood pressure.
3. Conservation of blood volume by reabsorption of sodium.
4. Natriuretic peptide inhibit sodium reabsorption and rennin-angiotensin system.
5. Impairment of renal excretory function will result in increased renal blood flow by increasing blood pressure to compensate for the reduced blood volume.



Vasculitis:

The pathogenesis of non-infectious vasculitis is:

1. Immune complex deposition.
2. Antineutrophil cytoplasmic antibodies.
3. Anti-endothelial cell antibodies.

Variants:

- Giant cell (temporal) arteritis; affecting mainly the temporal arteries with destructive giant cell granuloma.

- Takayasu's arteritis, involving the carotids and the subclavian arteries, with extension to the arch aorta, resulting in fibrosis of involved vessels (pulseless syndrome).

- Polyarteritis nodosa, involving medium sized arteries, frequently extending to involve the renal arteries, with necrotizing fibrinous inflammation.

- Kawasaki disease, happens in young children, involving the coronary arteries.

- Microscopic polyangiitis (leukocytoclastic vasculitis), occur in Henoch-Schonlein purpura and Churg-Strauss syndrome, involving small arterioles, capillaries and venules.

- Wegner's granulomatosis: is a destructive type of vasculitis usually involving the lungs and the kidneys, presented in the following forms: 1. Acute necrotizing granulomas of the upper and the lower respiratory tract. 2. Necrotizing or granulomatous vasculitis affecting small to medium-sized vessels. 3. Renal disease in the form of focal necrotizing, often crescentic, glomerulitis.

- Thromboangiitis obliterans (Buerger's) disease; segmental, thrombosing, acute and chronic inflammation of medium-sized and small arteries, principally the tibial and radial arteries, happens almost exclusively in heavy smokers.

So vasculitis divided into three categories according to the size of blood vessels:

1-Large Vessel Vasculitis: affects the body's large arteries, including the aorta and carotid arteries as (Giant cell arteritis , Takayasu arteritis)

2-Medium Vessel Vasculitis: affects the medium blood vessels in the body as: (Buerger's disease , Polyarteritis nodosa)

3-Small vessel vasculitis : affects the body's small blood vessels as:
(Churg-Strauss syndrome , Wegner's granulomatosis)

Diseases of The Heart:
All cardiac disorders can arise from the following mechanisms:

1. Failure to pump (heart failure).
2. Outflow obstruction (valvular stenosis, coarctation of aorta' systemic hypertension) resulting in increased workload on the affected chamber, with chamber hypertrophy.
3. Regurgitant flow due to valvular incompetence, resulting in increased residual volume with chamber dilatation.
4. Disorders of cardiac conduction causing arrhythmias.
5. Disruption of the continuity of the circulatory system.

Congenital Cardiac Diseases:

Malformation	%
Ventricular septal defect VSD	42
Atrial septal defect ASD	10
Pulmonary stenosis	8
Patent ductus arteriosus PDA	7
Tetralogy of Fallot TOF	5
Coarctation of aorta	5
Atrioventricular septal defect AVSD	4
Aortic stenosis	4
Transposition of great arteries TGA	4
Truncus arteriosus TA	1
Total anomalous pulmonary venous connection TAPVC	1
Tricuspid atresia	1

Diseases with left to right shunt include; ASD, VSD, PDA and AVSD.
Diseases with right-to-left shunting include; TOF, TGA, TA, tricuspid atresia and TAPVC.

Ischæmic Heart Disease:

Pathogenesis: The dominant influence in the causation of the IHD syndromes is diminished coronary perfusion relative to myocardial demand, owing largely to a complex and dynamic interaction among fixed atherosclerotic narrowing of the coronary arteries, intraluminal thrombosis overlying a disrupted atherosclerotic plaque, platelet aggregation, and vasospasm. Obstruction of 75% of the coronary artery lumen by atheroma leads to symptoms on exertion, while 90% obstruction causes symptoms even on rest (angina pectoris). Acute plaque change leads to thrombosis and total occlusion of the coronary artery lumen with myocardial infarction. Acute plaque changes include:

1. Rupture/fissuring, exposing the highly thrombogenic plaque constituents.
2. Erosion/ulceration, exposing the thrombogenic subendothelial basement membrane to blood.
3. Hemorrhage into the atheroma, expanding its volume.

Morphologic changes in acute MI:

Time	Gross Features	Light Microscope
Reversible Injury		
0-½ hr	None	None
Irreversible Injury		
½-4 hr	None	Usually none; variable waviness of fibers at border
4-12 hr	Occasionally dark mottling	Beginning coagulation necrosis; edema; hemorrhage
12-24 hr	Dark mottling	Ongoing coagulation necrosis; pyknosis of nuclei; myocyte hypereosinophilia; marginal contraction band necrosis; beginning neutrophilic infiltrate
1-3 days	Mottling with yellow-tan infarct center	Coagulation necrosis, with loss of nuclei and striations; interstitial infiltrate of neutrophils
3-7 days	Hyperemic border; central yellow-tan softening	Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border
7-10 days	Maximally yellow-tan and soft, with depressed red-tan margins	Well-developed phagocytosis of dead cells; early formation of fibrovascular granulation tissue at margins
10-14 days	Red-gray depressed infarct borders	Well-established granulation tissue with new blood vessels and collagen deposition

2-8 wk	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity
>2 mo	Scarring complete	Dense collagenous scar

Consequences of MI:

1. Contractile dysfunction.
2. Arrhythmias.
3. Myocardial rupture.
4. Pericarditis.
5. Infarct extension.
6. Infarct expansion.
7. Mural thrombus.
8. Ventricular aneurysm.
9. Papillary muscle dysfunction.
10. Progressive late heart failure.

Infective Endocarditis (IE):

Is characterized by colonization or invasion of the heart valves or the mural endocardium by a microbe, leading to the formation of bulky, friable vegetations. composed of thrombotic debris and organisms, often associated with destruction of the underlying cardiac tissues. IE can be classified into:

1. Acute endocarditis: Describes a destructive infection of previously normal heart valve by a highly virulent microaorganism leading to death of more than 50% of patients within few days. Such microorganisms produce necrotizing, ulcerative, invasive valvular infections that are difficult to cure by antibiotics and usually require surgery.

2. Subacute endocarditis: Caused by low virulent bacteria infecting an abnormal heart (deformed valves, VSD, ASD, etc…), pursuing a long course eventually to healing.

Ætiology And Pathogenesis:

Predisposing factors:

1. Rheumatic heart disease.
2. Myxomatous mitral valve.
3. Degenerative calcific valvular stenosis.
4. Neutropenia, and immunodeficiency
5. Malignancy.
6. Diabetes mellitus.
7. Alcoholism.
8. Intravenous drug abuse.

Causative microorganisms:

1. *Streptococcus viridans* (50-60%).
2. *Staphylococcus aureus* (10-20%), especially in deformed valves.
3. Others (enterococci, *Hæmophilus, Acinetobacillus*, etc…).
4. Gram negative bacilli and fungi.

Seeding of blood with microorganisms happens after dental extraction, surgical procedures, injection with contaminated needles or an occult source from the gut or oral cavity. In both forms of the disease friable, bulky, and potentially destructive vegetations containing fibrin, inflammatory cells, and bacteria or other organisms are present on the heart valves, resulting in small *microabscesses* in the underlying myocardium and *septic emboli* to distant organs, resulting in *septic infarcts*.