Disease	Definition	Risk Factors	Complications	Clinical features	Pathogenesis	Morphology
RF	An acute, **immune mediated**, multi-system inflammatory disease that occurs a few weeks after, group A-beta hemolytic streptococcal infection.	-	Repeated attacks or a single severe first attack can cause **chronic rheumatic heart disease** leading to **congestive cardiac failure.** →Valve regurgitation →Heart failure →LA hypertrophy → could cause brain stroke →Senile calcific aortic stenosis. →Bacterial infective endocarditis →Adhesive pericarditis	Chronic: Manifests years or decades after the initial episode of rheumatic fever. **Minor criteria:** ○ History of fever ○ Arthralgia ○ Leukocytosis ○ Increase in (ESR, CRP) ○ Long of PR segment). ○ Previous RF **Major criteria:** ○ Pancarditis. ○ Migratory polyarthritis. ○ Sydenham chorea. ○ Erythema marginatum. ○ Rheumatic nodules	**Immune mediated**. the causative organisms (streptococci) result in → **antibodies** → **cross react** with certain antigens in the heart and joints (i.e. **M-protein**) → activating **Th - CD4 cells.**	**Acute rheumatic fever** is characterized by discrete inflammatory foci within a variety of tissues. (Aschoff bodies) **Chronic rheumatic heart disease** Characterized by organization of the acute inflammation and subsequent scarring. Aschoff bodies are replaced by fibrous scar
IE	It's an infection of the cardiac valves or mural surface (الجدار السطحي) of the endocardium. Resulting in the formation of an adherent mass of thrombotic debris and microorganisms.	○ Congenital heart disease ○ Bicuspid aortic valve ○ Rheumatic heart disease. ○ Mitral valve prolapse. (Most common site for IE) ○ Atrial septal defect ○ The elderly diabetics and pregnant women ○ Prosthetic heart valves ○ Intravenous drug abusers. ○ Transient bacteremia	• Valve ulceration and perforation, rupture of chordae tendineae, • Arrhythmias • Valvular regurgitation • Congestive heart failure • Septicemia • Pulmonary emboli • Mycotic aneurysms of vessels. • Renal failure (glomerulonephritis)	***Acute Endocarditis:*** Caused by **highly virulent organisms** (staphylococcus aureus). ***Subacute Endocarditis:*** Infections by organisms of low virulence involving a previously abnormal heart, especially deformed valves. Streptococcus viridans	-	In both acute and subacute forms, there are friable bulky and potentially destructive vegetation (composed of fibrin, inflammatory cells and microorganisms) on the heart valves.

Disease	Definition	Risk Factors	Complications	Pathogenesis	Morphology
Marantic IE	It's a paraneoplastic syndrome, which causes sterile vegetations on the valves as a result of ↑ coagulability secondary to ↑ mucin production.	• Mucinous adenocarcinomas Immunocompromised. • Advanced chronic diseases.	• Chordae tendineae rupture. • Emboli. • Glomerulonephritis. • Suppurative pericarditis.	○ Subtle endothelial abnormalities. ○ Hypercoagulability. ○ Association with malignancy (50%) and other debilitating diseases. ○ This form of endocarditis associated with debilitating disorders, such as metastatic cancer and other wasting conditions. ○ Characteristics include small, sterile fibrin deposits randomly arranged along the line of closure of the valve leaflets.	Deposition of small masses of fibrin, platelets, and other blood components on the leaflets of the cardiac valves (sterile). There is no infective organism.
LSE	Sterile vegetations caused by systemic lupus erythematous (SLE).	-	○ Fibrosis causes retraction of chordae tendineae → causes incompetence → uncontrolled blood flow → heart failure. ○ Because these vegetation are very friable, they shoot septic emboli → could cause brain abscess.	-	Dystrophic Calcification: It's calcification of necrotic tissue associated with normal calcium level and caused by local inflammation.
VHD	It's the damage or defect in one or more of the four heart valves. Most commonly affected are mitral and aortic valves, rare in tricuspid valve, and almost never in the pulmonary valve	➢ Congenital. Most common is a bicuspid aortic valve. ➢ Secondary to thrombus and other diseases like infective endocarditis. ➢ Degeneration of the valve with age. ➢ Post inflammatory scarring (most common cause): A scar that occurs secondary or after an inflammatory process e.g. as a late result of rheumatic fever. ➢ Can occur even with prosthetic cardiac valves.	-	-	-

<table>
<tr><th>Disease</th><th>Definition</th><th>Risk Factors</th><th>Complications</th><th>Pathogenesis</th><th>Morphology</th></tr>
<tr><td>Atherosclerosis</td><td>Atherosclerosis is characterized by intimal lesions called atheroma, which protrude into and obstruct vascular lumens and weaken the underlying media</td><td>Major (imp):
• Non-modifiable:
- Age
- Genetics
- Family history
- Gender
• Modifiable:
- Diabetes
- Diet (hyperlipidemia)
- Hypertension
- Smoking</td><td>● MI
● Cerebral infarction
● Gangrene of extremities
● Angina
● Superimposed thrombosis
● Calcification
● Rupture or ulceration</td><td>○ Endothelial injury
○ Endothelial dysfunction.
○ Accumulation of LP
○ Monocyte adhesion and migration
○ Macrophages engulf lipid
○ Inducing an inflammatory reaction
○ Collagen deposition SMC proliferation
○ Fibrous plaque</td><td>The key characters of atheroma are: intimal thickening and lipid accumulation.
Atherosclerotic plaques contain 3 main components:
○ Cells: smooth muscle cells, foam macrophages, lymphocytes.
○ Extracellular matrix: collagen, elastic fibers.
○ Lipid: intracellular and extracellular lipid.</td></tr>
<tr><td>Angina pectoris</td><td>A type of IHD characterized by paroxysmal and usually recurrent attacks of substernal or precordial chest discomfort, described as constricting, crushing, squeezing, choking, or knifelike pain.</td><td colspan="4">1. Stable angina or typical angina pectoris:
○ Most common
○ It is caused by atherosclerotic disease with usually 70% to 75% narrowing of lumen.
○ The chest pain is episodic and associated with exertion or some other form of stress.
○ Is usually relieved by rest (thereby decreasing demand) or with a strong vasodilator like nitroglycerin.
2. Unstable or crescendo angina:
○ It is an unstable and progressive condition (90% narrowing (fixed) of lumen).
○ Pain occurs with progressively increasing frequency, and is precipitated with progressively less exertion, even at rest.
○ It is induced by disruption or rupture of an atheroma plaque with superimposed partial thrombosis.
○ Unstable angina is often the precursor of subsequent acute MI. Thus also called as preinfarction angina.
3. Prinzmetal or variant angina:
○ An uncommon pattern of episodic angina that occurs at rest due to coronary artery spasm.
○ Prinzmetal angina generally responds promptly to vasodilators, such as nitroglycerin and calcium channel blockers.
○ It is not related to atherosclerotic disease.
○ The etiology is not clear.</td></tr>
<tr><td>MI</td><td>Necrosis of heart muscle resulting from ischemia.</td><td>-</td><td>• Cardiac arrhythmia
• Left ventricular failure
• Cardiogenic shock
• Myocardial rupture
• Thromboembolism
• Pericarditis
• Ventricular aneurysm
• Progressive late heart failure in the form of chronic IHD.
• Right ventricular infarction
• Reperfusion injury</td><td>Most common cause is thrombosis on a preexisting disrupted atherosclerotic plaque.
• Exposure of the thrombogenic subendothelial basement membrane
• Myocardial necrosis begins within 20-30 minutes at the subendocardial region)
• Infarct reaches its full size within 3-6 hrs.
• Irreversible cell injury: When ischemia lasts for 20-40 min
• With more prolonged ischemia, the infarct can involve the entire wall thickness (transmural infarct).</td><td><table><tr><th>Time</th><th>Microscopic changes</th></tr><tr><td>0-4h</td><td>None</td></tr><tr><td>4-12h</td><td>Coagulation necrosis</td></tr><tr><td>12-24</td><td>More coagulation necrosis; Neutrophils come in</td></tr><tr><td>1-7d</td><td>Neutrophils die, macrophages come to eat dead cells</td></tr><tr><td>1-2w</td><td>Granulation tissue</td></tr><tr><td>2-8w</td><td>Collagen</td></tr></table></td></tr>
</table>

Hypertension

Definition

- Sustained diastolic pressure more than 90 mm Hg
- Sustained systolic pressure in excess of 140 mm Hg
- (>140/90)

Risk Factors

- **Hereditary,** Genetics-family history
- **Race.** African-Americans
- **Gender.** Men & postmenopausal women
- **Age**
- **Obesity**
- **Diet, particularly sodium intake**
- **Lifestyle-stressful**
- **Heavy alcohol consumption**
- **Diabetes**
- **Use of oral contraceptives**
- **Sedentary or inactive lifestyle**
- **Smoking**

Classification

1- **Based on etiology (cause):**
- **Primary/Essential (95%):** It is idiopathic.
- **Secondary (5-10%).**

2- **Based on clinical features:**
- **Benign**
- **Malignant (5%):**
  - → Organ damage (Kidney, Retina, Brain and Heart.)
  - → The diastolic pressure is usually over 120mmHg
  - → Complicates any type of HTN.
  - → It is associated with:
    - Widespread arterial necrosis and thrombosis
    - Rapid development of renal failure
    - Retinal hemorrhage and exudate
    - Hypertensive encephalopathy
    - Left ventricular failure
    - Leads to death in 1 or 2 years if untreated.

Causes of Secondary Hypertension

- **Renal:**
  - Glomerulonephritis
  - Renal artery stenosis
  - Renal vasculitis
  - Adult polycystic disease
  - Chronic renal disease,
  - Renin producing tumors
  - Primary renal disease
  - Renal artery narrowing
  - Adrenal disorders.
- **Endocrine:**
  - Adrenocortical hyperfunction
  - Hyperthyroidism/Thyrotoxicosis
  - Hypothyroidism/Myxedema.
  - Pheochromocytoma & Acromegaly
  - Exogenous hormones
  - **Pregnancy-induced**
- **Vascular:**
  - Coarctation of aorta &/ or rigidity.
  - Vasculitis e.g. **Polyarteritis nodosa**
  - Increased intravascular volume
  - Increased cardiac output
- **Nuerogenenic:**
  - Psychogenic & Sleep apnea
  - Increased intracranial pressure
  - Acute stress, including surgery

Pathogenesis

- Defect in sodium excretion: (common):
  - Decreased sodium excretion elevates blood pressure.
  - Defect in cell membrane function: affecting Na/Ca transport
- Increased sympathetic/ vasoconstrictive response:
  - Increased vascular resistance
- Rare gene disorders can cause HTN by increasing renal sodium resorption e.g. Liddle syndrome.

Complications

- **Cardiovascular:**
  - Left ventricular hypertrophy
  - Coronary heart disease
  - Aortic dissection
  - Heart failure (*hypertensive heart disease*)
- **Kidney:**
  - Benign nephrosclerosis (photo A).
  - Renal failure in untreated or in malignant hypertension.
- **Eyes:**
  Hypertensive retinopathy (photo B) is especially seen in malignant hypertension.
- **Brain:**
  Hemorrhage, infarction leading to Cerebrovascular accidents. (**Multi-infarct dementia)**

Morphology

- Large Blood Vessels (Macroangiopathy): HT is a major risk factor in AS.
- Small Blood Vessels (Microangiopathy):
  Arteriolosclerosis
  - → Hyaline arteriolosclerosis:
    - Characteristic of **benign hypertension**
    - Leads to benign nephrosclerosis
    - Marked by homogeneous, pink hyaline thickening of the arteriolar walls, with loss of underlying structural detail, and luminal narrowing.
  - → Hyperplastic arteriolosclerosis:
    - Characteristic of malignant hypertension.
    - Onion skin appearance
    - May be associated with necrotizing arteriolitis (fibrinoid necrosis), which are particularly prominent in the kidney.

Disease	Definition	Risk Factors	Complications	Pathogenesis	Morphology
Thromboembolism	A thrombus is a solid mass of blood constituents, which develops in artery or vein.	- **Hypercoaguable States:** Can be 1. **Primary/Genetic** 2. **Secondary/acquired states:** **a) High risk for thrombosis** ○ Prolonged bed rest or immobilization ○ Myocardial infarction, Atrial fibrillation ○ Tissue damage (surgery, fracture, burns) ○ Cancer ○ Prosthetic cardiac valves ○ Disseminated intravascular coagulation ○ Antiphospholipid antibody syndrome **b) Lower risk for thrombosis**	-	***Virchow triad*** predispose to thrombus formation: (1) Endothelial injury. (2) Stasis or turbulence of blood flow. (3) Blood hypercoagulability.	- **Lines of Zahn** - **May develop anywhere** - **Varies in size** - Arterial or cardiac thrombi usually begin at a site of endothelial injury (e.g., atherosclerotic plaque) or turbulence (vessel bifurcation) - Venous thrombi characteristically occur in sites of stasis.
Thrombophlebitis and Phlebothrombosis	An inflammation in a vein with blood clot formation inside the vein itself at the site of inflammation. Venous thrombosis often arises in the deep veins of the legs deep vein thrombosis (DVT).	1. Bed rest and immobilization. 2. Congestive heart failure 3. Trauma, surgery, and burns. 4. Pregnancy 5. Tumors. 6. Advanced age.	Such thrombi more often embolize to the lungs and give rise to pulmonary infarction.	-	-
Pulmonary thromboembolism	Usually the thrombus fragments in DVTs and get carried by blood to pass through the right side of the heart.. then it arrest at the pulmonary vasculature.	-	➢ It may occlude main pulmonary artery, or impact across the bifurcation (saddle embolus), or pass out into the smaller, branching arterioles of the pulmonary circulation. (may result in infarction.) ➢ Hypoxia, hypotension, and right-sided heart failure (60% obstruction) ➢ *paradoxical embolism*	-	-

Disease	Definition	Arises from	Complications	Where	Related syndromes
Systemic Thromboembolism	Emboli traveling within the arterial circulation.	(80%) arise from intracardiac mural thrombi.	Arterial emboli usually cause infarction of tissues supplied by the artery (The consequences of systemic emboli depend on the extent of collateral vascular supply in the affected tissue, the tissue's vulnerability to ischemia, and the caliber of the vessel occluded).	Major sites for arteriolar embolization are the lower extremities (75%) and the brain (10%)	-
Fat Thromboembolism	Fat is released by marrow or adipose tissue injury and enters the circulation through rupture of the blood vessels and act as an embolus	Microscopic fat globules may be found in the circulation after **fractures of long bones** (which have fatty marrow) or, rarely, in soft tissue trauma and burns.	-	Circulation	**Fat embolism syndrome** is characterized by pulmonary insufficiency, neurologic symptoms, anemia, and thrombocytopenia.
Air embolism	Gas bubbles within the circulation can obstruct vascular flow (and cause distal ischemic injury) acting as thrombotic masses. Bubbles may coalesce to form frothy masses sufficiently large to occlude major vessels.	Air may enter the circulation during ***obstetric procedures*** or as a consequence of ***chest wall injury***. An excess of 100 cc is required to have a clinical effect	➢ It may occlude main pulmonary artery, or impact across the bifurcation (saddle embolus), or pass out into the smaller, branching arterioles of the pulmonary circulation. (may result in infarction.) ➢ Hypoxia, hypotension, and right-sided heart failure (60% obstruction) ➢ *paradoxical embolism*	For caisson disease: the heads of the femurs, tibia, and humeri.	**Decompression Sickness:** ***Sudden changes in atmospheric pressure***. • Scuba and deep sea divers, and individuals in unpressurized aircraft in rapid ascent are all at risk. • ***Grecian Bend*** • A more chronic form of decompression sickness is called ***caisson disease*** in which, persistence of gas emboli in the skeletal system leads to multiple foci of ischemic necrosis.
Amniotic Fluid embolism	Infusion of amniotic fluid or fetal tissue into the maternal circulation via a tear in the placental membranes or rupture of uterine veins.	Labor and the immediate postpartum period	• Sudden severe dyspnea, cyanosis, and hypotensive shock, followed by seizures and coma. • If the patient survives the initial crisis, pulmonary edema develops, along with disseminated intravascular coagulation.	Presence in the pulmonary microcirculation	-

Disease	Definition	Affects	Clinical features	Treatment	Morphology
Giant-cell arteritis	Chronic, granulomatous inflammation of large to small arteries, especially in head particularly the branches of the carotid artery (temporal a. and branches of the ophthalmic a.) Most common type of vasculitis	Patients >50, F: M = 2:1.	+ Fever, weight loss, facial pain or headache, often most intense along the course of the superficial temporal artery. + Thickened and painful temporal artery + Jaw pain & Visual problems and vision loss	Corticosteroids or anti-TNF therapies	○ Granulomatous inflammation of the blood vessel wall. ○ Giant cells. ○ Disruption and fragmentation of internal elastic lamina.
Polyarteritis Nodosa	There is segmental necrotizing inflammation of arteries of medium to small size, in any organ (especially kidney and skin) except the lung.	Young adults	•Associated with hepatitis B or hepatitis C. - Fever & Weight loss - Abdominal pain and melena (bloody stool) - Muscular pain and neuritis. - In young-adults → Hypertension - Skin lesions associated with HBsAg.	Corticosteroid or anti-TNF therapies Fatal if untreated, but steroids and cyclophosphamide are curative.	- Segmental inflammation - Fibrinoid necrosis - Occlusion of the lumen of this artery. - Note that part of the vessel wall at the left side is uninvolved.
Wegner granulomatosis	○ A necrotizing vasculitis characterized by the triad of: 1) Necrotizing granulomas of respiratory tract & small to medium-sized vessels 2) Renal disease in the form of necrotizing, crescentic, glomerulonephritis.	M>F, at an average age of about 40 years.	- Persistent pneumonitis - Chronic sinusitis - Mucosal ulcerations of the nasopharynx - Evidence of renal disease. C-ANCAs (PR3-ANCAs) (antineutrophilic cytoplasmic antibodies) is positive in serum of more than 95% of patients.	Steroids, cyclophosphamide, TNF inhibitors and anti–B cell antibodies (Rituximab) Untreated: fatal - within 2 years	▪ Collection of epithelioid histiocytes = granuloma ▪ Fragmented smooth muscle ▪ Destroyed blood vessel by inflammation ▪ URT Lesions ▪ Renal Lesions: (Crescentic glomerulonephritis).
Thromboangiitis obliterans	• Medium-sized and small arteries, • Leg and hands. (specially tibial and radial arteries)	Heavy smokers before age 35.	Patients tend to have pain even at rest, due to the neural involvement. Chronic ulcerations of the toes, or fingers may appear, followed in time by gangrene.	Abstinence from cigarette smoking in the early stages of the disease brings relief from further attacks	Microscopically, there is acute and chronic inflammation, accompanied by luminal thrombosis. The inflammatory process extends into adjacent veins and nerves.
hypersensitivity vasculitis	• Necrotizing vasculitis of arterioles, capillaries, and venules. Can be cutaneous only or systemic • Inflammation of small blood vessels • Characterized by palpable purpura.	Immunologic reaction to an antigen	○ Idiopathic ○ It may be a part of a systemic disease: ▪ Collagen vascular diseases (lupus erythematosus, rheumatoid arthritis). ▪ Henoch-Schonlein purpura. • It affects many organs e.g. Skin (most common), mucous membranes, lungs, brain, heart, GI, kidneys and muscle.	-	▪ Skin biopsy is often diagnostic. . ▪ Extra vasated RBCs. ▪ Fragmentation of neutrophil nuclei in and around vessel walls. ▪ Leukocytoclasis = (karyorrhexis of neutrophils) in and around the vessels.
HSP	An IgA-mediated, autoimmune systemic small vessel hypersensitivity vasculitis of childhood	Children	Skin purpura, arthritis, abdominal pain, gastrointestinal bleeding, orchitis and nephritis Serum levels of IgA are high in HSP.	-	Immunoglobulin A (IgA) and complement component 3 (C3) are deposited on arterioles, capillaries, and venules.