**Atherosclerosis**

Atherosclerosis is a disease primarily 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. risk factors of atherosclerosis:

**Modified risk factors:**

* Diet and hyperlipidemia, high carbohydrate intake
* Hypertension
* Cigarette smokisng
* Diabetes mellitus
* Obesity
* Physical inactivities ,
* 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**
2. **Progression stage:** foam and platelet cells release mediators that cause migration of smooth muscle cell from media to intema with fibrin deposition covering the lipid plaque forming fibrin cap. **Macrophages** produces oxygen free radicles that **oxidize lipid (LDL)** , this oxidized LDL act as atherogenic as it:
   * 1. **chemotactic to blood monocytes**
     2. **inhibit macrophages motility preventing them from leaving the atheroma**
     3. **cytotoxic to endothelial cells increasing their permeability**

The plaque may enlarge causing narrowing or occlusion of the artery

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

**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**

**causes: (vessels, heart, blood)**

1. Reduction in coronary artery blood flow (90% of the cases) ………… vessels
2. Atherosclerosis (the main cause
3. Coronary artery spasm
4. Hemodynamic disorders (circulatory disorders)
5. Non atherosclerotic coronary diseases (arteritis)
6. Increase cardiac demand …………….. heart
7. Tachycardia
8. Ventricular hypertrophy
9. Reduced oxygen carrying capacity of the blood ……………. blood
10. Anemia
11. Cigarette smoking
12. Advanced lung diseases
13. Cyanotic congenital heart diseases
14. 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

**No.1 stable angina**: **chronic transient angina pectoris**, precipitated by physical activity or emotional upset (**increase cardiac muscle demand)**, relieved by rest within a few minutes. Usually occurs when about **75% of coronary artery lumen stenosed by atheroma (chronic cause).**

**No.2 prinzmetal (variant) angina:** Typical anginal discomfort, usually **at rest**, which develops because of coronary artery **spasm**, rather than an increase of myocardial oxygen demand.

**No.3 unstable angina**: **acute** coronary syndrome characterized by progressively increase in frequency and more prolonged attack of angina. It is usually occur **due to disrupted atherosclerotic plaque with superimposed thrombosis.** It has high frequency of **progression to myocardial infarction** if untreated

**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; may be first clinical manifestation of ischemic heart disease, or there may be a history of angina pectoris. 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 thrombous formation in **ruptured already present 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.

Morphological features of MI:

1. **macroscopical:** pale infarcted area including the **left ventricule** and **interventricular septum**. In subendothelial type the infarction is limited to the inner third of left ventricles. Infarcted heart less than 12 hour not suitable for gross examination.
2. **microscopical**: the myocardial cells show **coagulative necrosis** and this is not be detectable for the first 4 to 8 hours. The infarcted area **infilterated by acute inflammatory cells** and if the patient survive the infarcted area replaced by **granulation tissue** and **healed by fibrosis**.

**Sudden death**

**It is u**nexpected 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**

**Hypertension**

**Hypertension:** defined as increase in blood pressure

Blood pressure depends on cardiac output (CO) and systemic vascular resistance (SVR(

o BP = CO x SVR \* SVR= systemic vascular resistance

Cardiac output depends on heart rate (HR) and stroke volume (SV)

oCO = 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 increase both HR and (SVR(
2. Baroreceptor reflex - senses pressure changes in aortic and carotid arteries. It responsible for regulation of short term blood pressure fall and correct it. It Accommodate 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
2. Atrial natriuretic peptidego to practice 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 vasodilatory 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.
* atherosclerosis

**Stages of hypertention:**

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

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

**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