Thrombosis (lec#1)

*** Pathogenesis (called *Virchow's triad*): *Endothelial Injury*** *(Heart, Arteries),* ***Stasis*** *(abnormal blood flow),****Blood Hypercoagulability .***

* Endothelial cells can be **stimulated** by direct injury or by various cytokines that are produced during inflammation.

***** Pathologic effect of vascular healing→ Excessive thickening of the intima → luminal stenosis & blockage of vascular flow

***Stasis:** a *major factor in venous thrombi.*

*** Hypercoagulability**

A. Genetic (primary):

- Mutations in the **factor V gene** and the **prothrombin gene** are the most common

B. Acquired (secondary):

- Multifactorial and is therefore more complicated

* **Morphology of thrombi :**

- Can develop anywhere in the CVS , focally attached to the underlying vascular surface.

- *Arterial or cardiac* thrombi→ begin at sites of *endothelial injury* or turbulence; and are usually superimposed on an ***atherosclerotic plaque***.

- **Venous thrombi** → occur at sites of stasis. Most commonly the veins of the lower extremities (90%).

*** lines of Zahn**

-Thrombi can have grossly (and microscopically) apparent laminations called **lines of Zahn**; these represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers.

- Such lines are significant in that they represent thrombosis of **flowing** blood .
- Postmortem blood clots are bland non-laminated clots ***(no lines of Zahn)*** .

*** Mural thrombi:** thrombi occurring in heart chambers or in the aortic lumen.

*** Vegetations :** Thrombi on heart valves

- Types:

1- infectious (Bacterial or fungal blood-borne infections)→(e.g. infective endocarditis,).

2-Non-bacterial thrombotic endocarditis occur on sterile valves**.**

*** Venous thrombi:** (veins of the legs) are most common

a. Superficial*: e.g. Saphenous veins ,* can cause local congestion, swelling, pain, and tenderness along the course of the involved vein, but they rarely embolize .

b. Deep*: e.g. Popliteal, Femoral and iliac vein,* more serious because they may embolize , can occur with stasis or in a variety of hypercoagulable states .

Embolism (Lec#2)

- 99% due to dislodged thrombus.

*** Types:**

1.Thromboembolism (99%)

- Emboli result in partial or complete vascular occlusion.

A. **Pulmonary Thromboembolism**

- ***95% originate from deep veins of lower limb***
- ***Saddle embolus:*** *at bifurcation of Pulmonary artery*
- ***Paradoxical embolus:*** *Passage of an embolus from venous to systemic circulation through IAD, IVD*
- Most pulmonary emboli (60% to 80%) are clinically silent because they are small.

B. **Systemic thromboembolism**

- 80% due to intracardiac mural thrombi.
- The major targets are: *Lower limbs 75%, Brain 10%*

2.Fat embolism

- **Causes**: Skeletal injury (fractures of long bones), Adipose tissue Injury
- In skeletal injury, fat embolism occurs in 90% of cases, but only 10% or less have clinical findings.
- ***Fat embolism syndrome*** *is characterized by: Pulmonary Insufficiency,Neurologic symptoms, Anemia, Thrombocytopenia, Death in 10% of the case .*

3. Air embolism

- Causes: *Obstetric procedures, Chest wall injury, Decompression sickness*

* ***Caisson disease****:* gas emboli in the bones leads to multiple foci of ischemic necrosis, usually the heads of the femurs, tibias, and humeri .

4. Nitrogen embolism

5. Cholesterol embolism

6. Amniotic fluid embolism

- Due to infusion of amniotic fluid into maternal circulation via tears in placental membranes and rupture of uterine veins.
- Finding: squamous cells, languo hair, fat, mucin within the pulmonary microcirculation.

INFARCTION

- 99% of all infarcts result from thrombotic or embolic events
- **The dominant histologic characteristic of infarction is ischemic coagulative necrosis .**
- Most infarcts are ultimately replaced by scar. The brain is an exception, it results in **liquefactive necrosis .**

1- **Red infarcts** occur in : **venous occlusions** (such as in ovarian torsion) , **loose tissues** (like lung) that allow blood to collect in the infarcted zone , **tissues with dual circulations** (lung and small intestine), **Previously congested tissues** because of sluggish venous outflow, when flow is re-established to a site of previous arterial occlusion and necrosis .

2- **White infarcts** occur with **arterial occlusions , solid organs** (such as heart, spleen, and kidney).

3- **Septic infarctions** occur when bacterial vegetations from a heart valve embolize or when microbes seed an area of necrotic tissue.
- The infarct is converted into an abscess, with a correspondingly greater inflammatory response

*** Factors That Influence Development of an Infarct :** *nature of the vascular supply, rate of development of the occlusion (*collateral circulation*), vulnerability to hypoxia, the oxygen content of blood* .

Veins and lymphatics (Lec#3)

*** Pathology of veins**

A) Varicose Veins

- More common in females

- The superficial veins of the leg are most typically involved

- **RISK FACTORS** : Obesity ,Female gender ,Pregnancy, Familial tendency (premature varicosities results from imperfect venous wall development)
- **Microscopic Morphology** : spotty medial calcifications (phlebosclerosis) , venous valve deformities (rolling and shortening).
- Embolism is very rare complication

B) Thrombophlebitis And Phlebothrombosis

- ***Inflammation + thrombosis of veins***
- *The deep leg veins account for more than 90% of cases*
- The most important clinical **predispositions** are: congestive heart failure, neoplasia, pregnancy, obesity, the postoperative state, and prolonged bed rest or immobilization

- Thrombophlebitis of upper limb veins are usually associated with local risk factors like: catheter or canula site; or in some cases can be associated with systemic hypercoagulabilities.

*** Special thrombophlebitis types:**

1- Migratory thrombophlebitis (Trousseau sign): colon cancer

2- The superior vena caval syndrome : lung cancer

3- The *inferior vena caval syndrome:* hepatocellular carcinoma and renal cell carcinoma

*** Pathology of Lymphatics**

A) Lymphedema can occur as:

1- Primary (A congenital defect)*,* resulting from lymphatic agenesis or hypoplasia.

2- Secondary* or *obstructive lymphedema

B) Lymphangitis

- Most common are group A β-hemolytic streptococci.
- Red, painful subcutaneous streaks (the inflamed lymphatics), with painful enlargement of the draining lymph nodes *(acute lymphadenitis).*

C) Chylous

- Milky accumulations of lymph in various ***body cavities***
- Caused by rupture of dilated lymphatics, typically obstructed secondary to an infiltrating tumor mass
- **Types**: ***chylous ascites*** (abdomen), ***Chylothorax*** *(chest)*, ***Chylopericardium*** *(pericardium)*

ARTERIOSCLEROSIS (LEC#4)

*** Patterns:**

1-Arteriolosclerosis : affects **small arteries** and arterioles, most often associated with hypertension and/or diabetes mellitus .

2-Mönckeberg medial calcific sclerosis : characterized by calcific deposits in **muscular arteries** , typically in persons older than age 50, often palpable calcifications , do not encroach on the vessel lumen and are usually not clinically significant.

3-Atherosclerosis : most frequent and clinically important pattern , characterized by intimal lesions called ***atheromas*** (also called *atherosclerotic plaques*).

-**Pathogenesis**: initiation of inflammatory process => LDL particles and their content are susceptible to oxidation by free radicals => endothelial activation .

- **Epidemiology:** *Multiple risk factors have a multiplicative effect:* 2 risk factors increase the risk 4X. E.g. if 3 risk factors are present (e.g., hyperlipidemia, hypertension, and smoking), the rate of myocardial infarction is increased 7X.

- **Major Constitutional Risk Factors for atherosclerosis :**

A) Major Risks (Nonmodifiable):

1) Increasing age : between ages 40 and 60, the incidence of myocardial infarction in men increases 5 times, Death rates from IHD rise with each decade .

2) Male gender

-Premenopausal women are relatively protected against atherosclerosis compared with age-matched men unless they are otherwise predisposed by diabetes, hyperlipidemia, or severe hypertension.

3) Genetic abnormalities

- Familial predisposition to atherosclerosis and IHD is **multifactorial** either **familial clustering** of other risk factors such as (hypertension or diabetes) or **well-defined genetic derangements in lipoprotein metabolism**,e.g. familial hypercholesterolemia that result in excessively high blood lipid levels.

4) Family history

B) Potentially Controllable/modifiable: Hyperlipidemia ,Hypertension, Cigarette smoking ,Diabetes.

HYPERTENSIVE VASCULAR DISEASE (LEC#5)

- Cutoffs in diagnosing hypertension in clinical practice➔ sustained diastolic pressures >90 mm Hg, and/or sustained systolic pressures >140 mm Hg .
- **Malignant hypertension:** rapidly rising blood pressure , most commonly is superimposed on preexisting benign hypertension , **systolic pressures > 200 mm Hg or diastolic pressures > 120 mm Hg**

*** Types of hypertension:**

A- essential hypertension
- Most cases (95%) are idiopathic.

- Pathogenesis:
a. Genetic factors : linked to specific angiotensinogen polymorphisms and angiotensin II receptor variants; polymorphisms of the renin-angiotensin system , Susceptibility genes for essential hypertension: genes that control renal sodium absorption.
b.Environmental factors: stress, obesity, smoking, physical inactivity, dietary sodium intake

- Morphology: HTN is associated with **arteriolosclerosis** (small arterial disease)
- **Two forms of small blood vessel disease are hypertension-related:**

1- Hyaline arteriolosclerosis
- Associated with benign hypertension.
- Marked by homogeneous, pink hyaline thickening of the arteriolar walls, and luminal narrowing.
- Results from leakage of plasma components across injured endothelial cells into vessel walls
- Most significant in the kidneys➔ nephrosclerosis (glomerular scarring).

2- Hyperplastic arteriolosclerosis
- Associated with **severe (malignant)** hypertension
- Onionskin appearance : laminated thickening of arteriolar walls consist of smooth muscle cells and thickened **reduplicated basement membrane.**
- In malignant hypertension these changes are accompanied by fibrinoid deposits and vessel wall necrosis **(necrotizing arteriolitis),** which are particularly prominent in the kidney

B- Secondary hypertension:
- Due to renal disease, or renal artery narrowing **(renovascular hypertension**).

EDEMA

- **Extravascular fluid collection in body cavities**: pleural cavity (*hydrothorax*), the pericardial cavity (*hydropericardium*), peritoneal cavity (*hydroperitoneum*, or *ascites.*

- ***Mechanisms of edema*** *: Increased Hydrostatic Pressure ,Reduced Plasma Osmotic Pressure (Hypoproteinemia),Lymphatic Obstruction, Sodium Retention ,* Inflammation

1) Subcutaneous edema: the most common, signals potential underlying cardiac or renal disease, Can impair wound healing or the clearance of infections.

2) Pulmonary edema

- Common causes: left ventricular failure , renal failure, Acute Respiratory Distress Syndrom (ARDS) , inflammatory and infectious disorders of the lung.
- Can cause death by interfering with normal ventilatory function & impeding oxygen diffusion.

3) Brain edema

- Life-threatening→ brain *herniation* (extrude) through the foramen magnum.