Pathophysiology

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Lecture 9

I. Disorders of cardiovascular system

I. Hyperemia & Congestion

is a medical condition resulting from augmented tissue inflow because of arteriolar dilation or venous outflow obstruction; tissue is redder than surrounding areas because of engorgement with oxygenated blood.

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Hyperemia has two known types:

1- The active hyperemia

2- The reactive hyperemia.

Active hyperemia: is due to

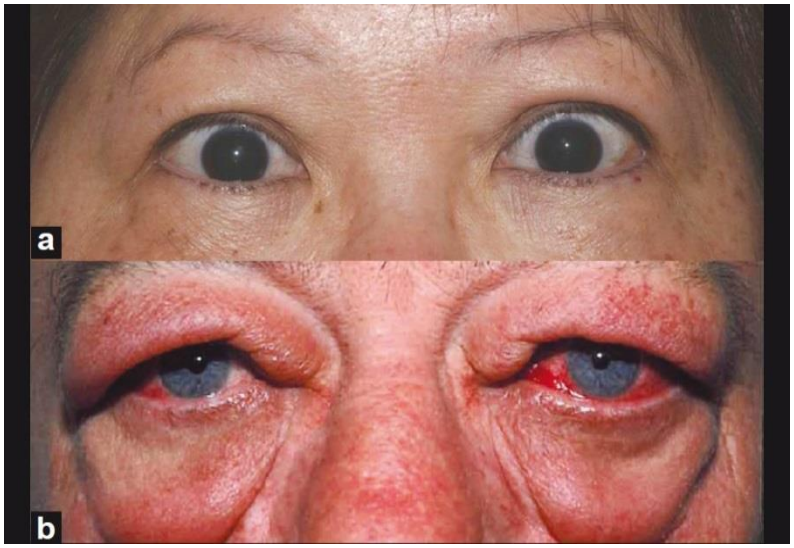
A. **Physiological:** exercise hyperemia or functional hyperemia. This type of hyperemia occurs due **to increase muscles contraction**. It is produced by the increase in the body's demand to oxygen resulting in vasodilation.
B. **Neurogenic**, hormonal (blushing, menopausal flush).
C. **Fever** – heat, chemical substances, UV, etc.
D. **Inflammation** ("tumor, Rubor, Calor") e.g. allergic conjunctivitis.

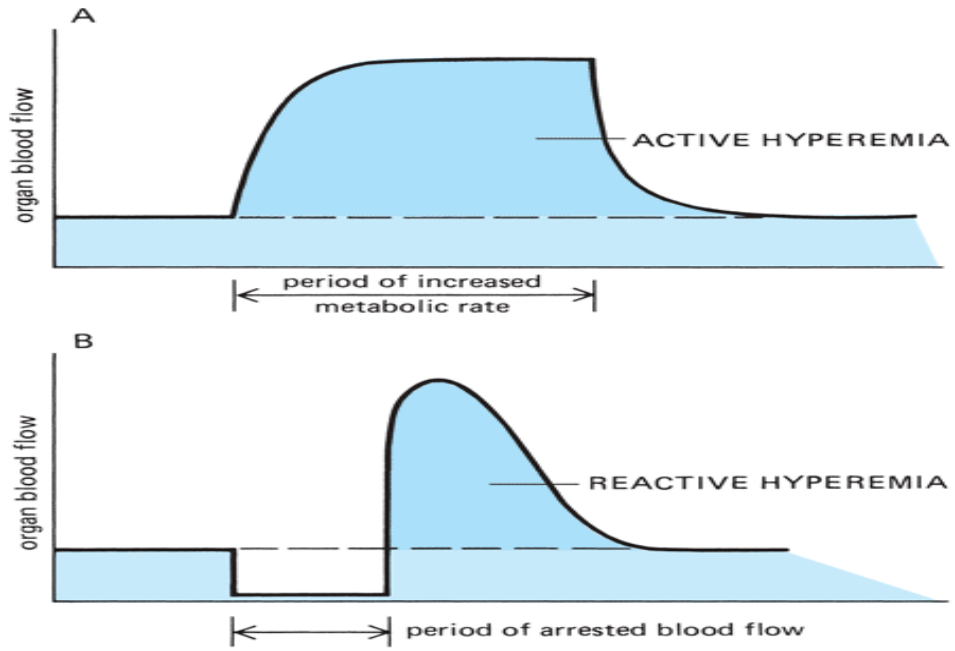
Reactive hyperemia:

*is also called as the passive hyperemia (**Congestion**). The blood collects in a certain organ of the body as a response to the veins being blocked causing the blood not to freely move about.* Reactive hyperemia occurs right after a person had an episode of ischemia, removal of a tourniquet.

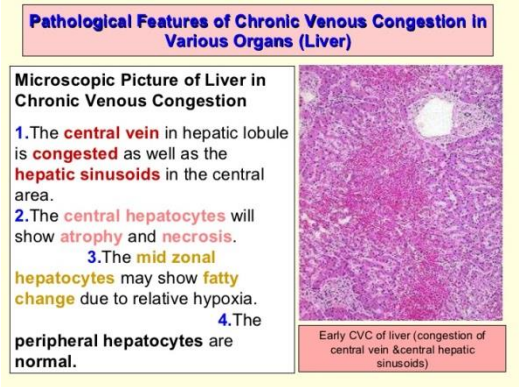
The oxygen content in the blood is reduced and the presence of metabolic waste in the tissue is increased, and build up in an organ and cause some veins to be blocked turning into blue-red (cyanotic), as worsening congestion leads to accumulation of deoxygenated hemoglobin.

a. Normal sclera
b. Hyperemia associated with allergic conjunctivitis



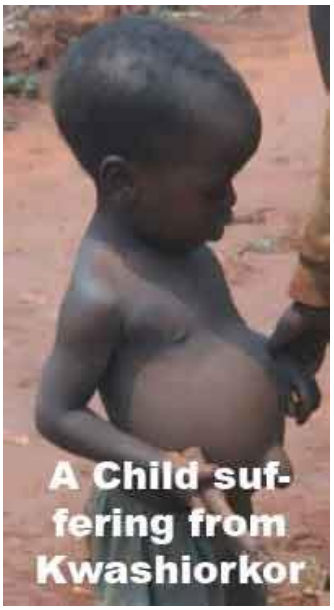


Long-standing congestion (**chronic passive congestion**) results in stasis of poorly oxygenated blood and chronic hypoxia which leads to parenchymal cell degeneration, cell death, Capillary rupture may cause small hemorrhagic foci and breakdown and phagocytosis of red cell debris may result in hemosiderin-laden macrophages.



II. Edema

A local or generalized condition in which an excessive amount of fluid accumulates in the extravascular compartment.



Causes of edema

A. **Increased Hydrostatic Pressure**
B. **Reduced Plasma Colloid Osmotic Pressure**
C. **Lymphatic Obstruction**
D. **Sodium Retention**
E. **Inflammation.**

Pathophysiologic of edema

1- Increased hydrostatic pressure

a) **Local** e.g., Impaired venous outflow, such as in deep venous thrombosis, or lower extremity inactivity with prolonged dependency.
b) **Generalized** e.g., Congestive heart failure, affecting right ventricular function

2- Reduced Plasma Oncotic Pressure

Excessive loss or reduced synthesis of albumin (which is the serum protein most responsible for maintaining colloid osmotic pressure). In **Nephrotic syndrome**: glomerular capillary wall losses its ability in preventing albumin loss which will lead to generalized edema. While in **Diffuse liver pathology or protein malnutrition** both lead to reduction in albumin synthesis.

Decreased albumin leads to reduced plasma oncotic pressure, with subsequent net movement of fluid into interstitial tissues and resultant plasma volume contraction.

In spite of sodium and water retention, plasma volume deficit cannot be corrected because low serum protein persists.

3. **Lymphatic obstruction** – usually localized; inflammatory versus neoplastic
   a) **Filariasis** – elephantiasis
   b) **Carcinoma**: Direct obstruction or Secondary to therapy – e.g., axillary node dissection at time of diagnosis (as with breast carcinoma) or post-irradiation
4. **Sodium and water retention**.
5. **Inflammation** is largely related to local increases in vascular permeability.

(Edema occurring in hydrodynamic derangements is usually a transudate: protein-poor, specific gravity < ~1.012 to 1.015, usually with few cells. Edema occurring in inflammatory conditions is usually an exudate: protein-rich, specific gravity >~1.015 to 1.020, often with inflammatory components.

6. Numerous medications can cause edema, including:

a) NSAIDs (ibuprofen, naproxen)
b) Calcium channel blockers
c) Corticosteroids (prednisone, methylprednisolone)
d) Pioglitazone and rosiglitazone *is an antidiabetic drug*
e) Pramipexole is a dopamine agonist.

Clinical types of edema

1- Localized

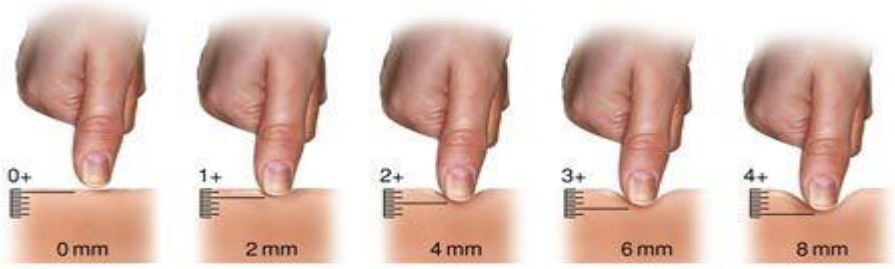
a) Involves one organ or part of the body.
b) Clinically important examples: brain edema, lung edema, hydrothorax, ascites.

2- Generalized

Involves the entire body (**anasarca**).

Clinical sign: pitting edema (depression in the skin by pressing on it with a finger) it is due to decreased serum protein, increased systemic venous pressure & increased Capillary permeability.

None pitting edema is caused by abnormalities in the lymphatic drainage (lymphedema). Characteristics: Non tender, painless, does not vary much during the day, Ulceration rare & Hyperkeratosis, thickening of skin.



0+ No pitting edema
1+ Mild pitting edema. 2 mm depression that disappears rapidly.
2+ Moderate pitting edema. 4 mm depression that disappears in 10–15 seconds.
3+ Moderately severe pitting edema. 6 mm depression that may last more than 1 minute.
4+ Severe pitting edema. 8 mm depression that can last more than 2 minutes.

III. Thrombosis

It is the formation of a blood clot in the intravascular compartment, obstructing the flow of blood through the circulatory system.

A thrombus is a clot consisting of fibrin, platelets, red blood cells, and white blood cells that forms in a blood vessel or in a chamber of the heart and can obstruct blood flow.

Pathophysiology

Any alteration in the: Virtue's trail.

1- Blood flow (Turbulence/Stasis),

2- Vascular Injury/Inflammation or

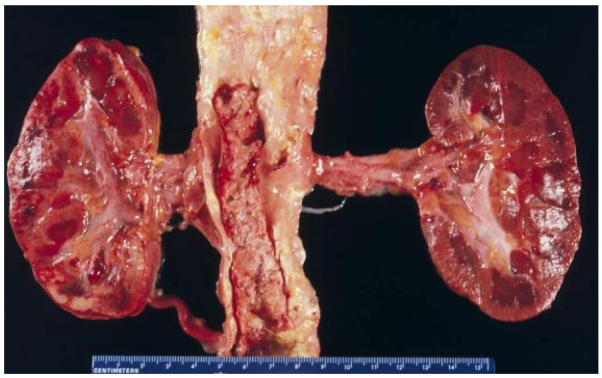
3- Hypercoagulability of the blood leads to thrombosis.

Thrombi can develop anywhere in the cardiovascular system (e.g., in cardiac chambers, on valves, or in arteries, veins, or capillaries). **The size and shape of a thrombus depend on the site of origin and the cause.**

Arterial or cardiac thrombi typically begin at sites of *endothelial injury or turbulence*;

Venous thrombi characteristically occur *at sites of stasis*. Thrombi are focally attached to the underlying vascular surface; arterial thrombi tend to grow in a retrograde direction from the point of attachment, while venous thrombi extend in the direction of blood flow (thus both tend to propagate toward the heart). The propagating portion of a thrombus tends to be poorly attached and therefore prone to fragmentation, generating an embolus.

Thrombi occurring in heart chambers or in the aortic lumen are designated **mural thrombi.** Abnormal myocardial contraction (resulting from arrhythmias, dilated cardiomyopathy, or myocardial infarction) or endomyocardial injury.



Arterial thrombi are frequently **occlusive** and are produced by platelet and coagulation activation; they are typically a friable meshwork of platelets, fibrin, erythrocytes, and degenerating leukocytes. Although arterial thrombi are usually superimposed on an atherosclerotic plaque, other vascular injury (vasculitis, trauma) can be involved.

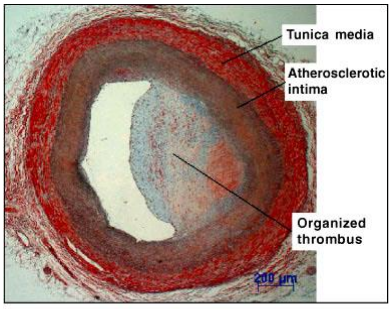
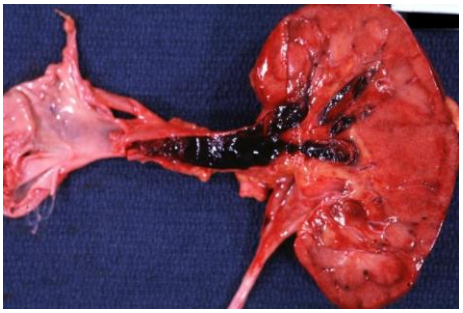


Figure 7 - Cross section photomicrograph of anterior interventricular branch first centimeter (anterior descending) of left coronary artery. Fibrotic atherosclerotic lesion and organized non-occlusive thrombosis are present. (Movat method coloring; objective lens augmentation - 2,5x).

Venous thrombosis (phlebothrombosis) is almost invariably occlusive, and the thrombus can create a long cast of the lumen; **venous thrombosis is largely** the result of activation of the coagulation cascade, and platelets play a secondary role. Because these thrombi form in the sluggish venous circulation, they also tend to contain more **enmeshed erythrocytes and are therefore called red, or stasis, thrombi**.



Thrombi on heart valves are called vegetations. Bacterial or fungal blood-borne infections can cause valve damage, subsequently leading to large thrombotic masses (infective endocarditis,).

Fate of the Thrombus: -

If a patient survives the initial thrombosis, in the ensuing days or weeks thrombi undergo some combination of the following four events:

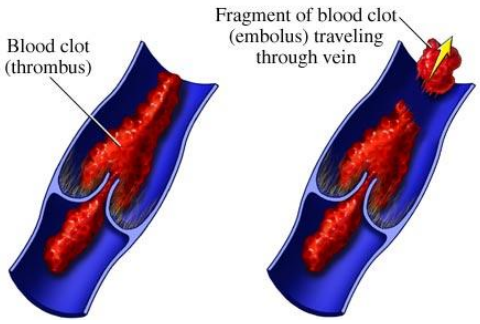
1. **Propagation**: Thrombi accumulate additional platelets and fibrin, eventually causing vessel obstruction.
2. **Embolization**: Thrombi dislodge or fragment and are transported elsewhere in the vasculature.
3. **Dissolution**: Thrombi are removed by fibrinolytic activity.
4. **Organization and recanalization**: Thrombi induce inflammation and fibrosis(organization). These can eventually re-canalize (re-establishing some degree of flow), or they can be incorporated into a thickened vessel wall.

IV. Embolism

Detached intravascular solid, liquid, or gaseous mass that is carried by the blood to a site distant from its point of origin. 99% are dislodged thrombi.

Types

a. Thromboembolism.
b. Fat and marrow embolism.
c. Bacterial embolism.
d. Air embolism (decompression sickness).
e. Amniotic fluid embolism.
f. Tumor cell embolism.
g. Foreign body embolism.



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In **Thromboembolism** the pathophysiology and clinical manifestations depend upon four main factors:

a) The extent of occlusion of the vascular tree and the size of the emboli.

b) The patient's pre-existing **cardiopulmonary condition**.

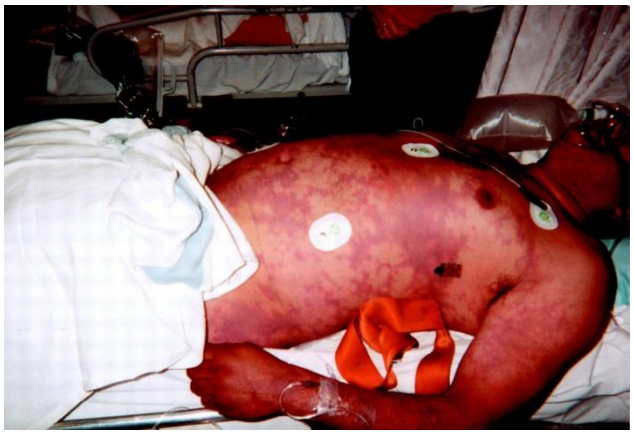
c) Chemical vasoconstriction due to the **release of serotonin and thromboxane from platelets** that adhere to the embolus, as well as to **fibropeptide B**, which is a product of fibrinogen breakdown.

d) The reflex vasoconstriction that is likely to occur as a consequence of artery dilatation.

Pulmonary Thromboembolism: 95% arise from deep leg vein thrombi above the knee. Systemic Thromboembolism 80% arise from intracardiac mural thrombi; remainder arise from aortic aneurysms, plaques or valve vegetations. 75% go to lower extremities and 10% go to the brain.

Fat Embolism occurs mostly after fractures of long bones, soft tissue trauma or burns. 90% of individuals with severe skeletal injuries, though <10% have any clinical findings. Fat embolism syndrome begins 1-3 days after injury with tachypnea, dyspnea and tachycardia, neurologic symptoms, diffuse petechial rash (20-50%), thrombocytopenia, anemia. The mechanical obstruction and biochemical injury. **Free fatty acids cause local toxic injury to endothelium, platelet activation**. **Prognosis: Syndrome fatal in 10%.**

Air Embolism



Decompression sickness, "**the bends**" or "**the chokes**", caisson disease**. Clinically needs an excess of 100cc of air to have a clinical effect**.

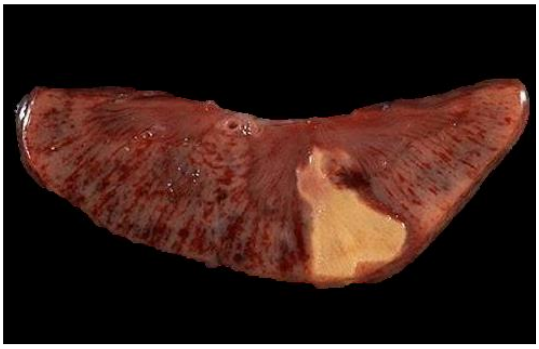
a. Painful muscle cramps,
b. Respiratory insufficiency.
c. Neurological symptoms.
d. Formation of gas bubbles within skeletal muscle, soft tissues and joints causes pain.
e. Focal ischemia to brain and heart.
f. Pulmonary edema and hemorrhage, focal atelectasis or emphysema.
g. Persistence of gas emboli in the skeletal system leads to **multiple foci of ischemic necrosis** (femoral head, tibia and humerus).

Amniotic Fluid Embolism Clinically 1 in 50,000 deliveries. 80% mortality rate. **Sudden severe dyspnea, cyanosis, and hypotensive shock, followed by seizures and coma.** Pulmonary edema and disseminated intravascular coagulation (DIC). Pulmonary microcirculation with epithelial squamous cells shed from fetal skin, lanugo hair, fat from vernix, mucin from GI tract.

V. Infarction:

An area of ischemic necrosis caused by occlusion of either arterial supply or venous drainage. 99% from thrombotic or embolic events. Remainder: local vasospasm, extrinsic compression, hemorrhage within a plaque, torsion, traumatic rupture. Infarcts caused by venous thrombosis are more common in organs with single venous outflows: e.g. testis, ovary.

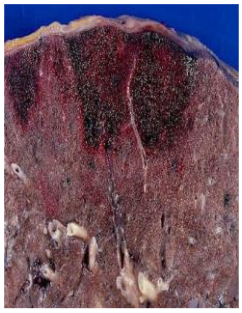
Types of infarction



1- White Infarct.
2- Red infarction.
3- Septic infarctions.

White Infarct: This type of infarction is due to **arterial occlusion**. It is referred as white due to lack of erythrocytes accumulation, it shows a Pyramid shape necrosis the apex of the pyramid points to the occluded artery while the base is at periphery it is a coagulative necrosis and can become red infarct when

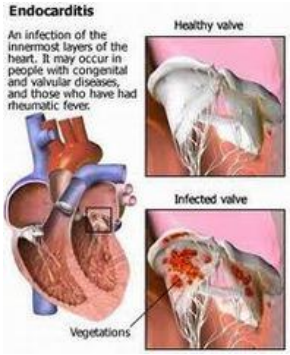
reperfusion occurs. It occurs in solid organs with no dual arterial blood supply such as the heart, Spleen and Kidneys. This is because solid organ may limit the amount of hemorrhage that can seep into the area of ischemic necrosis from adjoining capillary beds.



Red infarction is due to venous occlusion. Referred as red due to massive erythrocytes accumulation, it consists of numerous fibrin strands and often with irregular shape necrosis. It involves Loose organs with dual circulation such as the lungs, kidneys, GIT and brain. The loose tissue enables Erythrocytes to seep during injury and accumulate inside the tissue.

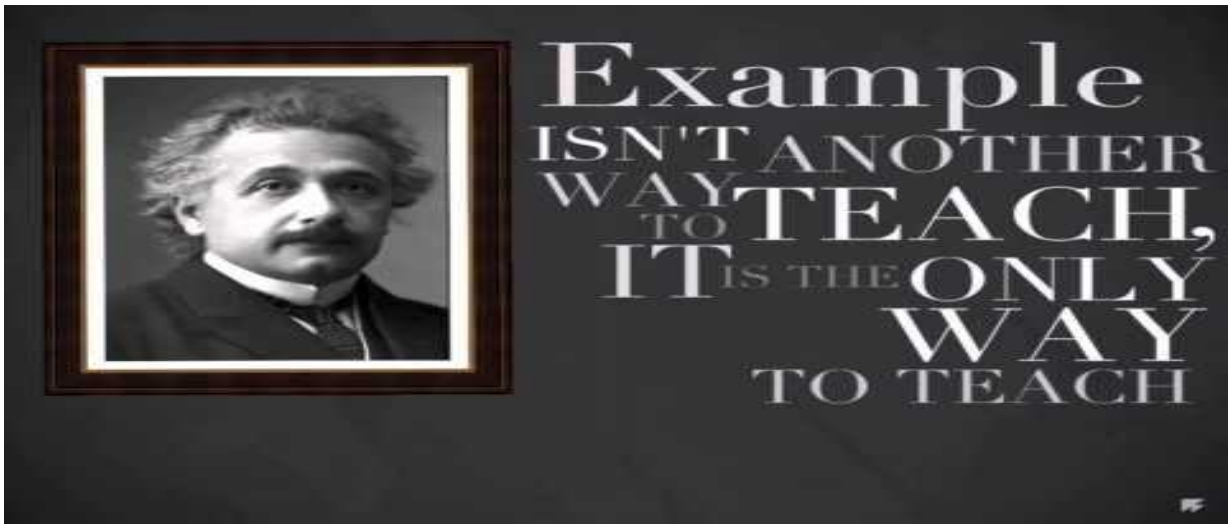
Septic infarctions may develop

a. When bacterial vegetation fragments.
b. When microbes seed necrotic tissue.
c. Infarct may be converted into abscess.



Factors That Influence Development of an Infarct:

1. Vascular supply.
2. Rate of development of occlusion (time for development of alternate perfusion pathways).
3. Vulnerability of the tissue to hypoxia (neurons 3-4 minutes, myocardium 20-30 minutes).
4. The blood oxygen content (e.g. ventilation).



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