Hemodynamic Disorders of Perfusion

1 Hemorrhage

Defined as a discharge of blood from the vascular compartment to the exterior of the body or into nonvascular body spaces. Consider:

- the amount of the blood lost
- where the bleeding goes (outside? into some body cavity?)
- the *speed* of bleeding (acute × chronic bleeding)

1.1 Basic vocabulary of bleeding

hemothorax into pleural cavity, similarly **hemopericardium, hemoperitoneum...**

hemarthrosis into a joint space

hematoma into soft tissues, brain...

purpura diffuse superficial haemorrhage in the skin

petechia a pinpoint hemorrhage (usually in the skin or conjunctiva). Larger is **ecchymosis**.

1.2 Etiology

- mechanical trauma
- inflammatory process
  - infectious agents weakens or destroys wascular walls (e.g. tuberculosis)
  - immune process (deposition of immune complexes on endothelial surfaces leading to destructive immune sequences)
- intrinsic diseases of blood vessesl and blood flow disorders
  - atherosclerosis
  - varicosities
  - passive hyperemia
  - hypovitaminosis
  - infarcts
- neoplastic processes
  - destruction and ulceration fo mucosal surface (GI tract, endometrium...)
  - bleeding into large tumor mass
- defects of the coagulation mechanism

1.3 Consequences

- acute bleeding with large blood loss leads to the hemorrhagic shock
- repeated loss of small amount of blood or chronic continuous bleeding leads to iron deficiency anemia.
- large hemorrhage into a blood cavity can have mechanical effects (hemocardium, hemothorax, intracranial hematomas)
- sometimes the absorption of the blood can cause sideeffects (azotemia after GIT bleeding in patients with cirrhosis of the liver)
- hyperbilirubinemia (and slight jaundice) during the absorption of large hematomas

2 Hyperemia

Defined as excess amount of blood within an organ or tissue. Classification:

active usually physiologic response to exercise, inflammation, heat, psychological stimuli
Dilated arterioles and capillaries.

passive (venous congestion) — caused by obstruction of venous drainage.
Dilated capillaries and venules.
Can be

- *localized* thrombophlebitis of the leg veins, thrombosis of hepatic veins (Budd-Chiari) — limited to certain body region
- *generalized* increased venous pressure, usually caused by chronic heart failure

Another important factor is the *duration* of hyperemia. Chronic, long standing hyperemia can cause typical changes in the organs:

- *the lung:* caused most often by chronic failure of the left ventricle or mitral stenosis. Increased pressure in pulmonary capillary bed leads to microhemorrhages, pulmonary edema and can lead to interstitial fibrosis called *brown induration*. Increased capillary pressure is transmitted to pulmonary arteries and *pulmonary hypertension* developes.
- *the liver:* passive congestion causes dilatation of liver sinuses centrilobularly with atrophy of the centrilobular hepatocytes. Grossly the cut surface of chronically congested liver shows dark foci (centrilobular blood) surrounded by paler peripheral normal parenchyma (with possible fatty degeneration). This picture is quite common and traditionally called *nutmeg liver*.
- *the spleen:* is usually enlarged, tense, the capsule is smooth, the cut surface is dark red with calcified foci of old haemorrhage (Gandy-Gamna bodies).
- *GIT mucosa:* active hyperemia is associated with inflammation, alcohol etc. Chronic passive hyperemia is typical fo portal hypertension (usually secondary to scarring of hepatic parenchyma). Leads to a variety of problems (bleeding, malabsorption...)
- *lower extremities:* chronic edema, fibrosis and degenerative changes in the dermis.

3 Thrombosis

Defined as *intravascular* and *intravital* coagulation of blood. The coagulated blood is called *thrombus*. It is necessary to differentiate between blood clot formed post-mortem or coagulated extravascular hematoma.

Thrombus

- adheres firmly to vascular wall
- has internal structure reflecting slow intravital grow

Blood clot

- can be separated from the endothelium easily
- has elastic, sometimes gelatinous consistence
- usually of typical appearance reflecting its formation after the blood flow was stopped: red bottom layer formed from blood cells (like „currant jelly“) and upper pale „chicken fat“ layer formed by coagulated plasma. Uniform, dark purple clots exist as well.

3.1 Pathogenic mechanisms

1. blood vessel wall (injured endothelium promotes coagulation)
2. platelet adherence and aggregation
3. activation of coagulation system of plasma

3.2 Etiology

- injury to endothelium

  - mechanical damage (cuts, bruises)
  - diseases of vessel (atherosclerosis, arteritis etc.)
  - infections
  - hypoxemia from stagnation
- alteration of blood flow
  - disruption of normal laminar blood flow
  - hypoxemia from stagnation
- hypercoagulability of blood as result of
  - increased viscosity (polycythemia, macroglobulinemia)
  - increased platelets (thrombocytosis)
  - increased thromboplastic substances from dead tissue
  - decreases fibrinolysis
- presence of foreign bodies in blood stream
  - catheters
  - arterial prostheses
  - cardiac valve prostheses
- red cell disorders such as sickle cell disease

3.3 Consequences

- *Obstruction*
  - arterial (hypoxemia — necrosis; the extent of damage modified by the extent of collateral circulation and metabolic needs of the ischemic tissue)
  - venous — passive hyperemia may in certain locations (bowel) impede arterial inflow as venous pressure rises
- *Propagation* (growing of the thrombus upstream (plateles, fibrin) and down stream (uniform, mainly erythrocytes and fibrin); may occlude tributaries or branches
- *Dissolution* plasma fibrinolysis may liquefy the thrombus especially in very small vessels
- *Embolization* detaching in whole or in part from the site of formation and impacting downstream
- *Organization*
  1. invasion of the thrombus by fibroblasts and endothelial cells with capillary formation
  2. conversion of the thrombus into richly vascular connective tissue
  3. begins peripherally and anchors the thrombus to the vessel wall
  4. occasionally a venous thrombus will become calcified and form „phlebolith“
- *Recanalization*
  1. the capillaries in the organization process anastomose and with time become transformed into larger arterioles
  2. eventually multiple new channels will coalesce and restore the vessel lumen to nearly its prethrombous state

4 Disseminated Intravascular Coagulation

- Is characterized by widespread thrombus formation (mainly loose knit fibrin) in small vessels; so called „hyaline thrombi“, which are *multiple* and of *microscopic dimensions.*
- It is a secondary manifestation associated with obstetrical complications (e.g. when amniotic fluid gets into the circulation of mother), infections, neoplasms, massive tissue injury and miscelaneous other conditions.
- The widespread formation of microthrombi is followed by rapid consumption and exhaustion of fibrinogen and other coagulation factors so that widespread hemorrhagic manifestation will then follow.
- Fibrinolytic mechanisms are activated → dissolving of the original fibrin thrombi → hemorrhagia is aggravated.
- Clinical consequences reflect tissue hypoxia and/or infarction; hemorrhagia is especially dangerous if DIC occures during surgery (complete stop of hemocoagulation)

5 Hemolytic-uremic syndrome (HUS)

Characterized by acute renal insufficiency, microangiopathic hemolytic anemia and thrombocytopenia.

In its typical form affects infants, adult forms are possible as well. The mortality of infantile form is about 5 %, that of the adult form is about 60 %. Follows a respiratory or gastrointestinal illness (children) or pregnancy, oral contraceptives intake (adults).

Features:

1. microthrombi in capilaries are formed, affecting the whole body, especially kidney glomeruli
2. fibrin and platelets are found in microthrombi, causing thrombocytopenia
3. erythrocytes are fragmented while passing through fibrin deposits (schistocytes), causing hemolytic anemia
4. blood does not coagulate, causing multiple hemorrhages (petechiae, GIT or urinary tract hemorrhage)
5. glomeruli are affected (mesangial proliferation), causing renal failure and uremia
6. neurologic symptoms, fever, hematuria are present

6 Toxemia of Pregnancy

Occurs in late pregnancy characterized by edema, proteinuria and hypertension — pre-eclampsia. May progress to eclampsia with coma, seizures, DIC. Pre-eclampsia can be managed, eclampsia has high mortality. The removal of the placenta (inducted delivery) can be the only cure of developed eclampsia.

Gross pathology:

- *placenta* is the site that iniciates the process[1]: infarcts, retroplacental hematomas
- *liver* focal hemorrhages
- *kidney* microinfarcts to bilateral cortical necrosis
- *brain* focal hemorrhages

Microscopic changes

- microscopic thrombi, fibrin deposits
- fibrinoid necroses of spiral arteries in uterus
- multiple ischemic necroses in various organs

7 Embolism

Defined as *intravascular migration* of undissolved material in blood (solid bodies, liquid, gas bubbles). Always follows the direction of blood flow. Ischemic necrosis (infarction) of target organ (supplied by embolized artery) is common.

Migration routes of normal emboli:

- peripheral veins → right heart or pulmonary artery (common)
- pulmonary veins (very rare) or left heart (common) → the main branches of aorta or more distal arteries
- mesenteric veins → portal vein (→ liver)

Paradoxical emboli bypasses a capillary bed between the site of origin and the site of impaction (e.g. thrombemboli passing through open foramen ovale, interventricular septal defect or artificial shunts created for renal dialysis).

Retrograde emboli where bloodstream reverts its flow (e.g. in thoracic vena cava while coughing — the thrombembolus can enter hepatic veins). Rare.

Liquid and gaseous thrombemboli can squeeze through one capillary bed and lodge in another (fat emboli from fractures lodging in the lungs, brain and kidney).

[1] *Toxemia* is a misnomer, no toxin was identified. Exact mechanism is still unknown, trophoblast is the responsible tissue, an immunologically mediated injury to spiral arteries of the placenta is possible

7.1 Types of emboli

- Solid:
  - thrombi (most common); if free of infectious microorganisms are called *bland*, if infected *septic*
  - marrow or bone fragments (bone fractured, CPR)
  - tumor (method of spread of certain malignant tumors: *hematogenous metastasis*
  - bacteria
  - cholesterol and atherosclerotic debris
  - foreign material (i.v. drug abusers (talc granulomas in lungs and liver), bullets, intravenous catheters
- Liquid
  - lipid (i.v. injection (oily substances given intravenously instead of intramuscularly)
  - traumatic (fat, bone marrow)
  - amniotic fluid (special situation: obstruction caused by lanugo and epithelia in lung capillaries is not important; the damage is caused by thromboplastin-like substance, which promotes DIC)
- Gaseous: aspiration of air into large veins in neck or thorax (trauma, surgery) or dysbarism

8 Infarction

Localized area (varying size) of ischemic necrosis.

8.1 Etiology

- thrombosis
- embolism (most usually thrombembolism)
- external pressure on artery
- venous occlusion by
  - twisting (torsion)
  - external compression (strangulation)

8.2 Appearance

Most common appearance is a segmental or wedge shaped area of *coagulation necrosis*, sometimes haemorrhagic. In CNS infarctions the liquefaction of necrotic tissue quickly follows. Sometimes necrotic tissue elicits an inflammatory response. Later is usually lysed and/or phagocytized and replaced by fibrous scar. In CNS a gliosis or cystic defect may result.

Septic infarction is usually caused by embolism of infected material; formation of an abscess may follow. Infarction which is not septic is *bland*.

9 Cyanosis

Cyanosis is *intravital* blueish color of the skin or mucous membranes. It is caused by abnormally dark color of blood in capillaries.[2] Dark color of blood is caused either by changes in hemoglobin or increased amount of reduced hemoglobin.

9.1 Cyanosis and hypoxia

Cyanosis is usually accompanied by hypoxia and vice versa. Sometimes, however, severe tissue hypoxia may occur without any noticeable cyanosis:

Anemia severe anemia leads to tissue hypoxia but cyanosis is not pronounced: the amount of *all* hemoglobin is decreased. Cyanosis requires at least 50 g/l of reduced hemoglobin to develop; this level is seldom reached. In **polycetemia vera**, where the number of blood corpuscles and the amount of hemoglobin is increased, tendency to cyanosis is high, especially if further suported by blood stasis and heart insufficiency (high blood viscosity).

[2] As opposed to pigmentations caused by deposition of some pigments in the skin or dermis.

Carbon monoxide (CO) poisoning CO binds firmly to hemoglobin forming *carboxyhemoglobin* the blood is brightly red, skin and mucous membranes are cherry red even in severe tissue anoxia.

9.2 Changed hemoglobin

Most often caused by *methemoglobinemia*. Causes: toxins, drugs — fenacetin, anilin, sulphonamids; nitrobenzen, NO_2 poisoning. NO_2^{++} can appear in water (fertilizers), in high concentrations small babies can be affected.

9.3 Increased level of normal reduced hemoglobin

1. heart diseases with right to left shunt
2. generalized heart failure
3. insufficient oxygenation of blood in the *lungs*
4. polycytemia
5. local disorders of blood circulation

9.3.1 Heart diseases with blood mixing

This topic will be discussed later. In some (most often congenital) heart diseases there is a communication enabling artero-venous blood mixing. Sometimes right to left shunt is present from the beginning, sometimes it developes later after a period of left to right blood flow through the shunt (late cyanosis). Important diagnostic sign: the tongue is cyanotic (never seen in generalized heart failure).

9.3.2 Heart failure

Cyanosis of peripheral type; acral. Most often found in lower extremities. Caused by blood stasis accompanied by increased amount of reduced hemoglobin in capillaries.

9.3.3 Pulmonary cyanosis

Pulmonary insufficiency: restrictive and obstructive lung diseases, diffusion blocks, sclerosis of pulmonary artery. Diagnostic sign: breathing of pure oxygen leads do improving or dissapearance of this type of cyanosis.

9.3.4 Polycytemia

See above.

9.3.5 Local cyanosis

Most often caused by venous thrombosis, sometimes by external obstruction of venous outflow. Asymmetric.