HEMODYNAMIC DISORDERS

Introduction

The health and well-being of cells & tissues depend not only on an intact circulation to deliver nutrients but also on normal fluid hemostasis. This chapter reviews the major disturbances involving the hemodynamic system.

Edema

Definition: Edema is increased fluid in the interstitial tissue spaces or it is a fluid accumulation in the body cavities in excessive amount. Depending on the site, fluid accumulation in body cavities can be variously designated as:

Clinical classification of edema:

One can also clinically classify edema into localized & generalized types.

A) Localized

a) Hydrothorax – fluid accumulation in pleural cavity in a pathologic amount.

b) Hydropericardium – pathologic amount of fluid accumulated in the pericardial cavity.

c) Hydroperitoneum (ascites) – fluid accumulation in peritoneal cavity**.**

d) hydrocephalus fluid accumulation in brain .

ex of disease cause localized edema

1) Deep venous thrombosis

2) Pulmonary edema

3) Brain edema

4) Lymphatic edema

B) Generalized

Generalized edema (anasarca) : is a sever & generalized edema of the body with profound subcutaneous swelling. **occurs due to**

a. Reduction of albumin due to excessive loss or reduced synthesis as is caused by:

1) Protein loosing glomerulopathies like nephrotic syndrome

2) Liver cirrhosis

3) Malnutrition

4) Protein-losing enteropathy

b. Increased volume of blood secondary to sodium retention caused by congestive heart failure

Ex of diseases cause generalized edema

1) Nephrotic syndrome

2) Liver cirrhosis

3) Malnutrition

4) Heart failure

5) Renal failure

Mechanism of edema formation:

Approximately 60% of the lean body weight is water, two-thirds of which is intracellular with the remainder in the extracellular compartment.

The capillary endothelium acts as a semipermeable membrane and highly permeable to water & to almost all solutes in plasma with an exception of **proteins**. Proteins in plasma and interstial fluid are especially important in controlling plasma & interstitial fluid volume. Normally, any outflow of fluid into the interstitium from the arteriolar end of the microcirculation is nearly balanced by inflow at the venular end. Therefore, normally, there is very little fluid in the interstitium.

Edema formation is determined by the following factors:

1) Hydrostatic pressure

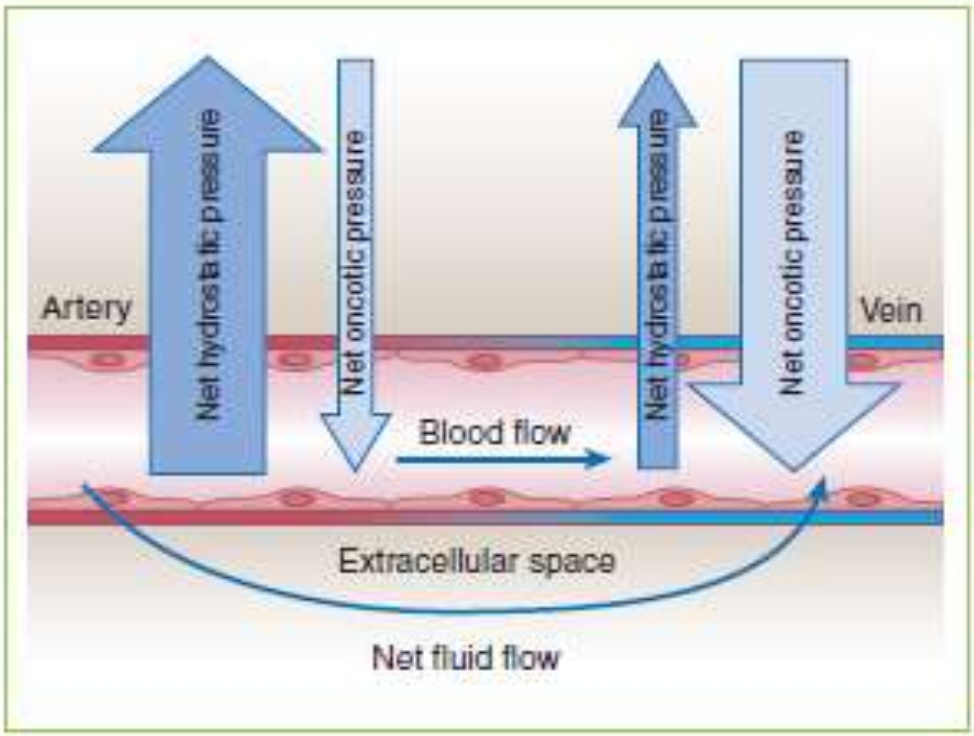
2) Oncotic pressure

3) Vascular permeability

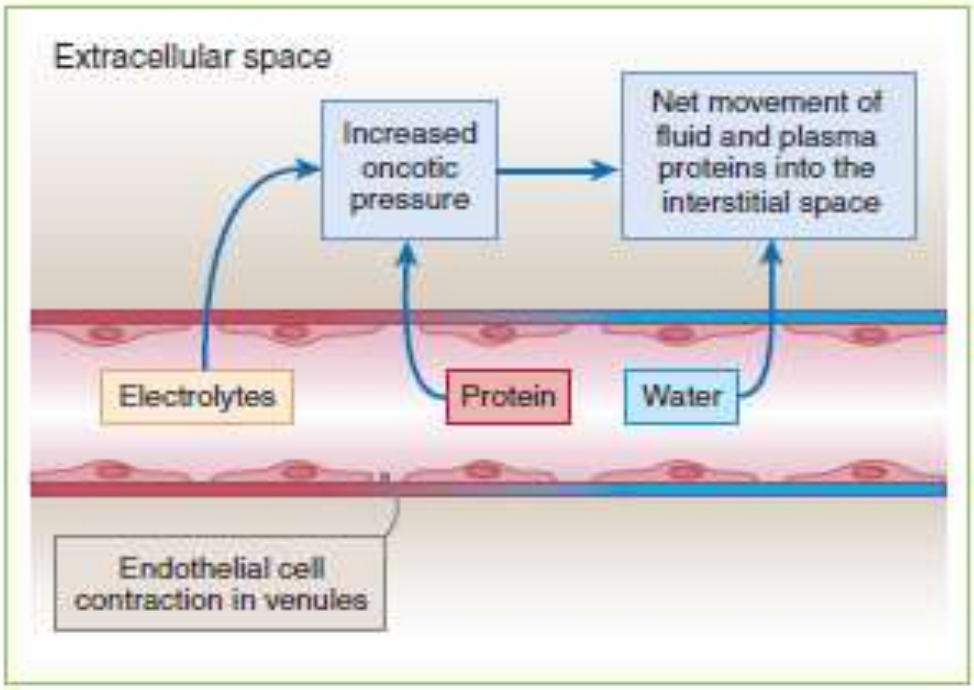
4) Lymphatic channels

5) Sodium and water retention

We will discuss each of the above sequentially.


Net hydrostatic pressure
Net oncotic pressure
Artery
Net hydrostatic pressure
Net oncotic pressure
Vein
Blood flow
Extracellular space
Net fluid flow

A


Extracellular space
Increased oncotic pressure
Net movement of fluid and plasma proteins into the interstitial space
Electrolytes
Protein
Water
Endothelial cell contraction in venules

1) Hydrostatic and oncotic pressures:

The passage of fluid across the wall of small blood vessels is determined by the balance between **hydrostatic** & **oncotic** pressures. There are primary forces that determine fluid movement across the capillary membrane. Any defect in these force lead to escape of the fluid in to interstitium .

2) Vascular permeability:

Increased vascular permeability usually occurs due to acute inflammation. In inflammation, chemical mediators are produced. Some of these mediators cause increased vascular permeability which leads to loss of fluid & high molecular weight albumin and globulin into the interstitium. Such edema (i.e. that caused by increased vascular permeability) is called inflammatory edema. Inflammatory edema differs from non-inflammatory edema by the following features

a) Inflammatory edema (exudate)	**b) Non-inflammatory edema (transudate)**
Due to inflammation-induced increased permeability and leakage of plasma proteins.	A type of edema occurring in hemodynamic derangement (i.e. increased plasma hydrostatic pressure & decreased plasma oncotic pressure
[protein rich	[protein poor]
Specific gravity > 1.012	Specific gravity < 1.012
Leukocyte and clotting fibrin is high	low
Odors putrefactive	Oder less
pH acidic	pH alkaline
Associated with inflammatory reaction	No inflammatory reaction

Causes of non-inflammatory transudate:

1- Hypoproteinemia (T.B, chronic fascilosis, starvation ,hepatitis , malnutrition).
2- Increase in capillary blood pressure (obstruction of vein ,obstruction of lymphatic vessels ,pressure on vein).
3- Water and Na retention .

3) Lymphatic channels:

Also important is the lymphatic system which returns to the circulation the small amount of proteinaceous fluid that does leak from the blood into the interstial spaces. Therefore, obstruction of lymphatic channels due to various causes leads to the accumulation of the proteinaceous fluid normally drained by the lymphatic channels. Such kind of edema is called lymphatic edema.

Lymphatic edema occurs in the following conditions:

1) Parasitic infection. E.g filariasis which causes massive lymphatic and inguinal fibrosis

2) Lymphatic obstruction secondary to neoplastic infiltration. E.g. breast cancer

3) post surgical or post irradiation, i.e surgical resection of lymphatic channels or scarring after irradiation

4) Sodium and water retention:

Sodium & subsequently water retention occurs in various clinical conditions such as congetive heart failure & renal failure. In these conditions, the retained sodium & water result in increased capillary hydrostatic pressure which leads to the edema seen in these diseases.

Morphology of edema

Gross appearance:

1- Pale white fluid fill the body cavities .
2- Swelling of edematous organ .
3- Clearing & separation of extracellular matrix.

Microscopy

(non inflammatory edema)

1- Present of fluid faint pink in color between cells and body cavities.
2- Few amount of fibrin and albumin homogenous .
3- Contain few amount of RBCs ,WBCs.

Hyperemia and Congestion

Definition: Both of them can be defined as a local increase in volume of blood in a particular tissue.

Hypermia (active)

Is an active process resulting from an increased inflow of blood into a tissue because of arteriolar vasodilation. commonly occurs in exercising skeletal muscle or acute inflammation. Affected tissue becomes red as there is engorgement with oxygenated blood.

Congestion (passive)

Is a passive process resulting from impaired outflow of blood from a tissue occurs systemically as in cardiac failure or locally as in isolated venous obstruction. Affected tissue appears blue-red due to accumulation of deoxygenated blood. It may be acute or chronic.

- In long-standing congestion (also called chronic passive congestion states), poorly oxygenated blood causes hypoxia → results in parenchymal cell degeneration or cell death.

Ex:

a) Pulmonary congestion

Cut surface: hemorrhagic & wet.

1. Acute pulmonary congestion:

 Alveolar capillaries engorged with blood

 septal edema

2. Chronic pulmonary congestion:

- Thickened & fibrotic septa

- Alveolar spaces contain hemosiderin-laden macrophages resulting in an appearance termed **brown indurations.**

- Can result in pulmonary hypertension.

b) Hepatic congestion

1) Acute hepatic congestion:

- Central vein & sinusoids are distended

- There may be even central hepatocyte degeneration.

- Peripheral hepatocytes better oxygenated & develop only fatty changes.

2) Chronic passive congestion of liver:

- Central lobules grossly depressed because of loss of cells and take white pale color whereas the surrounding hepatic tissue appear red brown this give picture of (**nutmeg liver**).

Hemorrhage

Definition: Hemorrhage is extravasation of blood outside the blood vessel.

Causes:

• Physical trauma – Stabbing

-Atherosclerosis

-Vasculitis

- Gunshot

- Motor vehicle accident

• Inadequacies in blood clotting which can be due to:

A. Too few or poorly functioning platelets (i.e. qualitative & quantitative defect of platelets)

B. Missing or low amount of clotting factors

E.g. Low levels of prothrombin, fibrinogen & other precursors.

Inadequate vitamin K leads to clotting factor deficiency because this vitamin is important in the synthesis of the clotting factors by the liver.

Type of hemorrhage.

A. External hemorrhage

Escape of blood outside the body .

1- Epistaxis: Bleeding from the nose .

3- Hemoptysis: Coughing of blood .

3- Hematemesis: Vomiting of blood .

4- Melena: Presence of dark digested blood in stools.

5- Bleeding per rectum: passage of red blood with stool

6- Hematuria: Blood in urine.

7- Menorrhagia: Excessive or prolonged menstrual bleeding

8- Metrorrhagia: Irregular uterine bleeding unrelated to menses

9- Bleeding from skin.

B. Internal hemorrhage

Bleeding into body cavities.

1- Hemothorax: Hemorrhage into the pleural sac.

2- Hemopericardium: Hemorrhage . into pericardial sac.

3- Hemoperitoneum: Hemorrhage . into peritoneal sac.

4- Hematocele: Hemorrhage . into tunica vaginalis sac.

5- Hemoarthrosis: Hemorrhage . into a joint cavity.

C. Interstitial hemorrhage

1) **Hematoma:** Hemorrhage enclosed within a tissue or a cavity .

2) **Petechial:** Minute 1-2 mm hemorrhages occurring in the skin, mucosal membrane, or serosal surface .

3) **purpura:** Slightly > 3mm hemorrhage occurring in the skin .

4) **Ecchymosis**: Larger than 1-2cm subcutaneous hematoma (bruises). It is typical after trauma.

Effects of haemorrhage: depend on the rate and amount of blood loss:

• If > 20% the total blood volume is rapidly lost from the body, it may lead to

hypovolemic shock & death. Chronic loss of blood leads to anemia.

Hemostasis and Blood Coagulation

Hemostasis

Definition: Hemostasis is the maintenance of the clot-free state of blood & the prevention of blood loss via the formation of hemostatic plug.

Hemostasis depends on three general components:

a) Vascular wall

b) Platelets

c) Coagulation pathways

Whenever a vessel is ruptured or severed, hemostasis is achieved by several mechanisms:

A. Vascular spasm

B. Formation of platelet plug

C. Formation blood clot as a result of blood coagulation

D. Eventual growth of fibrous tissue in to the blood clot to close the hole in the vessel permanently.

Thrombosis

Definition: Thrombosis is defined as the formation of a solid or semisolid mass from the constituents of the blood within the vascular system during life.

Postmortem clot: condensation of blood composition include (RBCs, WBCs platelets, fibrin) inside vascular system after death.

Postmortem clot	Chicken fat clot	Thrombus
After death	After death	During the life
Dark- red in veins	Yellow and red in hearts cavities of horse	Greenish- red
Unattached	Unattached	Attached
Homogenous	Homogenous	Laminated
smooth	smooth	Rough

Classification of thrombus

According to the intensity of thrombus can be classified as

1- Occluded thrombosis: which closed whole the lumen of blood vessels.
2- obturating: which closed the lumen of blood vessels partially .
3- Canalized: which closed the canal opening .

Pathogenesis:

Platelets leave the blood stream, agglutinate and adhere to the damaged endothelium. They form laminar, which are arranged vertical to the blood stream and called lines of Zhan. Soon, fibrin accumulates around them with red and white blood cells.

Cases of thrombus:

There are three factors that predispose to thrombus formation. These factors are called Virchow's triad:

A: Endothelial injury

B: Stasis or turbulence of blood flow

C: Changes in composition of blood:

A: Endothelial injury

 It is the most important factor in thrombus formation and by itself can lead to thrombosis.

 Endothelial injury is particularly important in thrombus formation in the heart & arterial circulation.

• In hemodynamic stress like severe hypertension & turbulence of flow over scarred valves directly damaging the endothelium.

• Bacterial endotoxin.

Endothelial damage may be:

Mechanical, inflammatory, or degenerative The injured endothelium becomes. swollen with rough surface.

B: Turbulence or Stasis (Alterations in normal blood flow)

Under physiologic conditions normal blood flow is laminar, that is, the cellular elements flow centrally in the vessel lumen separated from endothelium by slowing moving clear zone of plasma. Stasis & turbulence therefore:

a. Disrupt the laminar flow and bring platelets in to contact with the endothelium

b. Prevent dilution of activated clotting factors by freshly flowing blood

c. Retard or make a time lag in the inflow of clotting factor inhibitors and permit the build up of thrombi.

• Stasis is a major factor in the development of venous thrombi while turbulence contributes to arterial & cardiac thrombosis by causing direct endothelial injury or by forming countercurrents & local pockets of stasis.

d) Hypervisicosity syndrome, i.e an increase in hematocrit in excessive amount due to various reasons such as polycythemia causes stasis in small vessels.

C- Changes in composition of blood:

- ↑ platelets e.g. after operations.
- ↑ fibrinogen as in pregnancy.
- ↑ R.B.Cs. (polycythemia) → ↑ viscosity of blood → stasis → thrombosis.
- ↑ W.B.C. as in leukemia → ↑ viscosity of blood → stasis → thrombosis.

Hypercoagulability

Definition: Hypercoagulability is any alteration of the coagulation pathway that predisposes to thrombosis. Hypercoagulability is a less common cause of thrombosis

Classification of thrombi

A. According to the color & composition of thrombi

1- Pale thrombus: formed only of platelets and fibrin.

2- Red thrombus: formed mainly of red cells and fibrin.

3- Mixed thrombus: containing all blood elements.

B. According to the site of thrombus:

1-Venous thrombus (the most common): formed in veins as in varicose veins and after major abdominal operations.

2- Arterial thrombus: found in atherosclerosis and aneurysm.

3- Cardiac thrombus: found in the heart, either in the heart chambers called mural thrombus or on the heart valves called vegetations.

4- Capillary thrombi

C.According to presence or absence of bacteria:

1- Septic thrombus: containing pyogenic bacteria.

2- Aseptic thrombi: without bacteria•

• According to their location, thrombi can be divided into venous & arterial thrombi (Cardiac thrombi can be considered as arterial thrombi because of certain similarities between the two). The differences between arterial & venous thrombi are:

Arterial thrombi	Venous thrombi
Arise at the site of endothelial injury	Arise at area of stasis
Grow in a retrograde fasion, against	Grow in the direction of blood flow from its site of attachment. Flow towards the heart
Has firm attachment	Has loose attachment, hence, propagating
They usually occlude the blood flow tail may undergo fragmentation.	Almost invariably occlusive

The most common site of arterial thrombi in descending order are:

Coronary arteries

Cerebral arteries

Temporal arteries

Fates of a thrombus

A thrombus can have one of the following fates:

It depends upon its size & whether it is septic or aseptic.

● Septic thrombi:

Fragments by proteolytic enzymes into septic emboli → payaemic abscesses.

● Aseptic Thrombi: may undergo:

- Small thrombi is dissolved and absorbed.
- Large thrombus undergoes:

1- Organization ,canalization .

2-Calcification.

4- Fragmentation and embolism.