Disturbance of Homeostasis

Disturbances of Homeostasis

1. Disturbances of Body Water and electrolytes

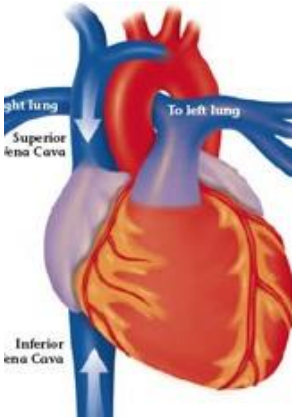
2. Disturbances of Haemostasis

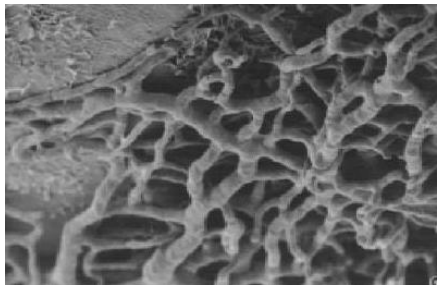
3. Disturbances of Blood Flow

Normal Distribution of Body Water

Physiology of Body Fluids:

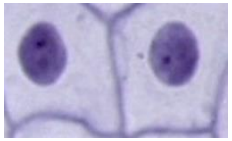
Normal Adult Weight = 70 Kg. Normal Adult Body Water = 60 %





Microcirculation

Intracellular water 43 % 30 liters



Extracellular water

- **Intercellular water (interstitial)** 13 % 9 liters
- **Intravascular water** 4 % 3 liters

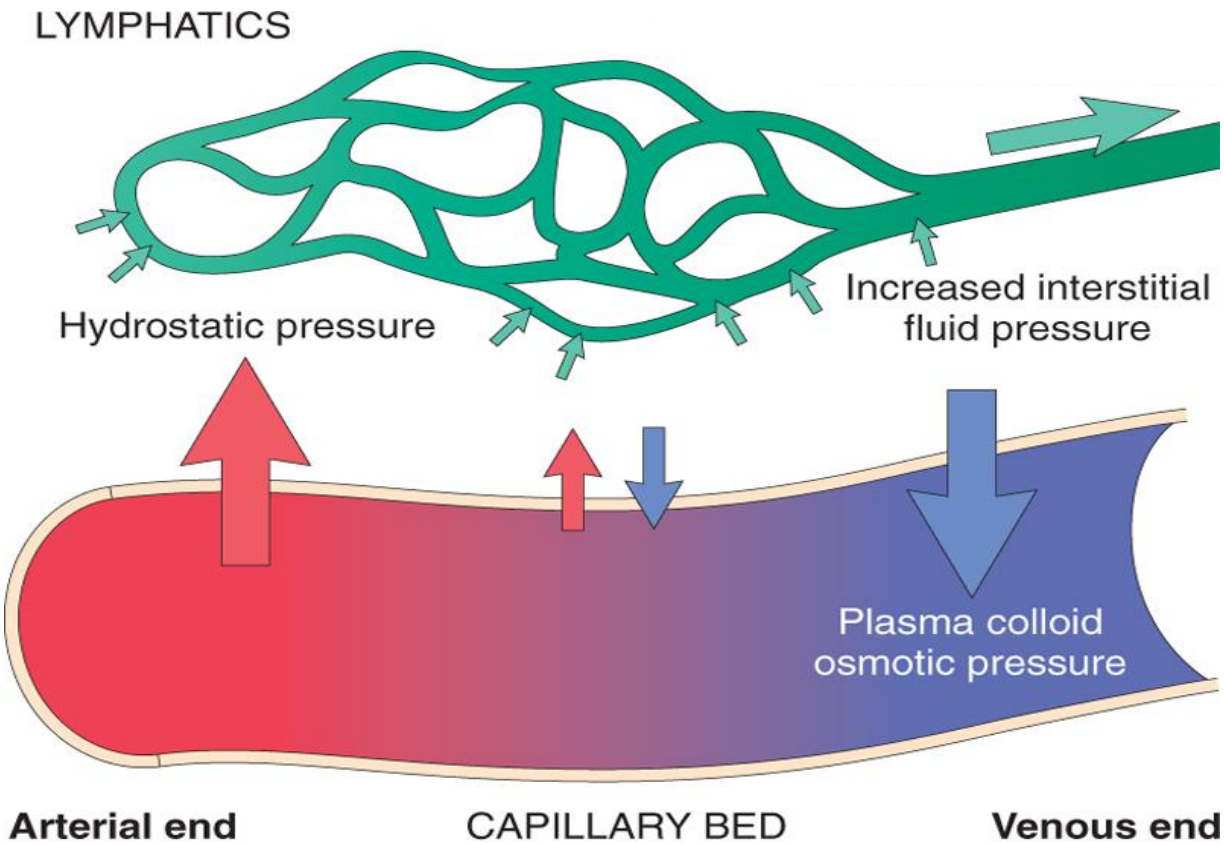
60 % 42 liters

Approximately 60% of lean body weight is water, two-thirds of which is intracellular and the reminder is in extracellular compartments, mostly as interstitial fluid; only 5% of total body water is in blood plasma.

Control of normal body water distribution

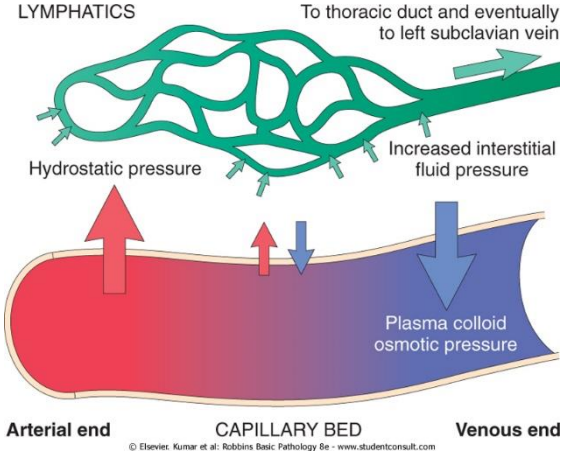
❖ The movement of fluid between vascular and interstitial spaces is controlled mainly by opposing effects of vascular hydrostatic pressure and plasma colloid osmotic pressure.

❖ Normally, the exist of fluid into the interstitium from the arteriolar end of the microcirculation is nearly balanced by inflow at the venular end. The lymphatics drain a small residual amount of excess interstitial fluid. In other words, there is no net loss or gain of fluid across the capillary bed.



Edema: introduction

- Edema is extra-vasation of fluid from vessels into interstitial spaces, or abnormal accumulation of fluid (mainly water) in interstitial tissue spaces
- Although any organ or tissue in the body may be involved, edema is most commonly encountered in subcutaneous tissues, lungs, and brain.
- The fluid may be protein poor (transudate) or may be protein rich (exudate)
- Fluid collections in different body cavities are variously designated *hydrothorax, hydropericardium,* or *hydroperitoneum* (*ascites*).



Causes of edema

- Edema results from any of the following conditions:

1. Increased hydrostatic pressure, caused by a reduction in venous return as in lower extremity deep venous thrombosis or by renal hypoperfusion as in **heart failure**.

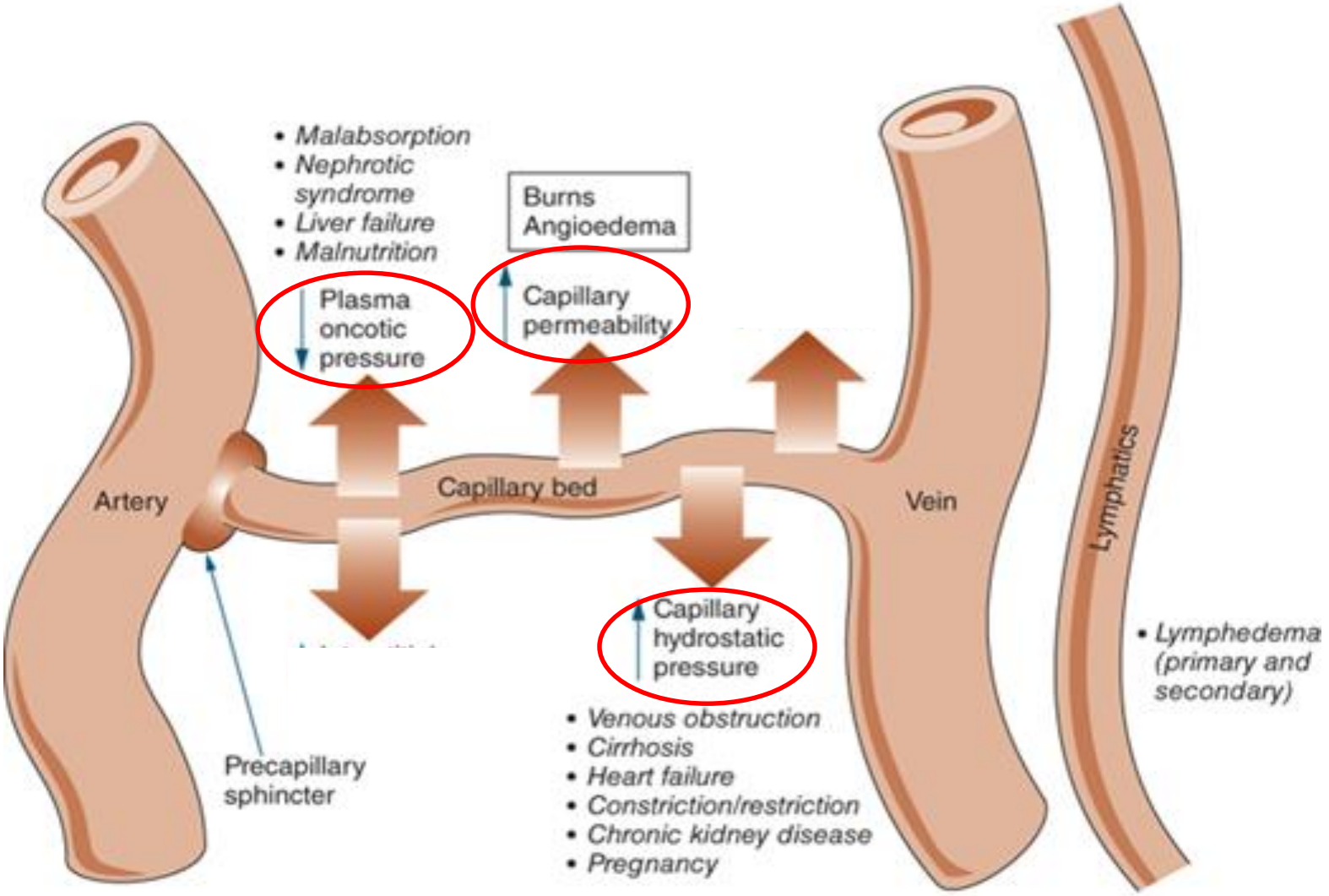
2. Decreased colloid osmotic pressure, caused by reduced concentration of plasma albumin (hypoalbuminemia) (due to decreased synthesis, as in **liver disease**, or increased loss, as in **kidney disease**). Edema precipitated by low protein is exacerbated by secondary salt and fluid retention.

3. Lymphatic obstruction that impairs interstitial fluid clearance (as in scarring, tumors, or certain infections).

4. **Primary** renal sodium retention (in **renal failure**) increasing hydrostatic pressure and reducing vascular osmotic pressure.

5. Increased vascular permeability (in inflammation).

Causes of edema



Edema Morphology

- Although any organ or tissue in the body may be involved, edema is most commonly encountered in subcutaneous tissues, lungs, and brain.

1. Subcutaneous edema:

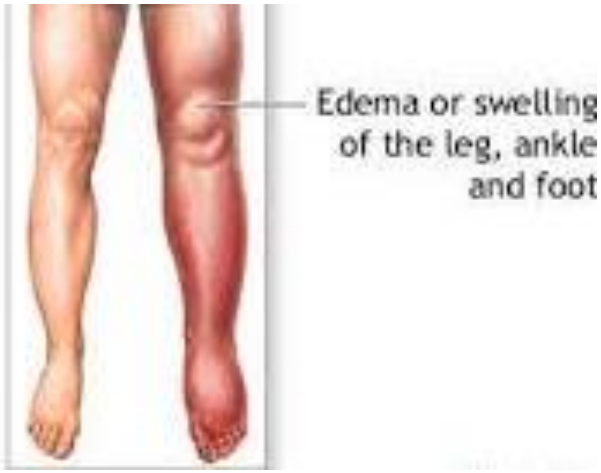
- It can be diffuse or more prominent in regions with high hydrostatic pressures; even diffuse edema can be more prominent in certain areas as a result of the effects of gravity and is called **dependent edema** (e.g., involving the legs when standing, or involving the sacrum when recumbent). **Dependent edema is a prominent feature of cardiac failure, particularly of the right ventricle.**
- **Pitting edema:** refers to finger pressure over significantly edematous subcutaneous tissue that displaces the interstitial fluid and leaves a finger-shaped depression.

2. Edema due to **renal dysfunction** or **nephrotic syndrome** is generally more severe than cardiac edema **and affects all parts of the body equally.** Nevertheless, severe edema early in the disease course can still manifest disproportionately in tissues with a loose connective tissue matrix (e.g., the eyelids, causing **periorbital edema** OR called puffy eyes).

Edema Morphology cont…

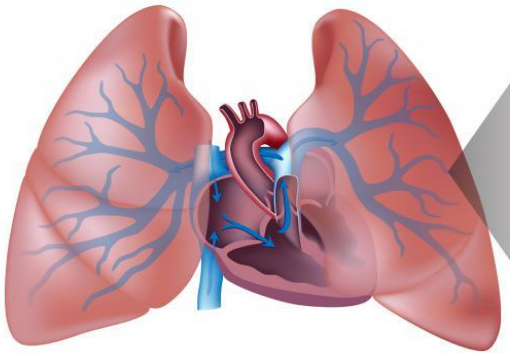
2. Pulmonary edema is a common clinical problem most frequently seen in the setting of *left ventricular failure* (with a dependent distribution in the lungs), but it also occurs in *renal failure* and *pulmonary infections*. The lungs typically weigh two to three times their normal weight, and sectioning reveals sometimes blood-tinged fluid representing a mixture of air, edema fluid, and extravasated red cells. This fluid collects in the numerous air sacs in the lungs, making it difficult to breathe

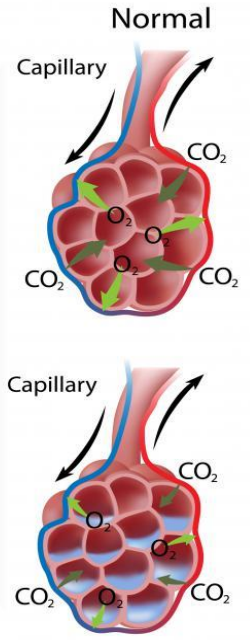
4. Edema of the brain may be localized to sites of focal injury (e.g., infarct, abscesses or neoplasms) or may be generalized, as in encephalitis, hypertensive crises, or obstruction to the brain's venous outflow. With generalized edema, the brain is grossly swollen with narrowed sulci and distended gyri.



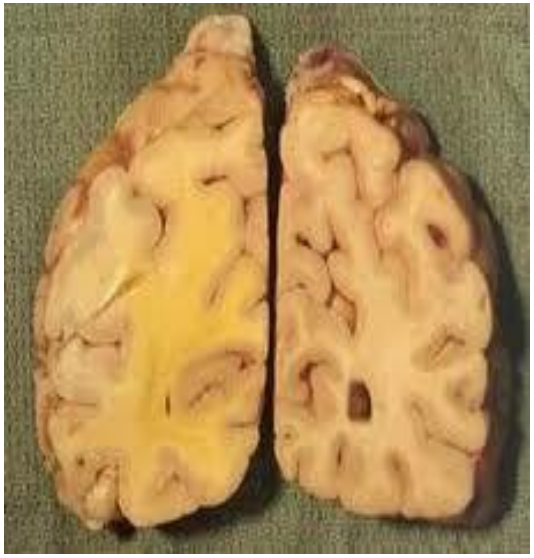
Subcutaneous pitting edema

Pulmonary Edema





Buildup of fluid
in the air sacs



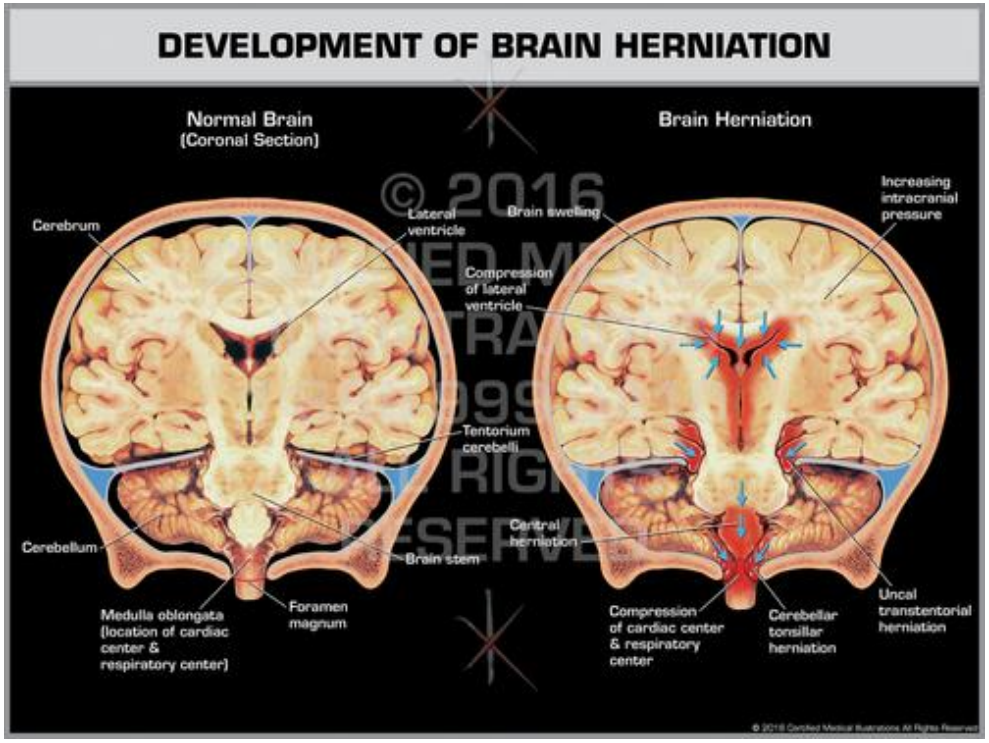
Clinical Correlation

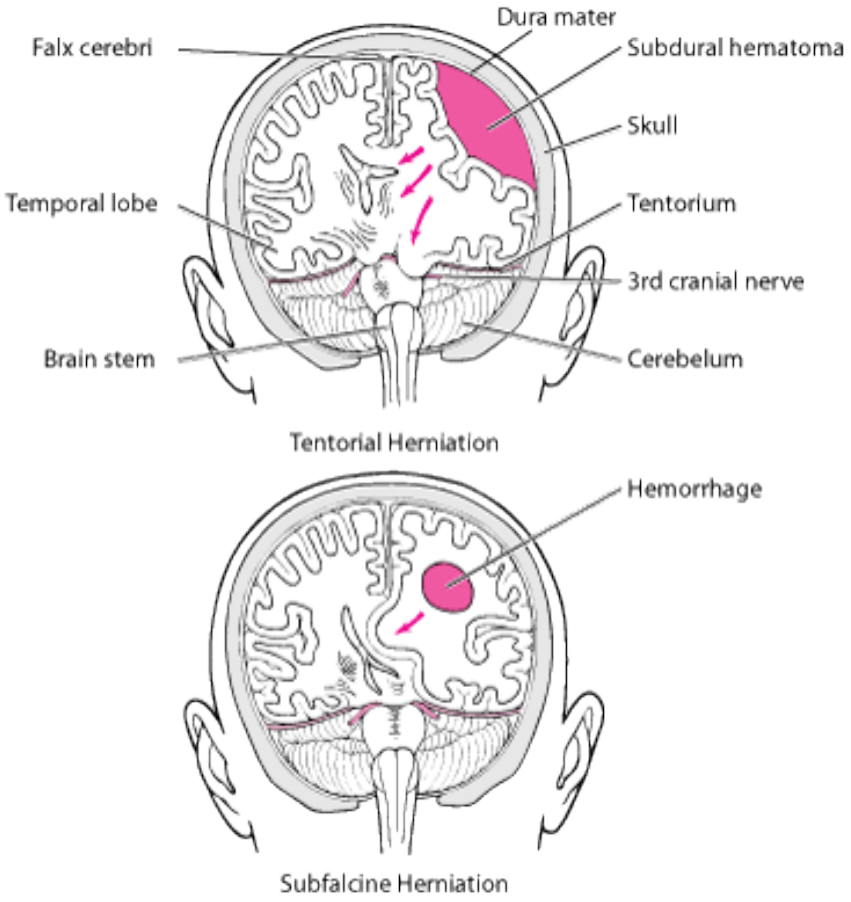
- The effects of edema may range from merely annoying to rapidly fatal.
- Subcutaneous tissue edema when significant it can impair wound healing or the clearance of infection.

- Pulmonary edema can cause death by interfering with normal ventilatory function. Not only does fluid collect in the alveolar septa around capillaries and impede (تعيق) oxygen diffusion, but edema fluid in the alveolar spaces also creates a favorable environment for bacterial infection.

- Brain edema is serious and can be rapidly fatal. If severe, brain edema can cause ***herniation*** (extrusion of the brain) through the foramen magnum; the brainstem vascular supply can also be compressed by edema causing increased intracranial pressure. Either state can injure the medullary centers and can cause death.
  (A brain herination is when brain tissue, cerebrospinal fluid, and blood vessels are moved or pressed away from their usual position inside the skull. It occurs when something inside the skull produces pressure that moves brain tissues.)

Brain herniation





Dehydration

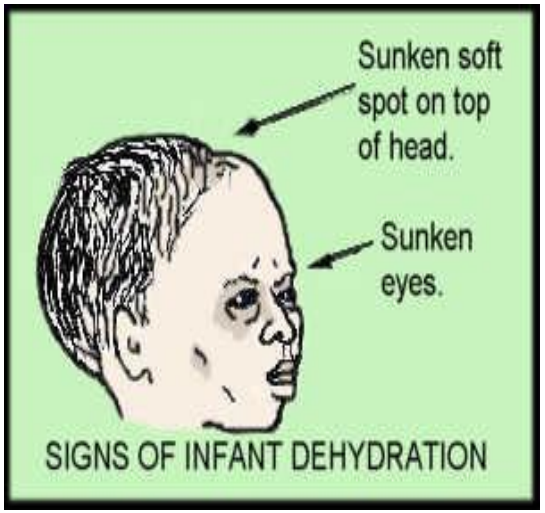
- It is a state of negative fluid balance of the body that may affect all body compartments at variable degrees.

- The decrease in total body water causes reductions in both the intracellular and extracellular fluid volumes.

- **Some Causes:**
  1. Decreased fluid intake.
  2. Increased fluid output (e.g., vomiting, diarrhea, severe sweating or insensible loss like in diabetes insipidus)
  3. Capillary leak states (e.g., burn).

Clinical picture of dehydration

1. Thirst.
2. Dry mouth and wooden tongue.
3. Rapid weak pulse.
4. Hypotension.
5. Sunken eyes (عيون غائرة).
6. Confusion.
7. Hypovolemic shock.



ELECTROLYTES AND ACID-BASE DISTURBANCES

Disturbances of serum sodium

- **Hypernatremia**: it is when serum sodium level exceeds 147mEq/L

➢ **Causes:**

a) Acute gain of sodium

b) Loss of water

➢ Therapeutic administration of sodium-containing solution may also cause hypernatremia.

➢ Is characterized by hypertonocity of the ECF and almost always causes cellular dehydration.

➢ Normally water deficit stimulates thirst and increases water intake.

➢ Therefore, hypernatrremia is more likely to occur in infants and in persons who can not express their thirst or obtain water to drink.

Disturbances of serum sodium

- **Hyponatremia**: It is when serum sodium level is below 135mEq/L.

➢ **Causes:**

a) Sodium deficit

b) Water excess

➢ Hyponatremia is particularly observed in the elderly population due to a decrease in renal function accompanied by limitations in sodium conservation.

➢ **Muscular symptoms include**: muscle cramps, weakness, depression of deep tendon reflexes and fatigue.

➢ **Brain and nervous symptoms include:** lethargy and headache and progress to confusion, ultimately with serum sodium levels reach extremely low levels seizures and coma occur.

➢ These severe effects, which are caused by brain swelling as a result of pronounced increase in intracellular water, may be irreversible.

Disturbances of serum potassium

- **Hyperkalemia:** It is when serum potassium above 5.5 mEq/L.
- **Causes:**
  a. Increase intake of potassium.
  b. Shifting from intracellular to extracellular compartments e.g. increased osmolality, acidosis, extensive tissue damage.
  c. Decrease body excretion of potassium.

- **Acidosis** is defined as an **increase in the concentration of hydrogen ions in the bloodstream**. In the body's attempt to correct the situation, **hydrogen is taken up by muscle cells** out of the blood in an **exchange mechanism** involving the **transfer of potassium ions into the bloodstream**. This can abnormally elevate the plasma's concentration of potassium ions. In acidosis, potassium excretion is also decreased.
- The effects are cardiac (tall peaked T wave, loss of P wave, widen QRS and neurological.

Disturbances of serum potassium

- **Hypokalemia:** It is when serum potassium level is below 3.5 mEq/L.
- **Causes**:
  a. Reduced dietary intake of potassium.
  b. Increased entry of potassium into the cell as a result of stimulating the Na+/K+ ATPase pump, e.g. alkalosis, insulin, beta-agonists (e.g., salbutamol).
  c. Increase body loss of potassium e.g. diuretics, hyperaldosteronism, theophylline, diarrhea
- **Pathophysiology hints:**

✓ Potassium is essential for many body functions, including muscle and nerve activity.

✓ In the **nerve**, the electrochemical gradient of potassium between the intracellular and extracellular space is essential for nerve function; in particular, potassium is needed to repolarize the cell membrane to a resting state after an action potential has passed. Lower potassium levels in the extracellular space cause **hyperpolarization** of the resting membrane potential. As a result, a greater than normal stimulus is required for depolarization of the membrane to initiate an action potential.

✓ In the **heart**, hypokalemia causes hyperpolarization in the myocytes' resting membrane potential. The more negative membrane potentials in the atrium may cause **arrhythmias**

✓ **Clinical Signs**: in the GI (constipation, distention), renal, musculoskeletal (muscle weakness or cramp), cardiac (ECG changes, flattened T wave, ST depression, prolonged QT, tall U wave, arrhythmia)

Disturbance of serum Calcium

Hypercalcemia: is when total serum calcium is above 12 mg/dl.

Causes:

a. Hyperparathyroidism (e.g., PTH-producing tumors)

b. Bone metastasis e.g breast. Local bone metastases induced osteoclastic activity causes bone resorption, raising calcium levels in the blood. This is the cause in 80 per cent of patients with hypercalcaemia of malignancy.

c. Sarcoidosis (Hypercalcemia occurs in **sarcoidosis** because of 1,25-dihydroxyvitamin D production by pulmonary alveolar macrophages.)

d. Excessive vitamin D intake

e. A variety of drugs elevate calcium levels: **Lithium** to treat bipolar disorders has caused hypercalcemia and hyperparathroidism. The **thiazide** diuretics increase calcium reabsorption in the distal convoluted tubule of the kidney. Although the thiazide diuretics seldom cause hypercalcemia, they can unmask hypercalcemia from other causes such as underlying bone disorders and conditions that increase bone resorption.

Disturbance of serum Calcium

Hypocalcemia: It is when total serum calcium is below 8.5 mg/dl.

Causes:

a) Inadequate absorption or intake of calcium
b) Decrease of parathyroid hormone (PTH) or vitamin D
c) Blood transfusion
d) Excessive phosphate intake leading to the production of calcium-phosphate crystals in the blood and soft tissue.
e) Pancreatitis
f) Alkalosis
g) Hypoalbuminemia

➢ **Pathophysiology hints:**

✓ PTH acts to increase the concentration of calcium (Ca^{2+}) in the blood. It enhances the absorption of calcium in the intestine by increasing the production of activated vitamin D.

✓ Because of the inverse relation between calcium and phosphate, serum calcium falls as phosphate level rise in renal failure >>> a side-effect of **hyperphosphatemia** is the formation of calcium-phosphate crystals in the blood and soft tissue.

Disturbance of serum Calcium

- ✓ Hypocalcemia can also occur with massive blood transfusions due to citrate binding (citrate used as anticoagulation in blood products) with serum calcium.
- ✓ **Acute pancreatitis** in which the pancreas is damaged and free fatty acids are generated which avidly chelate the calcium salts resulting in calcium deposition in the retroperitoneum and consequently a decrease in serum calcium.
- ✓ Alkalosis occurs due to hyperventilation. Alkalosis means less acids in the blood. These acids usually compete with Calcium in binding to albumin. If the acids are depleted then Calcium will have more room to bind to albumin and therefore less free ionised Calcium leading to hypocalcemia. This consequently may trigger tetany. Note: ionized form of calcium is able to leave the capillary and participate in body functions, so the biologic effect of calcium is determined by the amount of ionized calcium, rather than the total calcium.

- ✓ **A pseudohypocalcemia** describes the situation in which the total calcium is reduced because of hypoalbuminemia, but the ionized calcium remain within the normal ranges. However, it is asymptomatic.

Clinical manifestation of hypocalcemia

1. Tetany – neuromuscular irritability
- Trousseau's sign- Positive if carpopedal spasm resulting from inflated BP cuff above systolic pressure after 3 minutes
- Chvostek's sign – Positive if ipsilateral facial muscle spasms are elicited by tapping facial nerve just anterior to ear

2. Fatigue
3. Anxiety, depression and seizures

A. Positive Chvostek's Sign

B. Positive Trousseau's Sign

Disturbance of the acid-base balance

- **Acidemia**: Blood pH is below 7.35
- **Alkalemia**: Blood pH is above 7.45

There are two types of acid-base disorders:

1. Metabolic disorders: produce an alteration in the plasma [HCO_3^-] that result from the gain of alkali or loss of acid from the ECF.
2. Respiratory disorders involve an alteration in the PCO_2, reflecting an increase or decrease in alveolar ventilation.

Acidosis is either respiratory or metabolic

Alkalosis: is either respiratory or metabolic

Respiratory acidosis and alkalosis

- **Respiratory acidosis** is due to retention of CO_2 due to primary respiratory condition causing hypercapnia.

Causes:

a. Oversedation

b. Brain trauma

c. Respiratory muscle paralysis

d. Lung diseases

- **Respiratory alkalosis** is due to excessive washout of CO_2 due to primary respiratory condition causing hypocapnia.

Causes:

a. Heart failure

b. High altitude

c. Fever

d. Thyrotoxicosis

e. Salicylate intoxication

Metabolic acidosis and alkalosis

- **Metabolic acidosis** is abnormal decrease in $HCO3^-$ concentration or an increase in H+ concentration. Theses changes are not due primarily to respiratory condition.

Causes:

a. Increase H^+ load such as in lactic acidosis, ketoacidosis, NH4Cl, Salicylate.

b. Decrease H^+ excretion e.g. uremia, distal renal tubular acidosis

c. Bicarbonate loss e.g. diarrhea, renal failure, proximal renal tubular acidosis

- **Metabolic alkalosis** is abnormal increase in bicarbonate or decrease of H^+ concentrations in the blood.

Causes:

a. Prolonged vomiting

b. GI suction

c. Excessive $HCO3^-$ intake

d. Hyperaldosteronism

e. Diuretic therapy