

Министерство здравоохранения республики Беларусь  
Учреждение образования  
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии  
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Протокол №7 от 30.08.2017

**МЕТОДИЧЕСКАЯ РАЗРАБОТКА**  
Для проведения занятия со студентами  
3 курса ФПСЗС, обучающихся на английском языке  
по патологической физиологии

Тема: **Нарушения кислотно-основного состояния, водно-электролитного и минерального обменов**

Theme: **Disorders of acidbase balance, water-electrolyte and mineral metabolism**

Время 3 ак. часа

**Actuality of the theme.** The state of dehydration can arise in the person in time stay on place with hot climate owing to excessive of sweating and hyperventilation. However water deficiency is more often is observed for various pathological states - strong diarrhea, vomiting, complicated swallowing (tumour, atresia of the esophagus), extensive burns, significant blood loss, diseases of brain, which are accompanied by absence of thirst sensation, in the heavy patients and weakened children. This state especially is dangerous for children first two years life in connection with disorder of neuroendocrine regulation of water-electrolytes metabolism. Dehydration in them quite often lead to death.

**Learning goals of the lesson:** to know the main causes and mechanisms of ABS disturbances, main mechanisms of water, electrolyte and mineral metabolism disturbances in body.

**Educational goals of the lesson:** formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

**Objectives of the lesson:**

1. To know the basic mechanisms of violations of CBS and water-electrolyte exchange.
2. To study compensation mechanisms and methods for compensation of ions disbalance ( $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{P}^+$ ).
3. To know principles and methods of edema therapy.

**To repeat the following questions from related disciplines to ensure absolute mastery of the material:**

1. Anaerobic glycolysis, ways to utilize under-oxidized exchange products; buffer systems, classification, mechanisms of action (general and bioorganic chemistry discipline);
2. Renal mechanisms to maintain constancy of ABS (normal physiology discipline).

**Control questions of the lesson:**

1. Violations of the acid-base state (ABS): classification.
2. Gas acidosis and alkalosis: causes, mechanisms, manifestations.
3. Non-gase forms of acidosis and alkalosis: causes, mechanisms, manifestations. Mixed forms.
4. Compensatory reactions in acute and chronic violations of ABS.
5. Principles of correction of ABS changes (for various types of acidosis and alkalosis) in the body.
6. Disorders of water exchange: types, causes, mechanisms of development.
7. Disorders of electrolyte metabolism: causes, mechanisms, metabolic disorders and physiological functions.
8. Principles of diagnostics of typical violations of water-electrolyte exchange.

**Calculation of study time**

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes

## Additional materials:

### Mechanisms of Acid-Base Balance Regulation

Since the majority of intermediates (products of intermediate metabolism) are acids, the regulation of pH is provided continually. Many mechanisms (in liquid media, blood and cells) are constantly participating in acid-base balance regulation.

1. **Buffer systems** neutralize surplus of acids and alkalines, transferring them into a form, convenient for further secretion by lungs and kidneys.

- **Hydrocarbonate buffer system**  $\text{H}_2\text{CO}_3 / \text{NaHCO}_3 = 1/20$  maintains pH in blood plasma and interstitial fluid. This buffer has a *flying form of acid* ( $\text{CO}_2$ ), which can be easily excreted by lungs.
- **Phosphate buffer system**  $\text{NaH}_2\text{PO}_4 / \text{Na}_2\text{HPO}_4 = 1/4$  participate in acid-base regulation in kidneys.
- **Hemoglobin buffer** functions in erythrocytes.
- **Protein** buffer regulates intracellular pH.

2. **Lungs role** is in constant removing of carbon acid in form of carbon dioxide  $\text{CO}_2$ .

3. **Kidneys** role is in acid-base regulation through three mechanisms (schemes 16, 17, 18):

- **Acidogenesis** is a secretion of  $\text{H}^+$  ions into the renal tubules.
- **Ammoniogenesis** is a formation and secretion of ammonia ion  $\text{NH}_3$  into renal tubules. Then,  $\text{NH}_3$  reacts with  $\text{H}^+$  to form  $\text{NH}_4^+$ . Then it is accompanied by anion  $\text{Cl}^-$ . Neutral ammonium salt  $\text{NH}_4\text{Cl}$  is formed and is removed with urine.
- **Reabsorption of bicarbonate** ( $\text{NaHCO}_3$ ) in renal tubules.

Consequently, urine examination reflects the acid-base state. Two indices of urine are of practical use. They are urinary acidity, tested by titration, ammonium salts content.

4. **Aldosterone** (hormone of the adrenal cortex) supports acidogenesis in kidneys, participate in  $\text{H}^+$  and  $\text{Na}^+$  exchange ( $\text{H}^+$ -ion secretion and  $\text{Na}^+$  - ion reabsorption).

1. **Acidosis** — when excess  $\text{H}^+$  and decreased  $\text{HCO}_3^-$  causing a decrease in pH.

The Kidneys try to adjust for this by excreting  $\text{H}^+$  and retaining  $\text{HCO}_3^-$  base.

The Respiratory System will try to compensate by increasing ventilation to blow off  $\text{CO}_2$  (acid) and therefore decrease the Acidosis.

2. **Alkalosis** — when  $\text{H}^+$  decreases and excess (or increased)  $\text{HCO}_3^-$  base.

The kidneys excrete  $\text{HCO}_3^-$  (base) and retain  $\text{H}^+$  to compensate.

The respiratory system tries to compensate with hypoventilation to retain  $\text{CO}_2$  (acid) to decrease the alkalosis

### Compensation:

1. The respiratory system can effect a change in 15-30 minutes
2. The renal system takes several hours to days to have an effect.

**Normal pH: 7.35 - 7.45;  $\text{CO}_2$ : 35 – 45;  $\text{HCO}_3^-$ : 22 – 26**

### Classification of ABC violations

#### By direction of a change [ $\text{H}^+$ ] and pH:

- acidosis
- alkalosis
- mixed forms

#### By reasons and mechanisms:

- gas forms (respiratory)
- non-gas: metabolic, excretory (renal, gastro), exogenous

#### By degree of compensation:

- compensated (pH 7.35 - 7.45)
- subcompensated (pH 7.29-7.34 or 7.46- 7.56)
- decompensated (pH < 7.29 or > 7.56)

#### By current:

- acute
- chronic

### RESPIRATORY ACIDOSIS

**pH < 7.35 (Normal: 7.35 - 7.45)  $\text{CO}_2$  > 45 (Normal: 35 – 45)**

## Causes:

### Hypoventilation:

1. Depression of the Respiratory Center (sedatives, narcotics, drug overdose, CVA, cardiac arrest, MI)
2. Respiratory muscle paralysis (spinal cord injury, Guillain-Barre, paralytics)
3. Chest wall disorders (flail chest, pneumothorax)
4. Disorders of the lung parenchyma (CHF, COPD, pneumonia, aspiration, ARDS)
5. Alteration in the function of the abdominal system (distension)

### Pathogenesis of gas acidosis

Hypocapnia leads to the following changes:

- increasing the capacity of bicarbonate buffer
- protein, phosphate and hemoglobin buffer systems bind part of  $H^+$
- ↑ excitability of the respiratory center → breathlessness occurs → removal of excess  $CO_2$  from the body → pH remains for some time within the limits of normal
- in the kidneys,  $NH_4^+$  secretion is enhanced,  $H^+$  release in free form → ↑ reabsorption of  $HCO_3^-$ . Kidney retention of bicarbonate in chronic gas acidosis causes an even greater increase in its concentration in the plasma, which helps maintain a normal or close to normal pH (compensatory metabolic alkalosis is noted).

With an increase of hypocapnia:

- the buffer capacity of the hemoglobin system decreases → ↓ affinity of Hb to  $O_2$  → hypoxia is increased → underoxidized products accumulate in cells → metabolic acidosis is attached → vasomotor center is excited → spasm of arterioles → ischemia of internal organs
- the arterioles of the brain expand → arterial hyperemia → ↑ intracranial pressure (headache). Depression of brain substance activates the neurons n. vagus.
- Adrenoreceptor activity decreases and increases in tone of n.vagus → bradycardia and ↓ BP (for chronic respiratory acidosis)
- ↑ acetylcholine is manifested by spasm of bronchioles, allocation of large amounts of viscous mucus → deterioration of gas exchange → increase in  $CO_2$  production - "vicious circle"
- excess  $H^+$  + extracellular fluid is exchanged for  $Na^+$  + and  $Ca^{2+}$  + ions of bone tissue → osteoporosis (with chronic respiratory acidosis)

### Signs and Symptoms:

- a. CNS depression
- b. Muscle twitching which can progress to convulsions
- c. Dysrhythmias, tachycardia, diaphoresis (related to hypoxia secondary to hypoventilation)
- d. Palpitations
- e. Flushed skin
- f. Serum electrolyte abnormalities including elevated  $K^+$  (potassium leaves the cell to replace the  $H^+$  buffers leaving the cell)

### Treatment

- a. Physically stimulate the patient to improve ventilation
- b. Vigorous pulmonary toilet (chest PT, coughing and deep breathing, spirometer, respiratory treatments with bronchodilators)
- c. Mechanical ventilation (to increase the respiratory rate and tidal volume)
- d. Reversal of sedatives and narcotics
- e. Antibiotics for infections
- f. Diuretics for fluid overload

(NOTE: beware of  $NaHCO_3^-$  sodium bicarbonate—can compensate and cause metabolic alkalosis. Also, if patient has been hypoxic and this is a lactic acidosis;  $NaHCO_3^-$  can be dangerous)

## RESPIRATORY ALKALOSIS

pH > 7.45 (Normal: 7.35 - 7.45)  $CO_2$  < 35 (Normal: 35 - 45)

### Causes:

#### Alveolar Hyperventilation:

1. Psychogenic (fear, pain, anxiety)
2. CNS stimulation (brain injury, ETOH, early salicylate poisoning, brain tumor)
3. Hypermetabolic states (fever, thyrotoxicosis)
4. Hypoxia (high altitude, pneumonia, heart failure, pulmonary embolism)
5. Mechanical overventilation (ventilator rate too fast)

### Pathogenesis of gas alkalosis

Hypocapnia, which develops during hyperventilation, leads to:

- displacement of  $H^+$  ions from cells to the extracellular space in exchange for potassium ions → hypokalemia, intracellular alkalosis (hypokalemia is manifested by muscle weakness, extrasystole)
- ↑ affinities of hemoglobin to oxygen,  $O_2$  transition in tissues is hampered → hypoxia → metabolic acidosis, compensating pH shift
- ↓ respiratory center excitability →  $CO_2$  retention in the body
- decrease in the secretion of protons by the kidneys
- ↑ bicarbonate secretion → ↓ level in the plasma → pH returns to normal

Increasing hypocapnia, acting on the receptors of the vasomotor center, leads to

- decrease in tone of arterioles walls of organs and tissues → hypotension and collapse
- increase in tone of arterioles walls of brain → ischemia.

Hypocalcemia becomes the cause of increased neuromuscular excitability and can lead to convulsive phenomena (tetany)

### Signs and Symptoms

- Headache
- Vertigo
- Paresthesias (numb fingers /toes, circumoral, carpal pedal spasms and tetany)
- Tinnitus (ringing in the ears)
- Electrolyte abnormalities (decreased  $Ca^{2+}$ ,  $K^+$ )

### Treatment (treat the underlying cause)

- Sedatives or analgesics
- Correction of hypoxia (possible diuretics, mechanical ventilation to also decrease respiratory rate and decrease the tidal volume)
  - NOTE: patients with brain injury may need hyperventilation
- Antipyretics for fever
- Treat hyperthyroidism
- Breathe into a paper bag for hyperventilation

## NON-GAS ACIDOSIS

**pH < 7.35 (Normal: 7.35 - 7.45)  $HCO_3^-$  < 22 (normal: 22 – 26)**

**Causes:** Increased  $H^+$ , excess loss of  $HCO_3^-$

- metabolic: overproduction of organic acids (starvation, ketoacidosis, increased catabolism)
- renal: impaired renal excretion of acid (renal failure);
- gastro: abnormal loss of  $HCO_3^-$  (diarrhea, biliary fistula)
- exogenous: ingestion of acid (salicylate overdose, oral anti-freeze)

### Pathogenesis non-gas forms of acidosis

Excess  $H^+$  + extracellular fluid:

- exchanged for potassium ions of erythrocytes and tissue cells → ↑  $[K^+]$  in plasma
- depletion of  $HCO_3^-$  in erythrocytes reduces their exchange for chloride ions in venous blood → hyperchloremia
- stimulates central chemoreceptors → hyperventilation → gas alkalosis.
- in the kidneys, bases are actively reabsorbed and acidic equivalents are extracted → in urine ↑ the content of acids and their ammonium salts. Prolonged acidosis increases the breakdown of proteins → ↑ free amino acids in the blood → increased ammoniogenesis → preservation of sodium, potassium, calcium in the body
- exchanged for calcium and sodium bones → prolonged acidosis can lead to de-calcification of bones, if excretion of organic acids in urine is limited due to renal pathology

If the excess of  $H^+$  is not eliminated, then it develops:

- tachypnea → hyperventilation → ↓  $pCO_2$  blood → ↓ excitability of the respiratory center → respiration of Kussmaul
- due to hypocapnia, blood pressure and cardiac output decrease → circulatory insufficiency of brain, myocardium, kidneys
- Ventricular fibrillation (the causes are ↑  $K^+$  in the blood, ↓  $K^+$  in the myocardium, lowering the pH → increased secretion of catecholamines)
- suppression of high nervous activity occurs due to ↓ blood flow, imbalance of ions → energy deficiency, ↓ neuron excitability → coma
- Hyperosmia, hyperonkia, venous congestion, ↑ permeability of the vascular wall → edema.

### Signs and Symptoms

- CNS depression (confusion to coma)
- Cardiac Dysrhythmias (elevated T wave, wide QRS to ventricular standstill)

- c. Electrolyte abnormalities (elevated  $K^+$ ,  $Cl^-$ ,  $Ca^{2+}$ )
- d. Flushed skin (arteriolar dilatation)
- e. Nausea

**Treatment (Treat the underlying cause)**

- a.  $NaHCO_3^-$  (sodium bicarbonate) based on ABGs only and with caution
- b. fluids and insulin for DKA
- c. Dialysis for renal failure
- d. Antibiotics, increased nutrition for tissue catabolism
- e. Increased cardiac output and tissue perfusion for low CO states
- f. Rehydrate
- g. Treat dysrhythmias, support hemodynamic and respiratory status

## NON-GAS ALKALOSIS

**pH > 7.45 (Normal: 7.35 - 7.45)  $HCO_3^-$  > 26**

**Causes:** Loss of  $H^+$  or increased  $HCO_3^-$

1. Metabolic alkalosis - hyperaldosteronism resulting in increased secretion of  $K^+$ , hypothyroidism of parathyroid glands resulting in  $\downarrow Ca^{2+}$  and  $\uparrow Na_2HPO_4$
2. Renal alkalosis - a violation of the release of  $HCO_3^-$ , the release of excessive amounts of protons by the kidneys when taking diuretics
3. Gastroenteral alkalosis - loss of a large amount of  $HCl$  from stomach with intractable vomiting; pathological changes in an intestines, leading to losses of  $Cl^-$  and  $K^+$
4. Exogenous alkalosis - an introduction of large amounts of  $HCO_3^-$  (therapy with sodium bicarbonate solution), use of alkaline mineral waters

**Pathogenesis of non-gas forms of alkalosis**

Increasing the pH results in:

- neutralization of alkaline equivalents with carbonic acid  $\rightarrow \downarrow$  respiratory center excitability  $\rightarrow$  hypoventilation and difficulty of dissociation of oxyhemoglobin in alkaline environment  $\rightarrow$  hypoxia  $\rightarrow$  accumulation of under-oxidized products and increase of  $pCO_2$  partially compensates for excess bases. An increase in the content of  $CO_2$  stimulates breathing, and it is removed from the body, therefore respiratory compensation of metabolic alkalosis is insufficient
- in the kidneys increases the release of  $HCO_3^-$ , disubstituted phosphates, can develop in the loss of potassium, and in severe cases, sodium
- excessive formation of aldosterone enhances the reabsorption of  $H^+$  and contributes to the loss of potassium by the kidneys  $\rightarrow$  hypokalemia  $\rightarrow$  part of  $H^+$  enters the cells in exchange for the outgoing into the intercellular environment of the potassium ion  $\rightarrow$  alkalosis is aggravated and in parallel in the part of the tissues intracellular acidosis develops

Hypokalemia manifests atrial-ventricular arrhythmias, muscle weakness, hyporeflexia, impaired intestinal peristalsis up to dynamic obstruction. Along with this, there are signs of increased neuromuscular excitability, confusion of consciousness and stupor, as well as hypovolemia. If alkalosis reduces the level of  $Ca^{2+}$ , spasms, symptoms of tetany, hypocalcemic convulsions may develop.

**Signs and Symptoms: similar to the disease process**

- a. Diaphoresis
- b. Nausea and Vomiting
- c. Increase neuromuscular excitability ( $Ca^{2+}$  binds with protein)
- d. Shallow breathing (respiratory compensation)
- e. EKG changes (increased QT, sinus tachycardia)
- f. May also see confusion progressing to lethargy to coma
- g. Electrolyte abnormality (decreased  $Ca^{2+}$ ), normal or decreased  $K^+$ , increased base excess on the ABG

**Treatment: Treat the underlying cause**

- a. Replace potassium (KCl) losses in 0.9% NaCl (rehydrates and increases  $HCO_3^-$  excretion)
- b. Diamox (acetazolamide, increases  $HCO_3^-$  excretion)
- c. Monitor neuro status, re-orient, seizure precaution, monitor I and O

**Principles of diagnosis:**

- I. First, look at pH (normal is 7.35 - 7.45)
  1. If pH is < 7.35; it name is **ACIDOSIS**
  2. If pH is > 7.45; it name is **ALKALOSIS**

(NOTE: To have an absolutely perfect last name; pH needs to be 7.40. So, keep in mind that if her pH is 7.35 - 7.39 she's thinking about marrying into the **ACIDOSIS** family. If her pH is 7.41 - 7.45 she's thinking about marrying into the **ALKALOSIS** family)

II. Look at pH again.

1. If it is 7.35 - 7.45 (normal) it is **COMPENSATED**.
2. If the pH is < 7.35 or > 7.45 it is **UNCOMPENSATED**.

pH 7.34 - 7.29 subcompensated acidosis

pH 7.46 - 7.56 subcompensated alkalosis

pH < 7.29 decompensated acidosis

pH > 7.56 decompensated alkalosis

III. **Respiratory or Metabolic.**

First you need to look at the CO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup>. Remember : normal CO<sub>2</sub> 35 - 45; and HCO<sub>3</sub><sup>-</sup> 22 - 26.

2. If the CO<sub>2</sub> is < 35 or > 45; it is **RESPIRATORY**.

3. If the HCO<sub>3</sub><sup>-</sup> is < 22 or > 26; it is **METABOLIC**.

### **Water Balance**

Water composes 60% of body mass (45% in thin aged men to 70% in young). It is one of the most important constants of organism.

A person drinks about 1-2 liters of water. About 1 liter comes into the organism with a food and about 300 ml of water is produced from nutrient oxidation daily. The same amount of water (about 2.5 liters) is excreted from the organism by the kidneys (1-1.5 liters), skin vaporization (0.5-1 liter) and the lungs (about 400 ml) as well as feces (50-200 ml). Water is distributed in organism in such a way:

**Water of the blood** (intravascular) composes about 5%. It is a circulating blood volume. 93% of it is pure water. The rest is binding with blood cellular elements.

This volume must not be changed significantly since it determines a load on the heart. *Volumoreceptors* of the large vessel wall and atrium of the heart inspect this volume.

**Intracellular water** composes 35-45%. This volume is regulated most constantly and must not be changed. The intracellular fluid is presented in three conditions:

- Water of the cytoplasm bounded with hydrophilic structures,
- Water attracted on the surface of the colloid structures,
- Water in the cytoplasm lacunas, which is the most mobile, relatively free water of the cells.

In different pathologic conditions the intracellular fluid volume changes at the expense of the mobile water volume.

**Extracellular (interstitial) water** composes about 15%. Only in this space a water quantity may be changed significantly.

The interstitial fluid is close to the blood plasma (except protein contents) and washes the cells by ion and molecular substrates. This fluid is in a constant exchange with blood plasma so that approximately 20 liters of fluid with the dissolved substances come into the tissues from the vessels daily and the same amount returns into the systemic blood flow. Three liters of it return through the lymphatic vessels.

**Extracellular (transcellular) water** (1-3%) forms the digestive juice, cerebrospinal fluid, eye chamber humor, the kidney tubules fluid.

Intravascular and interstitial fluids are the most mobile, and just they are the first to change their volume.

The total body water amount decreases with aging. In old people the extracellular fluid amount is increased while the content of water in the cells is reduced.

### **Water Balance Regulation Mechanisms**

The water balance is regulated by many mechanisms. Some of them act locally in the tissues; some are systemic for the whole organism.

#### **Local Mechanisms**

Local (tissue) mechanisms regulate the water balance between the blood and the tissues through the capillary wall.

**Starling** and other scientists (Vidal, Fisher) studied factors, which determine the liquid passing from blood stream into the intercellular space (filtration) and its recovery into the vessels. This balance is regulated by physicochemical mechanisms:

- **Hydrodynamic pressure difference** between the blood and the extracellular liquid. The blood moves in the capillaries at a definite speed and under a definite pressure, which results in forming the hydrodynamic force, which makes the water go out from the capillaries into the interstitial space. The higher the blood pressure and the less the tissue fluid pressure, the more effect of hydrodynamic forces will be. The hydrodynamic blood pressure in the arterial section of the capillaries is 35-40 mm Hg and in the venous one 10-15 mm Hg (Starling).



- **Onkotic pressure** (of proteins) difference between the blood and interstitial liquid. An increase of the vascular permeability for proteins occurs with a number of pathologic processes and essentially influences this parameter (Starling).
- **Osmotic pressure difference** between the blood and interstitial liquid (Vidal).
- **Interstitial tissue pH**. Hydrophilic nature of colloids depends on  $H^+$  concentration and rises in the acid medium. Then colloids swell and detain more water (Fisher).
- Resulting force is called *filtration pressure*.

### **Systemic Mechanisms**

Systemic mechanisms regulate the water balance between the organism and the environment. One should understand, that entire organism water cannot be regulated by physicochemical laws mentioned above. It is regulated by biological (neurohumoral) mechanisms with the participation of such high level, as hypothalamus.

These mechanisms are the following:

- Participation of the **volumoreceptors** of vascular wall and the left atrium of the heart, which control the circulating blood volume.
- Participation of **osmoreceptors** of vascular wall (дуги аорты и каротидный синус), which control the blood osmotic pressure.
- Participation of **aldosterone** of the adrenal cortex, which regulates (increases)  $Na^+$  reabsorption from the primary urine into the blood.
- Participation of **hypothalamus**, which reacts both on decreased blood volume and increased blood osmolarity in response to the signals from volumo- and osmoreceptors. It release **vasopressin** (antidiuretic hormone ADH) by supraoptical and paraventricular hypothalamic nuclei. The point of vasopressin action is the epithelium of the renal tubules. Vasopressin increases a water reabsorption from the primary urine and thus regulates diuresis (primary urine quantity is 180 l daily and final urine is 1-2 l).
- Participation of **kidney** with its receptors and renin. Stimulation of the adducting **renal arteriole volumoreceptors and osmoreceptors** of the macula densa of the juxtaglomerular complex intensifies a synthesis and release of **renin**. Angiotensin II, which is formed under its influence, increases aldosterone secretion and stimulates the center of thirst located in the hypothalamic lateral part.

- Retention of water and  $Na^+$  in the organism is opposed by two mechanisms

- **Reno-medullar prostaglandins**,
- **Na-uretic factor of cardiac atria** (ANF, atriopeptide of 28 aminoacids).

All these mechanisms are in a constant functioning and provide water-electrolyte homeostasis restoration in the situation of blood loss and dehydration, water retention in the organism as well as osmotic concentration changes.

### **Classification of water disbalance:**

Water disbalance is divided into two variants – positive and negative.

**Positive water balance** (hyperhydration) is a water retention in the organism.

**Negative water balance** (hypohydration) is a water loss by organism.

Depending on the **osmotic concentration** divided into three types: **isoosmolar, hypoosmolar and hyperosmolar**. (the normal osmotic concentration of the blood and intercellular fluid is about  $0.3 \text{ osmol/l} = 300 \text{ mosmol/l}$ ).

In clinical practice it is manifested in form of two syndromes - **hyperhydration (edema)** and **dehydration**.

### **HYPERHYDRATION**

Hyperhydration is a positive water balance.

**Hypoosmolar hyperhydration develops in acute renal failure**. The vasopressin large dose injection into the blood results in the same. It is characterized by increased amount of water in the organism and decreased osmotic pressure in the extracellular space. The water excudes into the cells. Sodium-potassium balance gets changed on the membrane. Sodium passes into the cells and hence its amount in the blood plasma decreases.  $K^+$  passes out of the cells into the extracellular sector. The patient suffers headache, nausea, vomiting, arrhythmia, convulsions, and coma.

**Hyperosmolar hyperhydration** develops in drinking salt (sea) water in extreme situations. As a result, the osmotic pressure in the extracellular medium increases, and the water passes from the cells into the intercellular space. Dehydration of the cells develops.

**Edema** is a typical pathologic process, which is characterized by positive water balance and accumulation of water in interstitial space.

**Principal pathogenic factors of edema:**



- **Increased hydrodynamic pressure in the venous** part of the vascular flow (local venous hyperemia, inflammation as well as cardiac insufficiency).
- **Decrease of colloid-osmotic blood pressure** (in decrease of the plasma protein content - hypoproteinemia – especially of the albumins in fasting, nephritic syndrome, hepatic insufficiency, etc.).
- **Increased permeability of the capillary vessels**, which occurs
  - under the influence of BAS (histamine, serotonin, kinines, prostaglandins, etc.);
  - in capillary wall dystrophy (fasting, disorder of neurotrophic supply etc.).
- **Increase of colloid-osmotic pressure in the tissue** due to accumulation of osmotic and oncotic active substances: electrolytes, proteins, metabolic products (in inflammation, allergy).
- **Disorder of lymph outflow** (mechanic or dynamic lymphatic insufficiency).
- Disorder of the nervous and humoral regulation of water-electrolyte balance (impaired sensitivity of volumo- and osmoreceptors, secondary aldosteronism, hypothyroidism).

#### Types:

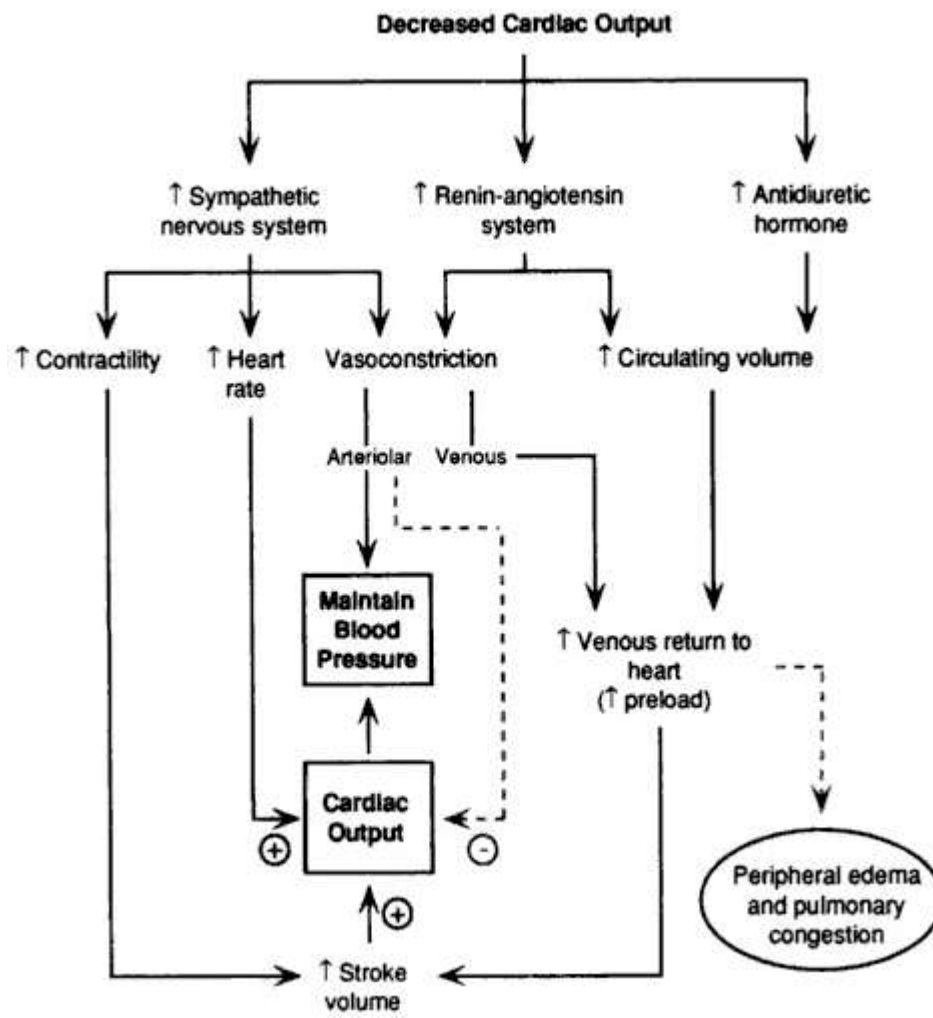
- Edema is divided into *local* and *systemic*.
- In accordance with pathogenesis (the main pathogenetic factor) edema is divided into *hydrodynamic*, *oncotic*, *osmotic*, *membranogenic*, *lymphogenic*.
- Clinical practice divides edema according to localization and causes into *inflammatory*, *allergic*, *toxic*, *venous*, *neurogenic*, *lymphogenic* (which are local) and *cardiac*, *fasting*, *nephritic*, *hepatic*, *endocrine* (which are systemic).

Etiology and pathogenesis of each type of edema are different.

**Inflammatory** and **allergic** types of edema. The leading component in pathogenesis of inflammatory and allergic edema is an **increased vascular permeability under BAS effect** (histamine, bradykinin and others). As a result, the **plasma proteins pass into tissue**. Blood oncotic pressure gets reduced. In the center of **inflammation** (allergic one also) **colloid-osmotic pressure rises**. Arterial and venous hyperemia, which are developed in the locus of inflammation, lead to an increase in the blood hydrodynamic pressure. Local acidosis contributes to colloid hydrophilia and an excessive binding of water.

**Toxic (membranogenic) edema** has analogous pathogenesis (edema after the bite of bee; phosgene causes selective increase of the pulmonary capillaries permeability and pulmonary edema).

**Venous edema** develops while the venous congestion, which is accompanied by an **increase in hydrodynamic pressure** and the filtration of the water.



**Neurogenic edema** develops as a result of the **nervous dysregulation of vessel trophicity** (angioneurosis) and **increase of the vessel permeability**. Edema of extremities in hemiparesis can be an example as well as edema of face in neuralgia of trigeminal nerve. Quincke's edema has the same pathogenesis.

**Lymphogenic edema** develops in the region of lymphostasis and disorder of lymph drainage, which compensates the accumulation of liquid in intercellular space in physiological condition.

Non-inflammatory fluid accumulated in different cavities and tissues is called **transudate**.

Pathologic accumulation of fluid in the serous cavities of the organism is called **hydrops**. The variants are **ascites** (in abdominal cavity), **hydrothorax** (in the pleural

cavity), **hydropericardium** (in the pericardium).

**Cardiac Edema** (Heart failure) **Hydrodynamic** factor is the main in pathogenesis (increase of hydrodynamic pressure in venous part of the capillaries). Due to decrease of contractile function of the heart, systemic increase of venous pressure develops (venous congestion). Resorption of liquid from interstitial space into the blood gets decreased.

**Nephrotic Edema.** **Hypoproteinemia** underlies the redistribution of water into the tissues according to the Starling's law, but positive water balance (total retention of water) has another explanation.

**Nephritic Edema Renin**, which is produced in **inflamed kidney** has two effects: an **increase of blood pressure** (by angiotensin II formation) and stimulation of **aldosterone** secretion.

#### **Pathogenesis of nephritic edema.**

→ ↓ number of functioning nephrons → reduced glomerular filtration → water and salt retention in the body → decrease blood flow in juxtaglomerular complex → activation of RAAS → delay electrolytes and water → increase BCV → arterial hypertension → increase hydrostatic pressure

**Hepatic Edema.** Limitation of the protein synthesis and hypoproteinemia underlie the pathogenesis. According to the Starling's law edema develops.

#### **Endocrine Edema**

The endocrine diseases are often accompanied by the development of edema.

**Myxedema** is a so-called *mucous edema* of the skin and subcutaneous cellular tissue which develops in hypofunction of the thyroid gland. **Colloids are accumulated** (collagen, glycosaminoglycans), which are **hydrophilic and bind enormous amount of the water**. Pressure by finger does not form a pit in the region of edema.

Diseases, which are accompanied by an increased aldosterone formation (primary or secondary hyperaldosteronism), are accompanied by edema.

**Starvation (Cachexic) Edema** Cachexic edema occurs in starvation and exhausting diseases. It develops during the **incomplete quantitative and qualitative (protein) starvation**. The pathogenetic basis of this form of edema is **hypoproteinemia** and decrease of oncotic blood pressure. According to Starling's laws the water leaves vascular channel and is accumulated in the interstitial space. During the first and the second periods of complete starvation with water, edema does not develop. On the contrary, the removal of excessive water from the organism and the reduction of edemas are observed. During the terminal period edema develops.

### **HYPOHYDRATION (DEHYDRATION)**

Hypohydration (dehydration, hypohydria, exicosis) is a negative water balance.

#### **Causes**

Hypohydration develops in the cases, when output of water exceeds its input into the organism. It may develop in water input limitation (water starvation, dysphagia, atresia of the esophagus, comatose condition, etc.). An increased water loss (diarrhea, vomiting, blood loss, loss of fluid with exudate in burn, etc.) has the same effect. The combination of these conditions may take place.

In dehydration, first of all, the extracellular fluid and sodium ions are lost. Ultimately, the cells may lose potassium and the intracellular fluid.

#### **Consequences**

Dehydration results in severe consequences connected with the decrease of the circulating blood volume (hypovolemia) and increase of its viscosity that may cause severe disorder of blood microcirculation. Collapse may eventuate.

Disorder of blood circulation results in the development of tissue hypoxia. The central nervous system suffers first of all. It is manifested by loss of consciousness, hallucinations and coma. The functions of the nervous centers, respiratory rhythm become disturbed. Body temperature rises.

The marked decrease of the arterial pressure may be accompanied by impairment of filtration in the nephrons, oliguria, hyperosmolemia and non-respiratory acidosis.

Compensatory reactions arise as a response. So, hypovolemia and reduction in renal blood flow promote hyperproduction of vasopressin and aldosterone. Water and sodium reabsorption in nephron tubules intensifies under the influence of these hormones.

#### **Isoosmolar Hypohydration**

**Isoosmolar hypohydration** occurs in proportional loss of fluids and electrolytes, as a rule, in the extracellular sector. Usually this condition arises **immediately after acute blood loss**. But it is changed for a short time and is substituted by hypoosmolar normovolemia due to compensatory mechanisms (immediate retention of water).

#### **Hypoosmolar Hypohydration**

Hypoosmolar hypohydration develops due to the loss of fluid enriched by electrolytes. This situation arises in **kidney pathology** (**increased filtration and decreased reabsorption of electrolytes**), **digestive tract** (**indomitable vomiting, diarrhea**), **adrenal glands insufficiency** (**decreased production of aldosterone**). Some of these conditions are accompanied by polyuria and hypoosmolar hypohydration.

Polyuria can lead to the extracellular hypoosmolar hypohydration. In case of a severe form of hypoosmolar hypohydration the water moves into the intracellular sector with development of the intracellular edema.

### Hyperosmolar Hypohydration

Hyperosmolar hypohydration develops due to the loss of fluid, which is poor in electrolytes. It may arise due to polyuria (deficit of ADH), diarrhea, profuse sweating, hyperventilation, vomiting.

Special attention should be drawn to diabetes mellitus as one of the causes of such pathology.

Under the conditions of hypoinsulinism osmotic polyuria develops but the level of blood glucose remains high. The increase of osmotic pressure in the extracellular fluid involves the movement of water from the cells into the extracellular sector. If the causative factor keeps on acting, the fluid is lost by the organism. It results in development of total hypohydration of the organism. The elevation of osmotic pressure of the extracellular fluid and dehydration of the cells causes thirst, protein lysis, fever, loss of consciousness, hyperosmolar diabetic coma. These disorders are based on hypoxia connected with hypovolemia and arterial hypotension.

Disorder of microcirculation, hemoconcentration, increasing of blood viscosity and stasis aventuate the tissue form of hypoxia. Hypoxia combined with tissue dehydration leads to dismetabolism: protein lysis and development of hypernitroemia (at the expense of ammonium because of kidney dysfunction), hyperproduction of urea (kidney dysfunction). Acidosis (due to the sodium and bicarbonates loss) or alkalosis (due to the potassium and chlorine loss) occur.

### Electrolyte Disbalance

Electrolyte	Excess	Deficit
Sodium	Hypernatremia > 147 mEq/L. Cellular shrinking may cause central nervous system irritability, tachycardia, dry and flushed skin, arterial hypertension, thirst, elevated temperature, weight loss, oliguria, anuria	Hyponatremia < 135 mEq/L. Cellular swelling may cause cerebral edema, polyuria, headache, stupor, coma, peripheral edema, absence of thirst, decreased body temperature, tachycardia, arterial hypotension, nausea, vomiting
Potassium	Hyperkalemia > 5.5 mEq/L. Depressed conductivity in heart, muscle cramping, parasthesia, nausea, diarrhea, metabolic acidosis	Hypokalemia < 3.5 mEq/L. Cardiac irritability, dysrhythmia, vomiting, paralytic ileus, thirst, metabolic alkalosis, inability to concentrate the urine
Calcium	Hypercalcemia > 12mg/dl. Decreased neuromuscular excitability, muscle weakness, central nervous system depression, stupor, coma, increased risk of bone fracture, vomiting, kidney concrements.	Hypocalcemia < 8.5 mg/dl Increased neuromuscular excitability, skeletal muscle cramps, tetany, laryngospasm, asphyxia, death.
Phosphate	Hyperphosphatemia > 4.5 mg/dl. ( See hypokalemia).	Hypophosphatemia < 2 mg/dl Skeletal muscle depression, muscle weakness, arterial hypotension, bradycardia, respiratory depression.
Magnesium	Hypermagnesemia > 2.5 mEq/L. Anorexia, muscle weakness, tremor, seizures, coma, anemia, bleeding, eukocytes alteration	Hypomagnesemia < 1.5mEq/L Hypocalcemia and hypokalemia, neuromuscular irritability, tetany, convulsions, tachycardia, arterial hypertension

### Questions for self-control of knowledge:

1. Blood buffer systems.
2. Genderson-Gesselbach's formula
3. Physiological mechanisms of acid-base balance control.
4. Mechanisms of lactate-acidosis development
5. Interactions between control mechanisms of acid-base balance and electrolyte-water exchange (give the examples).
6. Sodium metabolism impairments.
7. Potassium metabolism impairments.
8. Calcium metabolism impairments.
9. Magnesium metabolism impairments.
10. Etiology and pathogenesis of edema development (cardiac, nephritic, nephrotic, inflammatory, starvation, allergic).

### Tasks for self-managed student work:

1. Mechanisms of ABS violations in diabetic coma;
2. Edema: types, mechanisms of development, manifestations, modeling.
3. Principles of modern diagnosis and correction of ABS violations.

## Literature

### Basis literature:

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### Compiler:

senior lector

K.A. Kidun