S.V. LELEVICH, T.V. POPECHITS

CLINICAL BIOCHEMISTRY

Manual for 4th year students of the foreign faculty

GRODNO 2010

MINISTRY OF HEALTH OF THE REPUBLIC OF BELARUS

INSTITUTION OF EDUCATION
GRODNO STATE MEDICAL UNIVERSITY

Department of Anesthesiology and Reanimatology
with the course of Clinical Biochemistry

S.V. Lelevich, T.V. Popechits

CLINICAL BIOCHEMISTRY
Manual for 4th year students of the foreign faculty

Grodno 2010

УДК
ББК

Recommended by the Central Scientific- Methodical Soviet EI «GrSMU» (Protocol № 2010 yr.)

Authors: ass. of the Department of Anesthesiology and Reanimatology with the course of Clinical Biochemistry of EI «Grodno State Medical University», cand. of med. sciences S.V. Lelevich

ass. of the Department of Anesthesiology and Reanimatology with the course of Clinical Biochemistry of EI «Grodno State Medical University», T.V. Popechits

Rewiever: head of the Department of Physiology of EI «Grodno State Medical University», cand. of med. sciences, associate professor, O.A. Balbatun

This manual provides information about laboratory evaluation of acid-base balance and blood gases, protein, carbohydrate, water and electrolyte metabolism and enzyme tests. Manual also contains data about regulation of the main metabolic processes and laboratory parameters for their evaluation. Manual describes disturbances of acid-base balance and metabolism, their laboratory diagnostics. Moreover, this manual contains 170 tests with answers.

CONTENTS

PREFACE

Clinical biochemistry is a clinical and diagnostics subject, which aims to put forward, improve and use standard diagnostic methods, to monitor disease development and treatment by biochemical methods. Clinical biochemistry helps to make diagnosis, choice of treatment and prophylactic methods easier.

Clinical biochemistry is one of the most important parts of laboratory diagnostics together with laboratory haematology, immunology, clinical serology and microbiology, clinical toxicology. It possesses the largest number of diagnostic tests that help understand pathogenesis and etiology of different pathological processes. Information, obtained by biochemical methods help to evaluate the development of pathological process on molecular, cellular and organ level. It is essential for early diagnosis of a disease and also assessment of its therapy efficacy.

Clinical biochemistry is evolving rapidly in our era. During the last ten years, more than a hundred of new analytical methods have appeared, including DNA-diagnostics, determination of tumor markers, apoptosis tests. Biochemical tests are of great importance in diagnosis of endocrine, gastrointestinal, heart and renal diseases as well as in toxicology. Clinical biochemistry is closely linked to such theoretical subjects as general and bioorganic chemistry, biochemistry, histology, normal and pathological physiology, normal and pathological anatomy.

This manual provides useful information about modern principles of evaluation of protein and carbohydrate metabolism, water and electrolyte balance, acid-base balance and enzyme tests.

The information provided in this manual helps to come up with optimal schemes and algorhythms of laboratory diagnostics of numerous pathological conditions including their treatment efficacy monitoring.

LABORATORY EVALUATION OF ACID-BASE BALANCE AND ARTERIAL BLOOD GAS

Balance between acid and base is essential for many metabolic processes. Reaction of any solution depends on free hydrogen ions concentration ($[H^+]$). The term used to indicate $[H^+]$ is pH. pH is negative logarithm of hydrogen ions concentration:

$$\mathbf{pH = - lg\ [H^+]}$$

pH depends on balance between $[HCO_3^-]$ and CO_2. CO_2 concentration is regulated by lungs. Bicarbonate ion $[HCO_3^-]$ is a base, metabolized mainly in kidneys. CO_2 dissolves in plasma, forming carbonic acid (H_2CO_3), which is main acid component of blood. As it's difficult to determine H_2CO_3 concentration directly, acid component is expressed as carbon dioxide concentration.

In norm CO_2 to HCO_3^- ratio is approximately 1/20. In different cases of acid-base disturbances when acid content increases – acidosis will develop, if base – alkalosis.

The constancy of pH is maintained by several mechanisms. They are sensitive enough to minimal changes in pH, and allow keeping pH in normal range for a long time.

REGULATION OF ACID-BASE BALANCE

Physiological buffers

In the first instance pH is maintained by physiological buffers. Buffers may be intracellular and extracellular. Different buffer systems work in correlation with one another. It means that changes in one buffer system lead to changes in another.

Buffers are solutions of weak acids together with their conjugate bases which diminish the change in pH which would otherwise occur from the addition of acid or base.

The main buffer systems are the following:

1. ***Bicarbonate buffer:*** the most important extracellular buffer, produced by kidneys, has the largest buffering capacity.
2. ***Haemoglobin buffer:*** main intracellular buffer of the blood.
3. ***Protein buffer:*** is an extracellular buffer together with bicarbonate buffer, represented by plasma proteins.
4. ***Phosphate buffer:*** takes part in hydrogen ions excretion in renal tubules, is not of great importance in blood.

Table 1. **Main blood buffer systems**

Buffer system	Buffering capacity (%)
Bicarbonate	53
Haemoglobin	35
Protein	7
Phosphate	5

Cellular mechanisms of regulation of acid-base

Change in blood pH causes activation of cellular mechanisms of maintaining constancy of hydrogen ions concentration in extracellular fluid:

- If pH increases hydrogen ions move from cells to extracellular fluid in exchange of potassium ions that enter the cells. That's why alkalosis is usually accompanied by hypokalaemia.
- If pH decreases hydrogen ions enter the cells in exchange of potassium ions that leaves the cells. That's why acidosis may cause hyperkalaemia.

In such a way electroneutrality law is maintained by cellular regulation. According to it, the sum of the positive and negative charges (of cations and anions) is equal. So, hydrogen to potassium exchange between ECF and ICF should be equal.

Organ mechanisms of regulation of acid-base

Respiratory mechanisms

Lungs are responsible for volatile acid (carbon dioxide) elimination. CO_2 content in plasma depends on alveolar ventilation. Changes in pH lead to stimulation of chemoreceptors in the brain stem, causing a compensatory mechanism; therefore changing the respiratory rate.

In acidosis alveolar ventilation increases, $PaCO_2$ decreases and pH tends to return to norm. These changes occur rapidly, but it takes 12 to 24 hours to stabilize acid-base status.

Alkalosis causes hypoventilation and rise in $PaCO_2$, that leads to fall in pH.

Renal mechanisms

Renal mechanisms are the most complex and effective. Renal compensation occurs by three main mechanisms:

1. Bicarbonate ions reabsorption in proximal tubules
2. Bicarbonate ions regeneration in distal tubules
3. Hydrogen ions excretion.

CO_2 reacts with water to produce carbonic acid into the renal tubular cells. Carbonic acid dissociates to yield H^+ and HCO_3^-. Reaction is catalyzed by carbonic anhydrase. Bicarbonate ion enter the systemic circulation, H^+ is secreted into the lumen. The secretion of H^+ is coupled to the reabsorption of Na^+ and electroneutrality preserved. The secreted H^+ reacts with filtered bicarbonate to produce carbonic acid that dissociate into carbon dioxide and water.

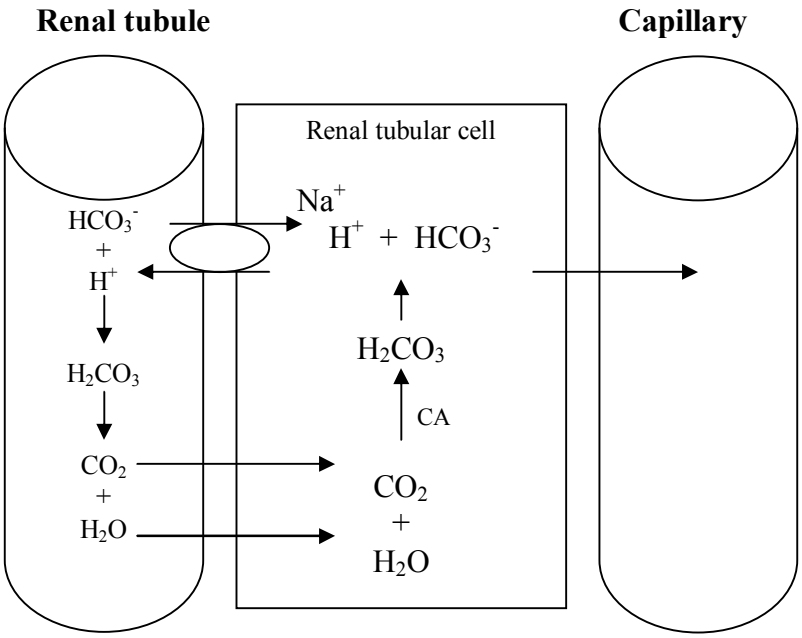


Fig. 1. **Mechanism of bicarbonate ions reabsorption in exchange of Na^+**

Hydrogen ions excretion begins at the second stage when the whole bicarbonate is reabsorbed.

HPO_4^{2-} ion can't be reabsorbed from renal tubules because of charge, but it can bind secreted hydrogen ions. Produced $H_2PO_4^-$ is excreted in urine, HCO_3^- - is reabsorbed into the blood. H^+ buffered by HPO_4^{2-} accounts for the titratable acidity (TA).

$H_2PO_4^-$/ HPO_4^{2-} is an ideal urinary buffer. This mechanism is able to decrease urinary pH to 4,8 (compared with blood pH 7,4). When this level is achieved, phosphate enters renal tubules as $H_2PO_4^-$ ion, which is not able to accept protons. This states depletion of the phosphate buffer reserve and activation of renal ammoniogenesis.

After depletion of the latter two mechanisms, the kidneys switch to ammonia buffer (NH_3/NH_4^+). The main source of ammonia is glutamine desamination. As NH_3 has no charge, it moves freely across the tubular cell membrane and appears in the urine, where it binds secreted proton to produce ammonium ions (NH_4^+). NH_4^+ can't be reabsorbed because of its charge. This process is termed as ammoniogenesis.

Tab. 2. **Main parameters for acid-base balance evaluation**

Parameter	**REFERENCE VALUES (for arterial blood)**
pH	7,35-7,45
pCO_2	35-45 mm Hg
HCO_3	21-27 mmol/l
BE (base excess or deficit)	0 ± 2,5 mmol/l

BE= BB – NBB

BB – actual buffer base
NBB – normal buffer base (pH=7,4 ед., pCO_2= 40 мм.рт.ст., t тела=37°)

Additional

- ***Anion gap (AG):***

$$\mathbf{AG = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])} \text{ (8-16 mmol/l)}$$

Anion gap is a sum of anions that can't be measured directly in blood serum (anions of organic and non-organic acids, proteins). AG consists of phosphates, sulfates, pyruvate, lactate, ketone bodies and others.

- ***Arterial blood gases parameters*** (PaO_2, ctHb, SO_2, PvO_2, lactate)
- ***Urinary parameters:***
- ***pH*** (4,5-7,5)
- ***Titratable acidity (TA)*** (10-30mmol/l)
- $[NH_4^+]$ (30-50 mmol/l)
- ***[H+]net*** – summary of hydrogen ions excreted in urine (30-80 mmol/24h)

$$\mathbf{[H^+] \text{ net} = ([NH_4^+] + TA) - [HCO_3^-]}$$

ACID-BASE BALANCE DISTURBANCES

There are several classifications of acid-base balance disturbances. The main ones are shown in table 3.

Tab.3. **Acid-base balance disturbances**

PARAMETER	TYPE OF DISTURBANCE
Blood pH	Acidosis Alkalosis
Primary disturbance	Respiratory Metabolic Mixed Combined
Compensation	Compensated Subcompensated Non-compensated

Compensation tends to normalize $[HCO_3^-]$ to pCO_2 ratio in extracellular fluid. If due to any pathological process any primary change of metabolic parameter (plasma bicarbonate concentration) occurs, respiratory parameter (pCO_2) also should change in the same direction due to compensation.

Table 4 presents compensatory changes of different types of acid-base balance disturbances**.**

Tab.4. **Compensation of acid-base balance disturbances**

Type of disturbance	**$[H^+]$**	**pH**	**Primary disturbance**	**Compensation**
Metabolic acidosis	↑	↓	↓$[HCO_3^-]$	↓pCO_2
Metabolic alkalosis	↓	↑	↑$[HCO_3^-]$	↑pCO_2
Respiratory acidosis	↑	↓	↑pCO_2	↑$[HCO_3^-]$
Respiratory alkalosis	↓	↑	↓pCO_2	↓$[HCO_3^-]$

Here the main types of acid-base balance disturbances are described more in details.

Respiratory Alkalosis

Respiratory alkalosis is defined as a pH greater than 7.45 with a pCO2 less than 35 mm Hg. Respiratory alkalosis appears if removal of CO2 is greater than it`s production by tissues.

$$\uparrow pH = pK + \lg \frac{[HCO_3^-]}{pCO_2 \times s\downarrow}$$

Acute Respiratory Alkalosis

$pCO_2 - \downarrow$; $[HCO_3^-]$ – normal or↓; pH – ↑

Chronic Respiratory Alkalosis

$pCO_2 - \downarrow$; $[HCO_3^-] - \downarrow$; pH – ↑ or normal

Any condition that causes hyperventilation can result in respiratory alkalosis. These conditions include:

1. Increased metabolic demands, such as high fever, sepsis, pregnancy, or thyrotoxicosis
2. Psychological responses, such as anxiety or fear
3. Central nervous system lesions, raised intracranial pressure, which may stimulate the respiratory center
4. Hysterical overbreathing
5. Mountain sickness
6. Lack of oxygen, hypoxia
7. CNS injury, neuroinfection, cerebral haemorrage, brain tumor
8. Salicylate overdosage or other respiratory stimulants (theophyllin, estrogens).
9. Excessive artificial respiration
10. Pulmonary diseases: lobar pneumonia, asthma, pulmonary oedema, pulmonary collapse or fibrosis, pulmonary embolism.

Compensatory mechanism: glomerular filtration of bicarbonate ion, lowering of bicarbonate regeneration, because the fall in pCO2 slows the carbonic anhydrase mechanism in renal tubules. The compensatory fall in $[HCO_3^-]$ tends to correct pH.

Respiratory Acidosis

Respiratory acidosis is defined as a pH less than 7.35 with a $PaCO_2$ greater than 45 mm Hg.

Acidosis is caused by an accumulation of CO_2, lowering the pH of the blood.

$$\downarrow pH = pK + \lg \frac{[HCO_3^-]}{pCO_2 \times s \uparrow}$$

Acute Respiratory Acidosis

$pCO_2 - \uparrow$; $[HCO_3^-]$ – normal; pH – $\downarrow$

Chronic Respiratory Acidosis

$pCO_2 - \uparrow$; $[HCO_3^-] - \uparrow$; pH – $\downarrow$

Any condition that results in hypoventilation can cause respiratory acidosis. These conditions include:

1. Respiratory center depression:

• Central nervous system depression related to head injury, neuroinfection, stroke, brain tumor, increased intracranial pressure;

• Central nervous system depression related to medications such as narcotics, tranquilizes, sedatives, barbiturates, or anesthetics;

2. Neuromuscular diseases:

• Impaired respiratory muscle function related to spinal cord injury, or neuromuscular blocking drugs, poliomyelitis, Guillian-Barr syndrome, muscular dystrophy, hypokalaemia.;

3. Chest abnormalities:

• Hypoventilation due to pain, chest wall injury/deformity (kyphoscoliosis), abdominal distension, pneumotorax, hydrothorax;

4. Pulmonary disorders:

• Atelectasis, pneumonia, bronchitis,asthma, pulmonary oedema, emphysema, or bronchial obstruction

• Massive pulmonary embolus

Compensatory mechanism: renal reabsorbtion of bicarbonate ion.

Metabolic Alkalosis

Metabolic alkalosis is defined as a bicarbonate level greater than 26 mEq/liter with a pH greater than 7.45. Either an excess of base or a loss of acid within the body can cause metabolic alkalosis.

$$\uparrow pH = pK + \lg \frac{[HCO_3^-] \uparrow}{pCO_2 \times s}$$

Causes of Metabolic Alkalosis

1. **Saline-responsive urinary chloride excretion < 20 mmol/l (chloride depletion):**

- gastric losses: vomiting, mechanical drainage, gastric aspiration;
- diarrhoeal states: villous adenoma, congenital chloridorrhoea;
- diuretic therapy, e.g. furosemide, chlorothiazide, bumetanide;
- cystic fibrosis (high sweat chloride);
- acute or chronic milk-alkali syndrome (in patients, who drink lots of milk or calcium- containing antacids;
- exogenous alkali (sodium citrate, lactate, gluconate, acetate);
- massive blood transfusion;
- bicarbonate ingestion : massive or with renal insufficiency.

2. **Saline-unresponsive urinary chloride excretion < 20 mmol/l (Potassium depletion/ Mineralocorticoid excess):**

- primary hyperaldosteronism (Conn`s syndrome);
- secondary hyperaldosteronism;
- Cushing`s syndrome;
- Liddle`s syndrome (hypermineralocorticism, hypertension and hypokalaemic alkalosis).

Compensatory mechanism: hypoventilation.

Metabolic Acidosis

Metabolic acidosis is defined as a bicarbonate level of less than 22 mEq/l with a pH of less than 7,35.

Metabolic acidosis is caused by either a deficit of base in the bloodstream or an excess of acids, other than CO_2.

$$\downarrow pH = pK + \lg \frac{[HCO_3^-] \downarrow}{pCO_2 \times s}$$

Causes of Metabolic Acidosis

1. Kidney dysfunction, that results in retention of nonvolatile acids; impairment of the ability of renal tubules to generate bicarbonate ions (distal renal tubular acidosis); renal losses of bicarbonate (proximal renal tubular acidosis).
2. Increased endogenous organic acids production:
   - ketoacidosis due to insulin deficiency (diabetic ketoacidosis) or due to lack of glycogen (starvation);
   - enzyme defects;
   - lactic acidosis due to tissue hypoxia
3. Intake of exogenous acids, their precursors, or substances, that block certain metabolic pathways, that leads to nonvolatile acids accumulation in the body (poisoning by salicylate, ammonium chloride, methanol, ethanol, ethylene glycol).
4. Gastrointestinal bicarbonate loss: diarrhoea, GIT drainage.

Classification of Metabolic Acidosis according to anion gap

1. High-anion-gap acidosis:
   - renal failure
   - ketoacidosis
   - lactic acidosis
   - poisoning by salicylate, methanol, ethanol, ethylene glycol.
2. Metabolic acidosis with a normal anion gap or acidosis with hyperchloridaemia:

with hypokalaemia

- diarrhoea;
- distal renal tubular acidosis;
- carbonic anhydrase inhibitors intake (acetazolamide);
- ureterosigmoidostomy, colono-vesical fistulae.

with hyperkalaemia

- uraemic acidosis;
- obstructive uropathy;
- NH4Cl, HCl overdosage;
- mineralocorticoid deficiency (renal tubular acidosis type 4);

Acidosis with high nonvolatile acids production includes:

- Metabolic ketoacidosis
- Metabolic lactic acidosis
- Metabolic acidosis of another etiology

Ketoacidosis classification by etiology:

- diabetic ketoacidosis

- ketoacidosis due to starvation
- ketoacidosis due to alcohol excess
- ketoacidosis of another etiology.

Lactic acidosis is defined as acidosis with high lactate level in arterial blood (more than 2,2 mmol/l).

Classification of lactic acidosis

1. *Lactic acidosis type A (because of lack of oxygen in the tissues):*

- cardiovascular failure (cardiogenic or hypovolaemic shock);
- septic shock;
- severe anemia;
- hypoxia.

2. *Lactic acidosis type B (because of impaired oxygen utilization in tissues):*

- drug-induced lactic acidosis(poisoning by salicylate, methanol, ethanol, biguanides);
- sodium hydrogen carbonate infusions
- inherited enzyme defects (G-6-PD deficiency, 1,6-diphosphofructokinase deficiency)
- insulin deficiency (diabetes mellitus)
- hepatitis;
- renal failure;
- haematological malignancies (leukemia).

Compensatory mechanism: hyperventilation through stimulation of central chemoreceptors.

LABORATORY EVALUATION OF BLOOD GASES

<u>Respiratory component of oxygen transport:</u>

- ***PaO_2*** – partial pressure of oxygen in arterial blood (80-107 mm Hg)
- ***% of intrapulmonary shunting (Shunt)*** (up to 5%)
- ***D (A-a)pO_2*** – alveolar to arterial oxygen gradient (5-15 mm Hg)

<u>Blood component of oxygen transport:</u>

- ***ctHb*** — total haemoglobin concentration:

$$ctHb = cH^{+}\text{-}Hb + cO_2\text{-}Hb + cCO\text{-}Hb + cMet\text{-}Hb$$

(m.- 130-160 g/l; f. - 120-140 g/l)

- ***SO_2*** – oxygen saturation (actual oxygen combined with haemoglobin) (95-98%)
- ***[2,3–DPG]*** – 2,3-diphosphoglycerate concentration in erythrocytes (4,1 -5,6 mmol/l)
- ***ctO_2 (tO_2)*** – oxygen content of blood (volume of oxygen combined with haemoglobin plus that physically dissolved)
  (m. - 8,4-9,9 mmol/l;
  f. - 7,1-8,9 mmol/l)

- p_{50} - partial pressure of oxygen in arterial blood at 50% saturation in standard conditions (25-29mm Hg)

Tissue component of oxygen transport:

- ***D (a-v)O_2*** – arterial to venous oxygen gradient (1,9-3,2 mmol/l)
- ***PvO_2*** – partial pressure of oxygen in mixed venous blood (35-45mm Hg)
- ***P_x*** – pressure of oxygen extraction (38 mm Hg)
- ***Cx*** — extracted oxygen concentration (volume of O_2 extracted from 1 liter of blood in following conditions: partial pressure of oxygen in mixed venous blood 38 mm Hg and constant pH and pCO_2)
  (2,3 mmol/l)
- ***Blood lactate concentration***
  (0,5-2,2 mmol/l)

LABORATORY EVALUATION OF WATER AND ELECTROLYTE BALANCE

Water is nearly 60% of body weight in adults. Water content decreases with age (Tab. 5).

Table 5. **Water content in the organism**

Age group	% of body weight
Newborns	75-80%
Adults under 60	60%
Adults >60 Male Female	 54% 46%

Water distribution mainly is observed between two compartments:

- Intracellular fluid (ICF)
- Extracellular fluid (ECF), which includes:
  - intravascular fluid;
  - interstitial fluid;
  - transcellular fluid.

The predominant ions of ECF are sodium cation, chloride anion and bicarbonate anion. The predominant ions of ICF are potassium cation (156 mEq/kg H_2O), phosphate anion (95 mEq/kg H_2O) and protein anion (5,5 mEq/kg H_2O). Ion distribution in extracellular fluid is not uniform. Protein concentration in plasma is 60-80 g/l, and in interstitial fluid − 15-20 g/l.

Difference in distribution of ions in different water compartments is achieved by selective permeability of biological membranes and active transport. In every fluid compartment the sum of anions and cations (positive and negative charges) are equal.

Table 6 represents ion composition of blood serum.

Table 6. **Anion and cation distribution in blood serum**

Cations	mmol/l	Anions	mmol/l
Sodium	135-145	Chloride	96-107
Potassium	3,5-5,2	Bicarbonate	21-27
Calcium	2,12-2,6	AG	8-16
Magnesium	0,8-1		

Osmotic pressure and osmolality

Osmotic pressure occurs due to osmotic active substances to selectively permeable membrane (permeable to water only). One mmol of a substance, diluted in one kg of water, if it is separated by a selectively permeable membrane from distillated

water on one side, provides pressure of 17 mm Hg. This amount of a substance is called ***milliosmole***.

Total osmolality of body fluids depends on:

- Concentration of free particles of diluted osmotic active substance;
- Activity of particles of diluted substance;
- Water content.

Total plasma osmolality is calculated according to the formula:

$$\mathbf{Osm_{pl}=2\ x\ [Na]+[glucose]+[urea]}$$

Osmolality also can be measured by osmometer cryoscopically. Freezing point of solution depends on its total osmolality.

Normal range – 285±5 mOsm/kg H_2O

Effective osmotic pressure of ECF is mainly provided by sodium ions. Effective plasma osmolality is calculated by the following formula:

$$\mathbf{Osm_{ef.}=2\ x\ [Na]+[glucose]}$$

Osmotic gap is the difference between measured and calculated osmolality. This parameter has clinical significance.

Normal values – below 10 mOsm/kg H_2O

Sodium metabolism regulation

If sodium intake is stable its excretion in the urine is equal to its intake. Total amount of filtrated sodium in primary urine is nearly 22500 mmol daily. 90 % is reabsorbed in proximal renal tubules, 9 % - in distal. Nearly 1 % of sodium is excreted in the urine. Such parameter as ***fractional excretion of sodium*** (**Fe_{Na}**) is used for sodium excretion estimation:

$$\mathbf{Fe_{Na} = [Na^+_{urine}] / [Na^+_{plasma}]\ \ x\ [Creatinine_{\ plasma}] / [Creatinine_{\ urine}]\ \ x\ 100\ \%}$$

Normal values – below 1%. Increase above 1,5 % is considered to be clinically significant.

In proximal tubules sodium reabsorption depends on glomerular filtration rate. In distal tubules it is regulated by aldosterone. Increased sodium reabsorption in this part of nephron is accompanied by increased excretion of potassium and hydrogen ions.

Aldosterone secretion is regulated mainly by renin-angiotensin-aldosterone system:

- Decreased plasma volume leads to decreased renal blood flow and total sodium charge. It results in stimulation of juxtaglomerular apparatus and high renin secretion.
- Renin converts angiotensinogen into angiotensin-I.
- Angiotensin-I is subsequently cleaved to angiotensin-II by angiotensin-converting enzyme (ACE).
- Angiotensin-II directly stimulates adrenal cortex to secrete aldosterone.

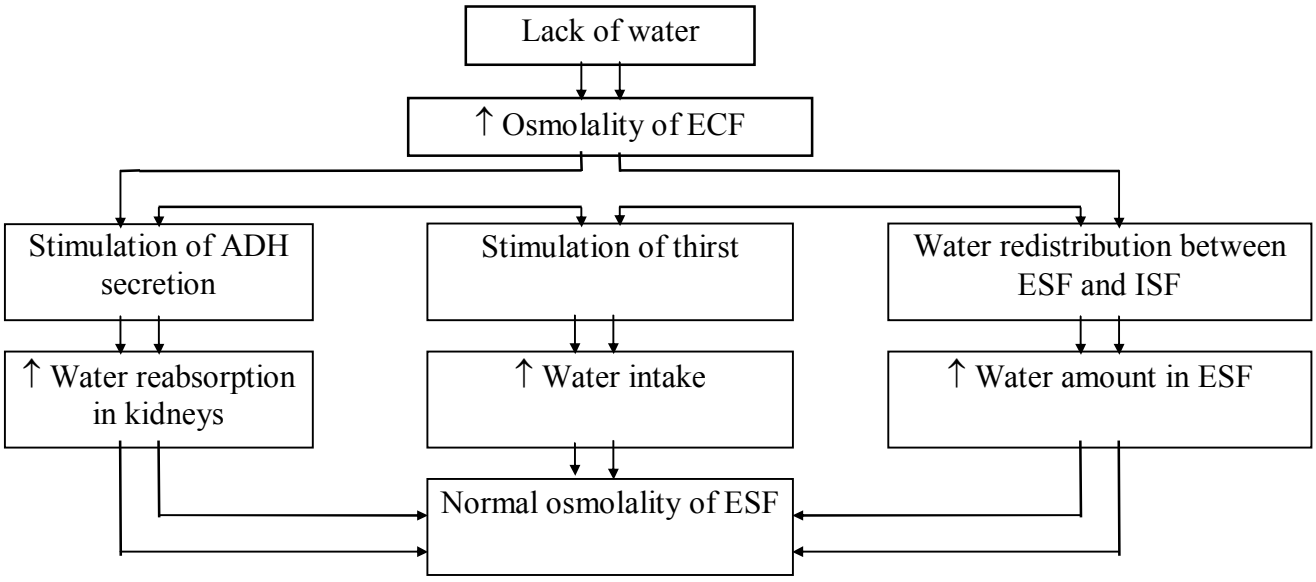
Increase in extracellular volume stimulates release of atrial natriuretic factor (ANF). It increases sodium excretion and excretion of an equivalent amount of water. It also suppresses aldosterone synthesis.

Water metabolism regulation

Water is excreted from the organism mainly by kidneys, GIT, lungs and skin. Water loss is compensated by water intake with food and beverages, and also some water is derived from metabolic processes (nearly 300 ml daily). If water intake is restricted, its excretion occurs mainly by kidneys and least – through lungs and skin.

Water excretion by kidneys is regulated by antidiuretic hormone (ADH). It stimulates water reabsorption in the distal part of the nephron (Fig.2).

Fig.2. **Physiological response to water depletion**



Parameters for the assessment of water and electrolyte metabolism

Extracellular fluid volume can be assessed using the following parameters:

- Red blood cells count in peripheral blood
- Total protein (albumin) concentration in plasma
- Haemoglobin concentration
- Haematocrit (depends on volume of extra- and intracellular fluid)

Intracellular fluid volume can be assessed with the help of:

- Sodium concentration in blood serum
- Plasma osmolality
- Mean corpuscular volume (MCV)
- Mean corpuscular haemoglobin (MCH)

Reference values of these parameters are showed in the following table 7.

Table. 7. **The main parameters for the assessment of water and electrolyte metabolism**

Parameter	Reference values
Erythrocytes	Male – 4,0-5,0 x 10^{12}/l Female– 3,7-4,7 x 10^{12}/l
Total protein	65-85 g/l
Haemoglobin	Male – 130-160 g/l Female – 120-140 g/l
Ht	Male – 45-55 % Female – 37-47 %
Na^+	135-145 mmol/l
Plasma osmolality	275-295 mosm/kg
MCV	80-93 fl
MCH	27-31 pg

Disturbances of water and electrolyte metabolism

The main types of disturbances of water and electrolyte metabolism are dehydration and hyperhydration.

Dehydration is a state of negative water balance.

Hyperhydration is a state of positive water balance.

Disturbances of water and electrolyte metabolism are divided into three groups according to sodium concentration and osmolality:

- **Isotonic –** plasma osmolality - 275-295 mOsm/kg, [Na] - 135-145 mmol/l. Sodium and water are lost in almost equivalent amount.
- **Hypotonic –** plasma osmolality <275 мОсм/кг, [Na]<135 mmol/l. Water loss or retention is predominant.
- **Hypertonic –** plasma osmolality >295 мОсм/кг, [Na]>145 mmol/l. Sodium loss or retention predominates.

Dehydration

The reasons of water deficiency are restricted water intake or increased water loss. Restriction of water intake occurs rarely in clinical practice.

The main reasons of water loss are:

1. Diabetes insipidus
    - Central
    - Nephrogenous

2. Increased perspiration
3. Profuse diarrhoea
4. Hyperventilation

In these cases hypotonic fluid is lost from the body. Increase in plasma osmolality causes intracellular water to move into the blood vessels, but it can not compensate hyperosmolality completely. As such dehydration is partially compensated by intracellular deposit, clinical signs will not be severe.

Central diabetes insipidus often occurs after neurosurgical operations and craniocerebral traumas. The reason of this disease is injury of pituitary gland or hypothalamus which is accompanied by decreased ADH secretion. These patients develop polydipsia and polyuria without glucosuria.

Nephrogenous diabetes insipidus usually develops as a result of chronic renal pathology. The reason of this pathology is low sensitivity of receptors to ADH in renal tubules. Clinical features are the same as in central diabetes insipidus. However, after ADH administration diuresis does not decrease.

Sodium deficiency

The reasons of sodium deficiency are increased sodium excretion or restricted intake.

Causes of sodium deficiency:

1. Renal losses
   - ARF, polyuric stage
   - Diuretic intake
   - Mineralocorticoids deficiency
   - Osmotic diuresis (in diabetes mellitus)
2. Skin losses
   - Dermatitis
   - Burns
   - Cystic fibrosis
3. Intestinal losses
   - Vomiting
   - Diarrhoea
   - Intestinal obstruction

Sodium can be lost with hypo- and isotonic fluid. In both cases the volume of extracellular fluid decreases. It leads to stimulation of volume receptors and aldosterone secretion.

In the cases of sodium loss its serum concentration does not reflect the total sodium level in organism, as the level depends on simultaneous water loss. If sodium is lost with hypotonic fluid its plasma concentration will be high. If sodium loss is combined with water retention, the level will be lower than normal. Loss of equivalent amount of water and sodium does not influence its plasma concentration.

Diagnostic of sodium and water loss predominance is shown in the table 8.

Table 8 . **Diagnostic of sodium and water loss predominance**

Parameter	Predominant saline loss (hypotonic dehydration)	Predominant water loss (hypertonic dehydration)
Serum sodium	N or ↑	↑
Haematocrit	↑↑	insignificant ↑
Serum urea	↑	N
Urinary volume	↓	↓↓
Specific gravity	↑	↑↑

In the case of excess water loss, the osmolality of ECF increases, which is based on water molecules movement from the cells to the interstitial fluid and vessels. In this case, the clinical features will be mild.

In clinical practice, the severity of dehydration of extracellular space is divided into three degrees. (Table. 9).

Table. 9. **Clinical diagnosis of severity of dehydration (WHO)**

Degree of severity of dehydration	% of weight loss	Clinical signs
I	3-6	Thirst, dryness of skin, tachycardia
II	6-9	Thirst, dryness of skin, tachycardia, oliguria, hypotension
III	More than 9	Thirst, dryness of skin, tachycardia, oliguria, hypotension, disorders of consciousness

Hyperhydration

This type of disturbance is usually due to water retention. Clinical signs of water intoxication present as a result of cerebral oedema. Risk of cerebral oedema appears if sodium concentration in serum approaches 120 mmol/l.

Sodium excess

The reasons of sodium excess are decreased sodium excretion or excessive intake.

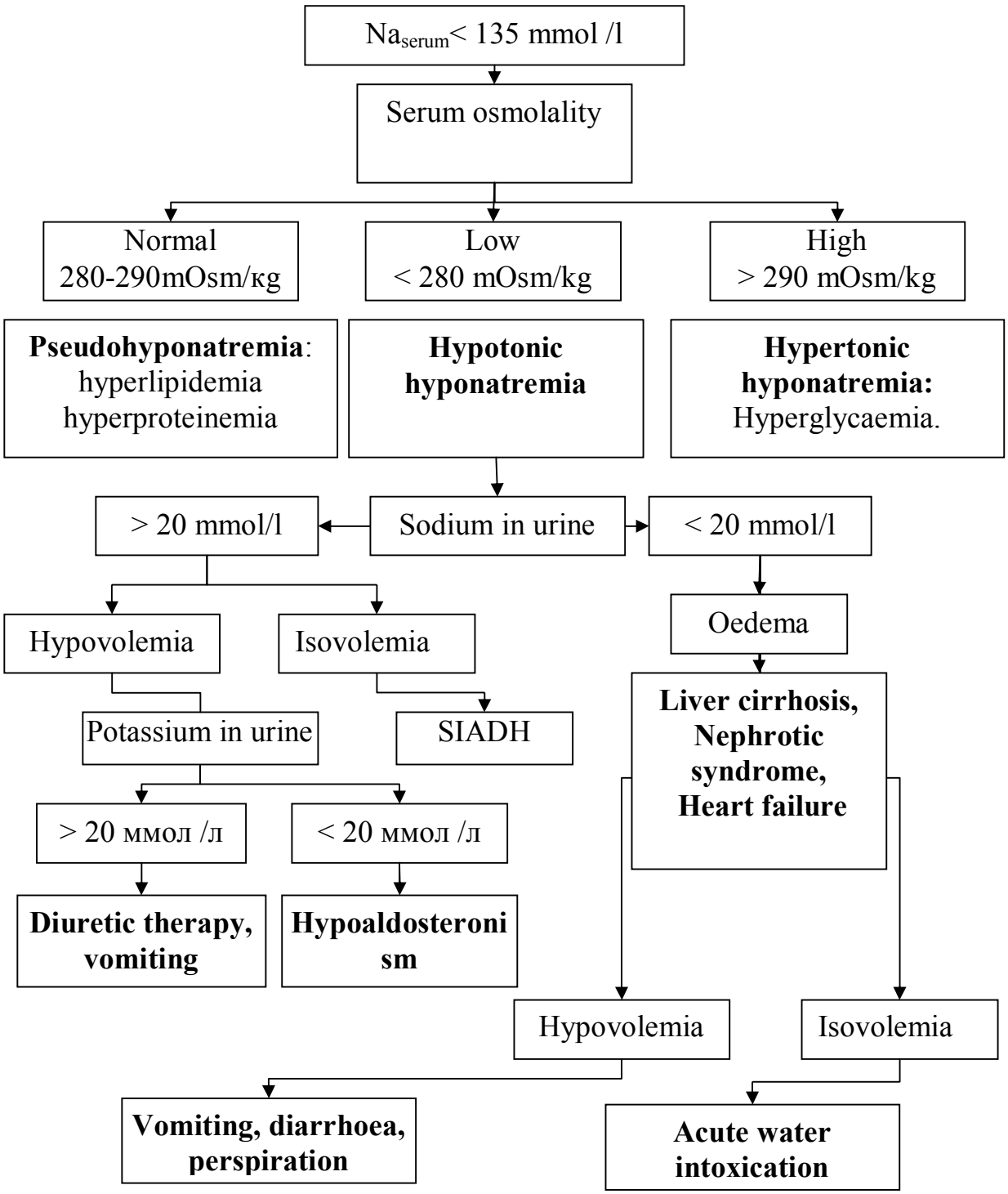
Causes of decreased excretion:

1. Decreased glomerular filtration rate (ARF, CRF)
2. Increased tubular reabsorption (mineralocorticoids excess, Conn syndrome, Cushing syndrome)
3. Secondary hyperaldosteronism
    - Congestive heart failure

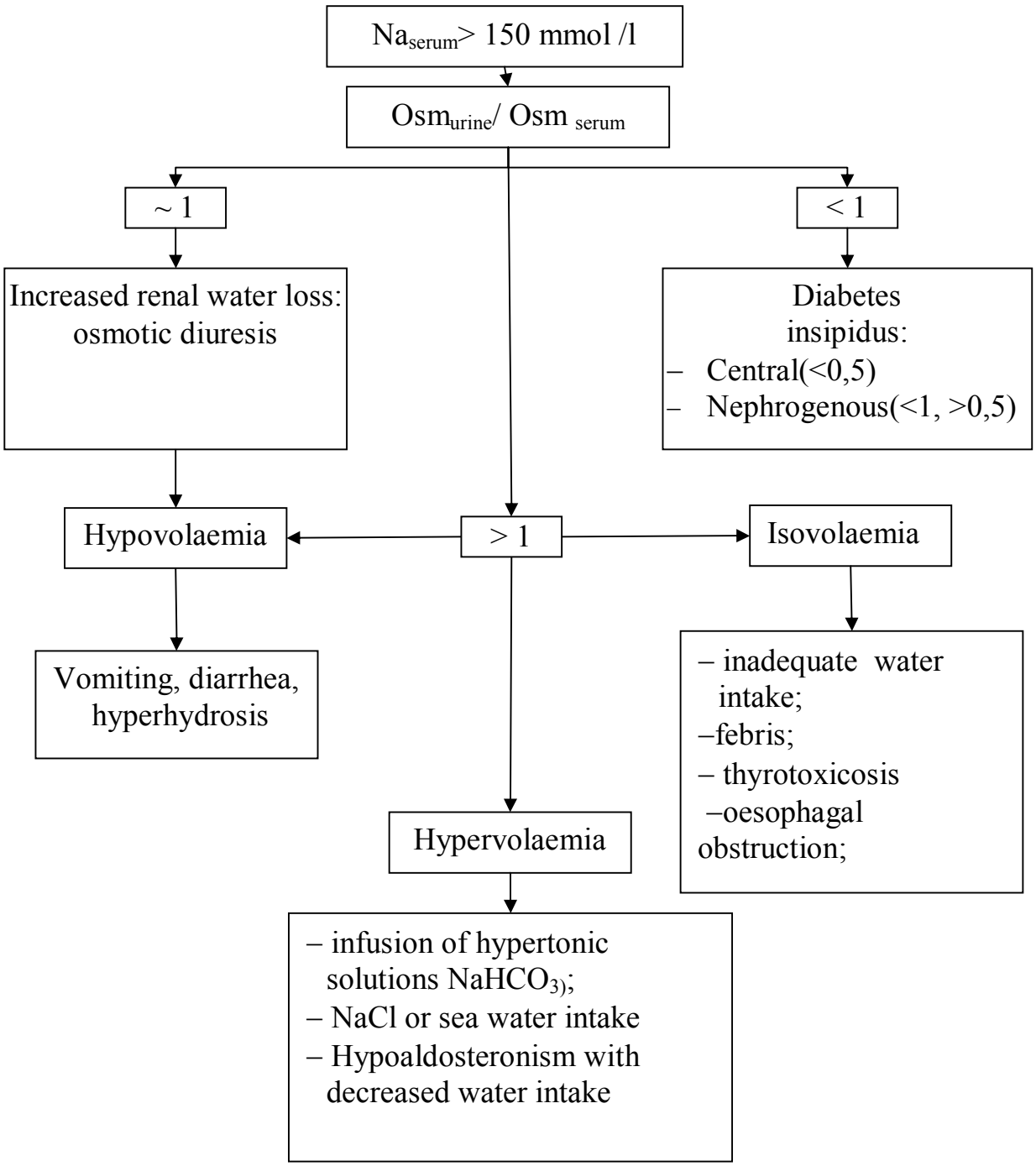
- Nephrotic syndrome
- Liver cirrhosis with ascites
- Stenosis of a.renalis

Decreased sodium excretion is the most frequent reason of sodium excess in the organism. The main reason of secondary hyperaldosteronism is fluid accumulation in the “third compartment”. It can be due to congestive heart failure, shock, sepsis, nephrotic syndrome, ascites. It leads to increased aldosterone secretion by adrenal cortex and sodium retention. As a result, plasma osmolality increases that stimulate osmoreceptors and causes ADH secretion. It leads to hyponatraemia despite of sodium excess in the organism. Treatment of such condition should be etiological.

Hyponatraemia



Hypernatraemia



Hypokalaemia – *serum potassium*< 3,5 mmol/l

A. Causes:

I. Reduced K^+ intake (Normal value of plasma [HCO^-_3], [K^+] in urine <20 mmol/l):

1. Inadequate i/v infusions;
2. Chronic alcoholism;
3. Anorexia nervosa.

II. K^+ redistribution into cells (Normal value of plasma [HCO^-_3], [K^+] in urine <20 mmol/l):

1.Drug therapy: insulin, salbutamol.

III. Extrarenal losses ([K^+] in urine <20 mmol/l):

– Decreased values of plasma [HCO^-_3]:
  1. Acute diarrhoea;
  2. Pancreatic fistulae.
– Increased values of plasma [HCO^-_3]:
  1. Chronic diarrhoea;
  2. Laxative abuse;
  3. Villous adenoma ileostomy or sigmoidostomy.

IV. Renal losses ([K^+] in urine >20 mmol/l):

– Decreased values of plasma [HCO^-_3]:
  1.Respiratory alkalosis;
  2.Renal tubular acidosis.
– Increased values of plasma [HCO^-_3]:
  1. Prolonged diuretic therapy (thiazides, loop diuretics);
  2. Increased mineralocorticoid secretion;
  3. Metabolic alkalosis;
  4.Vomiting;
  5. Diarrhoea.

*V.Another cases:*1. Gentamycin therapy;
2. Osmotic diuresis;
3. Release of urinary tract obstruction;
4. Subacute tubular necrosis;
5. Decreased Mg^{2+};
6. Chronic nephritis (pyelo- and glomerulonephritis);
7. Hyperaldosteronism;
8.Corticosteroids excess (Cushing`s syndrome, corticosteroid therapy);
9. Treatment of diabetic ketoacidosis without potassium administration.

B.Signs and symptoms:

– cardiovascular system :tachycardia, atrial and ventricular ectopic beats, ventricular fibrillation;
– skeletal muscles: muscle weakness ;

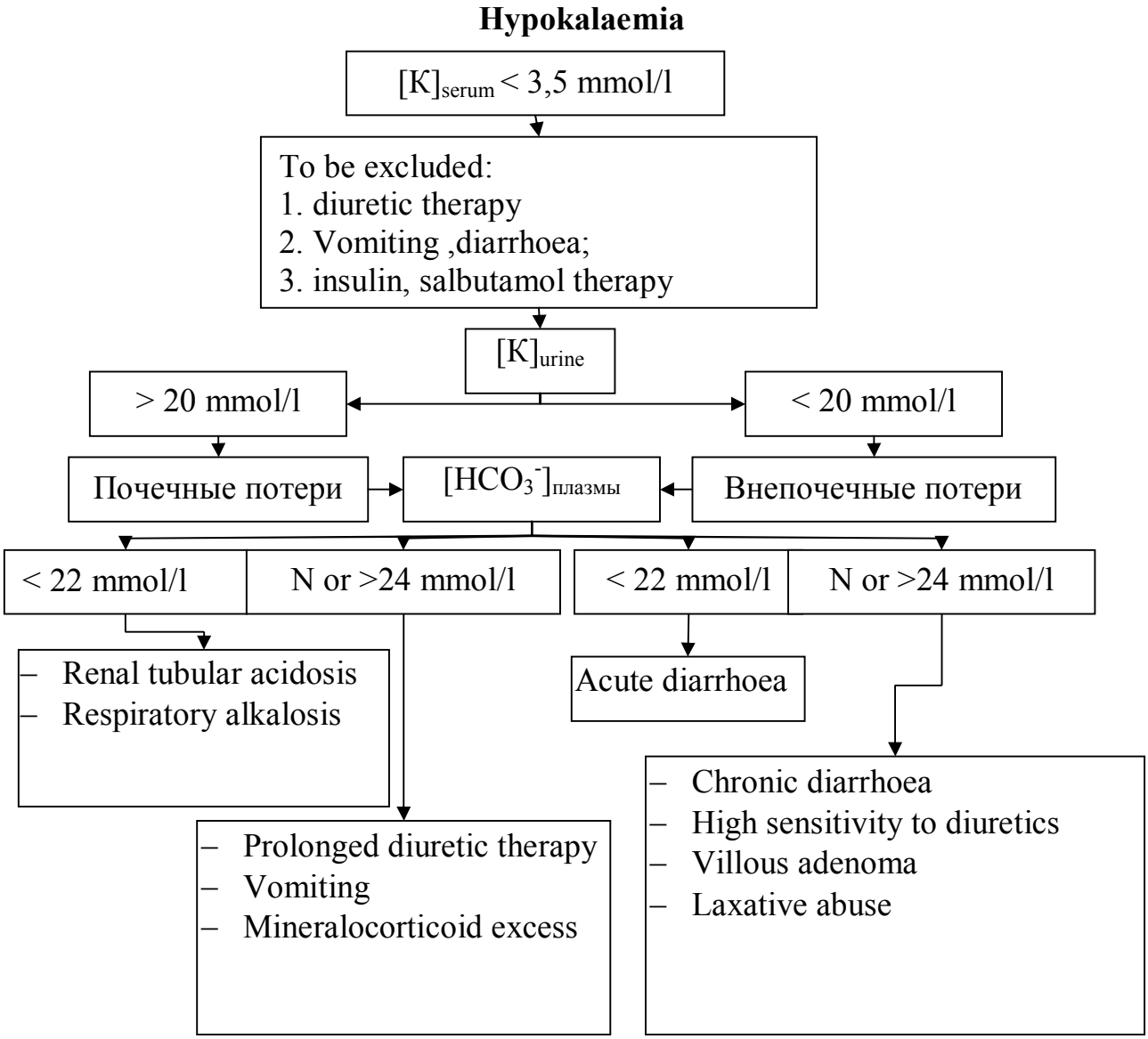
– intestinal atony, constipation;
– kidneys: decreased ability to concentrate urine;
– CNS: apathy, coma.

C.Laboratory findings:

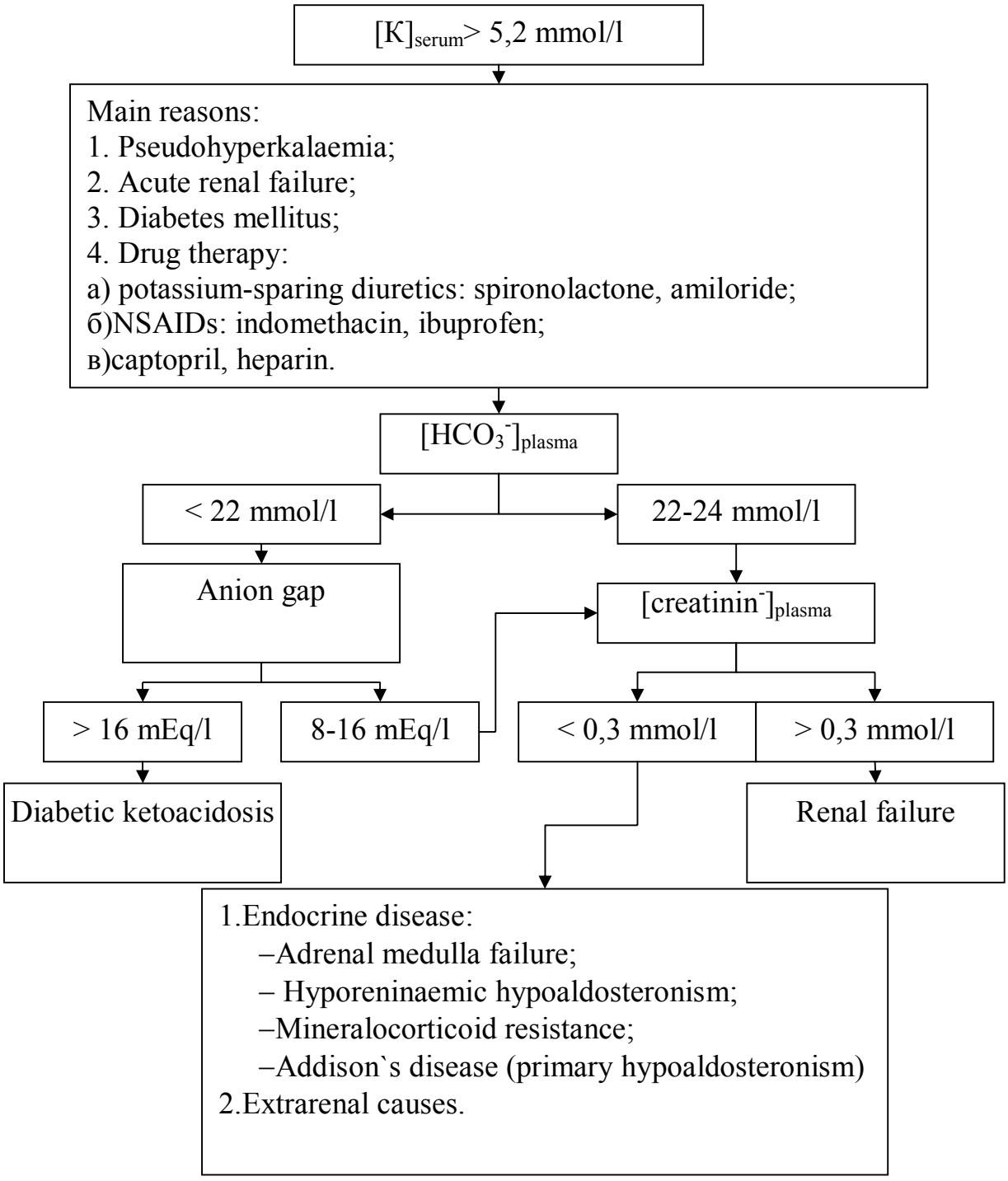
– low serum potassium concentration;
– often metabolic alkalosis;
– often hypochloridaemia.

D. Treatment:

– oral administration of potassium suppliments or i/v potassium replacement (not more than 20 mmol/h).
– normal saline infusion (0,9% NaCl) (if there is no hypervolaemia).
– Spironolactone



Hyperkalaemia



LABORATORY EVALUATION OF PROTEIN METABOLISM

Main functions of plasma proteins:

- Transport (albumin, TBP, transferrin)
- Protection (immunoglobulins)
- Control of body water distribution by maintaining the oncotic pressure (albumin)
- Enzymes (renin, coagulation factors, complement system)
- Inhibitors of plasma proteases (α1-antitrypsin)
- Buffers

Total protein – it is the concentration of all fractions of plasma proteins. Reference values are ***65-85 g/l.***

Normal level of total protein depends on balance between two main protein fractions: albumins and globulins (immunoglobulins). Hydrostatic blood pressure also significantly influences total protein and albumin concentration.

Composition of protein fractions and the main functions of individual proteins of blood serum are shown in following table 9.

Table. 9. **Protein composition of blood serum**

Fraction	Main components	Functions
Albumins		• Transport of hormones, bilirubin, fatty acids, bile acids, drugs • Maintaining of osmotic pressure
α1-globulins	α1-antitrypsine α -lipoprotein Prothrombin Transcortin Acid glycoprotein Thyroxin-binding globulin	Trypsin inhibitor Transport of lipids Coagulating factor Cortisol transport Progesterone transport Thyroxin transport
α2- globulins	Ceruloplasmin Antithrombin III Haptoglobin Plasminogen Retinol- binding protein Vitamin-D- binding protein	Copper transport Inhibitor of coagulation Binding of haemoglobin Plasmin precursor Vitamin A transport Calciferol transport
β- globulins	β –lipoprotein Transferrin Fibrinogen	Lipid transport Transport of iron Factor of coagulation

	C-reactive protein	Activation of complement system
γ- globulins	Ig A, M, G, E, D	Immune protection

Electrophoresis is one of the most widespread methods for separation of plasma proteins. Its basic principle is registration of movement of charged particles in the electric field. Proteins separate according to their different charge and molecular weight.

Electrophoresis is usually performed by applying a small amount of serum to a strip of cellulose acetate or agarose and passing a current across it for a standard time. Results are assayed visually by comparison with standard electrophoretic pattern or densitometrically.

The following slide presents normal electrophoretic pattern and densitogram.(Fig 3, table 10)

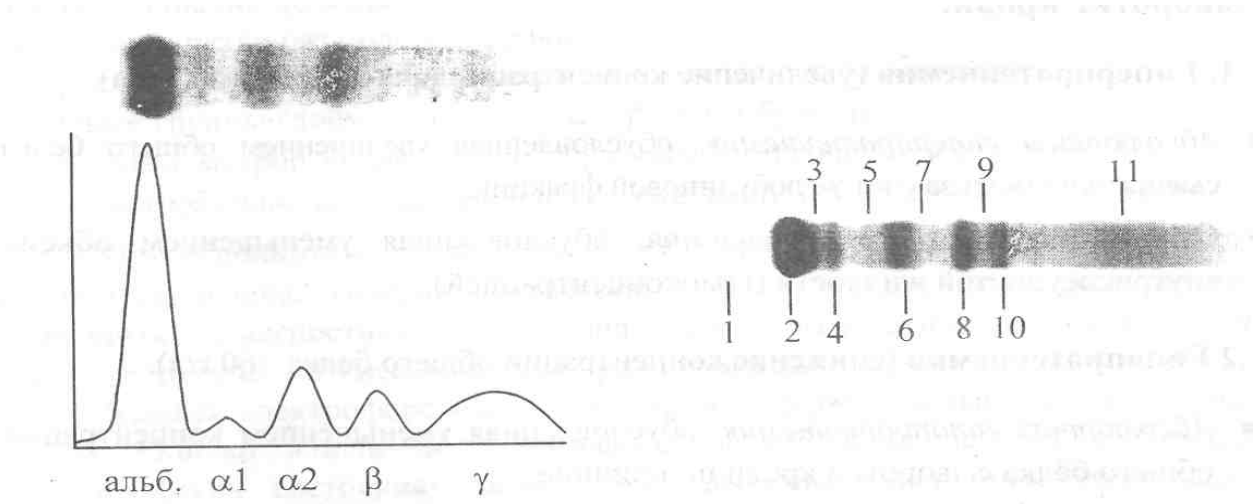


Fig. 3. **Electrophoretic separation of serum proteins**

1 –prealbumin, 2 –albumin, 3 – α-lipoprotein, 4 – Gc-globulin, 5 – α1-antitrypsin, 6 – α2-macroglobulin, 7 –haptoglobin, 8 – β-lipoproteins, 9 –transferrin, 10 –complement, 11 – γ-globulins

Табл. 10. **Main electrophoretic components of serum proteins**

Вид белка	**% of total protein**	**g/l**
Albumin	52-65	35-50
α1-globulin	2-4,5	1-3
α2- globulin	10-15	6-9
β- globulin	6-13	4-9
γ- globulin	10-19	6-13
Total protein		65-82

Disturbances of protein metabolism

Hypoproteinaemia

Hypoproteinaemia is a total blood protein decrease below 65 g/l. Low protein concentration may be relative due to haemodilution (hyperhydratation) and absolute in hypoproteinaemia (hypoalbuminaemia). Life threatening total protein concentration is ***below 40 g/l,*** albumin - ***below 20 g/l.*** In such concentrations oncotic pressure is too low, that is why water leaves the blood vessels. It results in oedema, transudation into body cavities and hypovolaemia. In majority pathological cases that result in hypoproteinaemia, altered ratio of plasma proteins fractions ***(dysproteinaemia)*** is observed.

Cases of absolute hypoproteinaemia are:

1. Decreased protein synthesis:

- Starvation, shortage of protein in diet
- Impaired absorption (infections of GIT, cystic fibrosis, celiac disease)
- Liver diseases

2.Increased protein excretion:

- Renal cases (glomerulonephritis, DM and others)
- Enteropathy with protein loss
- Burns
- Exudative dermatosis

Here, we will describe conditions, accompanied by high protein excretion in urine more in detail. Physiologically not more than 150 mg/24h is excreted in urine. ***Proteinuria*** is a high protein excretion.

Proteinuria is classified as follows:

1. By severity:

- Mild (less than 1 g/24h)
- Moderate (1-3 g/24h)
- Severe (more than 3 g/24h)

2. By the type of excreted protein:

- Selective(albumins)
- Non-selective(albumins and globulins)

3. By mechanism:

- Prerenal (large amount of protein passes through the kidney)
- Renal (glomerular and tubular)
- Postrenal (origins anywhere in urinary tract)

4. Functional:

- After heavy physical exercises
- Alimentary
- Febrile
- Orthostatic

Plasma protein deficiency assessment

Low level of total protein and albumin, except etiological treatment, requires protein replacement, especially if it is critical protein level.

A formula for total plasma protein content estimation is given below:

Plasma protein = [tot. plasma protein (g/l)] x V x 2,5

V – plasma volume (5% of body weight)

Plasma protein deficiency = actual content – due content of plasma protein (60 g/l)

Cases of hyperproteinaemia:

1. Hyper-γ-globulinaemia:

- Polyclonal:
  - Chronic liver diseases (cirrhosis, chronic hepatitis)
  - Response to infections of any kind
  - Autoimmune diseases
- Monoclonal:
  - Multiple myeloma
  - Waldenstrom's macroglobulinaemia
  - Heavy chain disease
  - Lymphosarcoma

2. Dehydration

3. Artefactual

Monoclonal hyper-γ-globulinaemia

A monoclonal increase occurs in several conditions. The term "paraprotein" describes these single types of immunoglobulins, which give an intense band on electrophoresis. The paraprotein band seen on electrophoresis is most often in γ region, then in diminishing frequency between β and γ, in β region and beyond β towards the α_2.

Types of monoclonal components:

- Ig light chains synthesis predominant (κ, λ)
- Ig heavy chains synthesis predominant (γ, α, μ, σ, ξ)
- Complete Ig molecules are produced (both light and heavy chains)

ACUTE PHASE PROTEINS – it is specific group of plasma proteins, which level changes (mostly grows) in response to acute inflammation.

Majority of acute phase proteins are non-specific. Concentration of acute phase proteins usually correlates with activity and stage of inflammatory process. It makes them better indicators of inflammation than other parameters (ESR, leukocyte count, differential WBC count). But diagnostic significance of these tests is limited because of low specificity.

CLASSIFICATION (APP):

1. ***Main reactants of acute phase, concentration increases 100-1000 times within 6-12 h:***
   - C-reactive protein(CRP)
   - Amyloid protein A
2. ***Moderate increase of concentration (2-5 times) within 24 h:***
   - α_1-acid glycoprotein
   - α_1- Antitrypsin
   - Haptoglobin
   - Fibrinogen
3. ***Mild increase of concentration (by 20 - 60%) within 48 h***
   - Ceruloplasmin
   - Complement system
4. ***Neutral reactants of acute phase***
   - Immunoglobulins G, A and M
   - α2 –macroglobulin
5. ***"Negative" reactants of acute phase, concentration decreases within 12 - 18 h***
   - Albumin
   - Transferrin

C- reactive protein (CRP) is the most responsive of the acute phase proteins, the most clinically significant.

- Normal CRP concentration is 0-10 mg/l
- This protein was so named because of its ability to bind the C-polysaccharide of the cell wall of Streptococcus pneumoniae
- Increases in CRP can be much greater than the other proteins. It may increase 100 times in bacterial infections, tissue damage, burns, tumors, necrosis.
- Increased levels usually appear within 24 to 48 hours after injury or infection, sometimes earlier than clinical signs
- Increase in CRP may give an additional band on electrophoresis between β and γ fractions, which can be mistaken for monoclonal protein

In the following cases CRP determination has maximal clinical significance:

1. ***Screening of neonatal sepsis:***
   - In a case of early sepsis (develops during 72hours) CRP level increases in the first 24 hours
   - CRP level should be determined twice during the first 24 hours after the beginning of disease to increase diagnostic value of a test
   - Late increase in the CRP level may indicate postnatal infection.
2. ***Diagnosis and differential diagnosis of bacterial infections:***
   - CRP level increases mainly in bacterial infections

- In viral infections, even severe ones, CRP concentration usually does not exceed 20 mg/l
- Significant increase of CRP in viral infections is an evidence of bacterial superinfection

3. ***Test for antibiotic therapy assessment:***
   - CRP has short half-life (19 hours), that's why it's concentration falls rapidly after successful elimination of infectious agent due to adequate antibiotic therapy
   - Decreasing of CRP concentration 12 hours after the beginning of antibiotic therapy by 30% or more reflects good effectiveness of antibiotic therapy
4. ***Test for assessment of antibiotic therapy duration:***
   - Antibiotic therapy should be continued until CRP level becomes normal (below 10 mg/l)
5. ***Diagnosis of bacterial infection in pregnancy:***
   - It's more informative parameter than ESR, because in pregnancy physiological increase of ESR is observed (up to 40 mm/h)
   - Increased level of CRP in pregnancy is an indicator of bacterial inflammatory process.

ENZYME DIAGNOSTICS

Enzyme diagnostics is one of the branches of enzymology. It has two main directions:

1) use of enzymes as reagents for determination of normal and pathological components in serum, urine, gastric juice etc.
2) determination of enzyme activity in biological material with a diagnostic purpose.

Serum enzymes are divided into 3 groups:

1. ***Cellular enzymes*** enter the blood from different organs. Their activity in serum depends on enzyme content in organs, molecular weight, intracellular localization, rate of elimination. Cellular enzymes are divided into non-specific and organ specific.
2. ***Secretory enzymes*** are synthesized by cells, enter the bloodstream and fulfill their specific functions in the circulatory system. These are enzymes of coagulation system and fibrinolysis, choline esterase etc.
3. ***Excretory enzymes*** are synthesized by glands of GIT and enter the blood (amylase, lipase).

Enzymes synthesis, functioning and breakdown take place continuously and simultaneously; providing their given concentration and activity. Enzymes are localized in different cellular compartments (cytoplasm, lysosomes, cellular membrane, mitochondrions). That is why increased activity of certain enzymes can indicate the degree of severity of cellular damage.

Here, we have provided information about enzymes which are most frequently used in clinical practice for diagnosis, prognosis and therapy monitoring of different pathologies. Their determination in blood serum has high clinical significance.

α-amylase

High activity of this enzyme is observed in the liver, skeletal muscles, microvillus of enterocytes, tears, secretion of mammary glands. Pancreas and salivary glands are richest in amylase. Plasma contains two isoenzymes of α-amylase: pancreatic (P-type)- secreted by pancreas and salivary (S-type)- produced by salivary glands. In norm pancreatic amylase constitutes 40 % of total serum amylase activity, and salivary – 60 %. Determination of α-amylase activity is very important for diagnosis of pancreatic pathology. Two times and more increased activity of α-amylase strongly indicates pancreatic damage.

In acute pancreatitis, α-amylase activity in the blood and urine increases 10-30 times. Initial increase of α-amylase activity is observed within 4-6 hours after the beginning of the disease, reaches peak within 12-24 h; then decreases and returns to norm within 2-6 days. Serum amylase level does not correlate with the degree of severity of pancreatitis. Pathogenetically hyperamylasaemia appears when oedema of interstitial tissue blokes the pancreatic ducts. It characterises fatty pancreatic necrosis. In haemorrhagical pancreatic necrosis, rise in α-amylase activity is observed in blood with subsequent rapid decrease. This reflects progressing pancreatic necrosis.

Aminotransferases (ALT and AST)

Aminotransferases catalyze the process of transamination, they are present in every organ and tissue. Isoenzymes of AST are localized both in cytoplasm and in mitochondrions. ALT predominates in cytoplasm. High concentration of AST is noted in heart and skeletal muscles, liver, kidneys, pancreas and erythrocytes. Damage of any of them leads to significant increase of AST in the blood serum. The most significant increase of AST is observed in myocardial damage. In myocardial infarction, AST activity in blood serum can increase 4-5 times. In acute myocardial infarction, 93–98 % of patients have high AST activity; the latter has the same dynamic as Creatine Kinase MB (CK-MB). However, CK-MB increase is more significant. Increase in AST activity reveals hepatic pathology. The most significant increase is observed in acute viral and toxic hepatitis. From mild to moderate increase in AST occurs in liver cirrhosis (2-3 times), obstructive jaundice and liver metastasis. It can be also so in skeletal muscular pathology, for example progressive muscular dystrophy; in pancreatitis; intravascular haemolysis.

Low AST activity usually reveals vitamin B6 deficiency, renal failure, pregnancy.

Highest concentration of ALT is noted in the liver cells. Skeletal muscles, kidneys and heart also contain ALT, but much less. Increased ALT activity is most frequently revealed in acute liver and biliary ducts diseases. ALT activity rises significantly in the early stages of acute viral hepatitis: in 50% of patients ALT increases 5 days before jaundice and hepatomegaly appear, in 90% of patients – 2 days before these symptoms. AST/ALT ratio is called de Ritis ratio. Its normal value 1 – 1,3. It decreases in liver diseases and increases in heart diseases. In toxic (alcoholic) liver damage AST activity rises predominantly,where de Ritis ratio exceeds 2. In viral hepatitis de Ritis ratio decreases. This ratio increases in obstructive jaundice, cholecystitis, liver cirrhosis, while ALT and AST activity increase slightly.

Alkaline phosphatase (ALP)

The isoenzymes of alkaline phosphatase (ALP) are produced by various tissues: intestinal mucous membrane, osteoblasts, biliary ducts, placenta, mammary gland during lactation. This enzyme is situated on the cellular membrane and takes part in transport of phosphorus.

Several isoenzymes of ALP are present in blood serum. Bone, liver and placental ones are the most significant for clinical and diagnostic purposes.

1. Bone ALP. In bones ALP is secreted by osteoblasts. It is possible, that ALP takes part in maturation of a bone matrix and its mineralization. ALP increases with bone formation. Its significant increase in blood serum results from high osteoblastic activity: growth of bones (children show higher ALP activity then adults; it also increases in the last trimester of pregnancy), reactivation after prolonged immobilization, fractures, deforming ostitis, rickets. It is also a characteristic for osteomalacia (malignant bone tumors, multiple myeloma), tuberculosis of bones, leukemia.

2. Liver ALP. There are two isoenzymes. The first one increases in blood serum in biliary obstruction, due to decreased elimination of enzyme with bile. It also increases

in pregnancy (the second half). It is the main indicator of biliary tract pathology. The second isoenzyme increases in hepatocellular pathology: viral hepatitis, liver cirrhosis. But this increase is less significant in comparison to aminotransferases. 1/3 patients with jaundice and liver cirrhosis show increase in ALP activity. Rise in ALP activity is also revealed in 20% of patients with primary liver cancer or liver metastasis.

3. Intestinal ALP. It originates from enterocytes, enters the intestinal lumen and is partially absorbed in the blood. It accounts for a small part of total ALP activity. Its activity can be increased in people with I or III blood groups; especially after meals; in intestinal diseases accompanied by diarrhoea.

4. Placental ALP. It normally appears in pregnancy. The highest activity is revealed during the third trimester. It is the most thermostable isoenzyme of ALP. The most significant increase develops in women with eclampsia as a result of placenta damage. Low ALP activity in pregnancy indicates placental insufficiency.

Gamma-Glutamyl Transpeptidase (GGT)

The determination of GGT is of great significance in diagnosis of hepatic and hepatobiliary pathology. This test is much more sensitive than either ALP or the transaminase test in detecting obstructive jaundice, cholangitis, cholecystitis.

The highest GGT activity is noted in kidneys - 7000 times higher than in blood serum. In healthy individuals serum GGT activity is low. The liver is considered as the main source of normal serum activity, despite the fact that the kidney has the highest level of the enzyme. Pancreas also contains GGT. Small enzyme concentration is detected in intestine, brain, heart, spleen, prostate gland, skeletal muscles. GGT is located in cellular membrane, lysosomes, cytoplasm. Membrane localization of GGT is characteristic for cells with high secretory, excretory or reabsorptional activity. Serum GGT activity increases in any pathology of liver and bile ducts. If GGT activity is normal, liver disease probability is very low. Thus, GGT is good marker for differential diagnosis of liver pathology. The most significant increase is observed in cholestasis and slight increase - in parenchymal liver disease (necrosis of hepatocytes). GGT activity rises on the early stage of the disease and remains high for a long time. Beside this, GGT is a specific indicator of liver disease, because in comparison to ALP its activity is normal in healthy children, pregnant women and patients with bone diseases.

Determination of GGT activity is also used for diagnosis of alcoholic liver disease and its therapy monitoring. Alcohol induces GGT synthesis in the liver and release from cell membranes. It leads to increase of enzyme activity in the blood serum without hepatic cell damage.

GGT test is also used for diagnosis of pancreatic pathology. Nowadays in Europe, this parameter is used even more often than α-amylase – traditional indicator of pancreatic pathology. 100% of patients with acute pancreatitis show GGT activity 10-20 times higher than normal.

This test can also be useful for laboratory diagnosis of renal pathology. It is proven that GGT activity in urine rises significantly in pyelonephritis, glomerulonephritis and renal calculi. Determination of GGT in urine allows to

diagnose the early stages of kidney disease, which is accompanied by proximal renal tubular damage.

Creatine Kinase (CK)

CK is a dimer and consists of 2 protein subunits: B (brain) and M (muscle), which combine to form 3 isoenzymes:

- CK-BB (CK-1) – brain
- CK-MB (CK-2) – cardiac
- CK-MM (CK-3) – muscle

CK-BB is present in large amount in brain tissue, prostate, stomach, lungs, urinary bladder, urethra, placenta, thyroid gland. CK-MB accounts for 25–46 % of total CK activity in cardiac muscle and less than 5% in skeletal muscle. CK-MM is present mainly in skeletal and cardiac muscle. CK-MM accounts for 94–96 % of total creatine kinase serum activity, CK-MB – 4–6 %, CK-BB – trace amount or is not detectable in serum. Total CK activity increases in different pathologies: traumas, surgical operations, myocardial infarction, reduced perfusion of muscles, myopathy, dermatomyositis, muscular dystrophy, myocarditis, intoxication, hypothyroidism, infectious diseases (typhoid fever). In some cases slight increase occurs in arthritis, congestive heart failure, tachycardia, pulmonary embolism. In myocardial infarction increase in CK activity occurs within 3–6 hours after an onset of pain. However, determination of its activity within 8 hours gives positive results in 31% of cases. CK is a reliable test for myocardial infarction diagnosis within 8-10 hours after onset of pain. It reaches maximal level within 24 hours and returns to norm within the next 48 hours even in extensive myocardial infarction. Relative increase of CK in myocardial infarction is higher than other enzymes. The determination of CK every 4-6 hours during 24 hours is most informative.

CK-MM increases in blood serum in the same cases, as total CK. CK-BB in blood serum slightly or moderately increases in cancer of certain localizations (lungs, intestine, urinary bladder, prostate gland), trauma of cardiac muscle, connecting tissue diseases. During parturition serum CK-BB may be 6 times higher than normal (the source of its activity are uterus and placenta). In neonates and infants the activity is considerably elevated, especially during the first 24 hr post-partum.

Lactate Dehydrogenase (LDH)

Lactate Dehydrogenase (LDH) catalyzes reversible reduction of pyruvate to lactate. LDH consists of two subunits – M (muscle) and H (heart). There are 5 isoenzymes in serum, which are distinguished by their subunit composition. They are identified as follows according to decreasing electrophoretic mobility (movement to anode): LDH-1 (H_4), LDH-2 (H_3M_1), LDH-3 (H_2M_2), LDH-4 (H_1M_3), LDH-5 (M_4).

LDH is present in cytoplasm of every tissue. In the liver, heart, kidneys, skeletal muscles and erythrocytes LDH activity is 500 times higher than in serum. That is why damage of these organs is accompanied by elevation of serum LDH. Increase in this enzyme occurs in tissue necrosis, especially in acute myocardial injury, haemolysis (erythrocyte damage), injury of kidneys, skeletal muscles, liver, lungs and skin. Significant increase is observed in hemolytic anaemias or B12- folate deficiency.

Normal proportion of LDH isoenzymes in serum is: LDH-1 – 15–30 %; LDH-2 – 22–50 %; LDH-3 – 15–30 %; LDH-4 – 0–15 %; LDH-5 – 0–15 %. In myocardial infarction increase in LDH occurs within 12-32 hours after an onset of pain and remains elevated during 8-14 days. LDH-1 is the most specific test for diagnosis of myocardial infarction. If within 8-24 hr after the onset of pain LDH (and also CK-MB and AST) level does not increase, we can exclude myocardial infarction. Some patients show correlation between LDH level and extensiveness of myocardial injury. In some cases LDH1/LDH2 ratio can give an additional diagnostic information. Its normal range is 0,6–0,7. In acute myocardial infarction it exceeds 1,0 and returns to norm after 2-3 weeks. LDH-1 also increases in tumors of reproductive organs: teratoma, testicle seminoma, ovarian dysgerminoma.

LDH-2, LDH-3 and LDH-4 have an intermediate properties. Activity of these enzymes grows in massive platelet destruction (pulmonary embolism, massive blood transfusions) and lymphatic system involvement. In non-lymphocytic leukemia, LDH-3 and LDH-4 levels increase. LDH-3 also increases in pancreatitis. LDH-4 level rises in viral, toxic and traumatic liver damage, exacerbation of chronic hepatitis, in active phase of rheumatism, in cardiosclerosis, severe diabetes mellitus, acute nephritis, tumors of the liver, prostate, uterine cervix, mammary gland, intestine.

Skeletal muscles, liver, skin, mucous membranes, some kinds of malignant cells contain small amount of LDH-5. Significant increase in LDH-5 occurs in traumas, inflammatory and degenerative muscular diseases and different liver diseases (hepatitis, cirrhosis and others). Oncologic diseases (i.e. lymphocytic leukemia) also can lead to increase in LDH-5. Its activity also grows in active phase of rheumatism, kidney tumors, rejection of kidney transplant, severe diabetes mellitus.

LABORATORY EVALUATION OF CARBOHYDRATE METABOLISM

Glucose level is the main parameter for carbohydrate metabolism evaluation. In clinical practice it is determined in following biological material:

Reference values of glucose (WHO, 1999):

- Whole blood – ***3,3-5,5 mmol/l***
- Plasma (serum) – ***4,0-6,1 mmol/l***
- Cerebrospinal fluid – ***60 % of plasma level***
- Urine – ***is not determined by routine methods***

The most frequently with diagnostic purposes glucose is determined in the blood. Factors that influence blood glucose level are:

1. Type of blood specimen, used for investigation (the whole blood or plasma, capillary or venous blood). Capillary blood glucose level is usually higher by 10-15% than venous.
2. If glucose level is determined in the whole blood haematocrit should be taken into account (Ht). If Ht is less than 35% blood glucose level will be higher, if more than 55% - lower.
3. In elderly patients after 60 years old every following ten years blood glucose level increases by 0,56 mmol/l.
4. Drug intake (especially hormonal) also influences glucose metabolism and it is blood level.

The main disturbances of carbohydrate metabolism are hypo- and hyperglycaemia.

HYPOGLYCAEMIA
THE MAIN CASES

Reactive hypoglycaemia	• Caused by drug intake: insulin, sulphonylurea. • After meals: alimentary, idiopathic • Caused by alcohol intake • Inherited metabolic disturbances
Fasting hypoglycaemia	• Liver or kidney diseases • Endocrine diseases (glucocorticoids deficiency) • Hyperinsulinism (insulinoma)
Hypoglycaemia in DM	• Insulin overdosage (inappropriate dose) • Hard physical exercises • Alcohol intake

HYPOGLYCAEMIA
DIAGNOSIS

Clinical signs	• Acute: fatique and general malaise, hunger, dizziness, vision disturbances and others. • Chronic (neurohypoglycaemia): psychosis, amnesia, personality or behavioral changes
Laboratory signs (glycaemia determination)	Neurohypoglycaemia symptoms appears: • In adults - < 2,2 mmol/l • In infants - < 1,5 mmol/l
Glucose administration	Disappearing of a symptoms

HYPERGLYCAEMIA
DIABETES MELLITUS

Diabetes mellitus (DM) – it is a group of metabolic disorders, characterized by hyperglycaemia due to insulin deficiency or defects in insulin action, or both of them (WHO, 1999).

DM classification (WHO, 1999):

Diabetes mellitus type 1	Destruction of β-cells of pancreatic islets, that usually leads to absolute insulin deficiency.
Diabetes mellitus type 2	Resistance to insulin action and relative insulin deficiency
Other types of DM	Genetic defects of β-cells function Exocrine pancreatic diseases Endocrinopathy Drug-induced diabetes Infections
Gestational DM	Appears in pregnancy

DIFFERENCES BETWEEN DM TYPE 1 AND 2

SIGNS	DM TYPE 1	DM TYPE 2
Age of beginning	Before 30 years	After 40 years
Insulin deficiency	Absolute	Relative
Body weight	Loss of body weight	Overweight
Beginning of the disease	Acute	Insiduous
Ketoacidosis	Often	Is not characteristic
Clinical course	Labile	Stable

LABORATORY DIAGNOSTIC CRITERIA:

- **Fasting hyperglycaemia:**

The whole blood - ***≥ 6,1 mmol/l***
Plasma (serum) - ***≥ 7,0 mmol/l***

- **Two hours after glucose load (OGTT):**

The whole venous blood - ***≥ 10,0 mmol/l***
The whole capillary blood - ***≥ 11,1 mmol/l***
Plasma (serum) - ***≥ 11,1 mmol/l***

ORAL GLUCOSE TOLERANCE TEST (OGTT)

This test is carried out in doubtful cases. Glucose level is determined before and two hours after taking a standard glucose load.

Test procedure:

1. The patient fasts overnight. Water, but no other beverage, is allowed.
2. A venous sample is withdrawn for plasma glucose estimation.
3. 75 g of glucose dissolved in 300 ml of water is given (for children 1,75 g/kg body weight up to a maximum of 75 g). The patient must drink it within about 5 minutes.
4. Futher blood sample is taken at two hours after the glucose load

IMPAIRED GLUCOSE TOLERANCE (WHO, 1999)

Two hours after glucose load (OGTT):

- The whole venous blood – ***6,7-10,0 mmol/l***
- The hole capillary blood – ***7,8-11,1 mmol/l***
- Plasma (serum) – ***7,8-11,1 mmol/l***

IMPARED FASTING GLUCOSE (WHO, 1999):

- The whole venous blood – ***5,6-6,1 mmol/l***
- The hole capillary blood – ***5,6-6,1 mmol/l***
- Plasma (serum) – ***6,1-7,0 mmol/l***

DEFINITIONS

- ***Fasting glycaemia*** – blood glucose level in the morning before breakfast after overnight fasting > 8 h
- ***Postprandial glycaemia*** – blood glucose level two hours after meals
- ***Glycemic profile*** – blood glucose level determination every 3-4 hours during the day
- ***Random hyperglycaemia*** – hyperglycaemia, revealed in any time of a day

DM MONITORING

PARAMETER	FREQUENCY OF INVESTIGATION	
	DM TYPE I	**DM TYPE II**
Glycemic self-control	In decompensation – every day	In decompensation – every day
HbA1c	Once a 3 months	Once a 3 months
Microalbuminuria	Once a year after 5 years from the beginning of the disease	Twice a year
Haemogram, urinalysis, biochemical blood tests	Once a year	Once a year
ESG, blood pressure control	Every visit to the doctor	Every visit to the doctor
Feet examination	Every visit to the doctor	Every visit to the doctor
Consultation of ophthalmologist, neurologist, cardiologist	Once a year within 5 years from the beginning of the disease	Once a year within 5 years from the beginning of the disease

PARAMETERS OF LIPID METABOLISM IN DM TYPE I and II
(European Diabetes Policy Group, 1998)

PARAMETR (mmol/l)	CARDIOVASCULAR DISEASES RISK		
	Low	Moderate	High
TOTAL CHOLESTEROL	< 4,8	4,8-6,0	> 6,0
CHOLESTEROL OF HDLP	> 1,2	1,2-1,0	< 1,0
CHOLESTEROL OF LDLP	< 3,0	3,0-4,0	> 4,0
TAG	< 1,7	1,7-2,2	> 2,2

COMPLICATIONS OF DM

- **EARLY:**
  1. Diabetic ketoacidosis
  2. Comas: ketoacidotic, lactacidotic, hyperosmolar non-ketotic, hypoglycaemic.

- **LATE:**
  1. Microangiopathy: neuropathy, nephropathy, retinopathy.
  2. Macroangiopathy: coronary heart disease, cerebrovascular diseases, peripheral angiopathy.

EARLY COMPLICATIONS OF DM

Diabetic ketoacidosis

The main reason – *absolute insulin deficiency*

Diagnosis

Clinical signs	Clinical signs of DM + smell of acetone in expired air
Routine urinalysis	Glucosuria Ketonuria
Biochemical blood analysis	Hyperglycaemia Hyperketonaemia
Acid-base status	Metabolic acidosis with high anion gap

Therapy control

Glycaemia	Once an hour until a level of 14 mmol/l is reached, then once every 3 hours
Acetone urine test	Once a day
Haemogram and routine urinalysis	Initial
Biochemical blood analysis	Initial
Acid-base status	1-2 times a day
Diuresis	Control hourly

Hyperosmolar non-ketotic coma

The main reason is relative insulin deficiency + severe dehydration.

Diagnosis

Clinical signs	Diabetes mellitus clinical signs
Biochemical blood analysis	Hyperglycaemia (> 50 mmol/l) Absence of ketonaemia and acidosis Hypernatraemia
Plasma osmolality	Increased
Routine urinalysis	Glucosuria

LATE COMPLICATIONS OF DM

Diabetic nephropathy

Diabetic nephropathy (DN) – specific renal blood vessels involvement in diabetes mellitus that is accompanied by nodular or diffuse glomerulosclerosis. Terminal stage of this process is characterized by development of chronic renal failure (CRF).

STAGES:

- Microalbuminuria
- Proteinuria (> 0,5 g/24 h)
- CRF

Tests

1. **pH reflects:**
   1. Free hydrogen ions concentration.
   2. Concentration of hydroxyl anions.
   3. Hydrogen ions concentration to hydroxyl anions concentration ratio.
   4. Hydrogen ions partial pressure.

2. **Which buffer system predominated inside cells?**
   1. Bicarbonate
   2. Acetate
   3. Protein
   4. Phosphate
   5. Haemoglobin

3. **pK of a bicarbonate buffer is:**
   1. 7,3
   2. 7,4
   3. 6,1
   4. 5,9
   5. 7,8

4. **Through which mechanisms do kidneys take part in regulation of acid-base balance?**
   1. Maintaining of pCO_2
   2. Bicarbonate ions reabsorption
   3. Hydrogen ions excretion
   4. Bicarbonate ions regeneration
   5. Nonvolatile acids formation

5. **Which enzyme in renal tubules catalyzes dissociation of carbonic acid?**
   1. Lactate Dehydrogenase
   2. AST
   3. ALT
   4. Lipase
   5. Carbonic Anhydrase

6. **Which anticoagulant is used for determination of parameters of acid-base balance?**
   1. Oxalate
   2. Citrate
   3. Heparin Li
   4. Heparin-Na
   5. EDTA

7. What are the main organs taking part in regulation of acid-base balance?

1. Lungs
2. Kidneys
3. Liver
4. Spleen
5. Small intestine

8. Acidosis is characterized by:

1. Increased blood pH
2. Increasing of blood hydroxyl anions concentration
3. Decreased blood pH
4. Increased hydrogen ions concentration in the blood
5. Decreased lactate blood level

9. Alkalosis is characterized by:

1. Decreased blood pH
2. Decreased blood hydroxyl anions concentration
3. Increased lactate blood level
4. Increased blood pH
5. Decreased hydrogen ions concentration in blood

10. Respiratory acidosis may develop due to:

1. Prolonged starvation
2. Pyelonephritis
3. Respiratory distress syndrome
4. Hepatitis
5. Hyperventilation

11. Reason of metabolic alkalosis may be:

1. CO_2 retention
2. Organic acids retention
3. Loss of potassium ions
4. Hyperventilation
5. Hypoventilation

12. Respiratory alkalosis develops due to:

1. Hyperventilation
2. Excessive vomiting
3. Tumors of oesophagus
4. Infusion of alkaline solutions
5. Hypoventilation

13. Patient suffering from respiratory failure should be given oxygen therapy if PO_2 in arterial blood is less than:

1. 50 mm Hg
2. 60 mm Hg
3. 70 mm Hg
4. 80 mm Hg
5. 100 mm Hg

14. Reference values of plasma bicarbonate concentration are:

1. 18-26 mmol/l
2. 21-27 mmol/l
3. 35-45 mmol/l
4. 25-30 mmol/l
5. 31-37 mmol/l

15. Reference values of arterial blood pH are:

1. 7,50-7,60
2. 7,35-7,60
3. 7,35-7,45
4. 7,25-7,45
5. 7,25-7,35

16. Life threatening bicarbonate ions concentration is above:

1. 35 mmol/l
2. 38 mmol/l
3 27 mmol/l
4 40 mmol/l
5. 29 mmol/l

17. Titrable acidity is:

1. Quantity of ammonium ions excreted in urine
2. Quantity of excreted phosphate anions
3. Quantity of excreted free hydrogen ions
4. Free hydrogen ions level in blood

18. Life threatening respiratory acidosis is characterized by:

1. pH less than 7,35
2. pCO2 is above 60 mm Hg
3. pCO2 is above 50 mm Hg
4. pH less than 7,20
5. pH less than 7,30

19. Life threatening respiratory alkalosis is characterized by:

1. pH less than 7,35
2. pCO2 less than 20 mm Hg
3. pCO2 less than 25 mm Hg
4. pH more than 7,60

5. pH more than 7,50

20. Life threatening metabolic alkalosis is characterized by:

1. pH more than 7,60
2. Plasma bicarbonate ions concentration is above 30 mmol/l
3. Plasma bicarbonate ions concentration is above 40 mmol/l
4. pH more than 7,45
5. pH more than 7,35

21. Life threatening metabolic acidosis is characterized by:

1. pH less than 7,20
2. Plasma bicarbonate ions concentration is less then 10 mmol/l
3. Plasma bicarbonate ions concentration is less then 20 mmol/l
4. pH less than 7,35
5. pH less than 7,30

22. Life threatening partial pressure of oxygen in arterial blood is:

1. Less than 60 mm Hg
2. Less than 40 mm Hg
3. Less than 50 mm Hg
4. Less than 70 mm Hg
5. Less than 80 mm Hg

23. Reference values of pCO2 in arterial blood are:

1. 25-35 mm Hg
2. 35-45 mm Hg
3. 45-55 mm Hg
4. 55-65 mm Hg
5. 65-85 mm Hg

24. Life threatening values of pCO2 are above:

1. 40 mm Hg
2. 45 mm Hg
3. 60 mm Hg
4. 55 mm Hg
5. 50 mm Hg

25. Life threatening plasma bicarbonate ions concentration is less than:

1. 20 mmol/l
2. 15 mmol/l
3. 10 mmol/l
4. 25 mmol/l
5. 30 mmol/l

26. Life threatening values of plasma lactate are above:

1. 6 mmol/l
2. 5 mmol/l
3. 4 mmol/l
4. 3 mmol/l
5. 2,5 mmol/l

27. Parameter D(A-a)pO2 reflects:

1. Intrapulmonary shunting
2. Alveolar to arterial oxygen gradient
3. Partial pressure of oxygen in mixed venous blood
4. Partial pressure of oxygen in arterial blood

28. Parameter D(a-v)pO2 reflects:

1. Intrapulmonary shunting
2. Alveolar to arterial oxygen gradient
3. Arterial to venous oxygen gradient
4. Partial pressure of oxygen in arterial blood

29. pH=7,22; pCO2=61 mm Hg; bicarbonate=23 mmol/l; BE= -1,2 mmol/l. This acid-base laboratory analysis is typical for:

1. Non-compensated metabolic acidosis
2. Non- compensated respiratory acidosis
3. Respiratory alkalosis and metabolic acidosis
4. Metabolic alkalosis and respiratory acidosis

30. pH=7,1; pCO2=66 mm Hg; bicarbonate=13 mmol/l; BE= -13 mmol/l. This acid-base laboratory analysis is typical for:

1. Non-compensated metabolic acidosis
2. Non-compensated respiratory acidosis
3. Respiratory acidosis and metabolic acidosis
4. Metabolic alkalosis and respiratory acidosis

31. pH=7,55; pCO2=55 mm Hg; bicarbonate=45 mmol/l; BE= +15 mmol/l. This acid-base laboratory analysis is typical for:

1. Subcompensated metabolic alkalosis
2. Non-compensated respiratory alkalosis
3. Respiratory alkalosis and metabolic acidosis
4. Metabolic alkalosis and respiratory acidosis

32. pH=7,41; pCO2=50 mm Hg; bicarbonate=30 mmol/l; BE= +7 mmol/l. This acid-base laboratory analysis is typical for:

1. Compensated metabolic alkalosis
2. Compensated respiratory acidosis
3. Non-compensated metabolic acidosis
4. Non-compensated respiratory acidosis

33. pH=7,36; pCO2=29 mm Hg; bicarbonate=16 mmol/l; BE= -8 mmol/l. This acid-base laboratory analysis is typical for:

1. Compensated metabolic acidosis
2. Compensated respiratory acidosis
3. Non-compensated metabolic acidosis
4. Non-compensated respiratory acidosis

34. pH=7,49; pCO2=42 mm Hg; bicarbonate=30 mmol/l; BE= +7 mmol/l. This acid-base laboratory analysis is typical for:

1. Compensated metabolic alkalosis
2. Compensated respiratory alkalosis
3. Non-compensated respiratory alkalosis
4. Non-compensated metabolic alkalosis

35. pH=7,30; pCO2=53 mm Hg; bicarbonate=35 mmol/l; BE= +6 mmol/l. This acid-base laboratory analysis is typical for:

1. Subcompensated metabolic acidosis
2. Subcompensated respiratory acidosis
3. Non-compensated metabolic acidosis
4. Non-compensated respiratory acidosis

36. pH=7,60; pCO2=36 mm Hg; bicarbonate=35 mmol/l; BE= +10 mmol/l. This acid-base laboratory analysis is typical for:

1. Compensated metabolic alkalosis
2. Non-compensated metabolic alkalosis
3. Compensated respiratory alkalosis
4. Non-compensated respiratory acidosis

37. pH=7,16; pCO2=60 mm Hg; bicarbonate=23 mmol/l; BE= -3,3 mmol/l. This acid-base laboratory analysis is typical for:

1. Non-compensated respiratory acidosis
2. Compensated respiratory acidosis
3. Compensated metabolic alkalosis
4. Subcompensated metabolic acidosis

38. pH=7,48; pCO2=25 mm Hg; bicarbonate=20 mmol/l; BE= -4 mmol/l. This acid-base laboratory analysis is typical for:

1. Subcompensated metabolic acidosis
2. Subcompensated respiratory acidosis
3. Non-compensated metabolic acidosis
4. Non-compensated respiratory alkalosis

39. Reference values of plasma glucose are:

1. 3,3-5,5 mmol/l

2. 4,0-6,1 mmol/l
3. 5,6-7,8 mmol/l
4. 5,6-6,7 mmol/l
5. 7,8-10,0 mmol/l

40. Reference values of glucose in whole blood are:
1. 3,3-5,5 mmol/l
2. 3,9-6,4 mmol/l
3. 5,6-7,8 mmol/l
4. 5,6-6,7 mmol/l
5. 7,8-10,0 mmol/l

41. Hypoglycaemia can be caused by:
1. Adrenaline
2. Glucocorticoids
3. Insulin
4. Somatotrophin (growth hormone)

42. In suspected diabetes mellitus it is necessary to determine:
1. Blood glucose level
2. Urinary glucose
3. Glycosilated haemoglobin
4. Cholesterol
5. Triglycerides

43. Methods used for blood glucose determination:
1. Glucose oxidase method
2. Ortotolidine method
3. Hexokinase method
4. Biuret method

44. The true statements about glycosylated hemoglobin are:
1. Revealed in diabetes mellitus type II
2. Not founded in diabetes mellitus type I
3. Revealed in the blood of healthy people
4. Decreases in patients with diabetes mellitus

45. Fructosamine is:
1. Fructose connected with proteins
2. Mucopolysacharides
3. Glycosylated albumin
4. Glycolipids

46. Reference method for blood glucose level determination is:
1. Hexokinase method

2. Ortotolidine method
3. Benedict's test
4. Glucose oxidase method
5. Glucose dehydrogenase method

47. Postprandial glycaemia is:
1. Blood glucose level 1 hour after meals
2. Blood glucose level 6 hours after meals
3. Blood glucose level 3 hours after meals
4. Blood glucose level 2 hours after meals

48. Renal threshold for glucose is:
1. 6,0-7,0 mmol/l
2. 7,0-8,0 mmol/l
3. 8,8-10,0 mmol/l
4. 11,0-12,0 mmol/l
5. 12,0-13,0 mmol/l

49. Diagnostic criterion of diabetes mellitus is plasma glucose level in fasting state:
1. >6,7 mmol/l
2. >5,6 mmol/l
3. >7,0 mmol/l
4. >5,5 mmol/l
5. >8,7 mmol/l

50. Diagnostic criterion of diabetes mellitus is whole blood glucose level in fasting state:
1. >6,1 mmol/l
2. >5,6 mmol/l
3. >7,8 mmol/l
4. >5,5 mmol/l
5. >8,7 mmol/l

51. Diagnostic criterion of diabetes mellitus is plasma glucose level in 2 hours after standard glucose load:
1. >6,4 mmol/l
2. >6,7 mmol/l
3. >7,0 mmol/l
4. >10,0 mmol/l
5. >11,1 mmol/l

52. Diagnostic criterion of diabetes mellitus is whole venous blood glucose level in 2 hours after standard glucose load:
1. >6,4 mmol/l

2. >6,1 mmol/l
3. >7,8 mmol/l
4. >10,0 mmol/l
5. >11,1 mmol/l

53. Diagnostic criterion of diabetes mellitus is whole capillary blood glucose level in 2 hours after standard glucose load:

1. >6,4 mmol/l
2. >6,7 mmol/l
3. >7,8 mmol/l
4. >10,0 mmol/l
5. >11,1 mmol/l

54. Glycosylated haemoglobin is:

1. Glucose combined with COHb
2. Glucose combined with HbA
3. Glucose combined with HbF
4. Fructose combined with HbA

55. Diagnostic significance of HbA1c :

1. Diagnosis of diabetic nephropathy
2. Estimation of hyperglycaemia duration
3. Diagnosis of diabetic ketoacidosis
4. Diagnosis of diabetic macroangiopathy
5. Diagnosis of diabetic retinopathy

56. One of the main laboratory criteria of diabetic nephropathy is:

1. Microalbuminuria
2. Proteinuria > 0,5 g/24h
3. Proteinuria > 1,0 g/24h
4. Proteinuria > 3,0 g/24h
5. Proteinuria > 2,0 g/24h

57. Microalbuminuria is:

1. Albumin excreted in urine in a quantity of 500-600 mg/24h
2. Albumin excreted in urine in a quantity of 600-800 mg/24h
3. Albumin excreted in urine in a quantity of 300-500 mg/24h
4. Albumin excreted in urine in a quantity of 30-300 mg/24h

58. Early complications of diabetes mellitus are:

1. Diabetic neuropathy
2. Diabetic nephropathy
3. Diabetic ketoacidosis
4. Diabetic retinopathy
5. Occlusion of femoral artery

59. Criterion of a compensated of diabetes mellitus type I is HbA1c level:

1. 8,0-9,0 %
2. 6,0-7,0 %
3. 7,1-7,5 %
4. 8,0-8,5 %

60. Criterion of compensated diabetes mellitus type I is when fasting blood glucose level is:

1. 5,0-6,0 mmol/l
2. 6,1-6,5 mmol/l
3. 6,5-6,9 mmol/l
4. 7,0-7,5 mmol/l
5. 7,5-7,8 mmol/l

61. How often HbA1c concentration should be determined in patients with diabetes mellitus type I?

1. Once a month
2. Once a year
3. Once a 6 months
4. Once a 3 months
5. Once a 2 weeks

62. How often HbA1c concentration should be determined in patients with diabetes mellitus type II ?

1. Once a month
2. Once a year
3. Once a 6 months
4. Once a 3 months
5. Once a 2 weeks

63. How often microalbuminuria should be determined in patients with diabetes mellitus type I ?

1. Once a year, 5 years after the beginning of the disease
2. Twice a year, 5 years after the beginning of the disease
3. Twice a year, 3 years after the beginning of the disease
4. Once a year, 3 years after the beginning of the disease
5. Once a month

64. Plasma lipids are:

1. Cholesterol.
2. Triglycerides
3. Glycogen
4. Fatty acids

65. Recommended serum cholesterol level is:

1. <6,5 mmol/l
2. <6,2 mmol/l
3. <7,0 mmol/l
4. <5,2 mmol/l
5. <7,6 mmol/l

66. Main risk factors of developing atherosclerosis are:
1. High level of HDL and low level of LDL in serum
2. High level of LDL and low level of HDL in serum
3. Existence of modified lipoproteins
4. High level of chylomicrons

67. Steatorrhoea is:
1. Bile and gall stones formation
2. Fatty infiltration of the liver
3. Excess of fat in stools
4. Increased blood lipoproteins concentration

68. Which conditions should be maintained while laboratory investigation of parameters of lipid metabolism?
1. Obtain blood from fasting patient
2. Use heparinised plasma for investigation
3. Use dry defatted tubes
4. Follow cholesterol-free diet 2-3 days before investigation

69. Screening tests for lipid exchange assessment include:
1. Total cholesterol
2. Phospholipids
3. Apolipoprotein A
4. Triglycerides
5. Fatty acids

70. What are the reasons of hypocholesterolaemia?
1. Nephrotic syndrome
2. Glomerulonephritis
3. Hard physical exercises
4. Insulin deficiency
5. Phaeochromocytoma

71. Which parameters should be determined in serum in order to identify the type of hypolipoproteinaemia?
1. α-cholesterol level
2. Total cholesterol
3. Main types of lipoproteins
4. LDL level

5. Triglycerides level

72. Apolipoproteins content may change in:
1. Coronary heart disease
2. Diabetes mellitus
3. Familial hyperlipidaemia
4. Pneumonia

73. Increased level of serum triglycerides may be revealed in:
1. Obesity
2. Alcoholism
3. Diabetes mellitus
4. Diabetes insipidus

74. In fasting serum from healthy individuals following types of lipoproteins are revealed:
1. LDL
2. Cholesterol
3. Chylomicrons
4. VLDL

75. Hypertriglyceridaemia may develop in:
1. Pancreatitis
2. Diabetes mellitus
3. Hepatitis
4. Thyrotoxicosis
5. Starvation

76. Atherogenous effect is characteristic for:
1. LDL
2. VLDL
3. Phospholipids
4. Polyunsaturated fatty acids
5. HDL

77. Antiatherogenous effect is characteristic for:
1. Triglycerides
2. Cholesterol
3. Pre-β- lipoproteins
4. β- lipoproteins
5. α- lipoproteins

78. Apolipoprotein is:
1. Protein that forms protein-lipid complex
2. Protein that determines properties of protein-lipid complex

3. Protein that causes hyperlipoproteinaemia in inherited defect or impaired apoprotein synthesis
4. Protein in fructosamine

79. VLDL are synthesized in:
1. Muscles
2. Fatty tissue
3. Hepatocytes
4. Lungs

80. LDL are synthesized in:
1. Kidneys
2. Fatty tissue
3. Plasma
4. Connecting tissue

81. Apolipoprotein A contains in:
1. Chylomicrons
2. VLDL
3. IDL
4. LDL
5. HDL

82. Apolipoprotein B is not present in:
1. VLDL
2. IDL
3. LDL
4. HDL

83. A 43-years old patient, plasma is transparent, cholesterol - 5,2 mmol/l, α-cholesterol - 0,94 mmol/l, atherogenity index – 4,5. Asses his lipid metabolism status.
1. Normal
2. Hyperlipidaemia
3. Hypocholesterolaemia
4. High atherogeneous risk

84. A 13-years old patient: obese, plasma is turbid (milky), hypertriglyceridaemia. Suspected type of hyperlipoproteinaemia is:
1. Type I
2. Type II
3. Type III
4. Type IV
5. Type V

85. A 49-years old patient was admitted to the hospital. He complains of frequent onsets of angina pectoris, eliminated by nitroglycerin. Laboratory investigation should include determination of :

1. Cholesterol, triglycerides, α-cholesterol
2. Cholesterol, cholesterol esters, total lipids
3. Cholesterol, total lipids, phospholipids
4. Cholesterol, ketone bodies, non-esterified fatty acids

86. A laboratory investigation gave the following results: cholesterol - 5,0 mmol/l, α-cholesterol – 1,83 mmol/l, triglycerides – 1,25 mmol/l, atherogenity index – 1,56. Risk of developing coronary heart disease is:

1. Extremely high
2. High
3. Moderate
4. Low

87. Biological functions of plasma proteins are:

1. Reception
2. Adoption
3. Enzymes
4. Transport

88. Reference level of total plasma protein is:

1. 25-45 g/l
2. 45-65 g/l
3. 62-85 g/l
4. 82-95 g/l

89. Life threatening total plasma protein level is less than:

1. 40 g/l
2. 60 g/l
3. 55 g/l
4. 50 g/l

90. During electrophoresis plasma proteins are separated into following fractions:

1. Albumin
2. α- globulins
3. Chylomicrons
4. γ- globulins
5. β- globulins

91. Reference level of plasma albumin is:

1. 15-25 g/l
2. 35-50 g/l

3. 30-40 g/l
4. 60-80 g/l

92. Life threatening hypoalbuminaemia is:

1. Albumin level is less than 50 g/l
2. Albumin level is less than 45 g/l
3. Albumin level is less than 20 g/l
4. Albumin level is less than 30 g/l

93. Proteinuria is:

1. Protein excreted in the urine in a quantity above 20 mg/24h
2. Protein excreted in the urine in a quantity of more than 150 mg/24h
3. Protein excreted in the urine in a quantity of more than 50 mg/24h
4. Protein excreted in the urine in a quantity of more than 30 mg/24h

94. Dysproteinaemia is:

1. Increased concentration of total plasma protein
2. Decreased concentration of total plasma protein
3. Decreased fibrinogen level
4. Altered ratio of plasma proteins fractions

95. Decreased level of γ-globulins is observed in:

1. Coronary heart disease
2. Gastritis
3. Radiation sickness
4. Tumors of oesophagus
5. Rheumatoid arthritis

96. Bence-Jones protein can be revealed by:

1. Reaction of agglutination
2. Dialysis of the urine
3. Electrophoresis of the urine
4. Concentration of the urine

97. Which diseases are accompanied by decreased fibrinogen level:

1. Myocardial infarction
2. Chronic liver diseases
3. Rheumatoid arthritis
4. Uraemia
5. Glomerulonephritis

98. Reference level of plasma fibrinogen is:

1. 2-4 g/l
2. 4-6 g/l

3. 6-8 g/l
4. 8-10 g/l

99. Increased level of fibrinogen is observed in:
1. Acute staphylococcus infections
2. Diabetes mellitus
3. Chronic hepatitis
4. Acute pancreatitis
5. Nephrotic syndrome

100. Paraproteins can be revealed in:
1. Waldenstrom's disease
2. Myeloma
3. Pneumonia
4. Light chain disease

101. Transferrin is:
1. Globulin combined with magnesium
2. Globulin combined with iron
3. Globulin combined with sodium
4. Globulin combined with cobalt
5. Globulin combined with calcium

102. Which pathological states lead to hyperproteinaemia:
1. Increased synthesis of paraproteins
2. Hyperhydratation
3. Malabsorption of proteins in the intestine
4. Increased permeability of blood vessel wall

103. The main physiological function of haptoglobulin is:
1. Binding of haemoglobin
2. Acute phase protein
3. Takes part in immunological reactions
4. Takes part in blood coagulation

104. Inherited α1-antitrypsin deficiency leads to:
1. Emphysema in young people
2. Pyelonephritis
3. Hepatitis of newborns
4. Inflammatory and infectious lung diseases

105. Acute phase proteins are divided into:
1. Positive reactants
2. Active reactants
3. Negative reactants

4. Non-active reactants
5. Weakly active reactants

106. What are the main diagnostic purposes of CRP determination?

1. Diagnosis of neonatal sepsis
2. Differential diagnosis of viral and bacterial inflammation
3. Assessment of antibiotic therapy efficacy
4. Assessment of hyperglycaemia duration

107. Increasing of which acute phase protein is the most remarkable in bacterial inflammation:

1. Haptoglobulin
2. Ceruloplasmin
3. CRP
4. Transferrin
5. Fibrinogen

108. The majority of enzymes reach maximal activity in the following range of pH:

1. 1,5-2,0
2. 8,0-9,0
3. Nearly neutral
4. If pH=7,0 only
5. 5,5-6,5

109. Isoenzymes are:

1. Multiple forms of enzymes catalyzing different reactions
2. Multiple forms of enzymes catalyzing the same reaction
3. Multiple forms of enzymes with different physical and chemical properties
4. Multiple forms of enzymes with the same physical and chemical properties

110. Enzymes activity is determined in:

1. Blood serum
2. Leucoconcentrates
3. Biopsy material
4. CSF

111. Maximal activity of ALT is revealed in:

1. Lungs
2. Liver
3. Skeletal muscles
4. Kidneys
5. Pancreas

112. Maximal activity of Creatine Kinase is revealed in:

1. Heart muscle
2. Prostate gland
3. Spleen
4. Kidneys
5. Pancreas

113. Creatine Kinase has following isoenzymes:

1. Muscular
2. Brain
3. Lung
4. Heart
5. Liver

114. Increased activity of γ-Glutamyl Transpeptidase in serum is revealed in:

1. Prostatitis
2. Gastritis
3. Pancreatitis
4. Cholestasis
5. Glomerulonephritis

115. Myocardial injury is accompanied by increased activity of:

1. Lipase
2. ALT
3. γ-Glutamyl Transpeptidase
4. α-Amylase
5. Heart isoenzyme of Creatine Kinase

116. Lactate Dehydrogenase molecule consists of such subunits:

1. B and M
2. H and M
3. B,M and H
4. B and H
5. B

117. How many isoenzymes does Lactate Dehydrogenase have:

1. 2
2. 3
3. 5
4. 10

118. Myocardium is rich in:

1. LDH-1
2. LDH-2
3. LDH-3
4. LDH-4

5. LDH-5

119. Acid Phosphatase activity increases in:

1. Prostatitis
2. Gastritis
3. Bronchitis
4. Meningitis

120. Patient complains of an onset of acute pain in the abdomen. Laboratory investigation revealed increased α-Amylase activity . Which diagnosis should be suspected?

1. Acute pancreatitis
2. Acute viral hepatitis
3. Renal calculi
4. Myocardial infarction
5. Acute pleuritis

121. Amylase isoenzymes are located in:

1. Prostate gland
2. Myocardium
3. Pancreas
4. Lungs
5. Salivary glands

122. Patient complains of an onset of acute retrosternal pain. Laboratory investigation revealed increased activity of serum Creatine Kinase. Suspected diagnosis is:

1. Acute pancreatitis
2. Acute viral hepatitis
3. Renal calculi
4. Myocardial infarction
5. Acute pleuritis

123. Which enzyme activity grows in increased bone resorption?

1. Alkaline Phosphatase
2. Amino Trasferases
3. Catalase
4. Acid Phosphatase
5. Lactate Dehydrogenase

124. Determination of which enzyme activity is the most significant in pancreatic injury?

1. Cholinesterase
2. α-Amylase
3. Creatine Kinase

4. LDH
5. γ-Glutamyl Transpeptidase

125. Which enzyme is considered to be early marker of myocardial infarction?
1. LDH-5
2. Cholinesterase
3. α-Amylase
4. Creatine Kinase
5. Alkaline Phosphatase

126. Which enzyme activity grows mostly in prostate gland cancer?
1. α-Amylase
2. Creatine Kinase
3. Alkaline Phosphatase
4. Acid Phosphatase
5. ALT

127. Which enzymes activity should be determined in serum in suspected toxic hepatic injury?
1. Cholinesterase
2. LDH
3. Creatine Kinase
4. γ-Glutamyl Transpeptidase
5. Acid Phosphatase

128. Which enzymes activity will increase in skeletal muscles injury?
1. Creatine Kinase
2. α-Amylase
3. LDH
4. Amino Trasferases

129. Increased activity of serum Creatine Kinase is revealed in:
1. Muscular traumas
2. Alcoholic intoxication
3. Muscular dystrophy
4. Pyelonephritis

130. Markers of cholestasis are:
1. Amino Trasferases
2. LDH and Creatine Kinase
3. Hystidase and Urokinase
4. γ-Glutamyl Transpeptidase and Alkaline Phosphatase

131. Which enzymes activity is increased in pancreatitis:

1. Urokinase
2. Acid Phosphatase
3. γ-Glutamyl Transpeptidase
4. Alkaline Phosphatase
5. α-Amylase

132. Which enzyme activity should be determined in serum in suspected chronic hepatitis?

1. ALT, AST, γ-Glutamyl Transpeptidase, Cholinesterase, Alkaline Phosphatase
2. LDH and Creatine Kinase
3. Acid Phosphatase and Urokinase
4. Alkaline Phosphatase isoenzymes

133. De Ritis ratio is:

1. ALT to AST ratio
2. Alkaline Phosphatase to Lipase ratio
3. γ-Glutamyl Transpeptidase to ALT ratio
4. AST to ALT ratio
5. AST to Acid Phosphatase ratio

134. Acid Phosphatase activity increases in:

1. Tumors of prostate gland
2. Pancreatitis
3. Pregnancy
4. Bone metastatic injury

135. Isoenzymes LDH-1 and LDH-2 content is high in:

1. Heart
2. Skeletal muscles
3. Liver
4. Tumor cells
5. Pancreas

136. γ-Glutamyl Transpeptidase activity increases in:

1. Toxic hepatic injury
2. Myocardial infarction
3. Intra- and extrahepatic cholestasis
4. Acute pancreatitis

137. Increasing of which Creatine Kinase isoenzymes is specific for myocardial infarction?

1. CK-MM
2. CK-MB
3. CK-BB

4. CK-CC

138. Increased activity of Alkaline Phosphatase bone isoenzyme is characteristic for:

1. Hepatic cirrhosis
2. Primary and secondary hepatic tumors
3. Intrahepatic cholestasis
4. Paget's disease

139. Water distribution in the organism depends on:

1. Osmotic pressure
2. Oncotic pressure
3. Blood cholesterol level
4. Permeability of blood vessel wall

140. Normal plasma osmolality is:

1. 140-180 mosmol/kg
2. 275-295 mosmol/kg
3. 350-385 mosmol/kg
4. 550-600 mosmol/kg
5. 600-650 mosmol/kg

141. Osmotic gap is increased in:

1. Ethanol intoxication
2. Hydrocyanic acid intoxication
3. Lead poisoning
4. Mercury intoxication

142. In norm osmotic gap does not exceed:

1. 10 mosmol/kg
2. 20 mosmol/kg
3. 30 mosmol/kg
4. 40 mosmol/kg

143. Reference values of plasma sodium are:

1. 120-130 mmol/l
2. 130-147 mmol/l
3. 135-148 mmol/l
4. 145-155 mmol/l

144. Life threatening hyponatraemia is:

1. <125 mmol/l
2. <130 mmol/l
3. <122 mmol/l
4. <120 mmol/l

145. Life threatening hypernatraemia is:

1. >150 mmol/l
2. >148 mmol/l
3. >155 mmol/l
4. >160 mmol/l

146. Physiological function of sodium is:

1. Regulation of oncotic pressure
2. Regulation of water and electrolyte balance
3. Regulation of acid-base balance
4. Nerve impulse generation

147. Which hormones regulate sodium level in plasma?

1. Aldosterone
2. Insulin
3. Adrenaline
4. Prostaglandins
5. Calcitonin

148. The main reason of hypernatraemia is:

1. Conn's syndrome
2. Pheochromocytoma
3. Addison's disease
4. Hypovitaminosis D
5. Parathyroid adenoma

149. The main reasons of hyponatraemia are:

1. Hypotonic hyperhydration
2. Hypertonic dehydration
3. Diuretic therapy
4. Addison's disease

150. Reference values of plasma potassium are:

1. 2,5-5,5 mmol/l
2. 3,0-5,2 mmol/l
3. 3,5-5,2 mmol/l
4. 5,0-6,5 mmol/l

151. Life threatening hypokalaemia is:

1. <3,0 mmol/l
2. <2,9 mmol/l
3. <2,7 mmol/l
4. <2,5 mmol/l

152. Life threatening hyperkalaemia is:

1. >3,5 mmol/l
2. >5,5 mmol/l
3. >7,5 mmol/l
4. >6,5 mmol/l

153. Biological functions of potassium are:

1. Nerve impulse generation
2. Affects neuromuscular activity
3. Cell membrane potentials formation
4. Takes part in lipid transport

154. The main reasons of hyperkalaemia are:

1. Haemolytic crisis
2. Metabolic acidosis
3. Shock
4. hyperemesis

155. Hypokalemia may develop in:

1. Vomiting
2. Acute and chronic renal failure
3. Sepsis
4. Crush syndrome

156. Clinical signs of hyperkalaemia are:

1. Vision disturbances
2. Paralysis
3. Myocardial function impairment
4. Gastrointestinal tract function impairment

157. Reference values of serum total calcium are:

1. 2,12-2,6 mmol/l
2. 3,5-5,5 mmol/l
3. 3,1-3,6 mmol/l
4. 3,3-5,5 mmol/l

158. Reference values of serum ionized calcium are:

1. 2,12-2,60 mmol/l
2. 3,57-4,59 mmol/l
3. 4,15-4,65 mmol/l
4. 3,33-5,55 mmol/l
5. 0,98-1,13 mmol/l

159. Serum ionized calcium concentration is influenced by:

1. pH

2. Plasma triglycerides level
3. Plasma potassium level
4. Plasma sodium level
5. Plasma chloride level

160. The main reasons of hypercalcaemia are:
1. Vitamin D deficiency
2. Rickets
3. Parathyroid adenoma
4. Administration of digitalis
5. Nephrotic syndrome

161. Physiological functions of phosphorus are:
1. Formation of energy rich bonds
2. Transport of glucose
3. Takes part in bone formation
4. Takes part in protein exchange

162. Reference values of serum phosphorus in adults are:
1. 0,55-1,5 mmol/l
2. 0,97-1,45 mmol/l
3. 1,45-2,45 mmol/l
4. 2,33-2,78 mmol/l

163. Which ion determines water transport process across cellular membranes?
1. Calcium
2. Potassium
3. Sodium
4. Hydrogen
5. Chloride

164. Reduced magnesium level results in:
1. Depression
2. Acid-base disturbances
3. Hypothyroidism
4. Renal calculi formation
5. Anemia

165. Reference values of serum magnesium are:
1. 0,5-1,5 mmol/l
2. 0,8-1,0 mmol/l
3. 1,4-2,4 mmol/l
4. 2,3-2,7 mmol/l

166. The reasons of hypochloridaemia are:

1. Myocardial infarction
2. Diabetic ketoacidosis
3. Chronic diarrhea
4. Renal failure

167. Hyperchloridaemia appears in:

1. Hypoventilation
2. Diabetic ketoacidosis
3. Lactic acidosis
4. Oedema

168. What should be taken into account while interpreting total calcium level?

1. Cholesterol level
2. Albumin concentration
3. Phosphorus concentration
4. pH

169. Increased magnesium level revealed in:

1. Malabsorption
2. Chronic alcoholism
3. Hypoparathyroidism
4. Primary adrenal hypofunction
5. Primary aldosteronism

170. Magnesium excretion in urine is reduced in:

1. Alcoholism
2. Starvation
3. Hypoparathyroidism
4. Hyperthyroidism
5. Magnesium deficiency

Answers

1. 1
2. 5
3. 3
4. 2,3,4
5. 5
6. 3
7. 1,2
8. 3,4
9. 4,5
10. 3
11. 3
12. 1
13. 2
14. 2
15. 3
16. 4
17. 2
18. 2,4
19. 2,4
20. 1,3
21. 1,2
22. 2
23. 2
24. 3
25. 3
26. 1
27. 2
28. 3
29. 2
30. 3
31. 1
32. 1
33. 1
34. 4
35. 2
36. 2
37. 1
38. 2
39. 2
40. 1
41. 3
42. 1
43. 1,2,3
44. 1,3
45. 3
46. 1
47. 4
48. 3
49. 3
50. 1
51. 5
52. 4
53. 5
54. 2
55. 2
56. 2
57. 4
58. 3
59. 2
60. 1
61. 4
62. 4
63. 1
64. 1,2,4
65. 4
66. 2,3
67. 3
68. 1
69. 1,4
70. 3
71. 3
72. 1,2,3
73. 1,2,3
74. 1,3,4
75. 2
76. 1,2
77. 5
78. 1,2,3
79. 3
80. 3
81. 5
82. 4
83. 1
84. 1
85. 1
86. 4
87. 1,3,4
88. 3
89. 1
90. 1,2,4,5
91. 2
92. 3
93. 2
94. 4
95. 3
96. 3
97. 2
98. 1
99. 1
100. 1,2,4
101. 2
102. 1
103. 1
104. 1,3,4
105. 1,3
106. 1,2,3
107. 3
108. 3
109. 2,3
110. 1
111. 2
112. 1
113. 1,2,4
114. 4
115. 5
116. 2
117. 3
118. 1
119. 1
120. 1
121. 3,5
122. 4
123. 4
124. 2
125. 4
126. 4
127. 4
128. 1,3,4
129. 1,2,3

130. 4
131. 5
132. 1
133. 4
134. 1
135. 1
136. 1,3,4
137. 2
138. 4
139. 1,2,4
140. 2
141. 1
142. 1
143. 3
144. 4
145. 4
146. 2,3,4
147. 1
148. 1
149. 1,3,4
150. 3
151. 4
152. 3
153. 1,2,3
154. 1,2,3
155. 1
156. 2,3,4
157. 1
158. 5
159. 1
160. 3
161. 1,3,4
162. 2
163. 3
164. 1
165. 2
166. 2,3,4
167. 1
168. 2,3,4
169. 4
170. 5

Literature

1. Acid-base status of the organism. Laboratory and clinical aspects: booklet / U.I. Stepanova, L.I. Alehnovich, V.S. Kamyshnikov. – Mn.: BelMAPO, 2008.
2. Alan, H. Gowenlock Practical clinical biochemistry, sixth edition / Gowenlock H. Alan – CBC: New Delhi, India, 2002.
3. Clinical biochemistry. Tests for 4th year students of general medicine and pediatric faculty / S.V. Lelevich. – Grodno: GSMU, 2007.
4. Kamyshnikov, V.S. Methods of clinical laboratory investigations / V.S. Kamyshnikov, – M.: MEDpress-inform, 2009.
5. Kamyshnikov, V.S. Manual of clinical biochemical laboratory diagnostics / V.S. Kamyshnikov, – Mn.: Belarus, 2000. – In 2 vol.
6. Laboratory diagnostics of carbohydrate metabolism disturbances. Metabolic syndrome, diabetes mellitus / V.V. Dolgov, A.V. Selivanov and authors. – M., 2006.
7. Marshall, V. J. Clinical biochemistry / V. J. Marshall, – SPb.: Nevski dialect, 1999.
8. Menshikov V.V. Manual of clinical laboratory diagnostics / V.V. Menshikov – M.: Medicine, 1982.
9. Tkachuk V.A. Clinical biochemistry / V.A.Tkachuk. – M.: GOETAR-MED, 2004.
10. Tits, U. Encyclopedia of clinical laboratory tests / U, Tits,– M.: Labinform, 1997.
11. Zylva, D.F., Pannal, P.R., Clinical chemistry in diagnosis and treatment / D.F. Zylva, P.R.Pannal, – M., 1988.