Poltava State Medical University

Lecture

# MAIN PRINCIPLES OF THE THERAPY OF ACUTE POISONINGS WITH MEDICINAL DRUGS. ANTIDOTES MEDICINAL AGENTS

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# POISONINGS

***Poisoning is a result of action of toxic agent or toxic dose of the drug on the organism.***

Poisonings may be acute and chronic. They are divided into household, environmental, industrial, pharmacological.

Poisoning with pharmacological agents results from: absolute overdose (administration of toxic dose of the drug) or relative overdose (caused by therapeutic dose under the conditions of drug accumulation, hepatic and renal insufficiency, etc.).

# Main syndromes accompanied acute poisonings

- CNS disturbances: coma, unconsciousness, seizures
- cardiovascular disturbances: heart failure, collapse, arrhythmia
- respiration disorders: spasm of bronchi, pulmonary edema, respiratory arrest, asphyxia
- GI disorders: vomiting, nausea, diarrhea, constipation, loss of appetite
- liver lesions: hepatic necrosis, hepatic insufficiency
- renal insufficiency
- lesions of skin and mucous membranes: necrosis, irritation, exfoliation, rash.

# Principles of poisonings treatment

- ***termination of poison exposure***
- ***fastening of elimination of toxic agent from the body***
- ***antidote administration***
- ***general supportive and symptomatic therapy.***

# Types of the therapy in acute poisoning

- detoxification therapy (non-specific)
- symptomatic therapy (non-specific)
- antidote therapy (specific).

# Detoxification therapy: reduction of poison absorption

- Irrigation of skin and mucous membranes with cold water, isotonic solution of sodium chloride, in some cases with special antidotes (e.g. weak solution of ammonia for neutralizing of formaldehyde; oil for washing out of phenol; 2% solution of sodium chloride for neutralizing of silver nitrate)
- Lavage of stomach with potassium permanganate (in poisoning with alkaloids), cold water (in poisoning with acids or alkalis), etc.
- Emesis induced with apomorphine (parenterally), solution of ammonia (dissolved in water, per os), or mechanically
- Use of adsorbents (activated charcoal, enterosgel)
- Use of astringents (tannin, milk, egg-white)
- Use of osmotic purgatives (magnesium sulfate) which form high osmotic pressure in the lumen of intestine and bowel and in such way inhibit absorption of toxic agent

# Detoxification therapy: enhancement of poison removal

- Forced diuresis with furosemide or mannitol
- Altering of urinary pH (alkalinization for acidic substances and acidification for alkaline drugs)
- Peritoneal dialysis, hemodialysis, hemosorbtion
- Use of osmotic purgatives (magnesium sulfate, sodium sulfate)
- Administration of drugs stimulating enzymes activity in the liver for fastening of poison metabolism (e.g., phenobarbital; glucose and vitamins in poisoning with ethanol)
- Analeptics for stimulation of respiration and increase of excretion of poison through lungs (Carbogenum, Aethimizolum).

# Symtomatic therapy

- It is aimed on supporting of damaged functions of the organism and resuscitation
- General supporting and symptomatic therapy is needed in the most cases of poisonings
- It is achieved according to main syndromes of intoxication and is the same in different poisonings.

# Antidote therapy

***Antidotes are drugs specifically interacting with some poisons.*** They act either by preventing of absorption or by inactivating or antagonizing the action of the poisons. Specific antidotes are not available for all poisons (e.g., acute poisoning with phenol).

# General mechanisms of antidote action

- binding to receptors (e.g., atropine, naloxone)
- acting on enzymes (e.g., cholinesterase reactivators)
- displacement from tissue binding sites (e.g., ethanol under the conditions of poisoning with methanol)
- exchanging with poison, binding with poison (e.g., chelating agents)
- replenishment of depleted essential substances (e.g., sulfur containing agents)

# Classification of antidotes

*1. Sulfur containing compounds*

– Unithiolum

– Sodium thiosulfate

– Acetylcysteine

*2. Chelating agents*

– Sodium edeteate (trilon B, EDTA–Natrium)

– Tetacin-calcium (Calcium-EDTA)

– Deferoxamine (desferral)

– Penicillamine

*3. Cholinesterase reactivators*

– Alloxim

– Dipiroxim

– Isonitrosine

*4. Antagonists of opioids*

– Naloxone

– Naltrexone

*5. M-cholinoblockers*

– Atropine sulfate

*6. Anticholinesterases*

– Neostigmine (Proserinum)

*7. Preparations of other groups*

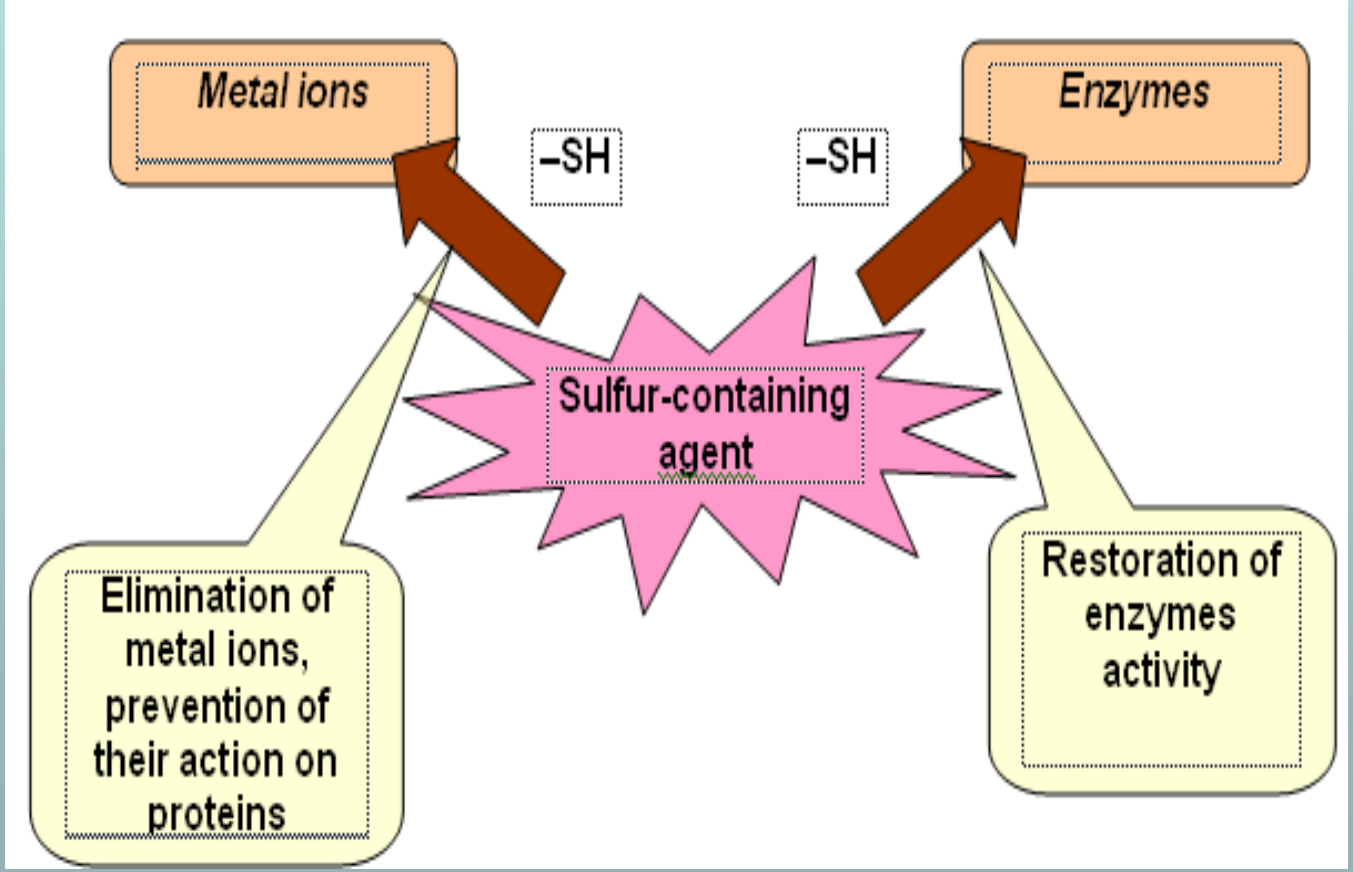
– Cromosmonum (Methyleni coeruleum)

– Ethanol (Spiritus aethylicus)

– Potassium permanganate

– Activated charcoal (Carbo activatus).

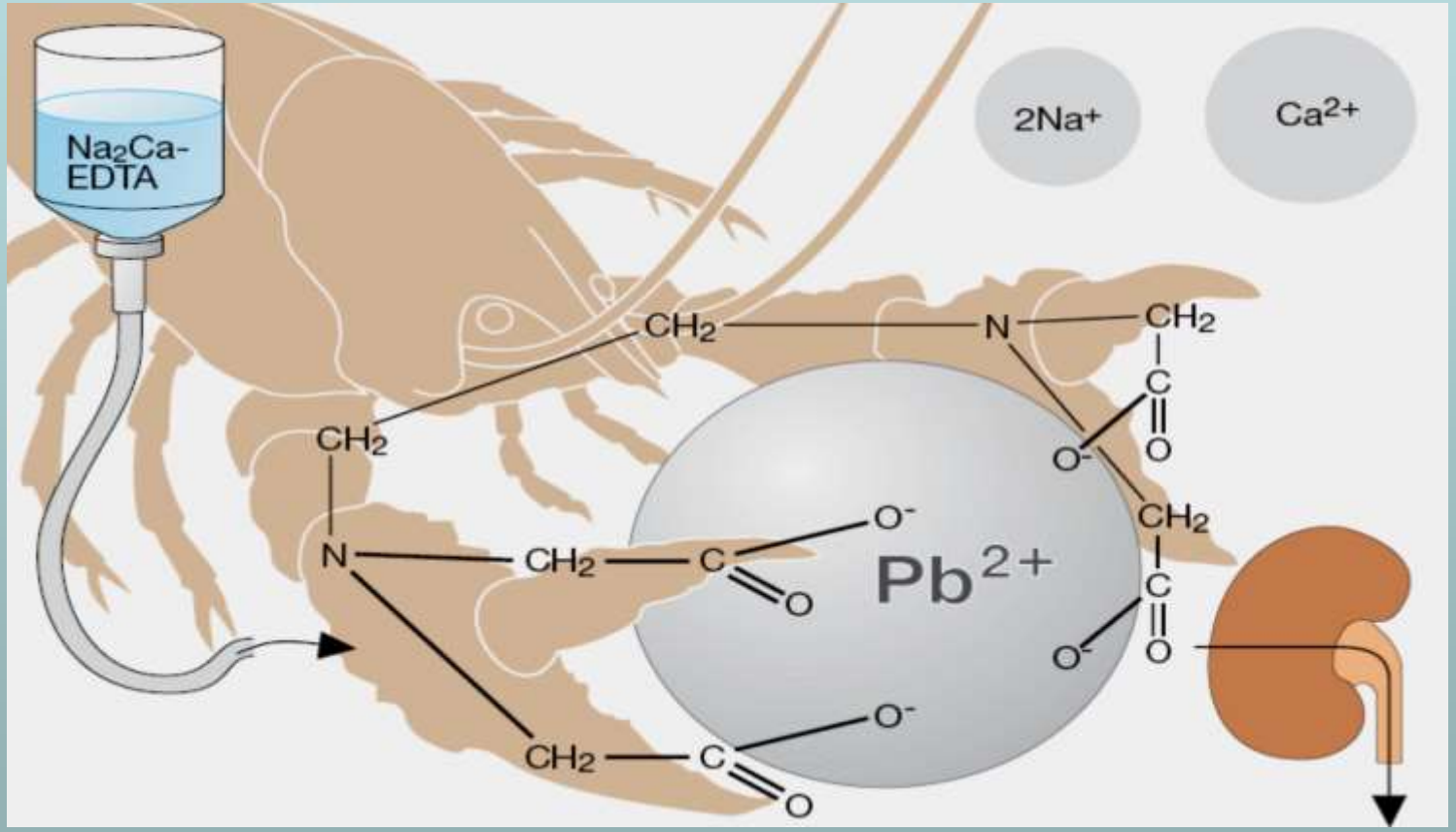
# Sulfur-containing drugs



# Unithiol

- is mercaptide on its chemical structure
- contains two SH-groups and forms two bonds with the metal ions
- is administered IM, orally (in chronic poisonings)
- has complex mechanism of action: 1) It forms bonds between SH-groups and metal ions with formation of inactive complexes which are excreted with urine; 2) It prevents metals binding to tissue proteins; 3) It restores the activity of SH-groups of enzymes as a donator of SH-groups
- is indicated in poisonings with arsenic compounds, mercury, lead, in cardiac glycosides poisoning, streptomycin poisoning, hepatocerebral dystrophy, treatment of alcoholism
- may cause nausea, tachycardia, dizziness, paleness.

# Chelating agents



# Sodium edeteate

- is administered by IV infusion
- forms complex compounds with different metal ions, especially with calcium
- is used in poisonings with metal salts, cardiac glycosides, as well as in pathological calcification
- can cause hypocalcemia and tethany in quick administration.

# Tetacin-calcium

- is administered IV and orally (in chronic intoxication)
- is used for treatment of poisonings with compounds of thorium, lead, cobalt, mercury, uranium, yttrium
- may cause gastrointestinal disturbances, toxic nephrosis, decrease in content of hemoglobin, ferrous, and vitamin B12
- is contraindicated for patients with diseases of the liver and kidney.

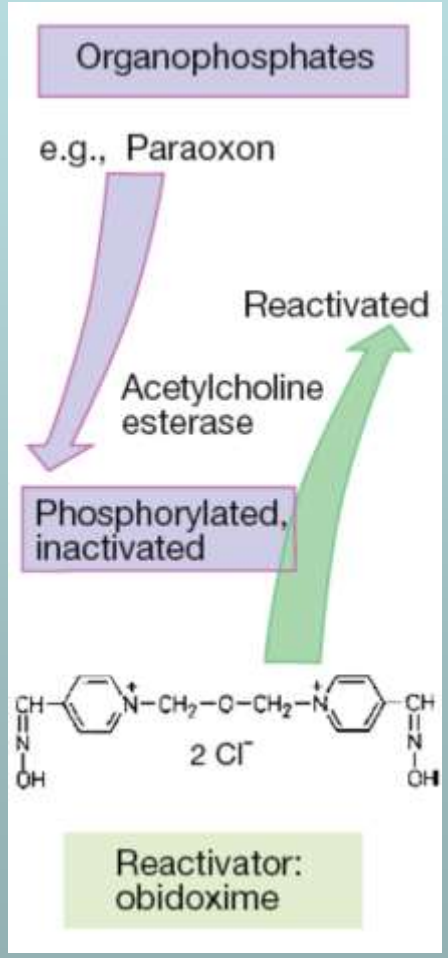
# Penicillamine

- is synthetic preparation similar to the fragment of penicillin's molecule
- is taken orally
- forms complex compounds with metal ions (copper, lead, mercury, iron, calcium)
- is used in acute and chronic poisonings with heavy metals, as well as in hepapocerebral dystrophy (Wilson's disease) and some collagen diseases (rheumatoid arthritis, scleroderma)
- may cause leucopenia, thrombocytopenia, hematuria, proteinuria, myalgia, arthralgia, itch, utricaria, gastrointestinal disturbances.

# Deferoxamine

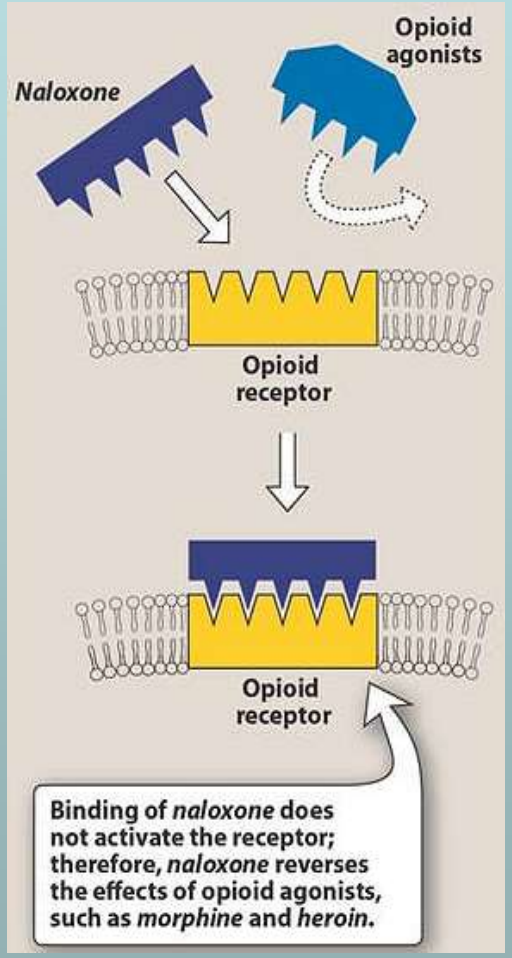
- is administered IM, IV, orally, or used for lavage of stomach
- binds with free ions of iron and with iron from ferrous-containing proteins (ferritin and hemosiderin); does not interact with iron from hemoglobin and enzymes; does not influence on content of other ions
- is used for treatment of acute poisoning with ferrous compounds, hemochomatosis, hemosiderosis
- may cause skin rash, collapse (after quick IV injection).

# Cholinesterase reactivators




- They interact with phosphor and split off phosphor from the etheric site of cholinesterase, cause reactivation of enzyme.
- They interact with poison and neutralize it.
- They are the most effective if are used for prophylaxis of poisoning or at the beginning of poisoning.
- Cholinesterase reactivators are administered together with atropine.

# Antagonists of opioid receptors




***Naloxone*** is an antidote of narcotic analgesics. It displaces drugs from opioid receptors

# Cholinergic drugs

**M–CHOLINOBLOCKERS**

***Atropine*** is an antidote to M-cholinergic agonists. It is also used in poisonings with anticholinesterases and morphine.

**ANTICHOLINESTERASES**

***Neostigmine, Physo-stigmine, galanthamine*** are antidotes to M-cholino-blockers and antidepola-rizing myorelaxants.

# Methylene blue

- is antiseptic with properties of donator and acceptor of hydrogen
- is administered IV in the form of sterile solution (**Cromosmonum**)
- is used for treatment of acute poisonings with cyanides, carbon oxide, hydrogen sulfide. Under the conditions of cyanide poisoning Methylenum coeruleum converts hemoglobin into methhemoglobin which interacts with cyanides and transforms them into non-toxic compounds.

# Potassium permanganate

- is an antiseptic from oxidazers group
- is an antidote in poisonings with morphine, some alkaloids, and phosphor
- is used for lavage of stomach as 0,1–0,5% solution
- is not effective in poisonings with atropine, cocaine, and barbiturates.

# Activated charcoal

- is adsorbent containing pores which absorb low weight molecules of toxic agents
- is taken orally in the form of aqueous suspension or tablets (in light intoxication or in chronic toxicity)
- is an universal antidote.

# Acute poisoning with organophosphates (irreversible anticholinesterases)

***Signs:***

hypersalivation, nausea, vomiting, spasm of bronchi, then edema of lungs, convulsions, unconsciousness.

***Emergency help:***

Reactivators of cholinesterase (dipyroxim, alloxim, izonitrozin), IM

Atropine, IM.

# Acute poisoning with ethanol

***Signs:***

specific odor; excitement, then sleeping and coma; hyperemia of the face, then paleness; decrease in BP; oppression of respiration; hyporeflexia; hypotermia; involuntary urination and defecation.

***Emergency help:***

Lavage of stomach with solution of potassium permanganate

Analeptics (Bemegridum)

Glucose, insulin, and vitamins preparations (IV)

Nootrops (piracetam, IV).

# Acute poisoning with morphine

***Signs:***

sleep or unconsciousness, normal or increased reflexes, normal muscles tone, miosis, bradycardia, Chain-Stocks breath, retention of urination, spasm of intestine and bowel.

***Emergency help:***

Lavage of stomach with 0,5% solution of potassium permanganate

Naloxone, IV ( an antagonist of narcotic analgesics)

Atropine (for decrease in vagal action of morphine).

# Acute poisoning with cardiac glycosides

***Signs:***

bradycardia, then tachycardia and arrhythmia (premature ventricular beats, fibrtillation); changes in ECG; increase in signs of CHF; anorexia, vomiting, nausea; headache, fatigue, hallucination; vision disturbances (xantopsia, micro- and macropsia).

***Emergency help:***

Abolishing of cardiac glycoside
Drugs containing potassium (potassium chloride, panangin)
SH-group donator (Unithiolum)
Anti-arrhythmic agents (phenitoin, lidocaine, propranolol, atropine for AV block)
Digoxin antibodies (digibind)
Glucose, vitamins preparations, oxygen inhalation.

# Acute poisoning with hypnotics (barbiturates)

***Signs**:*

sleeping, unconsciousness, hypotonia, lowering of reflexes, oppression of respiration, decrease in BP.

***Emergency help:***

Lavage of stomach

Alkalinization of urine and forced diuresis

Hemodialysis

Salt purgatives (magnesium sulfate).

# Acute poisoning with acids and alkalis

***Signs**:*

necrosis of skin and mucous membranes (coagulation necrosis caused by acid or coliquation necrosis caused by alkali); metabolic acidosis (if an acid is the toxic agent); severe pain.

***Emergency help:***

Neutralizing of acid by solution of sodium bicarbonate and neutralizing of alkali by weak solution of acid (acetic acid, citric acid) on the surface of skin

Lavage of stomach with cold water

Administration of covering drugs, astringents, and local anesthetics into the stomach

In poisoning with acids – sodium bicarbonate (IV) for correction of metabolic acidosis

Narcotic analgesics for decrease in pain.

# Acute poisoning with salts of heavy metals (e.g., mercury)

***Signs:***

severe pains in abdomen, vomiting and diarrhoea with admixtures of blood, metal aftertaste, hypersalivation, bleeding gums, 2-3 days after – acute renal failure, hypochomic anemia, irritateability.

***Emergency help:***

Lavage of stomach

Administration of activated charcoal and astringents in stomach

Unithiolum, tetacin-calcium, or sodium thiosulfate

Atropine for a decrease in spasm of GI tract

Morphine

Hemodialysis.

# Complications of drugs therapy in the oral cavity

- Direct action of preparations on mucous membrane and dental bone
- Effects resulting from drugs pharmacokinetics
- Effects resulting from systemic action of preparations
- Manifestation of general side-effects of preparations in oral cavity
- Special side-effects of some preparations.

# Direct toxic action on mucous membrane and dental bone

- Acids, alkalis, phenol, silver nitrate, arsenic compounds act directly on mucous membrane and cause necroses.
- Acids would be emergence washed off from the mucous membrane or skin by 0,5 -1% solution of sodium bicarbonate. Alkalis would be neutralized by 0,5% solution of weak acid (acetic acid, citric acid, or hydrocloride acid).
- Phenol is washed off from the surface of skin or mucous membrane by oil, or by 50% solution of ethanol.
- Silver nitrite is neutralized by 2% solution of sodium chloride.
- Toxic action of arsenic compounds may be decreased by usage of magnesium oxide, or alcohol solution of iodine.
- In the case of toxic action of iodine on mucous membrane of oral cavity it is processed by magnesium oxide in the form of very fine powder as well as by solution of sodium thiosulfate.
- Toxic action of fluorides is neutralized by 10% solution of calcium chloride.
- Ferrous preparations interact with hydrogen sulfide in oral cavity and forms black stains on gums and teeth. Chlorhexidine may cause grey-brawn color of teeth.

# Toxic effects resulting from pharmacokinetics of preparations

- Bismuth is excreted by saliva and causes gingivitis and grey “bismuth” streak on gums.
- Bromides also are excreted by saliva and cause rash on mucous membrane of oral cavity.

# Toxic effects resulting from systemic action of drugs

- M-cholinoblockers, ganglia blockers, central alpha adrenomimetics (Clophelinum), neuroleptics, antihistamines (Dimedrolum) cause dry mouth due decreasing in saliva secretion.
- M-cholinomimetics, anticholinoesterases, iodides, bromides, IV general anaesthetic ketamine may cause hypersalivation.
- Sympatholytics (Octadinum, Reserpinum) cause the increase in size of bigger saliva glands.

# Manifestations of general side-effects

- There are allergic reactions in oral cavity caused by antibiotics, or by sulfa drugs.
- Wide spectrum antibiotics, sulfa drugs, metronidazole inhibit normal microbes in a body
- That leads to activation of Candida albicans. Candidiasis is developed. It displays as stomatitis, or glossitis.
- In overdose of heparin and other anticoagulants we can see haemorrhagies, bleeding gums and petechiae in oral cavity.
- Inhibitors of leucopoiesis and anticancer drugs may cause necrotic processes in oral mucous due inhibiting of cell proliferation.

# Special side-effects of some preparations

- Antiepileptic drug Dipheninum cause hyperplastic gingivitis.
- Metronidazole and antifungal drug Griseofulvinum cause dysheusia (changes in taste).

# CONTROL TASKS

- An overdose of cardiac glycosides manifested as premature ventricular beats, an increase in signs of heart failure; anorexia, vomiting, nausea; and xantopsia. Unithiol was administered to a patient as specific pharmacotherapeutic agent for this poisoning. Which group of antidotes is it from?
- Sulfur containing compounds
- Chelating agents
- Cholinesterase reactivators
- Antagonists of opioids
- M-cholinoblockers.

# CONTROL TASKS

- A patient has taken strong acid with the attempt of suicide. She had coagulation necrosis of mucous membrane in oral cavity and severe pain lengthways the gullet and in the epigastral area. Biochemical analysis of blood detected metabolic acidosis. Which drug should be given intravenously for correction of this manifestation of poisoning?
- Sodium bicarbonate
- Ammonia chloride
- Sodium chloride (0,9% solution)
- Glucose (5% solution)
- Potassium chloride.

# CONTROL TASKS

- A patient was taken to the emergency room with such symptoms, as unconsciousness, paleness; low blood pressure; oppression of respiration; hyporeflexia; hypotermia; involuntary urination and defecation. Perspirated air has specific alcohol odor. The diagnosis is: Acute alcohol intoxication. Glucose, insulin, and vitamins preparations are administered intravenously to the patient. What is the purpose of this administration?
- Promotion of alcohol metabolism
- Neutralization of toxic agent
- Promotion of poison’s excretion
- Protection of brain tissue
- Inhibition of alcohol absorption in the gut.