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BASIC PRINCIPLES OF TREATMENT OF ACUTE POISONING AND URGENT STATES

ACUTE POISONING

More than 60 000 xenobiotics are used in the world; annually ≈ 500 novel substances are introduce into pharmaceutical market

Factors that determine toxicity:

- physico-chemical properties of toxin
- dosage (concentration), way and speed of toxin entrance to organism
- biological species (human, animal), age, gender, weight, individual pecularities (genetic predisposition, diet, concomitant diseases etc)
- other factors: geographic, temperature, circadian, ecologic, industrial etc

PHYSICO-CHEMICAL PROPERTIES OF THE TOXIN

(degree of dispersion, crystal polymorphism, volatility, dissolving in different fluids, ionization degree)

- potential toxicity of **gases** ↑ than in liquid and solid substances
- more > **dispersion** of solid toxins, than > degree of their toxicity
- **amorphic substances** develop stonger toxic effect
- if **volatility** ↑, than risk of toxicity ↑ (↑ **absorption)**
- molecules with **moderate coefficient of distribution (fluid/water)** have the best absorption rate
- higher **lipid-solubility**, associated with better penetration into organism

PHYSICO-CHEMICAL PROPERTIES OF THE TOXIN

- toxicity of water-soluble toxins directly associated with degree of their solubility in water (non-soluble barium sulfate is non-toxic, but its other salts are water-soluble and then toxic)
- reactive chemical groups of toxins ↑ its toxicity
- affinity of toxin for receptor, density of its binding etc
- ionization degree of toxin directly proportional to its toxicity; for instance, toxicity of metallic salts is determined by its capability to release metals' ions (metallic mercury even at I.V. injection is non-toxic, however small doses of mercury chloride and oxide can cause lethal outcome)

DOSES OF TOXINS

– the most important factor that determine substance's toxicity !

according to lethal dose (LD)* substances are divided on 6 categories *(according to Hodge and Gleason):*

1. **overtoxicity – LD_{100} = 3 mg/kg and less**
2. **extremely toxic – LD_{100} = 5-50 mg/kg**
3. **high toxic – LD_{100} = 50-500 mg/kg**
4. **moderate toxic – LD_{100} = 0,5-5 g/kg**
5. **low toxic – LD_{100} = 5-15 g/kg**
6. **practically non-toxic – LD_{100} > 15 g/kg**

*** – LD_{10}; LD_{50}; LD_{100} – doses that cause death of 10, 50 and 100 % animals correspondently; ED_{50} (effective or average therapeutic) – dose that cause necessary effect in 50 % of patients**

CONCENTRATON, WAY AND SPEED OF TOXIN PENETRATION INTO ORGANISM

Concentration **– dosage of liquid and gas-like substance is measured by concentration: 5 ml concentrated sulphuric acid; 0,2-0,3 % sol. – harmless**

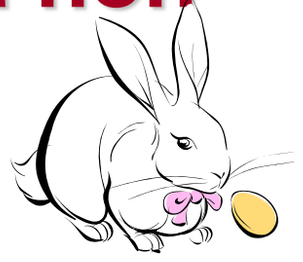
Way of entrance:

- ✓ **by toxicity: inhalation > I.V. > enteral > via mucosa > transdermal**
- ✓ **by frequency: 85,6 % – via GIT; 11,6 % – lungs; 2,7% – through skin; 0,1 % – others (placenta);**

Speed of entrance: **depend on physico-chemical properties of toxin (lipophylicity) and site of entrance (vascularization etc.)**

BIOLOGICAL SPECIES

- Digitalis et Belladonna pextremely toxic for human or harmless for herbivorous
- Datura stramonium contains atropine and scopolamine, toxic for human and non-toxic for animals
- atropine toxicity ↑ in rabbits, but Digitalis ↓ in rats
- phenylurea (rats venom) causes in rats pulmonary edema; for monkeys non-toxic (LD_{50} for rats – 5 mg/kg, rabbits – 40, hens – 100, guinea pig – 250)
- herbicide «paraqvat» is toxic for rats and non-toxic for human

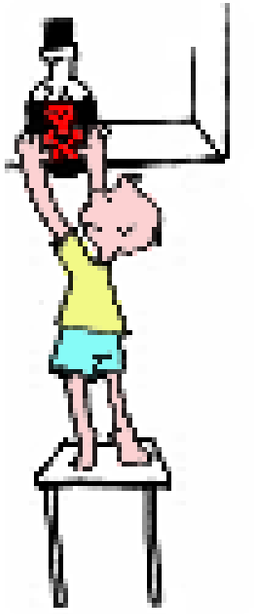


INDIVIDUAL CHARACTERISTICS

- ***age:*** **the most susceptible are kids (premature state of organs that determine toxins' absorption, biotransforation, and excretion), and aged persons (renal and liver diseases)**
- ***gender:*** **women are more susceptible (especially during pregnancy, lactation, mensis):**
  - ✓ **LD_{50} for rats male – 4,01, for female – 1,81 mg/kg**
- ***weight:*** **determine dosage of toxin**
- ***nutrition:***
  - ✓ **proteins ↓ toxicity**
  - ✓ **medicines ↓ alcohol toxicity**
  - ✓ **vitamins $B_{6,12}$ ↓ lead and isoniazid toxicity**
- ***genetic pecularities*** **(for example, alteration of enzyme system: «rapid» and «slow» acetylaters, oxidazers etc.)** ***and concomitant diseases*** **(especially those that affect liver and kidney function)**

TYPES OF POISONING

- clinical (acute, subacute, chronic)
- social-juridical:
  - ✓ intentional (suicide, killing, toxico- and narcomania)
  - ✓ unintentional or ocaisonal
- ethiology determined (poisoning by mushrooms, carbon monoxide, senile acid, methanol)



WHO statistics:

- ➢ more often poisoing at age under 16 yrs
- ➢ intentionally – 80 % (in women – 67 %, men – 33%); occasional – 20 % (in women – 40 %, men – 60 %)
- ➢ acute poisoning in 2-3 times more common in women (26 % – 17-20 yrs, 53 % – under 30 yrs, 6 % – 60 yrs and beyond)

COMBINATION OF POISONING

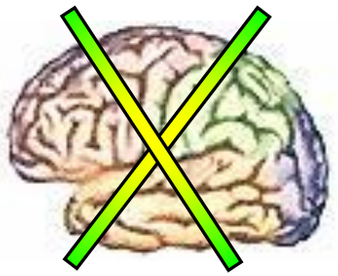
- **synergism:**
  - **summation (addition):** summation actions of toxins through the same mechanisms – 1+1 = 2 (tetrachlormethan and dichlorethan; adrenaline and noradrenalin; etc.)
  - **potentiation:** ↑ toxicity due to another toxin – 1+1 > 2 (alcohol and cyanamid calcium; tolyol and buthylacetate)
- **antagonism:** 2 and > toxins ↓, annul or inverse effects of each other – 1+1 < 2 or = 0 (citrate sodium and calcium; heavy metallic salts and SH-groups; etc.)
- **synergism-antagonism**

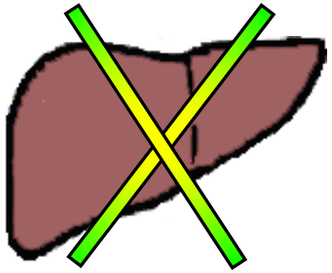
CLASSIFICATION OF TOXINS

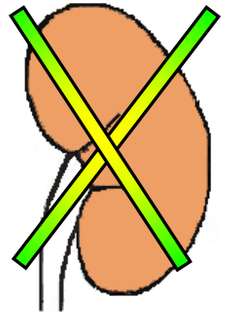
- **extremely toxic – chemical weapon of mass distraction, arsenical anhydrate, strychnin, today banned insecticides (thiophos, mercaptophos) etc.**
- **highly toxic – industrial toxins and chlorinated insecticides (tetrachlormethan (CCl_4), dichlorethan etc), air pollutants (ozone, carbon tetrachloride, nitrous dioxide, sulfur, etc.)**
- **moderately toxic – air pollutants (carbon dioxide, benzol, phenol etc.), phosphoorganic compounds, chlorphenoxyl herbicides etc.**
- **low toxicity – hydrocarbons of methane row, bipyridine herbicides (paraquat)**

EXAMPLES OF ORGANOTOXICITY

- **neurotropic** – chemical weapons, phosphoorganic compounds, opioids, barbiturates, etc.
- **hepatotropic** – industrial toxins and chlorinated insecticides: tetrachlormethan (CCl_4), dichlorethane; phosphorus etc.
- **nephrotropic** – mercury, acetic acid etc.
- **bone marrow** – air pollutant: carbon dioxide, benzol, phenol, tolyol, nitrates (methemoglobinemia), arsenicum (hemolysis) etc.







FREQUENCY OF ACUTE POISONING

- **medicines – 55,4 %:**
  - polymedicines – 25 %
  - benzodiazepines – 17 %
  - opioids – 15 %
  - phenothiazines – 12 %
  - barbiturates – 8 %
  - antidepressants – 7 %
  - different groups – 13 %
  - undetected – 3 %
- **insecticides* – 11,4 %**
  (out of them POC – 41,4 %)
- **ethanol – 8,6 %**
- **fungicides/raticides – 5,0 %**
- **toxic gases – 3,3 %:**
  - carbon monooxide – 80,7 %
  - household – 11,4 %
  - marsh (methane) – 5,3 %
  - sewerage – 0,8 %

FREQUENCY OF ACUTE POISONING

- **mushrooms – 2,6 %**
- **industrial hazard fluids (antifreeze etc.) – 2,1 %**
  (trichlorethylene – 28 %; formaldehyde – 23 %; ethylene glycol – 18 %; anylin – 8 %)
- **organic solvents – 2,4 %** **(turpentine – 58 %; aceton – 21%; CCl_4 – 4 %)**
- **methanol – 1,2 %**
- **detergents – 1,9 %**
- **petroleum products – 1,7 %**
  (gasoline – 69 %; kerosene – 16 %; diesel fuel – 9 %)
- **caustic fluids (greece. kaustikos – burning) – 1,7 %:**
  caustic soda – 40 %; calcinated – 18 %; sulfuric acid – 9 %
- **unknown venoms – 5,1 %**

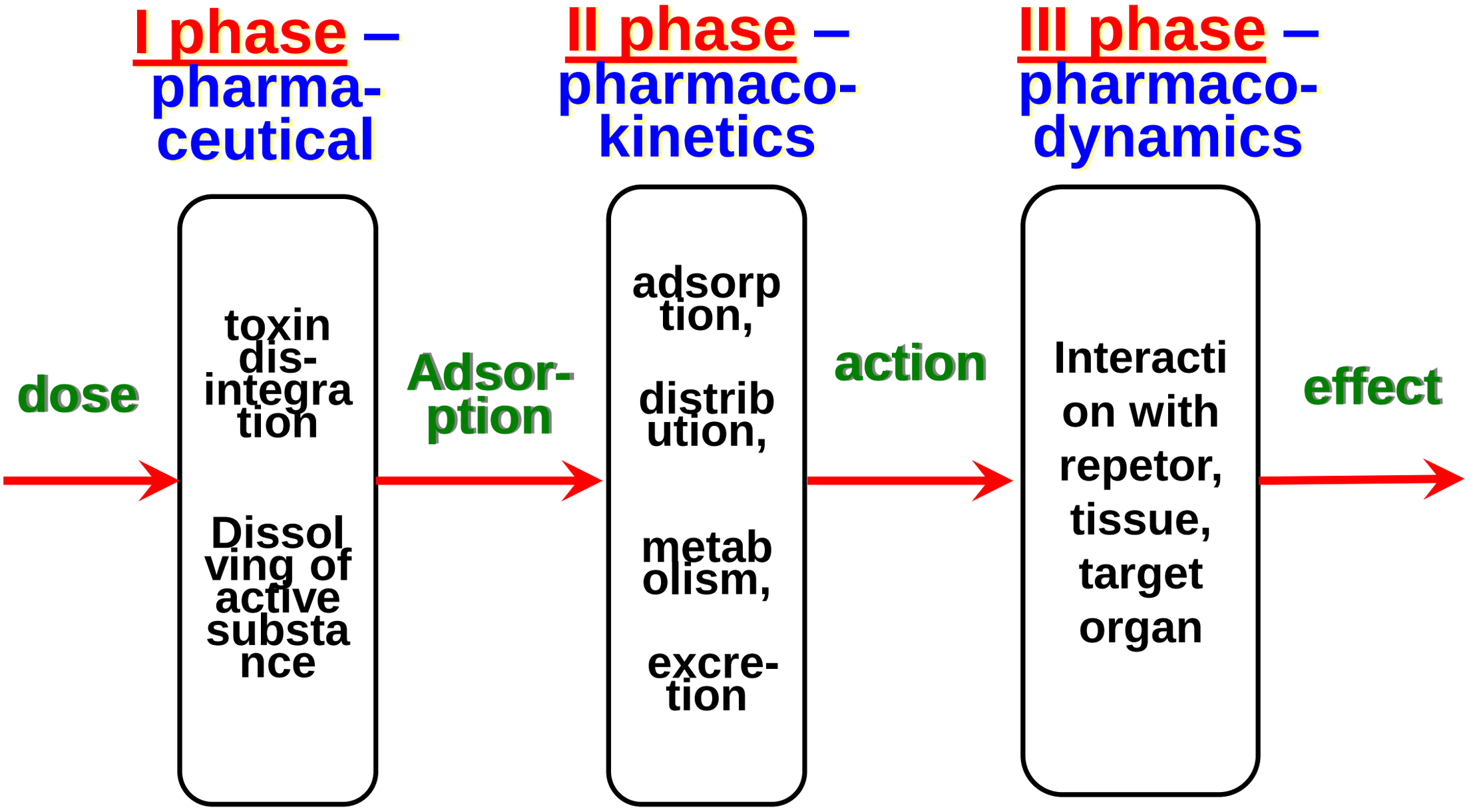
PESTICIDES

(от лат. pestis – зараза, caedo – убиваю) — химические средства для борьбы с вредителями и болезнями растений, сорняками, эктопаразитами домашних животных, переносчиками опасных заболеваний человека и животных, а также вещества, облегчающие уборку урожая (дефолианты и десиканты), регуляторы роста растений (ауксины, гиббереллины, ретарданты) и др.

Различают вещества для борьбы:

- **инсектициды** – с вредными насекомыми; **акарициды** – с клещами
- **гербициды** – с нежелательной растительностью
- **зооциды** – с вредными позвоночными (**родентициды** – с грызунами, **ратициды** – только с крысами)
- **фунгициды, бактерициды, вирусоциды, нематоциды** – с грибковыми, бактериальными, вирусными, нематодными заболеваниями растений
- **моллюскоциды** – с вредными моллюсками
- **репелленты** – отпугивающие вредных насекомых клещей, млекопитающих и птиц, и **антифидинги** – отпугивающие насекомых от растений
- **аттрактанты** – для привлечения членистоногих с целью их уничтожения
- **хемостерилизаторы** – вызывающие бесплодие у насекомых, грызунов, клещей

PHASES OF TOXINS ACTION

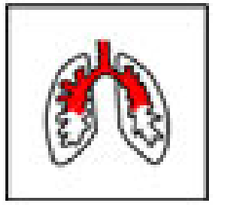


HELP IN ACUTE POISONING

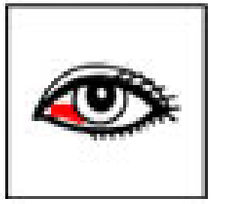
1. cessation of further entrance of poison into the body
2. speed up of poison excretion from the body
3. usage of anti-poisons (antidotes):
   - before absorption (impediment of its further entrance to the body)
   - after absorption
4. Normalization of the main physiologic functions of the body

PREVENTION OF TOXIN ENTRANCE DURING POISONING:

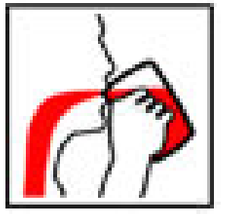
- **via lungs:** bringing out a victim on fresh air, oxygen inhalation



- **via skin, mucosa:** washing out by water
  if needed – by weak base (sodium bicarbonate) or acidic solution (citric etc. organic acids)



- **per os:**



  a) to induce vomiting (by mechanical way or hypertonic saline solution – 1 table-spoon of sodium chloride for cup of water);
  banned in unconscious persons or poisoning by caustic toxins

  б) stomach washing a few time up to full cleaning by warm water and/or in combination with agents bind and inactivate poison, in coma state – via probe

REMOVING OF TOXIN FROM THE BODY (1)

- ***those that is not absorbed:*** **usage of saline (!) laxatives (25,0 magnesium or sodium sulfate), enema, stimulation of intestinal motility**
- ***those that is absorbed :***
  - **enforced diuresis – first stage – "hydration" – I.V. infusion 400-800 ml of polyglucin, 1,5-2 l physiologic solution or 5 % glucose solution; second stage – "dehydration" – mannitol or furosemide**
  - **modification of urine pH for decreasing of poisons reabsorption in renal channels and ↑ their excretion:**
    - **at poisoning by weak acids (barbiturates, salicylates, sulfanilamides, herbecides etc.) – *urine alkalinization :* 1000 ml 4 % sodium bicarbonate solution**
    - **at poisoning by weak alkalines (alkaloids) – *acidification of urine:* ascorbic acid – 2 gr for 400 ml of isotonic solution of sodium chloride solution**

REMOVING OF TOXIN FROM THE BODY (2)

- **hemosorption – toxins' removing from blood and regulation of hemostasis by contact of blood with sorbent out of the body (poisoning by chloramphenicol, CNS suppressant, cardiac glycosides etc.)**
- **hemodialysis – is based on phenomenon of selective diffusion via semipermeable membrane, which on one side contact with blood, on another – with dialyzed solution – "artificial kidney" (poisoning by bromides, ethanol, ethylene glycol, methanol, lithium, heavy metallic salts)**
- **peritoneal dialysis – administration of dialysing fluid into abdominal cavity and further exchange between abdominal cavity and blood**
- **plasmopheresis – substitution of part or whole plasma volume in patients**
- **blood transfusion etc.**

ANTIDOTES (ANTIPOISONS) –

agents for the treatment of poisoning by inactivation of toxin and removing of its toxic effects; action is based on phenomenon of antagonism ⇒

according to mechanism of action:

- **physico-chemical:** usage of physico-chemical reaction (adsorption)
- **chemical:** usage of chemical reactions (oxidation, binding, neutralization) for inactivation of poison
- **physiologic (functional):** ϕfunctional antagonism for biological substrate of the organism (receptor, enzyme etc.)
- **immunologic:** anti-toxic serum

according to selectivity of action:

- **non-specific**
- **specific**

according to the time of action:

- **before toxin absorption –** physico-chemical and a few chemical (usually, non-specific)
- **after toxin absorption –** xchemical, physiologic (usually, specific)

INACTIVATION OF TOXIN IN GIT (1)

- **adsorption:** adsorbents (activated carbon 30-50 gr per 100 ml of water 10 before stomach washing) and enterosorbents (poisoning by alkaloids, glycosides, NSAIDs, heavy metallic salts etc.)
- **oxidation:** stomach washing by 0,1-0,25 % solution of potassium permanganate (universal oxidizer in case of poisoning by alkaloids)
- **neutralization:** stomach washing by:
  - ✓ weak acids (1 % acetic, citric) – poisoning by alkalines
  - ✓ weak alkalines (5 % solution of sodium bicarbonate) – poisoning by acids
  - ✓ thiosulfate sodium (30 % sol) – poisoning by iodides, metallic salts
  - ✓ soap solution – poisoning by detergents

INACTIVATION OF TOXIN IN GIT(2)

- **binding:**
  - ✓ **tanin precipitate glycosides, heavy metals**
  - ✓ **iodide solution (15 drops on 100 ml of water) – Pb, Ag, Hg, quinine, strychnine**
  - ✓ **starch – iodide**
- **precipitation (formation of insoluble compounds):**
  - ✓ **cupper sulfate – poisoning by phosphorus**
  - ✓ **magnesium sulfate – poisoning by barium salts**
  - ✓ **sodium chloride – poisoning by silver nitrtate, bromides, lithium**
  - ✓ **calcium gluconate – poisoning by oxalic acid, etc**
- **also bind and precipitate eggs protein (not less than 10 eggs), milk (banned in case of poisoning by lipid-soluble poisons), enveloping substances (mucilage, gel) – poisoning by irritating and caustic poisons κ(acids, alkaline, salts of heavy metallic salts)**

ANTIDOTES AFTER TOXIN ABSORPTION

antidotes	toxin	mechanism of action
chemical		
chelators: **EDTA (ethylene diamin tetraacetate), penicillamin**	**cyanides, cardiac glycosides, heavy metals**	**formation of chelating compounds**
Deferroxamine	**iron**	**-»- (100 mg bind 8,5 mg of iron)**
donators of SH-group: **unthiol, acetylcystein**	**metals, cardiac glycosides, paracetamol, dichlorethan**	**complex compounds with metals, toxic metabolites (paracetamol), competition for binding with SH-groups of proteins (↑ affinity)**
protamine sulfate	**heparin**	**forms stable complex (for 100 units of heparin – 1 mg of protamine)**
physiological		
atropine	**muscarin, POC**	**M-cholinblocker**
physiostigmin	**atropine-like**	**inhibitor of acetylcholine esterase**
proserin	**non-depolarizing myorelaxants**	**-»- ⇒ decreasing of neuro-muscular block**

ANTIDOTES AFTER TOXIN ABSORPTION

antidotes	toxin	mechanism of action
physiological		
dipyroxim, alloxim	POC, anticholin-esterases	cholinesterase re-activator
flumazenil	benzodiazepines	antagonist of benzodiazepine receptors
naloxon	opioids	antagonist of opioid receptors
sodium nitrite	cyanides	methemoglobin-maker, competition with cyanides for cytochromoxidase (forming of cyanohemoglobin)
sodium thiosulfate	cyanides, heavy metals	Transform cyanohemoglobin into thiocyanites; make insoluble sulfites with metals
methylene blue	cyanides; methemoglobin-makers (anilines, nitrates etc)	In high doses transform oxyhemoglobin into methemoglobin (in case of cyanides poisoning); in small doses – reduction of methemoglobin into hemoglobin

ANTIDOTES AFTER TOXIN ABSORPTION

antidotes	toxin	mechanism of action
physiological		
ascorbic acid	cyanides	see methylene blue
hydroxycobal-amine	cyanides	functional antagonist
vicasol	indirect (oral) anticoagulants	antagonist by mechanism of action
pyridoxin	isoniazid	removing of hypovitaminosis
calcium chloride	magnesium sulfate	antagonists, ↓ activity of dependent enxymes
sodium chloride	lithium, bromides	-»-; ↑ bromides excretion
ethanol	methanol	competition for alcohol dehydrogenase ⇒ ↓ production of toxic metabolites
bemegrid	barbiturates, general anesthetics	physiologic antagonists

ANTIDOTES AT POISONING

- **by heavy metallic salts:**
  - ✓ **SH-group donators – unithiol** (poisoning by Hg, As, Sb, Co, Zn, Cr, Ni), i.m. 7-10 ml 5 % sol. 4 times a day
  - ✓ **chelators – EDTA** (poisoning by Pb, Cd, Ni, Cr, Cu, Mn, Co) i.v. by drops 20 ml 5% sol. per 200 ml of physiologic sol.; **penicillamin** (poisoning by Cu, Hg, Pb) – 0,2 % sol. 1 ml i.v. or s.c.; **thiosulfate sodium** (poisoning by Hg, As Pb), i.v. 50 ml 30% sol.
- **by cyanides:** EDTA, i.v. by drops 20 ml 5% sol. per 200 ml of physiologic sol.; **sodium nitrite,** i.v. by drops 10-15 ml 3 % sol; **thiosulfate sodium,** i.v. 50 ml 30% sol; **methylene blue,** i.v. 50-100 ml 1 % sol. diluted in 25 % glucose sol. (“chormosmon"); as well as **ascorbic acid,** i.v. 1 gr. slowly; **cynocobalamin,** i.m. 100-1000 mg
- **by methanol, ethylene glycol:** ethanol, 30% sol. 50-100 ml orally, each 2 hrs 50 ml and I.V. by drops 100-400 ml 5 % sol. (up to 1 ml/kg/per day)
- **by paracetamol, dichlorethan:** acetylcystein, I.V. 10 ml 5% sol.

ANTIDOTES AT POISONING

- **by cardiac glycosides:**
  - ✓ **SH-group donators – unithiol (dimercaprol), I.M. 7-10 ml 5 % sol. each 6 hrs**
  - ✓ **chelators – EDTA, I.V. by drops 20 ml 5% sol. in 200 ml of physiologic sol. or 5% glucose sol.**
  - ✓ **potassium salts (panangin), I.V. 10-20 ml per 100 ml of physiologic sol.**
- **by iron-containing agents: deferroxamin, I.M. 1-2 gr with 12 hrs interval; I.V. 15 mg/kg in 1 hr (daily dose up to 80 mg/kg)**
- **by benzodiazepines: flumazenil, I.V. 0,2 mg during 30 sec up to 3-5 mg, 0,2% sol. 1 ml I.V. on physiologic sol. or S.C.; euphyllin, I.V. 1 mg/kg**
- **by opioids: налоксон, в/в 0,4-1,2 мг до 2 мг**
- **by barbiturates: бемегрид, в/в 10 мл 0,5% р-ра, 3-4 инъекции до восстановления рефлексов**
- **by magnesium sulfate, oxalic acid: calcium chloride, I.V. 5 ml 10% sol. I.V. during 3-5 min**

ANTIDOTES AT POISONING

- **by bromides:** sodium chloride, 0,9% sol. I.V. drip
- **by muscarin:** atropine sulfate, I.V., I.M., S.C. 0,6-1,2 mg after 15 min
- **by POC:** cholinesterase re-activators – aloxim, dipyroxim – 1 ml 15% solution I.M. or I.V., every 3-4 hrs, or drip I.V. 250-400 mg/hr; atropine sulfate, I.V. 0,6-2 mg
- **by atropine-like:** physostigmine, I.V., I.M., S.C. 1-2 mg every 1-2 hrs
- **by non-depolarizing myorelaxants:** proserin, I.V. 3ml 0,05% sol. per 10 ml of physiologic sol. or 10-12 ml 0,05% sol. S.C. during 20-30 min
- **by direct anticoagulants (heparin):** protamine sulfate, I.V. drip 1 ml 1% sol. (1 mg – 100 units of heparin)
- **by indirect anticoagulants(warfarin):** vicasol, I.M. 1ml 1% sol
- **by carbon monooxide:** inhalation of 100 % oxygen

SYMPTOMATIC THERAPY

- ***at respiratory disturbances of different origin*** **(airways obstruction, bronchospasm, pulmonary edema, respiratory center depression, respiratory muscles paralysis):**
  - ✓ **restoring of airways passability**
  - ✓ **endotracheal trial balloon and mechanical lung ventilation (in out-patient stage – respiratory analeptics)**
  - ✓ **when needed – oxygen, bronchodilators**
- ***at disturbances of vascular tonus:***
  - ✓ **↓ BP (poisoning by hypnotics, ganglionic blockers, adrenoblockers): if systolic BP under 80-90 mm – elevate legs on 20 sm; hemodynamic blood substitutive fluids; at hypervolemia – dobutamine I.V. 2,5-10 mcg/kg/min; for ↑ of renal bloodflow – small doses of dopamine (5 mcg/kg/min); if needed – alpha-adenomimetics, glucocorticoids; ↑ systolic BP up to 100 mm.**
  - ✓ **↑ BP (poisoning by vasoconstrictors, analeptics, amphetamine): hypotensive extreme aid (I.M., I.V. – myotropic, ganglionic blockers, diuretics, alpha-adrenoblockers; sublingually – beta-adrenoblockers, vasotropic calcium channels blockers etc)**

SYMPTOMATIC THERAPY

- ***at disturbance of cardiac activity*** **(disturbances of myocardium, tachy- and bradyarrhythmia, cardiac arrest): see anti-arrhythmics; in cardiac arrest – defibrillation**
- ***in case of acute convulsions*** **(poisoning by analeptics, anticholinesterases, phenothiazine neuroleptics etc): tranquilizers (diazepam, I.V. 2-4 ml 0,5 % sol. per 20-40 ml 40 % glucose sol.); barbiturates (thipental, I.V. 10 ml 1 % sol.), magnesium sulfate I.V., I.M. 25 % sol. 10 ml**
- ***at renal dysfunction:*** **catheterization, restoring of the circulated blood volume, in hypotension – dopamine**
- ***at body temperature disturbances:***
  - ✓ **hyperthermia (poisoning by tranquilizers, barbiturates, H1-antagonists): room ventilation, ice packs, "lytic" combinations (H1-antagonist+NSAID)**
  - ✓ **hypothermia (poisoning by neuroleptics, opioids, alcohols): environmental warming, rubbing by ethanol (30-40 %)**

SYMPTOMATIC THERAPY

- ***in metabolic disturbances:***
  - ✓ **acid-alkaline equilibrium: acidosis – 4 % sol. of sodium bicarbonate; alkalosis – 1 % sol. of citric, ascorbic acid**
  - ✓ **electrolyte balance: potassium-containing agents (panagin), calcium (calcium gluconate), sodium (sodium chloride)**
- ***in dehydration* (severe vomiting, diarrhea): hemodynamic blood substitutes**
- ***in severe pain syndrome:* narcotic analgesics (for prevention of shock)**
- ***at psychomotor excitement:* neuroleptics (aminazin, haloperidol, droperidol)**
- ***in hypoxia of different origin* (disturbances of respiration and blood flow, hemolysis, etc)*:* measures for correction of mentioned disturbances; antihypoxants**

ETREME CONDITIONS

acute heart failure (AHF)

- **A clinical syndrome with rapid ↓ cardiac output, insufficiency of tissue perfusion, ↑ of pressure in pulmonary capillaries (myocardial infarction, myocarditis, cardiac arrthythmia, cardiac valve abnormalities, decompensation of chronic heart failure etc.):**
  - ***with congestive type of hemodynamic:***
    - ✓ **right ventricular AHF – venous stagnation in systemic circulation**
    - ✓ **left ventricular AHF – cardiac asthma, pulmonary edema**
  - ***with hypokinetic type of hemodynamic:*** **cardiogenic shock**

ETREME CONDITIONS

general principles of AHF treatment

removing of hypoxia removing of fluid from lungs	→ breathing support
hemodynamic unloading of heart, decreasing of pressure in pulmonary capillaries	→ vasodilators (nitrates), opioids (morphine)
removing of fluid overloading	→ diuretics (furosemide)
supporting of sufficient cardiac output, increasing of myocardial contractility	→ cardiotonics (glycoside and non-glycoside)

ETREME CONDITIONS

treatment of AHF before hospital admition

- **right ventricular**: removing of main reason, ↓ hypoxia
- **left ventricular** (pulmonary edema):
  - stoppage of "respiratory panics" – narcotic analgesics (morphine)
  - ↓ preload and ↓ pressure in pulmonary artery – diuretics (furosemide), nitrates, morphine
  - ↓ after-load – nitrates and other vasodilators
  - inotropic stimulation of heart – cardiotonics: cardiac glycosides (digoxin), non-glycosides (dobutamine, dopamine*)
  - anti-foam therapy – ethanol vapor, synthetic anti-foam agents
  - oxygen therapy, mechanical lung ventilation

* - dopamine in doses: < 2,5 mcg/kg/min – renal effect (stimulation of dopamine receptors in renal vessels ⇒ ↑ renal blood flow and diuresis); 5-10 mcg/kg/min – «+» ino- and chronotropic effects (↑ β_1-adrenoreceptors); > 10 mcg/kg/min – vasopressive effect (stimulation of α-adrenoreceptors)

ETREME CONDITIONS

treatment of left ventricular AHF

- in cardiac arrhythmia: anti-arrhythmics
- AHF with hypertonic crisis: + usage of hypotensive agents (sodium nitroprusside)
- with low cardiac output (**cardiogenic shock**):
  - ✓ correction of hypovolemia (I.V. 200 ml of physiologic sol.) and stabilizing of hemodynamics
  - ✓ correction of arrhythmia (in bradycardia – 0,3–1 ml 0,1% sol. of atropine)
  - ✓ analgesia (morphine)
  - ✓ enhancement of cardiac output and oxygenation of tissues – non-glycoside cardiotonics (dobutamine, dopamine), vasodilators

ETREME CONDITIONS

- **myocardial infarction:** see topic «Antianginal agents»
- **acute vascular insufficiency – hypertensive agents**
- **spasm of smooth muscles of abdominal cavity organs (renal, hepatic, intestinal colics) - cholinolytics, miotropic spasmolytics, non-narcotic and narcotic analgesics**
- **hypertonic crisis:** see topic «Hypotensive agents»
- **anaphylactic shock:** see topic «Anti-allergic agents»
- **hyperglycemic (diabetic) and hypoglycemic comas:** see topic «Hormonal agents of protein and aminoacid origin»