

# General principles of poisoning treatment, specific antidotes of medicines, and the mechanisms of their effects

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# Pharmacology vs. Toxicology

- Interconnection of both disciplines
- They study the effects of chemicals on biological systems

Pharmacology - therapeutically useful effects, drugs

Toxicology - adverse, harmful (toxic) effects, poisons and toxins

Paracelsus (1493-1548):

“All substances are poisonous; there is none which is not a poison. The right dose differentiates a poison and a remedy”

# Causes of poisoning

1. drugs - 52%
2. Industrial Products - 30% (chemicals for cleaning, organic solvents, cosmetics etc.)
3. plants - 8%
4. Pure bulk chemicals -5%
5. funghi - 2%
6. Animal poisons (snakebite) -1%
7. others -1%

# General principles of acute poisoning treatment

Treatment has to be provided as quickly as possible but always with judgment so that therapeutical procedures do not cause worsening of the patient's state or even death  
!!!

# General principles of poisoning treatment:

- eliminate the substance from organism as quickly as possible (= decontamination)
- antidote (rapid counteraction for poison by means of specific actions);
  - „a drug, chelating substance, or a chemical that counteracts (neutralizes) the effects of another drug or a poison“
- vital functions + symptomatic treatment

# 1. Elimination of unabsorbed toxic substances from organism

- Gastric lavage and administration of emetic, preferably within 1 hour of intoxication (the first treatments should be done prior to transportation to the hospital)
- An average patient arrives only after 3 hours

# 1. Elimination of unabsorbed toxic substances from organism

## Induced vomiting

- in p.o. poisoning within 4 hours
- within 8 hours after anticholinergic agents
- within 12 hours of pylorospasm inducing agents (eg, salicylates)
- the patient is conscious, without spasms
- *Syrup of ipeca (emetin)*- non-reg., apomorphine (s.c.)
- mechanic stimulation of pharynx
- (red-eyed treefrog secretion)



Can not evacuate whole stomach content (max 30-50%) !

- **DO NOT INDUCE VOMITING IF ACIDS OR ALKALI WERE INGESTED**

## **OTHER CONTRAINDICATIONS OF INDUCED VOMITING:**

- Somnolence and loss of consciousness
- Intoxication with foaming agents
- Intoxication with hydrocarbons
- Attacks of spasms
- Alimentary intoxications in small infants



# 1. Elimination of unabsorbed toxic substances from organism

## Adsorbents

- With poisons ingested p.o.
- Charcoal (adsorbing carbon = Carbo adsorbens) / diosmectit → large active surface
- 50 – 100 g in 5 – 10% suspension, possibly with stomach tube, then repeatedly 50 g per 4 hours
- Up to 2.5 g/kg

**+**: paracetamol, salicylic acid, diazepam, amphetamine

**-** methyl/ethylalcohol, Li, strong acids and alkali



# Toxic substances that are poorly adsorbable by Charcoal

- acids
- alkali
- chlorates
- chlorids
- cyanides
- nitrates
- ethanol
- ethylenglycol
- isopropanol
- methanol
- fluorides
- iron
- ferrous sulphate
- potassium
- sodium
- detergents

# 1. Elimination of unabsorbed toxic substances from organism

- $\text{KMnO}_4$  – oxidation of strychnine and cyanides (light pink solution)
- Lime water -  $\text{Ca}(\text{OH})_2$  - binds  $\text{F}^-$  and oxalic acid into insoluble salts
- Flour/starches –binds iodine into insoluble iodides
- Paraffin oil binds phenols and organic solvents (benzene, toluene)
- Liquid paraffin (Paraffinum subliquidum – 100 – 300 ml) → it is a non-resorbable fatty substance → decreases resorption of poisons soluble in fats (simple and halogenated hydrocarbons)

# 1. Elimination of unabsorbed toxic substances from organism

## Gastric lavage

- In p.o. intoxications within 4 hours
- The patient is conscious, without spasms
- when unconscious, ONLY in lying position and intubated
- warm water (37°C), saline (preparation: 2 teaspoons of salt per 1 litre water), 300 ml
- Sample for toxicological analysis
- In the end (the last lavage) add adsorbent (30 g of activated carbon) or a laxative ( $\text{Na}_2\text{SO}_4$ )

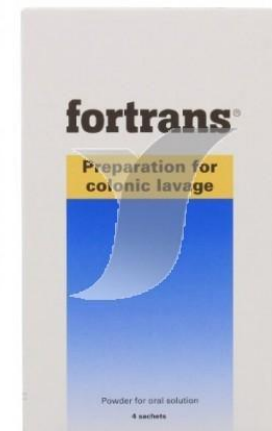
# 1. Elimination of unabsorbed toxic substances from organism - PEG - laxative , GIT dialysis

- PEG - polyethylene glycol in ionic solutions
- 4 liters / 2 hours
- until the evacuated rectal content is clear

Indications (toxic and lethal doses):

- rugs bound poorly by charcoal: iron, lithium

Retarded tablets: theophylline, calcium blockers - verapamil, diltiazem!

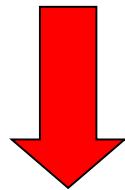


# 1. Elimination of unabsorbed toxic substances from organism

## Increasing the intestinal passage

The patient is conscious, with no spasms

- Administration of big doses of strong and quick-acting laxatives
- Sodium sulphate (20 – 30 g with a large volume of water)
- Mannitol (ca 50g per 1 litre water; 0.5 – 1 litre is administered p.o.)
- Castor oil (20 – 30 ml)



- Cl in poisons soluble in fats!!! (castor oil ↑ bile secretion and resorption of fats)

# 1. Elimination of unabsorbed toxic substances from organism

## Total intestinal lavage

- Large-volume solution (25 ml/kg)
- Through stomach tube, until clean solution flows off
- Without resorption, does not cause diarrhoea
- It only rinses the intestine
- polyethylenglycol + NaSO<sub>4</sub>, NaCl

# 1. Elimination of absorbed toxic substances from organism

## Forced osmotic diuresis

- Infusion of saccharide solutions (20% mannitol; possible combination with furosemide), physiological solution
- Up to several litres / day
- CI: brain and lung oedema, heart failure, anuria



# 1. Elimination of absorbed toxic substances from organism

## Forced alkali diuresis

- Speeds up elimination of slightly acidic poisons
- Alkalinisation of urine and blood (pH 7.5 – 9.0)
- NaHCO<sub>3</sub> solutions
- I: salicylates, barbiturates, sulphonamides, antipsychotic drugs,...
- Cl: pulmonary oedema, shock, serious impairment of kidneys

# 1. Elimination of absorbed toxic substances from organism

## Forced „acidic“ diuresis

Speeds up elimination of slightly alkaline poisons

- Acidification of blood and urine
- 5% Glc solutions with ammonium chloride in i.v. infusion
- I: amphetamines, quinine, quinidine, nicotine, morphine,...
- Cl: serious impairment of kidneys

# 1. Elimination of absorbed toxic substances from organism

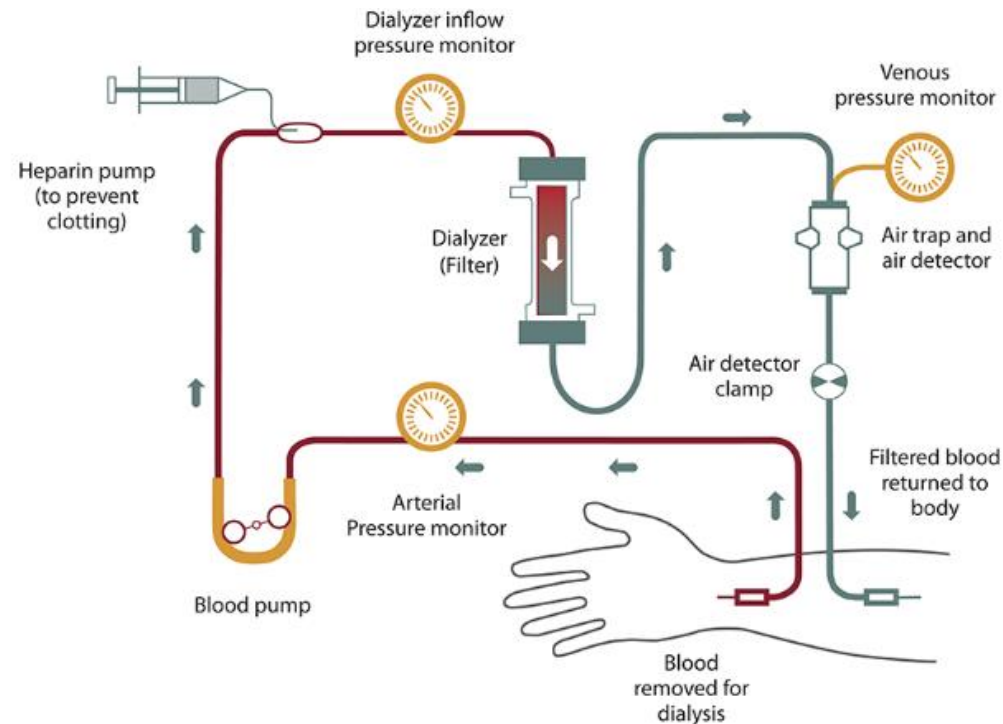
## Peritoneal dialysis

- dialysis solution via catheter into abdominal cavity
- Intestinal mucosa and peritoneum serve as a membrane
- Replacement after 2 hours
- I: unavailability of haemodialysis in case forced diuresis cannot be applied
- For poisoning with some analgesics, hypnotics, barbiturates,...
  
- -: low efficiency, risk of infection

# 1. Elimination of absorbed toxic substances from organism

## Haemodialysis/CRRT

- I: salicylates, barbiturates, alcohols, ethylenglycol, toluene, mushrooms



# INDICATION OF HAEMODIALYSIS

- Acute renal failure – e.g. rapidly progressing glomerulonephritis
- hypercalcemia > 6 mmol/l that cannot be managed by conservative therapies
- hypercalcaemia > 3.5 mmol/l
- hyperuricemia > 1000 µmol/l
- uncorrectable metabolic acidosis, pH < 7.1
- hyperhydrating with heart failure
- oliguria lasting more than 3 days

# INDICATION OF HAEMODIALYSIS – cont.

Indication for dialysis (sooner in diabetics):

- urea > 30 mmol/l,
- creatinine 600–800  $\mu\text{mol/l}$ ,
- Creatinine clearance < 0.25 ml/s.

Patient on dialysis

Diseases that lead to dialysis are as follows:

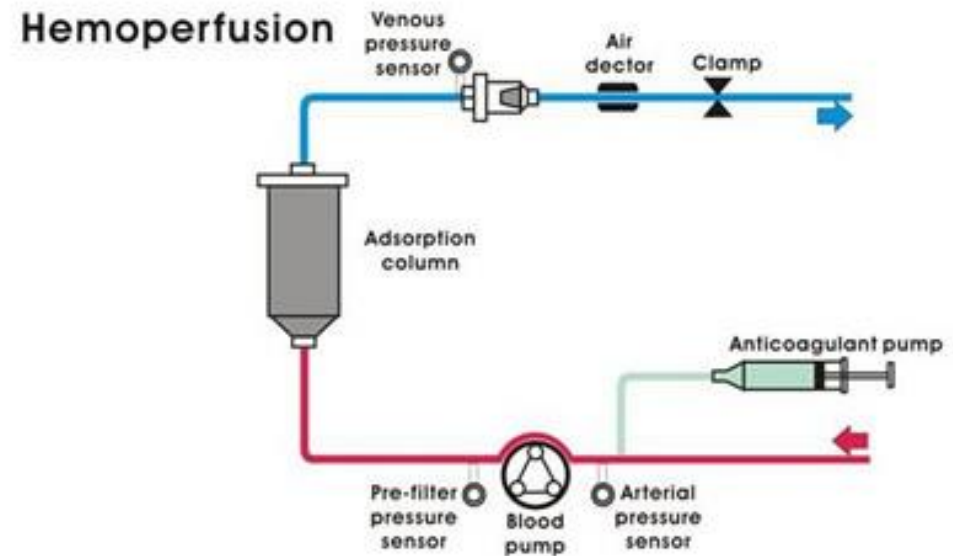
- diabetic nephropathy,
- hypertension nephropathy,
- chronic glomerulonephritis,
- rapidly progressing glomerulonephritis (RPGN) – when irreversible fibrotic changes occur,
- Autosomal dominant polycystic disease of kidneys.



# 1. Elimination of absorbed toxic substances from organism

## Haemoperfusion

- Perfusion of blood through a capsule containing sorbents
- I: barbiturates, theophylline, phenothiazines, paracetamol, salicylates, phenobarbital, carbamazepine
- +: highly efficient



# Haemodialysis, haemoperfusion

## Indication (on fulfilment of at least 3 criteria):

- Clinical picture of severe intoxication (deep unconsciousness, hypotension, hypothermia, hypoventilation in intoxications with depressant substances)
- Clinical state can only be influenced by a complex resuscitation care
- Clinical state becomes worse despite complex resuscitation care
- Protracted unconsciousness with pulmonary complications (pneumonia, diffuse alveolar damage, COPD)
- Proven high plasmatic level of toxic substance that can be eliminated applying available methods



# Haemodialysis, haemoperfusion

## Contraindication of extracorporeal elimination methods:

- Effective antidote is available
- The toxic substance is quickly metabolised and its metabolites are not toxic
- Toxicity appears quickly and irreversibly
- Intoxication is caused by a substance with low toxicity
- The toxic substance has a large distribution volume
- Shock
- Severe haemocoagulation disorders

# Lipidic (micro)emulsions

- Novel (Commercial RMP) – decreases the free fraction of lipophilic drugs in serious intoxication. (Intralipid®)
- for the treatment of severe arrhythmias (e.g. ventricular tachycardia, atrial fibrillation, cardiac conduction system block, asystole)
- in lipid soluble drugs
- if conventional therapy fails.
- Free drug fraction - binding by lipid emulsion a
- reducing the pharmacological effect
- commonly used to treat a topical toxicity of local anaesthetics
- Cardiotoxicity of local anesthetics, some beta-blockers, TCA

# Lipidic (micro)emulsions

- however, the blood in the blood abolishes the possibility of hemodialysis or ECMO - hence this therapy is preferred over lipids when other options fail

## 2. Neutralization of poison through administration of antidote

- **Antidote – a substance that neutralises the effect of poison**
  - specific (using antagonistic effects of pharmaceuticals – antidotes that can counteract the effects of poison either partly or completely)
  - Non-specific (adsorption – activated – medicinal carbon = carbo adsorbens – carbo activatus – carbo medicinalis)  
RATIO OF CARBON : TOXIC SUBSTANCE = 10 : 1  
(usually 50g / 3 – 4h; most often intoxications with medicines, chemicals)
- It is necessary to administer antidote as quickly as possible
- Dosage according to plasmatic level of toxin

## 2. Neutralization of poison through administration of antidote

- Decrease bioavailability of the toxic substance
- Increase rate of elimination of (especially non-transformed) toxic substance
- Slow down biotransformation of the toxic substance leading to activation of the tox. substance
- Incr. rate of biotransformation to inactive metabolite
- Influence the distribution of the toxic substance within the organism

# Specific Antidotes

[https://www.annemergmed.com/article/S0196-0644\(17\)30657-1/fulltext](https://www.annemergmed.com/article/S0196-0644(17)30657-1/fulltext)

# Specific antidotes

- (<http://www.farmakologie.net/lecbaotrav.php>)  
Lékové informační centrum 3. LF UK (Information Centre for Pharmaceutical Drugs at the Third Faculty of Medicine, Charles University)

# 3. Symptomatic treatment

- Check vital signs
- Intubation
- Entry into bloodstream
- Support of CVS (inotropics, vasopressors)
- Therapy of spasms



# Toxicological Information Centre

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Welcome at the website of the Toxikologické informační středisko TIS).

## Acute poisoning - what to do?

Dial +420 **224 91 92 93** or **224 91 54 02**

To receive advice on first aid and what to do next.

### Prepare:

- precise information on the accident
- **full name**
- **birth identification number**
- **health insurance company**
- healthcare professional also their IČP (organization identification number)

In order to facilitate the consultation, the doctors are asked to calculate (provided it can be ascertained) the quantity of medication (active substance) that intoxicated the patient. Also please try to estimate or find out the body weight of the patient.



# Toxicological Information Centre

- A 24/7 nationwide telephone medical information service to consult cases of **acute human and animal intoxications**
- For both laypersons and doctors
- The goal of the TIS is **to decrease the number and severity of intoxications** and to favourably effect **the course of accidents. The Centre provides information on the chemical composition of commercial products and on the therapy of acute intoxications with these products**
- **It does not deal with:**
  - the influence of chemical compounds on foetus
  - cancerogeneity
  - adverse effects of medicinal drugs
  - impact of chemical compounds on the environment

# Toxicological Information Centre

- 120 00 Praha 2, Na Bojišti 1
- <http://www.tis-cz.cz/>
- E-mail: [tis@vfn.cz](mailto:tis@vfn.cz)
- Phone: +420 **224 91 92 93** or +420 **224 91 54 02**

- **Snakebite poisoning**

Anaesthesiology and Resuscitation Clinic

1st FM CU in Prague and VFN in Prague

Praha 2

Phone: 224 962 243

- **Lékové informační centrum (Information Centre for Pharmaceutical Drugs)**

Lékárna FN U sv. Anny

Brno

Phone: 543 182 175-7

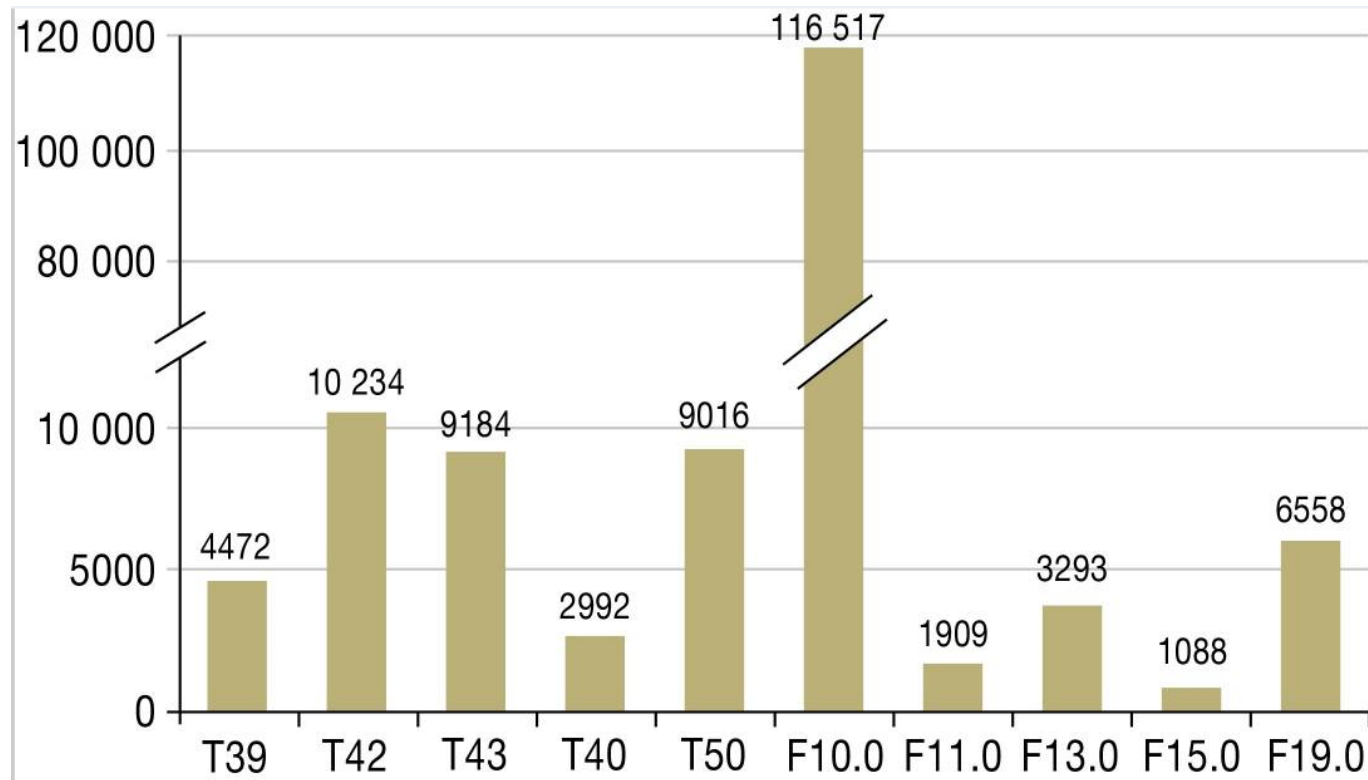
- Poisoning causes 10% of deaths !!!
- Coincidence
- Suicide
- Criminal act
- Abuse of habit-forming substances
- Occupational injury
- ...

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- 2/3 of all intoxications are related with children!

- Most frequent entry: p.o. or inhalation

# Intoxication with drugs (in German hospitals in 2011)



T39 = analgesics (ca. 40% 4-aminophenol derivatives)

**T42 = hypnotics (ca. 50% benzodiazepines) and antiepileptic drugs**  
**T43 = antidepressants, neuroleptic drugs, psychotropic substances (not further classified)**

**T40 = narcotics, methadone, hallucinogens (especially morphine and codeine)**

- T50 = other medications, not further specified
- **Mental and behavioral disturbances due to acute intoxication with: F10.0 = alcohol (ethanol)**
- F11.0 = opioids
- F13.0 = hypnotics, sedatives
- F15.0 = stimulants
- F19.0 = multiple substance use

# General overview of neurologic symptomatology at unknown poison intoxication

- **Convulsion** – spasms of skeletal muscles: substances with excitatory effects (strychnine, HCN, organophosphates, psychotomimetics, psychostimulants [caffeine included!])
- **Excited state** – states similar to ebriety (often during intoxication with solvents, benzene, alcohol, atropine, scopolamine, PS-lytics, cocaine, hashish, fly agaric [*amanita muscaria*])

- **Hallucination, delirious states** – analeptics, atropine(*Atropa belladonna*), scopolamine, panther mushroom (also causes states of confusion), organophosphates, ergot alkaloids, yohimbine
- **Manifestations of depression** – sedation, somnolence, sopor to comatose states with depression of breath and blood circulation – hypnotics, „narcotics“, sedatives, antipyretics, analgesics, codeine antitussives, alcohol, CO, poisoning...



- **Vision disorders** – atropine (transitory disorder – mydriasis, focusing disorder), H<sub>2</sub>S, As, myorelaxants (focusing disorder), alcohol (vision hallucinations), amphetamines (tactile hallucinations: bedbugs creeping below one's skin → excoriation),
- **Hearing disorders** – streptomycine (and other AMG - at ↑doses), quinine and salicylates (transitory worsening of hearing, tinnitus)

# Intoxication with medicines

# Intoxication with medicines

**Most often:** *sedatives, hypnotics, analgesics*

Causes of death:

- Injury to CNS – *psychotropics*
- Injury to CVS – *cardioglycosides antiasthmatic drugs*
- Liver injury – *paracetamol, nimesulide, pretease inhibitors,*

# TOXICITY of MEDICATIONS

## 1. ANALGESICS:

**a) paracetamol** 10 - 15 tb. (15 – 20 tb. of Panadol 500mg → serious to lethal intoxication)

– hepatotoxicity; it changes into N-acetyl-p-benzochinone imine(minor metabolite) =hepatotoxic

– GIT problems (vomiting, renal failure)

– Th.: activated carbon + N-acetylcysteine

**b) salicylates:** breath stimulation, hyperventilation,

– alkalosis = brain and lung oedema

– Th.: alkalizing of urine + activated carbon +  
haemodialysis

**c) opioids** – see Psychopharmaceuticals

## 2. PSYCHOTROPICS

a) antipsychotic (neuroleptic) drugs, TCA antidepressants

- depressed consciousness, sedation, somnolence, sopor

- (it is difficult to wake up the patient), coma + increased muscle tone, convulsions, cardiotoxicity

- Th.: act. carbon, laxatives, symptomatic treatment    antidote = physostigmine – mitigates anticholinergic symptoms, haemoperfusion

b) psychostimulants (amphetamines, cocaine)

- ↑ endogenous catecholamine secretion, stimulation of sympathetic nervous system

- euphoria, hallucination, unconsciousness, hypertension, arrhythmia

c) opioids

- euphoria, breath depression, miosis, BP decrease, heart rate decrease, apnoea, coma

- Th.: naloxone

## 2. PSYCHOTROPICS

### d) Hypnotics, sedatives

- BZD:
- CNS depression
- Th.: flumazenil
- BARBITURATES:
- CNS depression
- Th.: charcoal, alkali forced diuresis, haemoperfusion

# Selected CVS pharmaceuticals and the related intoxications

## **Beta-blockers (BB)**

- AE: bronchial asthma, shortness of breath
- heart failure, bradycardia, blocking of transmission of impulses in the heart
- hypoglycaemia
- peripheral circulation disorders, sleeping disorders, depression (lipophile substances)
- fatigue, cold extremities, dizziness, paresthesia
- skin rashes, fever, and other manifestations of allergy (rare)
- sudden interruption of therapy – „rebound phenomenon“

# Intoxication with BB:

- hypotension
- bradycardia
- A-V blocks
- ventricular dysrhythmias (ventricular tachycardia to fibrillation)
- pulmonary oedema, renal failure (at prolonged hypotension)
- diplopia, mydriasis
- bronchoconstriction, shortness of breath, cyanosis
- spasms or CNS depression



# Therapy of intoxication with BB:

- gastric lavage at potentially lethal doses (within 2 to 3h from ingestion), in patients with spasms and comatous patients
- Add Carbo adsorbens (50-100g) to the last dose of lavage
- At hypotension Trendelenburg position + i.v. liquids on a massive scale
- At persisting hypotension – dopamine or NA
- At bradycardia atropine i.v. (some cases require a temporary stimulation)
- At hypoglycaemia – i.v. glucose (or glucagon)

# Selected CVS pharmaceuticals and the related intoxication

## ACE Inhibitors (ACEI) AE:

- hypotension (usually reacts to dose modification)
- cough
- hypercalcaemia
- decrease in renal functions to acute renal failure
- angioneurotic oedema
- neutropenia - rarely
- liver function abnormalities

# Intoxication with ACEi:

- hypotension
- hypercalcaemia (mainly in patients with acute renal function abnormalities)
- renal function abnormalities (important factors of severity are as follows: dose, age of the patients, concomitantly administered medications -NSAIDs, diuretics)
- Increase in nitrogen compounds (haemodialysis)
- oliguria, anuria

# Therapy of intoxication :

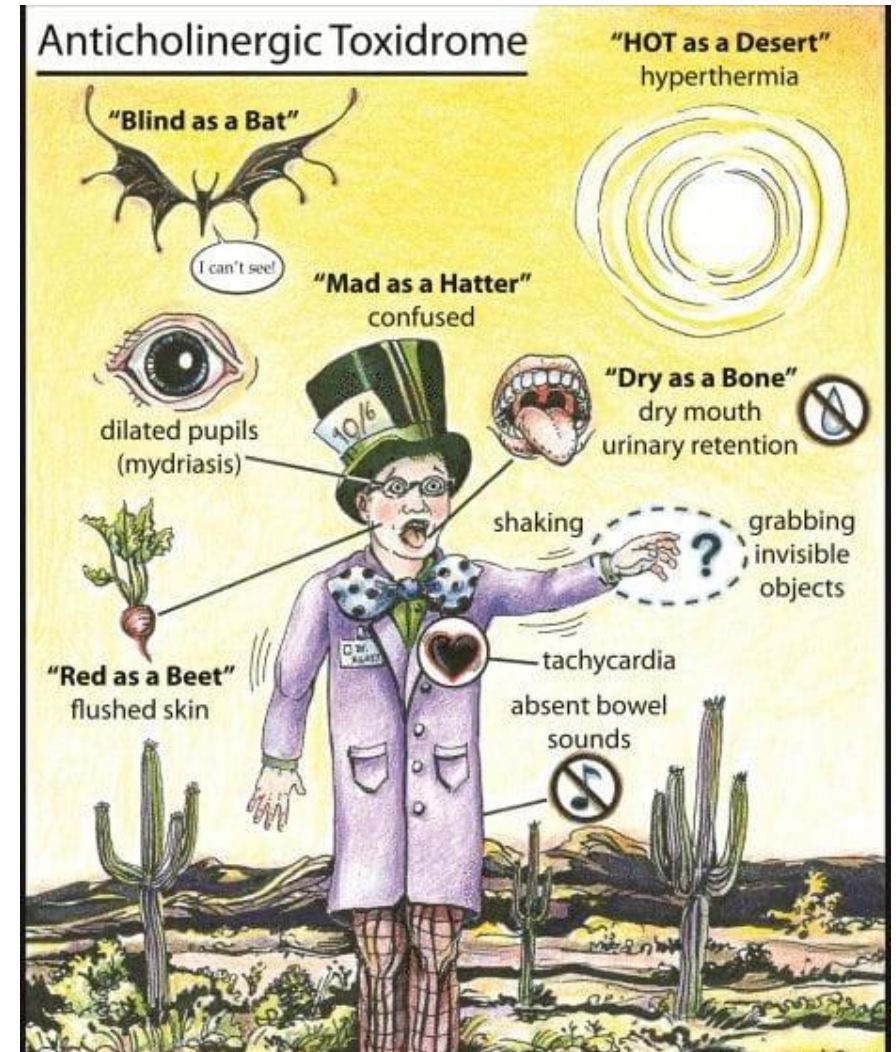
- discontinuation ACEI (or NSAIDs, diuretics)
- rehydration (saline, ballanced inf. solution – ringer/ ringer lactate)
- persisting hypotension – catecholamines ( dopamine, dobutamine, NA)
- Gastric lavage, administration of adsorbents
- monitoring of BP, electrolytes, and creatinine
- vital functions (breath, ECG)

# Prognosis of intoxication:

- promising with early diagnose
- promising in patients with nitrogen compounds retention who have no significant hypotension
- hypotension – impairment of renal tissue + ischemia
- unfavourable at concomitant administration of NSAIDs and diuretics
- Unfavourable in elderly patients, at dehydration, in inflammatory complications and other comorbidities

# Intoxication with anticholinergic drugs

- Anticholinergics (atropin, TCA, antihistaminics, antipsychotics)
- HOT as a hare (hypertermia)
- RED as a beet (flush)
- DRY as a bone (dry skin, mucosas)
- BLIND as a bat (mydriasis)
- MAD as a hatter (delirium)
- tachycardia, urinary retention
- urine, absence of peristalsis



# Intoxication with serotonergic drugs – serotonergic toxidrome

- Serotonin increase within CNS (antidepressants MAOIs, SSRIs, triptans, TCAs, ecstasy, dextromethorphan, opioids, prokinetics)
- mydriasis, agitation / coma, confusion, hallucinations,
- tachycardia, hypertension, hyperthermia, tremor, hyperreflexia,
- convulsions, tachypnea, diaphoresis

Th.: discontinue 5-HT agonists,

Symptomatic treatment: lorazepam, propranolol, cyproheptadine



# Serotonin Syndrome

Mental Status Changes	Autonomic Instability	Neuromuscular Hyperactivity	Causes
confusion agitation lethargy coma	hyperthermia tachycardia mydriasis <b>diaphoresis</b> <b>nausea &amp; vomiting</b> <b>diarrhea</b>	hyperkinesia hyperreflexia trismus myoclonus cogwheel rigidity	SSRI Lithium Meperidine Triptans MAOI Cocaine SSRI + MAOI = ↑ Risk

Similar to Anticholinergic OD. However, this has **Diaphoresis, Nausea and Vomiting**. I'm **dry as a bone** and she's **hot and wet!**

My medication was increased 6 hours ago!

Onset in 6 hrs.

Passes in days.

hyperreflexia

bruxism (grinding teeth)

sweat

cog wheel rigidity

tachycardia

VOMIT

Rx Treatment  
Cyproheptadine

5HT 1a  
5HT 2a  
Agonism



## Selected CVS pharmaceuticals and the related intoxication - Digoxine

### Pharmacokinetics of digoxine

- 60 - 75% absorbed from GIT
- $t_{1/2} = 36$  hours
- 75 % renal elimination (both GF and efflux transport)
- therap.plasm. [0.6-2.0 nmol/L]
- binding to albumine 20 - 40%
- metabolised < 20%

# Increased plasm. concentration of digoxine

- Dose not corresponding with muscle mass
- Decreased renal excretion
  - hypocalcemia  $< 3$  mmol/l
  - chinidin, amiodaron
  - decreased GFR - elderly, renal failure
- Decrease of extraren. clearance - AA
- Decrease of intestinal degradation – broad spectrum ATB

# Signs of intoxication with digoxine

- GIT
  - anorexia, nausea, vomiting, diarrhoea
- CNS
  - fatigue, depression, yellow vision
- HEART
  - arrhythmia

# Arrhythmia at treatment with digoxine

- Ventricular extrasystoles (VES) (bigeminia)
- atrial tachycardia with block
- AV tachycardia
- SA and AV blocks

# Treatment of intoxication with digoxine

- discontinue digoxine
- adjust plasm. levels of potassium
- SV tachycardia, tachyFis - phenytoin
- VES and KT – lidokain, mesokain, phenytoin
- bradycardia and blocks – temporary stimulation (try atropine prior to that!)
- to renew a stable rhythm – chinidin, prokainamid
- DIGIDOT - ovine PL against DG

# Risks of treatment with digoxine

- status after AMI
- thyreopathy
- hypoxemia (lung disease)
- drug interaction (chinidin, CAA, ATB )
- older age (lower GF and muscular mass)
- changes in K and Ca concentrations
- other – obesity, renal failure

# Mushroom poisoning

- Quite frequent in this country
- Less frequent after ingestion of edible mushrooms that developed toxic products due to metabolic processes
- Death cap mushroom – *Amanita Phalloides*  
=phaloidine, amanitine alpha, beta, gamma, ...
- Most frequently confused with champignons



## **POISONING with Amanita phalloides "destroying angel"- „death cap“**

**A quarter to half of mushroom of average 30 - 35 g mass causes a serious poisoning in an adult person !**

- Lethal intoxication – caused by ingestion of only 1 mushroom (children are more sensitive!!!)
- prognosis: very serious especially in children, death rate 60 - 80% !!!



## POISONING with Amanita phalloides "destroying angel"- „death cap“

- **Th.:**

- gastric lavage.
- forced diuresis
- PNC G (displaces amanitine from its binding to serum albumine)
- silymarine → hepatoprotective – 20 mg/kg/day in 4 infusions, other hepatoprotectives,
- CRRT- haemoperfusion
- charcoal

## Symptoms of muscarine intoxication

- Typical for excessive stimulation of PS (?):
- (identification of muscarine in plasma, but in a very low concentr.)
  - salivation, lacrimation, sweating
  - bradycardia, hypotension
  - Decr. breathing (bronchoconstriction, hypersecretion of bronchial glands)
  - Diarrhoea (hypermotility and hypersecretion in the GIT)
  - Muscular tremor

Poisoning with amanita results from joint action of muscarine, ibotenic acid with muscimole and also mykoatropine (but atropine poisoning symptoms may be also present (PL effects))

# Plants

- Nearly all plants that are used in traditional medicine can be toxic in higher doses (primarily in children)
- „red berries“ – common rue, perfoliate honeysuckle (or fly, Japanese h.), bittersweet – solanum, common yew, lily-of-the-valley
- „blue berries“ – privet (*Ligustrum*), common juniper, deadly nightshade (*Atropa Belladonna*)
- Datura, daffodil, raw and green haricot beans = toxic dose 3-10 beans

# Poisoning with organophosphates (insecticides)

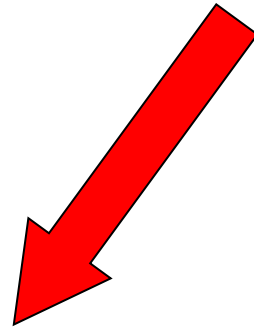
**Cholinergic crisis** (organophosphates, carbamates, pilocarpine)

i **AChE** – SLUDGE-M:

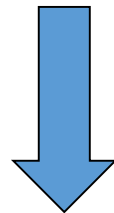
salivation, lacrimation, **u**rination, **d**iarrhea/**d**iaphoresis,  
**e**mesis, **m**iosis.

Bradycardia, bronchosecretion

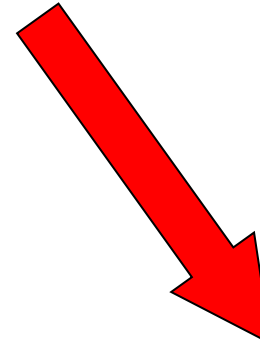
# *AchE INHIBITORS*



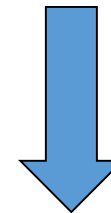
**SHORT-TERM  
(REVERSIBLE)**



**Competitive inhibition  
of enzyme**



**LONG-TERM  
(IRREVERSIBLE)**



**„Ageing“ of the  
inhibitor + enzyme complex**



**COVALENT BOND**

# Poisoning with organophosphates (insecticides)

- Irreversible inhibition of Ach-esterase – cumulation of Ach
- Late neurotoxic effects – 1-2 weeks (paresis of extremities)
- Th.:
  - atropine – antagonist on Ach receptors
  - reactivators of Ach-esterase (trimedoxin, pralidoxim)
  - reversible inhibitors of AchE
  - symptomatol. treatment (e.g. treatment of spasms – BZD)

# Intoxication with organic solvents and alcohols

- ethylalcohol (alcohol, ethanol)
  - alcohol → (alcohol dehydrogenase) → acetaldehyde + acetic acid + CO<sub>2</sub> + H<sub>2</sub>O
  - Th.: artificial respiratory support, glc infusion, BZD (to dampen restlessness+ convulsions), fomepizol (competitive inhibitor of ADH)
- methylalcohol (methanol)
  - methanol → ADH → formaldehyde + CO<sub>2</sub> + H<sub>2</sub>O + formic acid
    - Metabolic acidosis
    - Damaged eye
    - Th.: gastric lavage, laxatives, paraffine, ethylalcohol, fomepizol, haemodialysis
- organic solvents: **petrol, trichlorethylene, toluen, xylen, benzene, hexane...**
  - Th.: paraffine oil – not absorbed