CLINICALLY RELEVANT DRUG INTOXICATIONS & INTERACTIONS

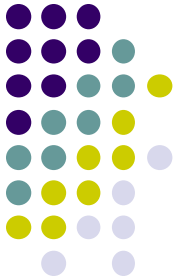
Ladislav Mirossay

P.J. Šafárik University
Faculty of Medicine
Department of Pharmacology
Košice

DRUG INTOXICATIONS
(Basic principles)

- **stop** further poison **exposure** & **absorption**
- **start** poison **elimination**
- **counteract** poisoning with an **antidote**
- **correct** disorders with **symptomatic** therapy
- **maintain vital functions** (consciousness, breathing, circulation, liver & kidney functions)
- **prevent complications**

Decontamination
(General principles)



- **surface decontamination**
- **skin, eyes** - remove contaminated clothing, rinse with wather or saline (in eyes - 1 l each, apply anaesthetic)
- **inhalation - interrupt exposure** (apply oxygen)
- **gastric lavage** (contraindicated in unconscious patients, convulsions, in organic solutants & raw or refined oil products – risk of aspiration pneumonia)
- **sorbents - activated charcoal** (1 g/1 kg^{-1}, repeat after 1-2 hours, contraindicated in ileus)

- **elimination procedures**
- **forced diuresis** (in case the kidneys are the main excretion way)
- **haemodialysis** (applicable for low molecular weight, low albumin binding & water soluble substances)
- **haemoperfusion** (not affected by above mentioned properties)
- **peritoneal dialysis** (less effective than 2 previous methods)

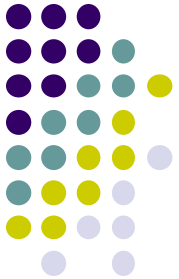
Opioid analgesics
(morphine, heroin)

- **acute intoxication symptoms**
  - dizziness, anxiety/euphoria, **miosis**
  - face flush, itching
  - drowsiness, conscience disturbances, **coma**
  - ↓ GI motility, vomiting, nausea
  - cyanosis, cell hypoxia, lung edema, respiratory **inhibition**/apnea – death

- **therapy**
  - **antidote - *naloxone, nalorphine* *(naltrexone - in dependences)***
  - **symptomatic therapy, vital function support**

Analgesics-antipyretics

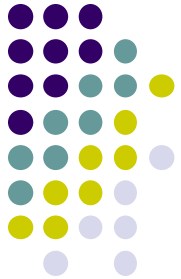
(paracetamol)



- **acute intoxication symptoms**
  - **anorexia, nausea, vomiting – in first 24 h**
  - **⇧ ALT, AST, ALP**
  - **⇧ billirubin, icterus**
  - **encephalopathy, exitus**
  - **rarely kidney failure**
- **therapy**
  - **antidote - *N-acetylcysteine***
  - **must be applied up to first 12 h**
  - **hemoperfusion is also effective**

Analgesics-antipyretics

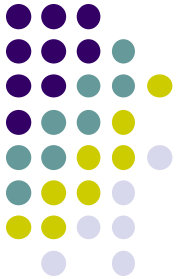
(salicylates - aspirine)



- **acute intoxication symptoms**
  - **hyperventilation ⇨ respiratory alcalosis ⇨ compensation & shift to metabolic acidosis**
  - **vomiting, throat & stomach burning**
  - **headache, vertigo, tinnitus**
  - **sweating, thirst**
  - **coma, cramps, hyperthermia, hypoglycemia - in severe intoxication**
  - **uncoupling of oxidative phosphorylation (lactate production, lipolysis) ⇨ acidosis ⇨ possible exitus in children**
  - **CNS paralysis, cardiovascular colaps – exitus**

- **therapy**
  - **no antidote available**
  - **respiration support**
  - **stomach lavage, charcoal**
  - **prevention of acidosis & urine alcalisation**
  - **bleeding control**
  - **hemoperfusion is effective**

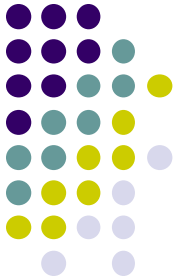
Psychostimulants
(amphetamine, metamphetamine, ephedrine)



- **acute intoxication symptoms**
  - euphoria, restlessness, anxiety, mydriasis, headache, convulsions
  - hyperthermia, coma
  - erythema, sweating, tremor, tachypnoe
  - fasciculation, rigidity, dysrhythmia, MI, intracranial bleeding
  - rhabdomyolysis & kidney failure

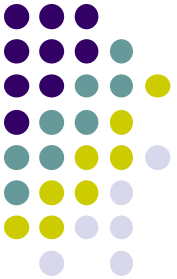
- **therapy**
  - **no antidote available**
  - **gastric lavage, sorbents**
  - ***diazepam* & symptomatic therapy (tachycardia = *β-blockers*)**
  - **assisted ventilation & forsed diuresis**

Anxiolytics
(benzodiazepines)



- **acute intoxication symptoms**
  - **lethargy, speech problems**
  - **hypothermia**
  - **coma, respiratory arrest**
  - **combination with alcohol !!!**
  - **respiratory arrest in newborn – during delivery medication**
- **therapy**
  - **symptomatic**
  - **antidote – *flumazenil* (in case of coma)**

AChE inhibitors
(organophosphates)



- **acute intoxication symptoms** **(intoxication with endogenous ACh)**

M-receptors

- **anorexia, nausea, vomiting**
- **abdominal cramps, diarrhea**
- **bradycardia, bronchospasm, miosis**
- **salivation, bronchial secretion, sweating**

N-receptors

- **muscle, tremor, convulsions**
- **muscular weakness**
- **respiratory muscle paralysis**

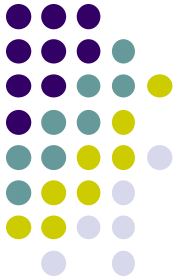
CNS

- **confusion, irritability, coma, exitus**

- **therapy**

- **decontamination, charcoal (oral ingestion), ventilation**
- **antidote - *atropine***
- ***oxims***
- ***diazepam*** **(in case of cramps)**

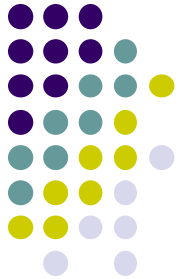
Antimuscarinics
(atropine)



- **acute intoxication symptoms**
  - **dry skin & mucosa, thirst, red face**
  - **tachycardia & tachypnoe**
  - **mydriasis, photophobia**
  - **fever, urine retention, intestinal motility**
  - **restlessness, muscle twitches, excitation, hallucinations**
  - **↑ BP, circulation failure (in severe intoxications)**

- **therapy**
  - **stomach lavage & charcoal (oral ingestion)**
  - **antidote - *physostigmin* 1-2 mg slow i.v. inj. (0,02-0,04 mg/kg in children)**
  - **cathetrize urinary blader**
  - ***metoprolol* or *atenolol* slow i.v. inj. (in case of tachycardia)**
  - **patient in a dark room**

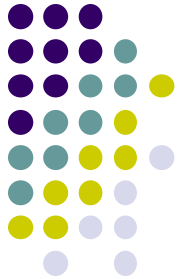
Anticoagulants
(warfarin)



- **acute intoxication symptoms**
  - bleeding from different organs, mucosa, hematuria
  - hematemesis, melena, petechiae, intracranial bleeding, hemorrhagic shock

- **therapy**
  - **gastic lavage & activated charcoal**
  - **prothrombin complex activity control**
  - **antidote -** ***vitamin K*** (p.o. 10-20 mg 2x a day; 10-20 mg i.v. 2-4x a day in severe cases)
  - ***plasma*** **&/or** ***concentrated coagulation factors*** **in case of severe bleeding & tranexamic acid** (competitively inhibits the activation of plasminogen to plasmin)

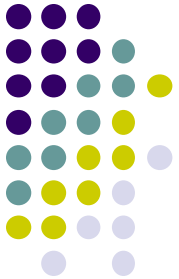
Anticoagulants
(heparine)



- **acute intoxication symptoms**
  - **bleeding**
  - **thrombocytopenia**
  - **antithrombin III consumption**

- **therapy**
  - **control thrombocytes, hemoglobin & serum electrolytes**
  - **antidote – *protamine sulfate* (in massive bleeding)**
  - **1 mg of protamine neutralizes 100 (to 150) I. U. of heparine**
  - **neutralizes also LMWH**

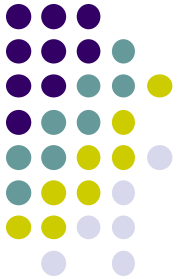
Alcohol
(ethanol)



- **acute intoxication symptoms**
  - overall depressive effect
  - mental confusion, stupor, coma, or person cannot be roused
  - vomiting
  - seizures
  - slow breathing (fewer than eight breaths per minute)
  - irregular breathing (10 seconds or more between breaths)
  - hypothermia (low body temperature), bluish skin color, paleness

- **therapy**
  - no antidote available
  - fluids, glucose, Mg^{2+}, K^{+}, thiamin
  - acidobasis
  - warming
  - assisted ventilation
  - stomach lavage (up to 30 min. after ingestion)
  - hemodialysis, no hemoperfusion
  - metabolic acidosis – *bikarbonate sodium*

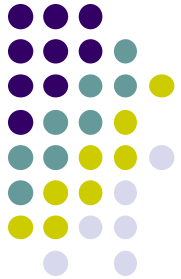
Alcohol
(methanol)



- **acute intoxication symptoms**
  - **metabolism - similar (slower) to *ethanol***
  - **formaldehyde, formic acid**
  - **acidosis**
  - **optic nerv damage – blindness**

- **therapy**
  - **elimination of *methanol* residues**
  - **compensation of acidosis**
  - ***ethanol***
  - **hemodialysis**

Cardioglycosides
(digoxin)



- **acute intoxication symptoms**

a) moderate intoxication

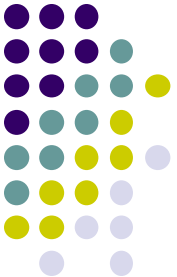
- anorexia, nausea, vomiting
- bradycardia
- headache

b) severe intoxication

- disturbance of vision, disorientation
- diarrhea
- ventricular tachycardia, fibrilations
- SA & AV block

- **therapy**
- stop drug medication
- stomach lavage + charcoal
- antidote - antibodies - *antidigoxin Fab* (Digitalis-Antidot)
- *potassium chloride*
- antidysrrhythmics, Mg^{2+} (in case of dysrrhythmias)
- ECG & serum electrolyte control

POISON/DRUG	ANTIDOTE
paracetamol *(acetaminophen)*	***N-acetylcysteine***
warfarin	***vitamin K***
opioids	***naloxone***
iron (& other heavy metals)	***desferoxamine*** (other chelating agents)
benzodiazepines	***flumazenil***
ethylene glycol	***ethanol*** or ***fomepizole*** & ***thiamine***
methanol	***ethanol*** or ***fomepizole*** & ***folinic acid***
cyanide	***amyl nitrite, sodium nitrite*** & ***sodium thiosulfate***
magnesium	***calcium gluconate***
verapamil, diltiazem	***calcium gluconate***
β-blockers *(propranolol, sotalol)*	***calcium gluconate*** and/or ***glucagon***
isoniazid	***pyridoxine***
thallium	***Prussian blue***
antimuscarinics	***cholinergics*** (& vice-versa)



http://en.wikipedia.org/wiki/Poison