Forensic toxicology

Toxon *(Greek)* – bow

- Forensic toxicology is a part of forensic sciences concerned on the study of thousands of toxic substances or poisons and application this knowledge to the law purposes.

- Toxicology encompasses theoretical considerations, methods and procedures from many disciplines including analytical chemistry, biochemistry, epidemiology, pharmacodynamics, pathology, and physiology.

- **Toxicology**

the study of the toxic or harmful effects of chemicals

- action of toxic substances

- occurrence of their harmful effects

- the symptoms and treatment of poisoned

- analysis: identification of the substances, quantitative determination

"All substances are poisons: there are none to be not a poison. The right dose differentiates between a poison and a remedy"

- **The toxic and the fatal dose**

- Is not fixed for every drug or poison – different people have a wide range of sensitivity or resistance and it may vary from time to time for one person

- LD_{50} is determined in experiments on particular species of animals, so can't be simply extrapolated to humans

- It's almost impossible to „calculate backward" from a drug blood concentration what dose was used and when

- **What substances are most frequently detected in autopsy samples in cases of suspected poisoning?**

The list is not closed; it is continuously verified and modified

- **medications**
  - **sedatives, hypnotics**
    - **benzodiazepines**
    - **zolpidem, zopiclone**
    - **barbiturates**
  - **antidepressants**
    - **TCA – amitriptiline, imipramine, desipramine, clomipramine, doxepine**
    - **SSRI – fluoxetine, paroxetine, fluvoxamine, sertraline, citalopram**
    - **SNRI – wenlafaxine**
    - **IMAO – moclobemide**
    - **other – mirtazapine, mianserine, trazodone**
  - **neuroleptics**
    - **phenotiazines (chlorpromazine, promazine, perazine, methotrimeprazine, perphenazine, thioridazine**
    - **thioxanthenes (chlorprothixene, flu[enthixol, zuclopenthixol**
    - **butyrophenones (haloperidol, droperidol)**
    - **benzamides (sulpiride)**
    - **atypical (clozapine, olanzapine, risperidone, quetiapine)**

- **anticonvulsants**

(valproic acid, carbamazepine)

- **cardiovascular**
    - **β - antagonists - metoprolol, acebutolol, propranolol**
    - **Ca - channel blockers - diltiazem, verapamil**
    - **ACE – enalapril, trandolapril, perindopril**
    - **antiarrythmics – propafenone**
    - **glycosides – digoxine, digitoxine**
    - **diuretics – indapamide, hydrohlorothiazide**
    - **other – trimetazidine**
- **drugs of abuse**
    - **opioids**
        - **opiates (morphine, codeine, heroine, oxycodone, buprenorphine)**
        - **synthetic (tramadol, pethidine, pentazocine, methadone, phentanyls, propoxyphene)**
    - **amfetamines**
        - **amphetamine, metamphetamine**
        - **designer drugs – MDMA, MDA, MDEA, PMA, PMMA and many others**
    - **cocaine**

- **hallucinogenes**
    - **LSD-25**
    - **psilocine, psilocybine**
    - **mescaline**
    - **salvinarine (Salvia divinorum)**
- **cannabinoids**
- **GHB (γ-hydroxybutyric acid – analogue of GABA, acting like alcohol, popular „date rape drug")**

- **metamphetamine**
- Marihuana, hashish
- cannabinols
- Δ9-THC

(Δ9-tetrahydrocannabinol)

main psychoactive substance in Cannabis sp.)

- GHB (γ-hydroxybutyric acid)
- white powder
- very soluble in water
- solution is colorless, water-like
- the taste is only light salty, undetectable in drinks, beer, food

- alcohol-like acting, but doses are 100 x greater
- drug facilitating sexual assault
- no good screening tests
- is normally detected in the body
- „legal highs”
- ketones (analogs of amphetamines) – mephedrone, methedrone, buphedrone, methylone, buthylone
- synthetic cannabinoids:
    - (CP-47,497 i its 3 analogues („Spice”, „K2”)
    - JWH-018, JWH-073, JWH-200, JWH-250, JWH-398
    - HU-210

☞ acting like classic drugs (amphetamines, cannabinoids, deliriums)

☞ unknown toxicodynamics and toxicokinetics

☞ unpredictable symptoms especially when mixed with another drugs and alcohol

☞ lack of specific therapy

- **pesticides**
    - phosphoroorganics (very toxic, inhibitors of acetylcholinoesterase)
    - carbamates
    - chlorinated hydroarbons

        - triazines
        - phenylacetic acids derivatives
        - pyretroides
        - other
    - **ethylene glycol**
        - **substitution of ethanol,**
        - **fixed (non-volatile), of sweet-burning taste,**
        - **available – component of the cooler liquid,**
        - **onset of intoxication – similar to ethanol abuse**
        - **toxic metabolites, causing excessive acidosis: glycol aldehyde, glyoxalic acid, glycolic acid (level of acidosis - prognosis as to life, not the blood concentration of glycol),**
        - **lesion of kidneys – deposition of calcium oxalate crystals (late metabolite) – oliguria, anuria**
        - **the quicker diagnosis – the better prognosis for recovery (hemodialysis)**
- **Carbon monoxide**
- chemical nature
    - colorless and odorless gas
    - slightly lighter than air
    - easily penetrating
- source:

- incomplete combustion (cookers, heaters, etc., insufficient ventilation, blocked chimney)
- car exhaust fumes (4-8% co)
- leakage from containers (ex. laboratory cylinders)
- fire (co toxicity is related to cyanide and hypoxia)

- **Carbon monoxide**
- mode of action
  - displacement of oxygen from hemoglobin
  - 200-300 times higher affinity than oxygen
  - very stable binding
- **Carbon monoxide**
- Toxicity
  - Headache, nausea, drunken-like symptoms, coma
  - Survivors: cystic degeneration of basal ganglia → parkinsonism
- Death
  - Cardio-respiratory failure (a kind of forensic asphyxia)
- Autopsy
  - Cherry pink color of the lividity, intensive red color of the blood and tissues
- **Carbon monoxide**

- Lab test
    - Quick – spectroscopy (very simple, but low sensitive method)
    - Hospitals - CO-meters (not O2-meters!)
    - Spectrophotometry (for ex. Wolff's method, Fretwurst-Meineck's metod)
    - Gas chromatography (CO is converted and detected as methane)
- **Carbon monoxide**
- COHb (carboxyhaemoglobine concentration)
    - Normal range (non-smokers) < 4%
    - Smokers ≤10%
    - Symptoms of toxicity ~20-30% (headaches, dizziness, nausea
    - Loss of consciousness 40-50%
    - death 50-60%
- **Post-mortem signs suggesting poisoning**
- <u>Stomach</u>
    - remains of plants, mushrooms, tablets, capsules
    - atypical color or/and smell (chemicals agents)
    - gastritis and/or oesophagitis (irrigative agents)
- <u>Liver</u>

- fatty changes, cirrhosis, necrosis (toxins of Amanita phalloidea, heavy metals, arsenic, Cl-derivatives of organic solvents, acetaminophen, NSAID)

- Kidneys
    - Necrosis, inflammation (mercury, chromium, ethylene glycol)

- Lungs
    - Oedema (corrosive gases)

- **solutions of cyanide salts of sodium and potassium have a high pH value (11-12) and its very irritable for gastric mucosa**

- Samples for toxicological analysis

- 10-15 ml

- better collect small but fully filled bottle than half-empty large bottle

- urine

- vitreous body

- stomach with contents

- piece of liver

- bile

- kidney

- piece of brain

- piece of lung

Lung and brain are important when volatile organic compounds are suspected

- <u>in some special cases</u>

- Skin with underlying tissues – intramuscular or subcutaneous injections

- Nails and hair

    - suspicion of chronic poisonings - arsenic, thallium, antimony, mercury (hair must be orientated in one direction and root must be determined)

    - living people

        - control of abstinence from drugs

        - anti-doping tests

        - suspicion of exposure on GHB (rapes)

- **material from exhumed bodies**

- the same like from normal autopsy if body is not decomposed

- in case of decomposition

    - tissues from abdomen cavity

    - skeletal muscles

- embalming fluids may contains: formaldehyde, methanol, iodide compounds

- samples should be collected in glass clean tightly closed containers (jars, vials)

- all containers should be described

    - name of deceased

    - date of autopsy
    - name of the sample
- addition of any preservatives is forbidden
- samples should be refrigerated or (better) frozen
- is a passive process
- mean time of absorption after single bolus of alcohol: 30-90 min.
- the gastric mucosa contains alcohol dehydrogenate which partly decomposes alcohol before it is absorbed into bloodstream
- The effects of alcohol
- Methods of alcohol analysis in biological samples (at least two):
- **Widmark's method**
- **ADH enzymatic**
- **Gas chromatography – preferred**

- **Widmark's method**
- Simple, cheap
- Linear in the range of 0-5 promiles
- Unspecific (false positive due to other reducing agents: H2S, mercaptans, other alcoholes, aldehydes etc)
- Enzymatic ADH

EtOH +NAD EtCHO (acetaldehyde) +NADH

- **Volume is not weight!**
- Widmark's equation

C – blood alcohol concentration [‰]

A – amount of consumed alcohol [g])

p – body weight [kg]

r – body weight reduction coefficient – volume of distribution individually calculated for each person

R – resorption deficit (10-30%, ie R= 0,9 to 0,7)

- **Rate of metabolism (β_{60})**
- **0,1 – 0,2 ‰ per hour**
- **may be lower or greater (up to 0,6 ‰ per hour in rare cases)**
- **may be different at the same person**
- **Alcohol-like acting substances (driving skills impairment)**
- Road-side screening tests of saliva (immunochemical qualitative tests)
- Urine tests (immunochemical qualitative tests)
- Confirmatory examination blood/saliva/urine test conducted in laboratories:
    - Forensic Medicine Departments (Medical Universities)
    - Institute of Forensic Research (Cracow)

- Central Laboratory of Police

- **Substances to be monitored in blood according to the amendment to the Polish Law on Road Traffic**

- opiates (LOD of morphine = 20ng/ml)

- amphetamine and derivates (LOD = 50ng/ml)

- cocaine and its metabolite benzoylecgonine (LOD of cocaine =50ng/ml)

- cannabinoids (LOD of Δ9THC = 2 ng/ml)

- benzodiazepines

LOD = limit of detection