



JESSENIUS FACULTY
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Industrial Toxicology

**Intoxication due to:
Organic solvents,
Pesticides**

Rýchle vyhľadávanie

Výučbové webstránky

Digitálne video

Materiály k prednáškam

E-learningové kurzy

Online videokonferencie

Univerzita tretieho veku

Obrazové kazuistiky

Selected Chapters in Toxicology

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





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The first edition of the university textbook "Selected Chapters in Toxicology" aims to serve as a concise, lucid, and compendious study material intended to teach students general and dental medicine. The use and presence of various chemicals in the living and working environment has been a serious long-term environmental problem that will also be present in the future. Therefore, all junior doctors should be well aware of all the necessary information, not only on acute poisonings they may encounter in emergency medicine, but also on the long-term and chronic effects of chemicals that need to be considered in the differential diagnosis of diseases.



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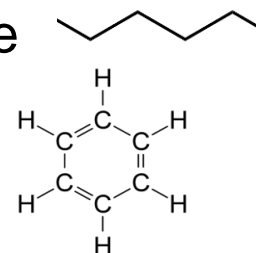
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Organic solvents - characteristic

- Usually a liquid at room temperature, dissolves another substance resulting in a solution (oils, fats, rubber, plastics)
- Properties
 - low molecular weight, lipophilicity, and volatility
- They may be divided into:
 - **Aliphatic-chain compounds**, such as n-hexane
 - **Aromatic compounds** with a 6-carbon ring, such as benzene or xylene
 - Both group may contain
 - a substituted halogen element – halogenated hydrocarbons
 - a substituted hydrogen group – alcohols, ketones, glycols, esters, ethers, aldehydes...



Flammability, explosiveness

- some of them may be used as fuels, other fire - extinguishing agents

Organic solvents-examples

Class of chemical substances	Compound	General effects
Aromatic Hydrocarbons	Benzene,	Carcinogenic, Anesthetic, Irritative
	Toluene, Xylene	Renal acidosis, persistent cerebellar ataxy
Alcohols	Methyl alcohol	Anesthetic, Irritative
	Ethyl alcohol	
Glycols	Ethylene glycol	Acidosis
Ketones	Acetone	Anesthetic, Irritative
Chlorinated Hydrocarbons	Trichloroethylene	Carcinogenic, Hepatotoxic, Nephrotoxic. Cardiotoxic
	Tetrachloroethylene	
	Chloroform	

Organic solvents - absorption

Pulmonary – inhalation of vapours of organic solvents

- the pulmonary retention and absorption for most organic solvents ranges 40-80% at rest
- organic solvents - volatile liquids, lipid soluble – well absorbed across alveolar-capillary membrane
- physical labour and exercise increase pulmonary ventilation and blood flow, more molecules are delivered to the alveoli, more molecules are absorbed the pulmonary uptake of many solvents increase by a factor of 2-3 times that at rest

Percutaneous – is determined by lipid or water - solubility and by volatility

- high absorption of solvents is when which are soluble in both lipid and water
- low absorption of highly volatile substance (they tend to evaporate from the skin unless evaporation is prevented by occlusion e.g. cloths)
- absorption of vapours in very high airborne concentrations e.g. in enclosed space with respiratory protection

Organic solvents

Distribution

- Distribution via the blood
 - To organs with large blood flows (cardiac, skeletal muscle)
 - To lipid - rich tissue (adipose tissue, nervous system, liver)
 - Adipose tissue accumulate greater amounts of a solvent and excrete large amounts at a slower rate after cessation of exposure
 - Lipid solubility increases with
 - length of carbon chain,
 - substitution with halogen or alcohol,
 - presence of unsaturated carbon bonds
 - Most solvents cross placenta, enter to breast milk

Metabolism

- Some of them are extensively metabolised by cytochrome P450 in liver, some not at all metabolised
 - Alcohol (aldehyde dehydrogenase enzyme)

Organic solvents – excretion

- Exhalation of unchanged compound
- Elimination of metabolites in urine
- Combination both ways
- The biological half- life of parent compounds varies from a few minutes to several days.
- Bioaccumulation beyond a few days is not an important determinant of adverse health effects for most solvents.

Organic solvents

Skin disorders

- Up to 20% of cases of occupational dermatitis are caused by solvents.
- Solvents are primary skin-irritants; they cause - **acute irritant dermatitis**
- It depends on concentration, duration of exposure, occlusion of the exposed area of skin, such as by clothes and leaking protective clothing
- **Allergic contact dermatitis** (skin tests)
- The most common work practice leading to solvent dermatitis is washing the hands with solvents, then painting, printing, mechanics, and dry cleaning.

Dg - History of direct contact, typical appearance of the skin, patch tests

- symptoms and signs- erythema, edema, chronic dry, cracked eczema
- secondary bacterial infection – these areas are more permeable to chemicals than unaffected skin

Dif.dg.- other sources of irritants or non-professional allergens

Treatment – the same as for contact dermatitis /topical corticosteroids, emollients, skin care

Prevention – education of workers about proper handling, engineering controls, alternatives to washing, using of solvent-resistant barrier creams, protective clothing

Organic solvents – effects on CNS

Acute effects

- Nonspecific depression of the CNS /both brain, spinal cord/
- General anaesthesia

Symptoms and signs – the same as those from drinking alcoholic beverages

- Headache, nausea, vomiting, dizziness, light-headedness, vertigo, disequilibrium, slurred speech, euphoria, fatigue, sleepiness, weakness, irritability, nervousness, depression, disorientation, confusion to loss of consciousness, death from respiratory depression, secondary-increasing of risk of accidents
- Many solvents exposure are to mixtures of solvents and that the effects of each solvents are at least additive and may be synergic.

Dif.dg. – alcohol, psychoactive drugs

Th. – Removal from exposure (until the signs and symptoms have completely resolve)

- avoid of using alcohol or other central nervous system depressant
- medication
- analgesics

Organic solvents – effects on CNS

Chronic effects

- Chronic toxic encephalopathy, presenile dementia, chronic solvents intoxication, painter's sy., psychoaffective disorder, neurasthenic sy.
- Changes in personality or mood, impaired intellectual function as assessed by batteries of neurobehavioral test, decrements in short-term memory and psychomotor function
- Chronic brain damage - cortical atrophy, Alzheimer's disease, vestibulo-oculomotor disturbances, due to effects on the cerebellum
- Dizziness, nausea, weakness after exposure to minimal solvent vapor concentration with normal vestibular test results

Symptoms - headache, mood disturbance /depression, anxiety, fatigue, memory loss /short-term/, difficulty in concentrating

Signs - impairment in recent memory, attention span, motor or sensory function

Dg - neurobehavioral tests, encephalography, CT, cerebral blood flow studies showing evidence of diffuse cerebral cortical atrophy, EEG abnormalities

Dif.dg. - Organic brain dysfunction, drug, alcohol, Alzheimer's d., Creutzfeld-Jacob d.

Organic solvents

Effects on peripheral n.s., cranial nerves

- Sensory - motor polyneuropathy of the axonopathy
- Centripheripheal distal axonopathy of the nerves in the spinal canal
- Trichloroethylene caused isolated trigeminal nerve anesthesia
- Vestibular dysfunction- hypacusis sensorineural /toluene/
- Color- vision disturbances /central rather than peripheral site of damage
- Disturbances of olfactory function /hyposmia, anosmia/

Symptoms - numbness, paresthesias, weakness, pain and muscle cramps

Signs - Symmetrical decrease in sensitivity and strength, decrease in distal reflexes, trigeminal neuropathy

Dg - history of exposure and illness, clinical examination,
neurophysiologic tests, EMG, test of olfactory function

Diff.dg. - DM, alcoholism, drugs, familiar neuropathy, renal failure

Th - removal of exposure to all substances toxic to the peripheral n.s.,
Physical th

Organic solvents

Respiratory system

- Irritation
- Acute pulmonary edema
- Exacerbation of asthma
- Chronic bronchitis
- Symptoms and signs - sore nose and throat, cough, chest pain,
• irritation of the eyes- tearing, dyspnea, cyanosis
- Examinations - X- ray, arterial blood gas analysis
- Dif.dg. infectious bronchitis, infectious / aspiration pneumonitis
- Th. Administration of oxygen, bronchodilators, ...

Organic solvents

Effects on the heart

- Arrhythmogenic effect
- Unexplained death
- Higher risk of coronary artery disease
- Symptoms and signs - dizziness, palpitation, faintness, loss of consciousness
- Lab. ECG

Dif.dg. primary cardiac disease

Effects on the liver

- Hepatocellular damage in sufficient doses.
 - Acute hepatic injury
 - Acute hepatic necrosis and death from liver failure
 - Toxic hepatitis subacute, chronic
- Lab.- liver function tests

Organic solvents

Effect on kidneys

- Acute renal failure from acute tubular necrosis (polyuria, proteinuria, glycosuria, acidosis, electrolyte disorders, hypokalemia, hypophosphatemia, hyperchloremia, hypocarbonatemia...)

Effects on blood

- Aplastic anaemia (benzene)
- Leukaemia
- Haemolytic anaemia (glycol)

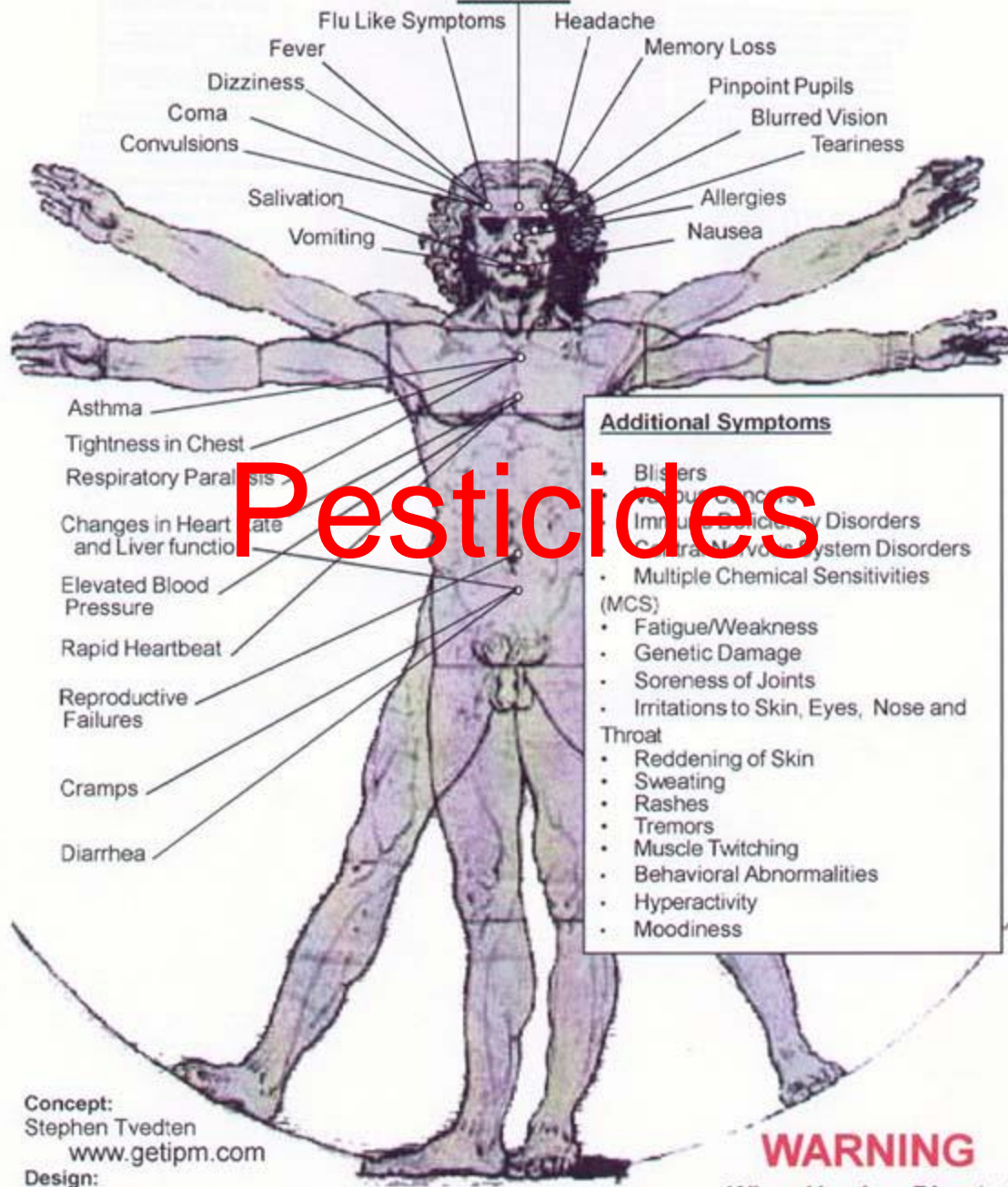
Cancer potential

- Benzen - all types of acute and chronic leukaemia
- Halogen hydrocarbons – hepatocellular carcinomas in mice
- Mixed solvent exposure – lymphatic and hematopoietic malignancies

Effect on reproductive system

- Teratogenity “fetal solvent sy”
- Spontaneous abortion
- Male reproductive capacity, sperm damage.

DEATH



Concept:
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WARNING
When Used as Directed
Pesticides Kill

Pesticides (nerve agents)

- Organophosphorus esters with low freezing-points
- Color – from pale yellow to colorless, essentially odorless
- Destruction
 - slowly broken down by hydrolysis on less toxic products
 - rapidly by strong alkalis and bleaching powder
- Penetration – liquid and vapor well penetrate the skin, leather and fabric. The protective clothing is safe till 6 hours.
- Damaging effects – caused through inhibition of acetylcholinesterase (ACHE) activity, effects are cumulative
- Death is from block of the airways with fluid secretions.
- The first intoxication is through respiration route, later mainly through the skin, possible through the digestive system.
- Muscarinic, nicotinic and central nervous symptoms

Pesticides (nerve agents) – signs and symptoms

Bronchial tree	Tightness in chest, with prolonged wheezing expiration, slight pain in chest, increased bronchial secretion, cough, lungs swelling,
Gastrointestinal system	Nausea, vomiting, abdominal cramps, diarrhea, involuntary defecation
Sweat, salivary, lacrimal glands	Increased sweating, salivation, tearing
Heart	Slight bradycardia
Pupils	Slight miosis, later marked miosis
Bladder	Frequency, involuntary micturition
Striated muscle	Fatigue, mild weakness, cramps, weakness of all muscles
Central nervous system	Tension, anxiety, emotional instability, insomnia, headache, tremor, apathy, confusion, slurred speech

Pesticides (nerve agents) respiratory route of the intoxication

Mild intoxication – few minutes of inhalation of low concentrations

Symptoms:

- **Miosis within dimming of vision**, difficulty in accommodation
- Frontal headache
- Tightness of the chest
- Nasal discharge and salivation

Symptoms persist for only a few hours

Headache and visual difficulties persist up to 3 days

Pesticides (nerve agents) respiratory route of the intoxication

Severe intoxication – all symptoms are more expressive

- Nasal discharge and salivation are profuse that watery secretions run out of the mouth and nose
- Excessive bronchial secretion with audible wheezing
- Severe sweating
- Profuse and uncontrollable vomiting, severe abdominal pain
- Involuntary defecation and micturition
- Muscular weakness occurs fasciculation, convulsions and paralysis
- Anxiety and depression, psychological disturbance

Pesticides (nerve agents) other route of intoxication

- **Cutaneous route**

- Symptoms are preceded by general malaise and are same as described at severe intoxication
- Miosis is not significant symptom for this route of intoxication
- Progress of intoxication is slower than in case of intoxication through respiratory route

- **Gastro-intestinal route**

- Symptoms are similar as described at severe intoxication
 - Symptoms develop faster than in the case of intoxication by the skin route
 - Vomiting may occur
 - Abdominal pains are well-marked at this route of intoxication
 - Miosis is not significant symptom for this route of intoxication

Nerve agents – casualties – Tokyo

TOKYO METRO 1995

– terrorist attack

Sarin was placed in 5 subway cars on three separate lines in plastic bags so that it could evaporate

Treated was more than 5000 persons of them

984 - moderately intoxicated

54 - seriously intoxicated

12 - people died



Nerve agents – self aid

The most effective treatment is within 30 minutes of exposure

Self aid – immediately after exposition or after first symptoms

- To use the full - face gas mask
- Self-inject needle with antidote (Atropine, Pralidoxime chloride)
- Get into protective suit
- Self-inject needle with 5 mg Diazepam (Combopen) or use 5 mg tablet
- Use decontamination KIT

Nerve agents – first aid

- **First aid - rescuers**

- Quickly ensure a free airway
- Stabilize the cervical spine
- Supplemental O2 must be administered
- Must be given antidote **Atropine + Obidoxime and Diazepam**

- **Treatment in hospital**

- Must be given first or continue - Atropine each 5-10 min.
- Administration of oximes must be continued (Obidoxime, Pralidoxime)
- Keeping free airway - suction of secretions from the respiratory tract is important
- Supplemental O2 must be administered
- Monitoring of vital functions