

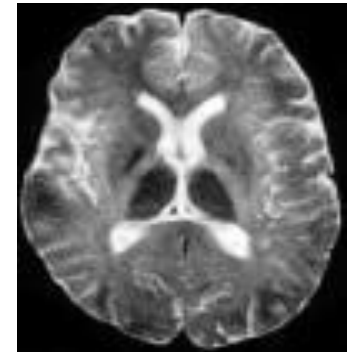
Organic solvents

Daniela Pelclová

Organic solvents



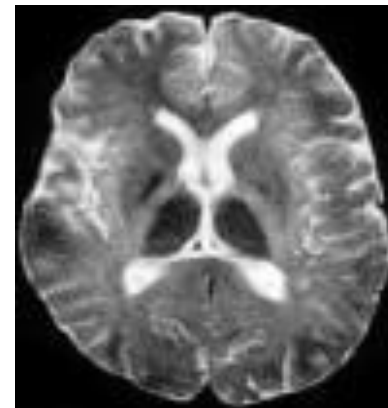
- **Exposure:** manufacture and formulation of chemical products, work with glues, cleaners, thinners, degreasers
- Most common route of exposure: inhalation
- **Etiopathogenesis:** lipid solubility, distribution to lipid-rich tissue-
- adipose tissue, nervous system.



Common effect : CNS NEUROTOXICITY

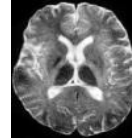
Acute exposure:

- 1. **excitation**
- 2. **depression** - sedation, coma



- **Chronic exposure**
- 1. **reversible neurobehaviour dysfunction**
- 2. **irreversible toxic encephalopathy (organic psychosyndrome)**

Acute exposure:

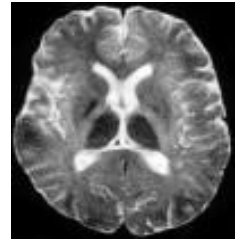


- 1. **excitation** of the CNS, euphoria, ebriety, hallucinations – music, images
 2. **depression** - sedation, coma

- **Treatment: symptomatic**
- **No milk for first aid – fat increases the absorption of solvents.**
- **No antidote for most solvents (except glycols and methanol), monitoring and support of vital functions.**

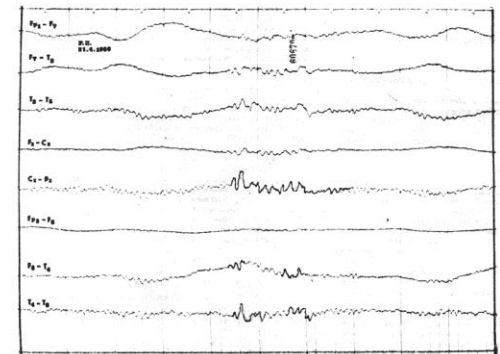


2. Chronic exposure:



- 1. **reversible neurobehaviour dysfunction** – nervousness, sleeping disorders
- 2. **toxic encephalopathy - irreversible organic psychosyndrome** (NMR and CT cerebral cortical and white matter atrophy) – IQ lowering, memory loss, personality degradation.

- PSYCHOL. TESTS
- EEG – slow theta waves
- impaired vision of blue-violet colors (Lanthony test)



- EXPOSURE MUST BE WELL DOCUMENTED

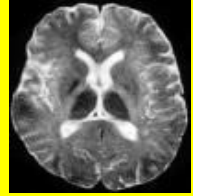
Biological exposure tests -BET



- Most organic solvents are biotransformed in the liver, their metabolites eliminated by the kidneys, are used for **biological monitoring- BET**.
- **Toluene: hippuric acid**
- **Trichlorethylene: trichloroacetic acid and trichloroethanol**
- **Benzene: phenol**
- **Exceptions: gasoline and other petroleum distillates (elimination without biotransformation by the lungs**
- .

SOLVENTS WITH LOWER TOXICITY

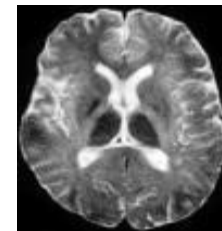
lethal dose: 200-300 ml



Commonly used solvents have no hepatotoxicity and no nephrotoxicity.

COMMONLY USED SOLVENTS

LOWER TOXICITY

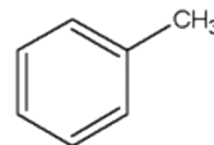


- ELIMINATION AFTER OXIDATION WITH LIVER ENZYMES TO METABOLITES
- EXCRETED INTO URINE



1. TOLUENE methylbenzene

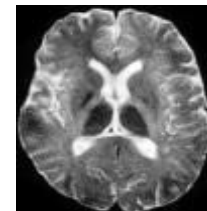
- metabolite: hippuric acid



2. TRICHLOROETHYLENE $\text{Cl}-\text{CH}=\text{CCl}_2$

- metabolites: trichloroethanol + trichloroacetic acid

COMMONLY USED – LESS TOXIC 2



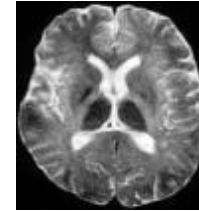
3. TETRACHLOROETHYLENE – PERCHLOROETHYLENE

- $\text{CCl}_2=\text{CCl}_2$ LD: 300 ml
- for degreasing in dry cleaners and in the industry
- metabolites: low amounts, not used for monitoring
- Double bond in chlorinated organic solvents prevents hepatotoxicity and nephrotoxicity.



SOLVENTS WITH LOWER TOXICITY

LD: 500 ml



4. PETROLEUM DISTILLATES

aliphatic and aromatic hydrocarbons (petroleum naphtha, gasoline, white spirits, etc.) – **LOW VISCOSITY, EASY ASPIRATION!**

ELIMINATION BY INHALATION

Acute inhalation exposure (after accident):

Chemical pneumonitis – symmetrical, rare

Ingestion: – common aspiration bronchopneumonia!!!

No vomiting induction, no gastric lavage!

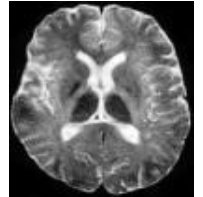
Conservative approach: fever? cough?

Then X-ray, and antibiotics treatment



SOLVENTS WITH HIGH TOXICITY

LETHAL DOSE: 1 sip – 30 ml



- May damage further organs:
- Liver (CCl_4 , CCl_3)
- Kidneys (CCl_4 , CCl_3)
- Bone marrow (benzene)
- Peripheral nerves (CS_2)

RARELY USED - VERY TOXIC

LETHAL DOSE: 5-20 ml

CARBON DISULPHIDE CS₂



Use: production of viscose rayon fibres and cellophane

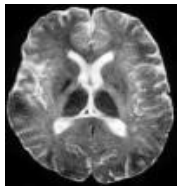
Health effects:

- CNS changes resembling manic depressive syndrome
- **peripheral neuropathy**: ascending symmetric paresthesias, sensory loss, weakness
- EMG



RARELY USED - VERY TOXIC

LETHAL DOSE: 5-20 ml



BENZENE



Use: production of ethylbenzene and styrene, chemical analyses

Health effects:

- 1. reversible pancytopenia, aplastic anaemia
- 2. acute or chronic **leukaemia**

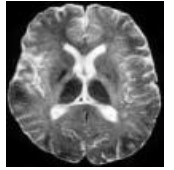
Laboratory

- urine: phenol,
- S-phenylmercapturic acid

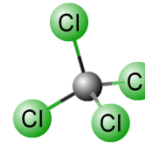


RARELY USED - VERY TOXIC

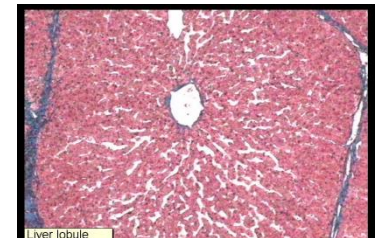
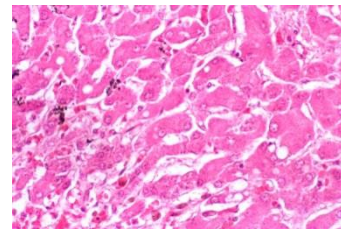
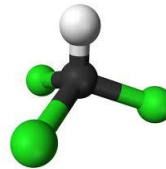
LETHAL DOSE: 5-20 ml



- Simple structures: hepatonephrotoxic
- **CARBON TETRACHLORIDE CCl_4**
- Use: chemical analyses, pharmaceutical industry



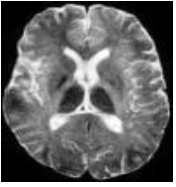
- **CHLOROFORM CCl_3**
- Health effects:
 1. hepatotoxicity, nephrotoxicity
 2. by oxidation - phosgene COCl_2
- - pulmonary oedema
- Laboratory : 0



Centrilobular necrosis
reversible

ETHANOL

- Pathogenesis:
- depression of the CNS, hypoglycaemia due to impaired gluconeogenesis, vasodilatation
- Risks: vomiting, aspiration, hypoglycemia, vasodilatation
- Metabolised
- by **alcohol dehydrogenase** to acetaldehyde,
- by **aldehyde dehydrogenase** to acetic acid, CO₂, H₂O
- Fixed rate of elimination about 5-7 g/hour
- Toxicity: lethal dose 3-13 g/kg (8 litres of beer,
- 3.5 litres of wine, 1litres of distillate – individual variability)

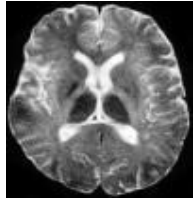


Clinical effects:

- 1 promile = 1g/l blood
- 1 promile - euphoria, mild incoordination
- impaired gluconeogenesis
- 2 promiles - ↓ judgement, ataxia, ↓social inhibition
- 2-3 prom. – respir. depression, aggressive behaviour
- 3-5 prom. - coma, respir. arrest, pulmonary aspiration,
- ↓ temperature ↓blood pressure ↓pulse rate
- consider : head trauma, hypothermia, meningitis, other intoxications

Treatment:

- mainly supportive care
- glucose, thiamine (esp. in chronic abusers)
- Haemodialysis – above 4 promile (4 g/l)
- no charcoal (no effect)
- no forced diuresis and no hemoperfusion (no effect)




ETHYLENE GLYCOL

Toxicity : LD 100-200 ml



- Sources:
- antifreeze for cars,
- brake fluids
- Biotransformation:
- by **alcohol dehydrogenase** to glycolaldehyde by **aldehyde dehydrogenase** to **glycolic and oxalic acid** – severe metabolic acidosis
- High osmolarity
- Unchanged partly excreted by urine

Clinical presentation:

- inebriation, gastritis, elevated osmolar gap
 - after 4 –12 hours severe anion gap metabolic acidosis, seizures, oxalate crystals in urine,
 - renal failure (anuria),
 - hypocalcemia, coma, death
- 
- A microscopic image showing numerous oxalate crystals in urine. The crystals are characterized by their elongated, needle-shaped or dumbbell-like morphology, which is typical of calcium oxalate. They are distributed throughout the field of view against a light background.
- In case of survival: polyuria, slow restoration of kidney functions (1-2 years)

FOMEPIZOLE EUSA Pharma 5 mg/ml
 5 ampoules / ampoules à 20 ml
 5 fl.oz 20 ml
 EUSA Pharma

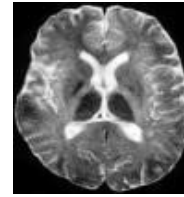
or

- **first aid** 100-200 ml 40% alcoholic beverage

- maintain the level of 1-1.5 promile (per os, gastric tube, or i.v.)
- (ADH saturation at 1 promile)

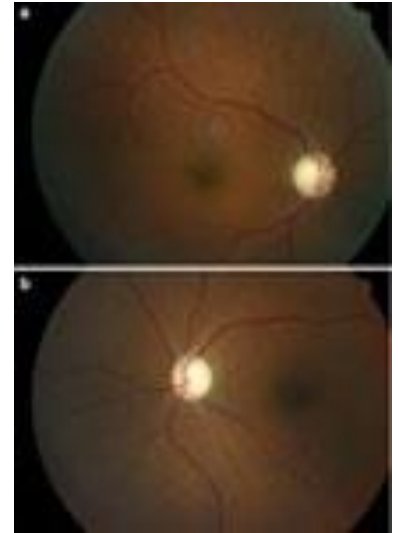
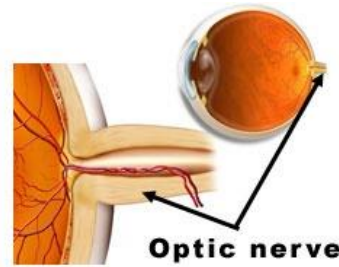
- replacement of kidney function
- removes EG, toxic metabolites, improves pH, osmolarity (ethanol treatment doses must be then multiplied by 2)
- Supportive care (no effect of charcoal, and HP)

METHANOL



- Source: Adulterated spirits, ingredient of some solvents, in laboratories
- Biotransformation:
- by **alcohol dehydrogenase (ADH)** to **formaldehyde** and
- **aldehyde dehydrogenase** to **formic acid**
- (inhibition of cytochromoxidase and depletion of GSH in retina –oxidative stress and optic nerve damage)
- metabolized 0,01g/kg /h (10x slower than ethanol)
- Metabolic acidosis, increased osmolarity
- Unchanged from 10-20 % eliminated by breath, 3% urine

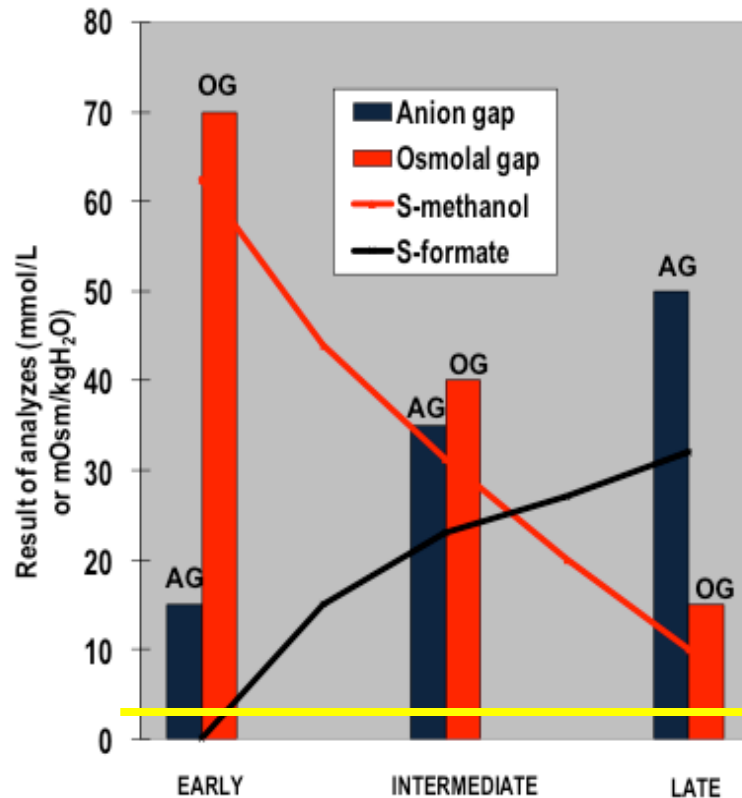
Clinical presentation:



- 1. inebriation, gastritis, headache
- 2. after 6-30 hours (delayed with alcohol intake):
- **visual disturbances** foggy, black and white snowfield, scotomas, blindness,
- dyspnoea, chest pain, sudden coma, cardiac arrest,
- multiorgan failure, brain edema, death
- **Eye fundus**: hyperemia, oedema of the retina (vessels, macula lutea)
- **Visual field** – scotomas – central and paracentral, decreased vision
- Toxic levels: methanol above 200 mg/l

3 stages of methanol poisoning

in the late stage **methanol disappears from the serum**
diagnosis is confirmed **by serum formic acid**



Limit of detection
2 mmol/l = 60 mg/l

Treatment:



1) **Antidote – Fomepizole (4-methylpyrazole)** – inhibitor of ADH – no side effects (more expensive)

- or

2) **Ethanol** (ADH affinity 5x higher) per os or 5% i.v.,

- **first aid** 100-200 ml 40% alcoholic beverage

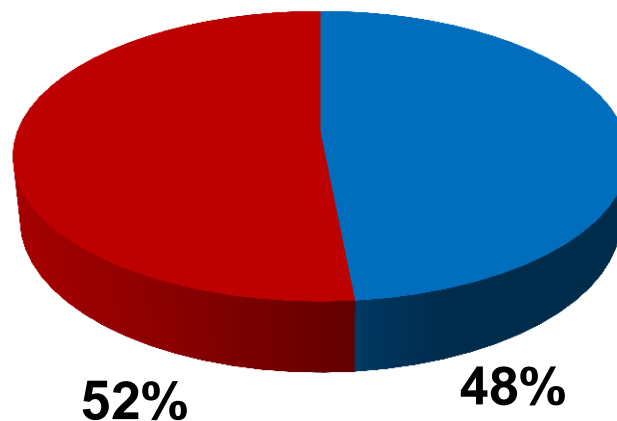
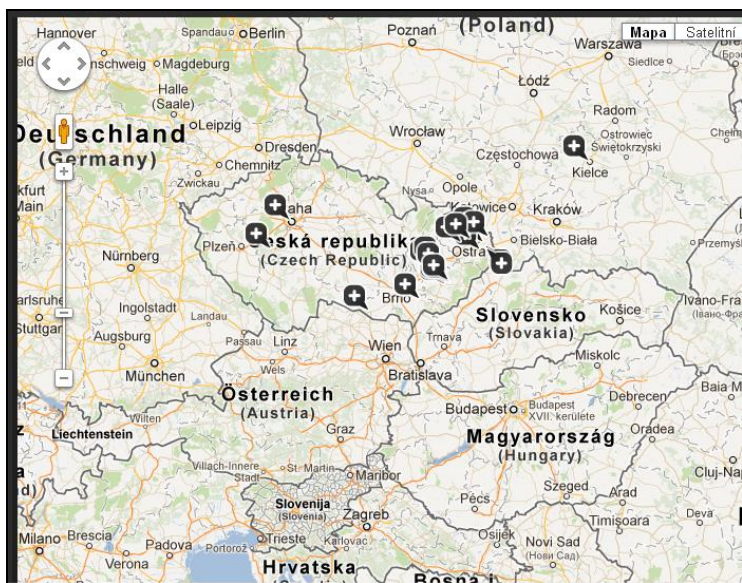
- maintain the level of 1-1.5 promile (per os, tube, or i.v.)
- (saturation of ADH at 1 promile)

Haemodialysis (methanol level above 400 mg/l)

- removes methanol, toxic metabolites, improves osmolar gap and severe metabol. acidosis
- (ethanol treatment doses must be then multiplied by 2)
- **Folic acid** – enhances conversion of formic acid to CO_2 and H_2O
- Supportive care (no effect of charcoal and HP)

Methanol poisonings outbreak in the Czech Republic in 2012

- Adulterated spirits
- About 90 persons hospitalized
- 39 deaths (half at home)



■ In the hospital
■ Before hospital

Outcome

Survivors after dismissal:

