LEARNING TOXICOLOGY THROUGH OPEN EDUCATIONAL RESOURCES

Mercury

Marie Vopršalová
Department of Pharmacology and Toxicology
Faculty of Pharmacy in Hradec Králové, Charles University,
Heyrovského 1203, 500 05 Hradec Králové, Czech Republic

e-mail: marie.voprsalova@faf.cuni.cz

MERCURY *(Lat. Hydrargyrum, Hg)*

= metal named after the planet Mercury

Hg = hydrargyros (name given by Aristotle) = water silver (liquid metal at room temperature)

Hg has been known about 2000 years, its properties have been described by Aristotle, Pliny the Elder, Paracelsus, etc. Alchemists used mercury in attempts in which they tried to convert common metals to gold.

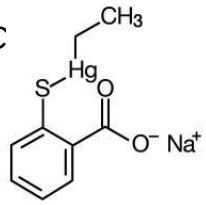
1. Uses:

Hg and Hg compounds have valuable physicochemical properties:

- **in the industry** (in thermometers, barometers, vapor lamps, batteries, as a catalyst in the production of chlorine)

EU banned Hg in glass thermometers according Directive EC 2007/51/EC

- **in the medicine** - antiseptic agent thiomersal in vaccines
- **in the dentistry** - component of amalgam



thiomersal

2. Types of mercury compounds:

Historically Hg compounds were responsible for numerous outbreaks of mercurialism (= mercury poisoning):

- *In mirror-makers in 17th century (at Venice on the Island Murano where huge mirrors were made by the means of Hg compounds).*
- *In hatters in 18th century (in England mercury salts were used in the preparation of felt for hats). The psychological symptoms - tremors, mental disturbances "mercury madness", jerky walk, stammering speech - associated with mercury poisoning inspired the phrase "mad as a hatter".*

The Mad Hatter from Alice's Adventures in Wonderland, by Lewis Caroll © duncan 1890

Hg exists in the three forms:

Elemental mercury → **mercury vapor**

= a silver gray liquid at room temperature

Vaporizes readily

Inorganic mercury compounds:

monovalent mercurous salts (Hg_2Cl_2, calomel)

divalent mercuric salts ($Hg(NO_3)_2$, $HgCl_2$)

Organic mercury compounds:

alkylmercury salts (fungicides)

methylmercury = CH_3Hg^+ (fish and shellfish contaminant)

Methylmercury: pollution and poisoning

1950 - CH_3Hg^+ poisoning was first described in the inhabitants of Minamata Bay, Japan:

Methylmercury is biosynthesized by aquatic microorganisms from inorganic Hg^{2+} waste and subsequently bioaccumulates in fish. High consumption of fish may lead to high CH_3Hg^+ uptake in humans → Minamata disease with >1500 death after consumation methylmercury contaminated seafood.

First the cats died → this species is more sensitive to CH_3Hg^+ than humans.

Unborn children are also at risk. CH_3Hg^+ readily crosses the placenta from mother to fetus and it damages especially the developing brain. Children born with Minamata disease can have growth deficiency and severe mental retardation.

Share video: https://www.youtube.com/watch?v=a3g0F8McXrs

https://www.youtube.com/watch?v=iD7QDlbtbn8

For more see : http://keywordsuggest.org/gallery/501477.html

Other sources of exposure to methyl mercury:

- *flour made from seed grain treated with methyl mercury (affected at least 6,500 people in Iraq), 1971*
- *meat from livestock that was fed mercury-tainted grain (in New Mexico, USA), 1969*

3. Toxicokinetics:

Why do the different forms of mercury cause different effects?

Because of different fate in the organism

Elemental mercury (Hg^0)

- low absorption from the gastrointestinal tract
- inhaled mercury vapor - absorbed by the lung,
  crosses the cell membranes → distribution to the brain

Inorganic salts of mercury (Hg^{2+}, Hg^{+})

- Absorption: after ingestion only 10% is absorbed in the intestine
- Distribution: the highest concentration of Hg^{2+} → in the kidneys.
  Inorganic mercurials do not readily pass the blood-brain barrier or the placenta.
- Excretion: in the urine ($T_{1/2}$ = 60 days).

Organic mercurials

- More lipid soluble → more completely absorbed from the gastrointestinal tract, through the skin.
- Cross the blood-brain barrier and the placenta → more neurological and teratogenic effects.
- Excretion of methylmercury: in the feces (through bile duct and in the form of conjugate with glutathione GSH).
  $T_{1/2}$ of methylmercury in man: 40 and 105 days.

4. Laboratory determination:

Elemental + inorganic Hg:

Follow a biphasic elimination rate (initially rapid, then slow)

The urinary Hg $T_{1/2}$ = 40 days

Whole blood and preferably urine Hg levels are useful in confirming exposure, but correlate poorly with the appearance of clinical symptoms

Organic Hg:

Methylmercury undergoes biliary excretion and enterohepatic recirculation → ≥ 90% in the feces

Urinary levels are not useful !

Hg concentration in red blood cells is 20 times higher than in plasma

The blood Hg $T_{1/2}$ = 50-70 days

5. Mechanism of toxic action:

- Formation of covalent bonds with -SH groups → the inactivation of metabolic enzymes, denaturation of structural proteins and disruption of cell membranes in the target organs. The inhibition of SH- enzymes is reversible after removal of Hg
- Interruption of protein and DNA synthesis and autoimmune responses
- Local corrosive action on the GIT

6. Intoxication:

Each of three forms produces an unique profile of toxicity

Elemental mercury

- ***Short-term exposure*** to vapor of elemental Hg (in high concentration): **pulmonary toxicity** (cough, dyspnea, bronchitis, pneumonitis)
- ***Chronic exposure*** to Hg vapor: **neurological effects** (asthenic vegetative syndrom - tremor, ataxia, tremor, emotional instability, insomnia, memory loss + goiter + tachycardia, gingivitis)

Inorganic salts of mercury

- ***Acute toxicity*:** **GIT local corrosive effect**: ashen-gray appearance of the mucosa of the mouth, pharynx and intestine, vomiting, mucosal sloughing in the stool → hypovolemic shock and death
- ***Systemic toxicity*:** **renal toxicity** (renal tubular necrosis leading to oligouria and anuria)

In children, chronic exposure to Hg is the cause of acrodynia together with some other predisposing factors such as hypersensivity. Acrodynia is characterised by pink hands and feets (also called **„pink disease"**), photophobia, pain in the extremities.

Additional reading:

http://www.cmaj.ca/content/168/2/201.full.pdf+html

Organic mercurials

- Adult: neurotoxicity – both hearing and visual loss, dysarthria, paresthesia
- Fetus and child: methylmercury is teratogenic → mental retardation of the fetus

For more see:

http://www.oocities.org/minoltaphotographyw/

http://ehp.niehs.nih.gov/121-a304/

http://www.who.int/mediacentre/factsheets/fs361/en/

Share video: https://www.youtube.com/watch?v=ihFkyPv1jtU

7. Treatment and decontamination:

Elemental mercury liquid

It passes through the gastrointestinal tract with minimal absorption in healthy persons → no gut decontamination needed

Elemental mercury vapor

Termination of exposure → immediately remove the victim from exposure

Indoor spills of elemental mercury can result in hazardous airborn levels → cover the spills with the tape (or powdered sulphur) and carefully clean up.

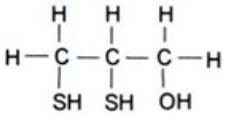
Do not use a home vacuum cleaner (it can disperse the liquid Hg in the air) !

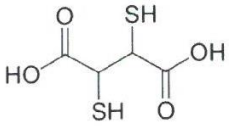
For more see:

https://www.health.ny.gov/environmental/chemicals/hsees/mercury/docs/cleaning_up_a_small_mercury_spill.pdf

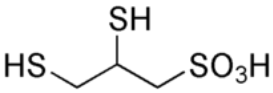
Chelation therapy:

- ***Dimercaprol*** - for high-exposures or symptomatic patients, i.m. administration





- oral derivatives, such as DMSA = ***dimercaptosuccinic acid*** or DMPS = ***dimercaptopropane sulfonate***



Each of these agents contains thiol groups that compete with endogenous -SH for mercury

Inorganic mercury

Do not induce emesis because of the risk of serious corrosive injury

Gastric lavage

Chelatation therapy: ***BAL, DMSA, DMPS***

Hemodialysis may be helpful in renal insufficiency, but it has no value for removing Hg because it is bound tightly to proteins in plasma and tissues.

Organic mercury

Dimercaprol is contraindicated: increases brain concentrations of methylmercury and may worsen neurotoxicity.

Methylmercury compounds undergo the enterohepatic recirculation → repeated oral administration of a non-absorbable mercury-binding substance should facilitate their removal from the body. A polythiol resin is effective in enhancing Hg elimination by **interrupting enterohepatic recirculation**.

References:

- Bernhoft, R.A.: Mercury Toxicity and Treatment: A Review of the Literature. Journal of Environmental and Public Health. 2012, Volume 2012, 1-10 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3253456/pdf/JEPH2012-460508.pdf
- Klaassen, C D..: Casarett and Doull's toxicology: The Basic Science of Poisons, 7th ed., McGraw-Hill: New York, 2008, 931-980
- Shannon, M.W., Borron, S.W., Burns, M. J.: Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose, 4th ed., Sunders/Elsevier: Philadelphia, 2007,1111-1170
- Bryson, P.D.: Comprehensive Review in Toxicology for Emergency Clinicians, 3rd edition, Taylor and Francis: London, 1997, 579-642
- Olson, K. R. at al.: Poisoning & Drug Overdose, 5th Edition, McGraw-Hill, New York, 2006, 213-216
- Reichel, F-X., Ritter, L.: Illustrated Handbook of Toxicology, 4th edition. Thieme, Stuttgart, 2011, 160-182
- Timbrell, J.: The Posion Paradox: Chemicals as Friends and Foes, 1st edition, Oxford University Press, New York, 2005, 348

https://toxoer.com

Project coordinator: Ana I. Morales
Headquarters office in Salamanca.
Dept. Building, Campus Miguel de Unamuno, 37007.
Contact Phone: +34 663 056 665