LEARNING TOXICOLOGY THROUGH OPEN EDUCATIONAL RESOURCES

Cadmium

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CADMIUM *(Lat.cadmium, Cd)*

1. Sources and uses:

Environmental source

- Cd occurs in nature in association with zinc, lead and extraction and prossesing of these metals thus often lead to environmental contamination with cadmium.
- Coal and other fossil fuels contain cadmium and their combustion releases the element into environment.
- Cd is a component of cigarette smoke.

  1 cigarette contains 1 to 2 µg Cd, 10% of Cd in a cigarette is inhaled (= 0,1 - 0,2 µg)

- Moreover, animal liver, kidney, shellfish are among foods that have higher concentrations of cadmium. Cd is readily absorbed and accumulated in plants.

Industrial use

- Cadmium has valuable electrochemical properties (manufacture of rechargeable nickel-cadmium batteries).
- Cd is used in alloy fabrication (corrosion protection), metal plating, paint pigments (cadmium yellow), rubber and plastic.

Cadmium pollution related disease:

1946 Fuchu, Japan : → „itai-itai“ („ouch-ouch“) disease:
Victims (predomintly women) complained of severe pains
Itai = painful
They suffered from severe osteomalacia, osteoporosis, skeletal deformation.
Cause: Cadmium poisoning from contaminated rice (cadmium had contaminated the local rice fields from the effluent from a lead-zinc processing plant).

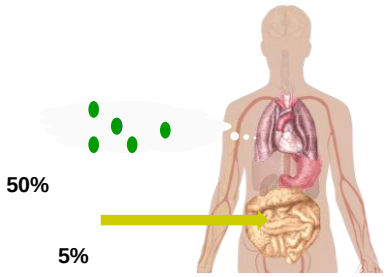
One of the markers of „itai-itai disease" was osteomalacia. There may be an interaction among Cd, nutrition and bone disease. Body stores of calcium have been found to be decreased in subject exposed to Cd occupationally. This presumed effect of cadmium may be due to interference with renal regulation of calcium and phosphate balance.

Share video:

https://www.youtube.com/watch?v=zCsps94OogY&index=2&list=PLSNnN9ZEWEghzVer7EbHplMm4R2gK37NS

2. Toxicokinetics:

Cadmium occurs only in one valence state, 2+, and does not form stable alkyl compounds or other organometallic compounds of known toxicological significance.



Absorption:

- Cd is well absorbed after inhalation (up to 50%). Cigarette smokers may absorb Cd from smoke.
- However only about 5% of an oral ingested dose is absorbed.
- GIT absorption is enhanced by low intake of Ca, protein and Fe.

Distribution:

After absorption, cadmium is transported in blood, bound mainly to blood cells and albumin.

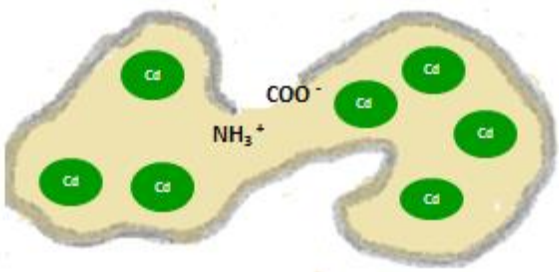
Cd is stored bound to **metallothionein**. The main storage organs are the liver and the kidneys.

Metallothionein (MT) = intracellular, low-molecular-weight protein, rich in amino acid cysteine and thus with –SH groups (> 30%).

- high affinity for essential metals - Zn, Cu and toxic metals Cd, As, Hg.
- inducible by exposure to Cd and other metals.

Biological role:

- storage of essential metals (Cu, Zn)
- detoxification of heavy metals (Cd, Hg, As)



For more see:

https://cadmium-binding.wikispaces.com/Metallothioneins

Excretion:

Cd is poorly excreted from the body (0,001% of the body burden/day). The half-life of cadmium in the body is 10-30 years. Consequently, with continuous environmental exposure, concentrations of the metal in tissues increase throughout life.

3. Intoxication

Acute cadmium poisoning:

Acute poisoning usually results from:

- inhalation of cadmium dusts and fumes (usually cadmium oxide)
- ingestion of cadmium salts

Cadmium is more toxic when inhaled. The early toxic effects are due to local irritation.

Oral intake: within minutes after exposure → nausea, vomiting, salivation, abdominal cramps, diarrhea (sometimes bloody). Death results from shock or acute renal failure.

Inhalation: within a few hours after exposure → irritation of the respiratory tract with cough, fever, severe chest pains, chemical pneumonitis and pulmonary edema.

Chronic cadmium poisoning :

Depends on the route of exposure:

Kidney damage → after inhalation or ingestion

Lung → after inhalation

Kidney are the major target organ after long-term Cd exposure → acute tubular necrosis → interstitial inflammation and fibrosis. Renal tubular dysfunction → proteinuria with a loss of ß$_2$- microglobulin, N-acetyl-ß-D-glucosaminidase (NAG). Urinary excretion of proteins and Cd are biomarkers for Cd exposure.

For more see:
http://www.kanazawa-med.ac.jp/~pubhealt/cadmium2/itaiitai-e/itai02.html

Lung: the consquence of excessive inhalation of cadmium fumes and dusts are obstructive lung disease, dyspnea and pulmonary fibrosis.

Bone: Cd interferes with calcium metabolism → calcium loss from renal dysfunction. Disrupted production of active metabolite of vitamin D (= calcitriol) in the kidney → stimulation osteoclastic activity.

Carcinogenesis:

IARC: Cd is human carcinogen → lung, prostate carcinoma

Additional reading:
https://rais.ornl.gov/tox/profiles/cadmium.html

4. Laboratory determination:

Whole-blood Cd levels: confirm the exposure.

Urine Cd levels: little value, because there is little excretion in the urine.

ß$_2$- microglobulin, N-acetyl-ß-D-glucosaminidase (NAG) – markers of tubular microproteinuria and toxic effects of Cd on the kidney.

5. Treatment of cadmium poisoning:

Involves the use of chelating agents, which binds the metal forming a complex that is then excreated into the urine.

Chelating therapy no evidence, that it is effective

Some clinicans recomend chelation therapy with **$CaNa_2EDTA$**. Chelatation therapy should be instituted as soon as possible after Cd exposure, because there is a rapid decrease in the effectiveness of chelatation therapy with time, due to distribution of the metal to sites that are not accesible to the chelators.

Dimercaprol is contraindicated because it increases nephrotoxicity.

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