

3 rd International Summit on Toxicology CHICAGO Oct 2014

TRACK 4 : Industrial and Metallic Toxicology

**A NEW CHALLENGE :
ASSESSMENT of Metallic Toxicity**



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INTRODUCTION (Environmental exposure)

- Cobalt is a hard lustrous, gray metal
- Cobalt is naturally found in rocks, soil, water, plants, animals



INTRODUCTION (Environmental exposure)

- Cobalt is present in trace amounts in human diet
- (fish, vegetable, drinking water ...)



PHYSIOLOGY

- cobalt is a part of vitamin B 12
(necessary for neurological function, brain function,
and blood formation...)
- Require for oxygen transport in metabolism



USES

- cobalt containing products include corrosion and heat resistant alloys (metal industries)
- hard metal alloy :
 - cobalt – tungsten – carbide



OTHER USES

- magnet
- grinding/ cutting tools
- pigments / paint
- colored glass
- catalyst / batterie
- cobalt – coated metal
- surgical implants



OCCUPATIONAL EXPOSURE

- hard metal industry
- diamond polishing
- ceramic industry



INDUSTRIAL PROCESS

- First step : forming wolfram carbide (WC) from the ore
- WC is then milled to fine powder
- secondly mixed with metallic cobalt (size 1 – 2 mm)



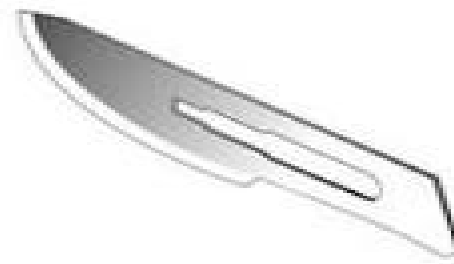
INDUSTRIAL PROCESS

- mixed powder is pressed to obtain desired shapes
- after heated under pressure to 1000 °
- this « product » could be drilled
- finelly heated again (1500°C)



End of the PROCESS

- pieces obtained are ground to very exact shapes (material is very hard and only diamond grinders can be used)



Mechanism of cobalt toxicity

- high affinity for sulfhydryl groups
- inhibition of crucial enzymes
(oxidative phosphorylation)
- inhibition and competition with calcium binding
- generation of oxygen species
- direct cyto-toxicity



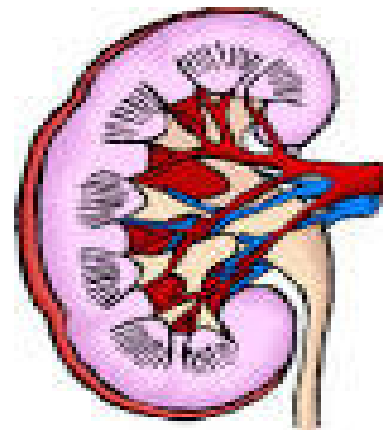
Effects of cobalt on cells

- inhibit osteoblast function
- reducing alkaline phosphatase activity
- inducing secretion of proteins IL8 and MCP
(osteoblasts)



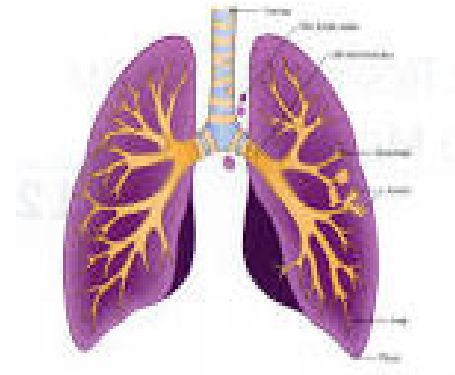
Chronic systemic exposure

- accumulation liver
- accumulation Kidney



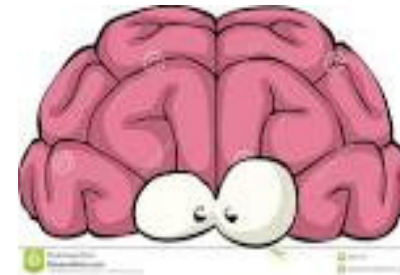
Adverse effects of cobalt and pulmonary diseases (interstitial fibrosis)

- tightening of the chest
- cough
- shortness of breath
- fatigue
- production of sputum
- weight loss



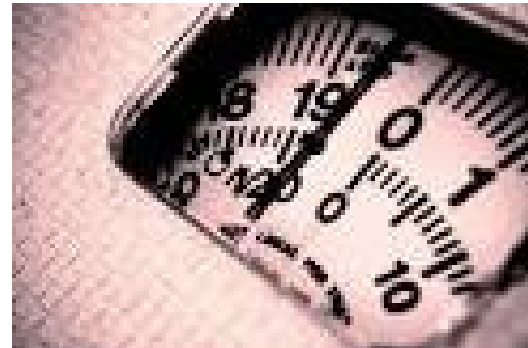
Adverse effects of cobalt

- neurological symptoms
 - severed headaches
 - cognitive decline
 - memory difficulties (remembering names)
 - poor concentration
 - depression



Adverse effects of cobalt

- metal taste in the mouth
- anorexia
- weight loss



Adverse effects of cobalt

- hearing loss
- visual changes
- arrhythmias and cardiopathy
- endocrine symptoms (hypothyroidism ...)
- abnormal lymphocyte function



Adverse effects

- releasing micro particulate metal debris :
 - development of pseudotumors
 - hypersensitive reaction
 - nanoparticles consequences
 - * cytotoxic
 - * genotoxic
 - * immunological (vigilance after long latency)



Hip prostheses

- conventional total hip prostheses :

- metal head

- fits into polyethylene cup

- (but with time require revision)



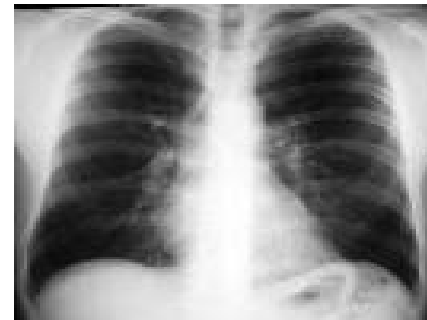
Hip prostheses

- metal on metal bearing (made with cobalt and chromium)
- release a variety of metal ions into :
 - local tissue
 - general circulation



Metal hip assessment

- well fixed (x-rays)
- well aligned implant
- mild osteopenia around acetabular component



Case report

- 60 years old women
- total hip prosthesis containing cobalt
- three years ago



Case report clinical symptoms

→ none symptom



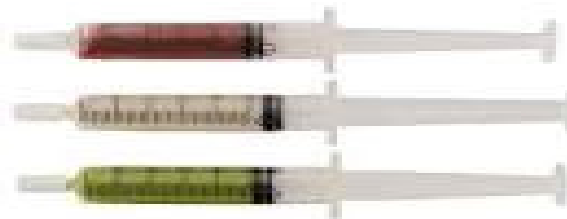
Case report routine biomonitoring

- 1) Blood cobalt level : 3.2 ug/l
(non exposed population < 0.6 ug/l)
- 2) Blood cobalt level : 4.64 ug/l
(three months later)
- 3) Blood cobalt level increases : 8.29 ug/l
(patient with cobalt hip : 7 ug/l)



References biomonitoring

- Problem from : 60 ug / l
(up to 100 times that of physiologic levels)



Intravenous injection

- 40 % eliminated within first 24 hours
- 70 % eliminated within one week
- 80 % eliminated one month
- 90 % eliminated one year



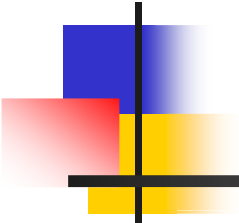
Treatment of cobalt toxicity

- No consensus
- To treat the systemic symptoms :
 - * thyroid replacement therapy
 - * beta-blockers
 - * angiotensin-converting.....

(no established indication for chelation therapy)



Conclusion

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- No current consensus regarding management of patients with cobalt alloy, hip prostheses and elevated circulating cobalt metal ion levels
 - Removal of implanted hardware if :
 - * endocrinopathy
 - * cardiopathy(persistence of neurologic symptoms)
 - Improved surveillance is needed