COPPER

Michaela Králíková, MD
Department of Biochemistry
Faculty of Medicine
Masaryk University

- **Cu^{+}, Cu^{2+}**
- **80 - 100 mg in organism, 90% in body tissues**
- **reference values Cu/S = 820 – 1400 μg/l**
  males 11 - 22 μmol/l
  females 12.5 - 24 μmol/l
- **Afroamericans 8 - 12% ↑**
- **90-95% in ceruloplasmin**
- **ceruloplasmin /S = 240 - 400 mg/l**

Metabolism

- **Absorption**
- **Transport and distribution in organism**
- **Excretion**

Absorption

- 10 - 70% of intake Cu
- RDI about 2 mg/d
- sources: sea fish, cereals, nuts, cocoa, liver

- small intestine
- chelate complex with aminoacids (His), or metalothionein bounded
- competition with zinc

Transport and distribuiton in organism

- chelate Cu – AA transported to portal circulation, where Cu binds to albumin, His or transcuprein
- in liver 90% binds to newly synthetized ceruloplasmin
- in blood 90-93% in ceruloplasmin

Excretion

- faeces (1.5 - 2 mg/d) – bile and shed mucosal Cu
- urine - 1 - 2% Cu absorbed ~ < 100 μg/d assesment for dg and therapy control of Wilson´s disease

Importance

- Part of enzymes: **cyt c-oxidase, SOD, MAO, tyrosinase, dopamine-β-hydroxylase, lysyloxidase**
- Part of pigments, for example keratin
- Necessary for catecholamines metabolism, production of connective tissue , CNS and ercs function
- Antioxidative function

SOD

$$2\ O_2^{\cdot -} + 2\ H^+ \rightarrow O_2 + H_2O_2$$

SOD 1(cytosol), EC-SOD: contains Cu and Zn

$$E\text{-}Cu^{2+} + O_2^{\cdot -} \rightarrow E\text{-}Cu^{+} + O_2$$
$$E\text{-}Cu^{+} + O_2^{\cdot -} \rightarrow E\text{-}Cu^{2+} + H_2O_2$$

Zn^{2+} - stabilisation function

SOD 2 (mtch): $Mn^{2+} \leftrightarrow Mn^{3+}$

← antioxidative activity

ceruloplasmin –

catalyses

$$Fe^{2+} \rightarrow Fe^{3+}$$

(protects Fe^{2+} from participation in Fenton reaction)

← antioxidative activity

Cu in Fenton reaction

$$H_2O_2 + Cu^{+} \rightarrow OH^{-} + {}^{\cdot}OH + Cu^{2+}$$

← prooxidative activity

Deficiency

- inborn: Menkes disease
- obtained

Menkes disease
(Kinky (steely) - hair disease)

- GR heredity
- gene mutation of transport IC ATPase 7A → intestinal absorption impairment
- PCR prenatal dg
- ↓Cu, ceruloplasmin and Cu-enzymes
- most of children die within 3 years
- growth and skeletal defects, mental and physical retardation, brain and typical hair symptomatology

Obtained deficiency - causes

- malnutrition
- parenteral nutrition without Cu supplementation
- zinc or long-term D-penicilamine therapy
- diarrhoea

Obtained deficiency – clinical symptoms

- hypochromic normocytic anemia
- neutropenia
- bone metabolism disorders (lysyloxidase)
- GIT disorders
- depigmentations
- demyelination

Toxicity

- ↑ Cu in hepatitis, acute leukemias, lymfoms, MM, melanoma, schizophrenia
- **Acute intoxication** - >250 mg Cu, nausea, emesis diarrhoea, epigastrium pain; shock, coma and acute hepatal and renal failure
- **Chronic intoxication** - cirrhosis (children in India, milk and water stored in brass vessels)

Wilson´s disease

- **AR heredity**
- **gene mutation of transport IC ATPase 7B →**
- **↑ Cu absorptin, Cu bile elimination disorder, Cu-ceruroplasmin bound defect, ↓ or none ceruloplasmin synthesis**
- **manifests usually between 10th – 20th year**
- **↓ total Cu /S** (6.3 – 9.4 μmol/l), **↑ free Cu /S, ↓ ceruloplasmin /S** (<0.2 g/l) , **↑ urine excretion** (> 1.57 μmol/d = > 400 μg/d)

Wilson´s disease

- **free copper attacks:**
- **liver:** icterus, anorexia, nausea, weight loss, haemorrhagic diathessis, cirrhosis
- **brain:** basal ganglion dysfunction → rigidity or tremor, dystonia, speech disorder
- **kidneys:** ↑ urine excretion
- **cornea:** brown-greeen Keyser-Fleischner ring

Wilson´s disease

- ATP7B gene molecular PCR analysis – detection of latent disease
- Examination of relatives (brothers and sisters) is necessary!
- (Cu/S, ceruloplasmin/S, Cu/U; PCR)

- Therapy: D-penicilamine (1 - 2 g/d)

  Zn (25 - 50 mg 3x per day between meals)

  vit. B_6 (penicilamine is it´s antimetabolite)