Trace Elements

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Trace Elements

- a naturally occurring, homogeneous, inorganic substance required in humans in amounts less than 100 mg/day
- Essential nutrients in trace amounts
• Assessment of trace mineral status is difficult and requires specialized analytical instruments (atomic absorption spectrometry).
• Serum measurements are complicated by associated disease states that affect levels of circulating binding proteins (e.g., albumin).
• Diagnosis is dependent on high degree of suspicion, careful inspection for signs and symptoms, thorough understanding of predisposing causes and resolution of symptoms with therapeutic trial.

Copper
Copper Metabolism

- Intestinal absorption/membrane translocation mediated by specific transporters
- Copper circulates bound to ceruloplasmin
- Relative tissue distribution of copper reflects levels of cuproenzymes
- Excretion occurs via transport of copper into bile and elimination in feces

Copper: Biochemical Functions

- Essential catalytic cofactor for many cuproenzymes including:
  - Cu, Zn-superoxide dismutase (antioxidant)
  - Cytochrome C oxidase (ATP synthesis, neurologic function)
  - Ceruloplasmin (6 atoms per molecule)
    - Functions to oxidize Fe^{2+} to Fe^{3+} for binding to transferrin.
      - Congenital absence of this protein leads to tissue iron accumulation and iron overload syndrome (hemochromatosis)
  - Lysyl oxidase (cross links and stabilizes connective tissue proteins)
  - Tyrosinase (melanin synthesis)
Copper Physiology/Deficiency

- Acquired deficiency is rare. Causes include:
  - Omission from TPN
  - High intake of Zinc
  - Renal dialysis patients
  - Use of copper chelating agents (penicillamine)
- Manifestations:
  - Hypochromic microcytic anemia
  - Neutropenia
  - Hypopigmentation of hair and skin
  - Structural abnormalities in connective tissue (hair, teeth, bone demineralization, vascular system with arterial aneurysms with risk of hemorrhage and thrombosis)
  - Fetal and neonatal deprivation leads to neurologic dysfunction
  - Reduced levels of circulating copper and ceruloplasmin

Food Sources

- organ meats, seafood, nuts, seeds, cereals, whole grains, cocoa
Inborn Errors of Copper Metabolism: Wilson’s Disease (Hepatolenticular Degeneration)

• Autosomal recessive defect in ATP7B resulting in copper storage disease (primarily liver, CNS, cornea of eye)
• Inability to transport copper out of liver results in deficiency in some organs (bones with demineralization, anemia and low levels of ceruloplasmin)
• Diagnosis based on:
  - Low Ceruloplasmin levels
  - Corneal copper deposition (Kayser-Fleisher Rings)
  - High liver copper levels
• Treatment:
  - Zinc
  - D-penicillamine (chelation increases urinary copper excretion)
  - Copper deficient diet of little value
Inborn Errors of Copper Metabolism: Menkes Kinky Hair Syndrome

- X-linked neurodegenerative disease associated with all symptoms of copper deficiency including:
  - Brittle, kinky hair characterized by pili torti or cork screw hair (this feature is unique to MKH syndrome and is not seen in other copper deficiency syndromes)
  - Death by year 3 of life is usual
- Disease is due to mutation in ATP7A transporter resulting in low serum copper levels and accumulation in intestinal cells.

Pili torti (Menkes Disease)
Iodine

- body normally has 20-30 mg of iodine and more than 75% is in the thyroid gland
- the rest is in the mammary gland, gastric mucosa, and blood
- it’s only function is related to thyroid hormone
Iodine

- Required for synthesis of thyroid hormone
  - Thyroxine (T₄) – 4 atoms of iodine per molecule
  - Triiodothyronine (T₃) – 3 atoms of iodine per molecule

Absorption and Excretion

- iodine is absorbed in the form of iodide
- occurs both as free and protein-bound iodine in circulation
- iodine is stored in the thyroid where it is used for the synthesis of T₃ and T₄
- the hormone is degraded in target cells and in the liver and the iodine is conserved if needed
- excretion is primarily via urine
- small amounts from bile are excreted in the feces
Food Sources

- foods of marine origin (seaweed), processed foods, iodized salt

Deficiency

- goiter—enlargement of the thyroid gland
- deficiency may be absolute—in areas of deficiency, or relative—adolescence, pregnancy, lactation
- goiters are more prevalent in women and with increased age
- goitrogens occurring naturally in foods can cause goiter by blocking absorption or utilization of iodine (cabbage, turnips, peanuts, soybeans)

- severe deficiency during gestation and early postnatal growth: cretinism—mental deficiency, spastic diplegia, quadriplegia, deaf mutism, dysarthria, shuffling gait, short stature, hypothyroidism

**Endemic Cretinism**

- Note normal man and three adult women with cretinism:
  - Short stature
  - Protuberant abdomen
  - Swollen features
Iodine deficiency is the most common nutrient deficiency in the world!

### Iodine Excess and Toxicity

- Humans are remarkably tolerant to high iodine intakes
- In iodine deficiency, repletion must be done slowly to prevent hyperthyroidism
- Paradoxical goiter (enlarged thyroid as a result of very high intakes of iodine)
  - Occurs in Japan and China with high intake of seaweed (50,000 - 80,000 µg/day)
Toxicity

- Iodine has wide margin of safety

Goiter

- Endemic to parts of S. America and India
- Sporadic cases in U.S.
- Selenium deficiency (needed to convert T4 to T3)
Goiter - Complications

- Usually asymptomatic
- Acute pain from thyroidal hemorrhage
- Dysphagia (trouble swallowing)
- Dyspnea (trouble breathing)

Chromium
Chromium--Functions

- required for normal lipid and CHO metabolism and for the fxn of insulin
- can supplementation raise HDL

Absorption and Excretion

- 10-25% absorption in its trivalent form
- amount absorbed remains constant at dietary intakes >40 ug (micrograms) at which point excretion in urine is proportional to intake
- increased intake of simple sugar, strenuous exercise, or physical trauma also increase urinary excretion
- both chromium and Fe are carried by Tf, however albumin can also assume this role
Food Sources

- cereals, meats, poultry, fish, beer

Deficiency

- altered CHO metabolism, impaired glucose tolerance, glycosuria, fasting hyperglycemia, increased insulin levels and decreased insulin binding
- impaired growth, peripheral neuropathy, negative nitrogen balance
- increased chromium losses in stress
- hyperglycemia and wt loss reverse with IV supplementation in TPN
Toxicity

- chronic renal failure

Cobalt
Cobalt

- most stored with vitamin B12
- component of B12—cobalamin
- essential for maturation of RBC’s and normal function of all cells

Absorption and Excretion

- shared with Fe
- absorption is increased in pts with deficient Fe intake, portal cirrhosis with Fe overload, and hemochromatosis
- excretion is mainly thru the urine
- small amts in feces, hair, sweat
Sources and Intakes
- microorganisms are able to synthesize B12
- ***humans must obtain B12 and cobalt from animal foods such as organ and muscle meat
- ***takes a long time to become deficient—happens in vegetarians

Deficiency
- related to vit B12 deficiency
- **macrocytic anemia
- genetic defect: pernicious anemia
- tx: massive doses
- discussed in the vitamin lecture
Toxicity

- polycythemia
- hyperplasia of BM
- reticulocytosis
- increased blood volume

Selenium
Selenium

- glutathione peroxidase
- acts with other antioxidants and free radical scavengers
- overlaps with vit E for antioxidant effects
- fxn with vit E to protect cell and organelle membranes from oxidative damage

Selenium – Biochemical Functions

- Serves as a catalytic component in enzymes and proteins
- Iodothyronine 5’- deiodinase
- Thioredoxin reductase
- Glutathione peroxidase (destroys hydrogen peroxide)
Selenium – Metabolism

- Selenium is stored in the body as selenocysteine in selenoproteins
- Excreted in urine and in breath as dimethyl selenide with a garlic-like odor

Relationship of glutathione peroxidase, selenium, and vitamin E

![Diagram showing the relationship between glutathione peroxidase, selenium, and vitamin E]

GSH peroxidase contains selenocysteine

Figure 33.7 The relationship between glutathione peroxidase, selenium and vitamin E
Absorption and Excretion

- upper segment of the small intestine
- increased absorption with deficiency
- status is measured by measuring selenium or glutathione peroxidase in plasma, platelets, and RBC’s or selenium levels in whole blood or urine
- RBC selenium is an indicator of long-term status

Food Sources

- Food content tends to follow Se content of soil – richest food sources are organ meats and sea foods, followed by cereals and grains, dairy products, fruits and vegetables
- Se content of grains can vary by 10,000 fold
  - Requirements determined based on serum glutathione peroxidase activity
Selenium Deficiency Diseases

- Major problem in livestock
- Human deficiency is rare except in areas with low Se content in soil
  - Keshan disease occurs in Keshan China: endemic cardiomyopathy and muscle weakness (due to oxidized lipids)
  - Aggressive supplementation has eliminated disease
- Iatrogenic deficiency
  - TPN without supplemental Se

### TABLE S-4 Tolerable Upper Intake Levels (UL) by Life Stage Group

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Vitamin C (mg/d)</th>
<th>α-Tocopherol (mg/d)</th>
<th>Selenium (mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 through 6 mo</td>
<td>ND</td>
<td>ND</td>
<td>45</td>
</tr>
<tr>
<td>7 through 12 mo</td>
<td>ND</td>
<td>ND</td>
<td>60</td>
</tr>
<tr>
<td>1 through 3 y</td>
<td>400</td>
<td>200</td>
<td>90</td>
</tr>
<tr>
<td>4 through 8 y</td>
<td>650</td>
<td>300</td>
<td>150</td>
</tr>
<tr>
<td>9 through 13 y</td>
<td>1,200</td>
<td>600</td>
<td>280</td>
</tr>
<tr>
<td>14 through 18 y</td>
<td>1,800</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>19 through 70 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
<tr>
<td>&gt;70 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-18 y</td>
<td>1,800</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>19 through 50 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
<tr>
<td>Lactation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-18 y</td>
<td>1,800</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>19 through 50 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
</tbody>
</table>

*The UL is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the risk of adverse effects increases. Unless specified otherwise, the UL represents total nutrient intake from food, water, and supplements.

*The UL for α-tocopherol applies to any form of supplemental α-tocopherol.

*ND. Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food and formula in order to prevent high levels of intake.
Selenium Toxicity

Range of dietary Se intake without toxicity is narrow

Acute selenium poisoning can result in cardiorespiratory collapse (gram amounts)

Chronic toxicity (selenosis) changes in nail structure and loss of hair (intakes ~6x UL)

Hair and nail brittleness

**Selenium and Cancer Prevention**

- Epidemiologic evidence indicates low intakes of Se are associated with higher risk of prostate cancer
- Prospective study of Se supplementation demonstrated 42% reduction in cancer incidence
- Small sample size and other confounding factors have diminished enthusiasm for the results of these studies
Molybendum

- relationship with copper and sulfate
- cofactor of many enzymes involved in the catabolism of sulfur AA, purines and pyridines
- Toxicity: gout-like syndrome, reproductive SE’s
- Deficiency: increased risk with co-existing copper deficiency, TPN
Silicon, Vanadium, Arsenic, Boron

- see handouts posted on the web
- will not be on the exam!!!