Iodine and Selenium

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Micronutrients
- Required by the human body in small amounts
- Body can’t produce them, obtained through the diet
- Do not provide energy, yet essential for life!
- 2 types:
  - Vitamins (‘vital’=life, ‘amine’=nitrogen-containing compound):
    - Fat-soluble; Water-soluble
  - Minerals

Vitamins

<table>
<thead>
<tr>
<th>Fat-soluble</th>
<th>Water-soluble</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Absorption and metabolism requires dietary fat intake</td>
<td></td>
</tr>
<tr>
<td>• Excess not easily excreted (toxicity possible)</td>
<td></td>
</tr>
<tr>
<td>• Stored in adipose tissue</td>
<td></td>
</tr>
<tr>
<td>• Dissolve easily in water</td>
<td></td>
</tr>
<tr>
<td>• Excess amounts are excreted</td>
<td></td>
</tr>
<tr>
<td>• Consistent daily intake is required</td>
<td></td>
</tr>
</tbody>
</table>

Minerals
- Inorganic
- 4% of the body’s weight
- 15 essential minerals (i.e. can’t be synthesized in the body)
- Food sources: Meat, fish, milk, cheese, green leafy vegetables, legumes
- Higher concentration and bioavailability in animal sources
- Retain their chemical identity – not destroyed by heat, air, acid, mixing

Functions
- Structure of body tissues - bones, teeth, nails, blood, nerves and muscles - Calcium
- Osmotic balance – Sodium (Na), Potassium (K)
- Nerve impulse – Calcium (Ca), Sodium (Na)
- Muscle contraction – Calcium, Sodium
- Oxygen transport - Iron
- Physical and mental development - Iron
- Maintain immune function - Zinc

Hidden Hunger
- "The chronic lack of vitamins and minerals that often has no visible warning signs so that people who suffer from it may not be aware of it"
- Can lead to mental impairment, poor health, productivity, or death
- 1 in 3 people in the world suffer from hidden hunger
- Women and children from the lower income groups in developing countries are most affected

www.micronutrient.org
Micronutrient Deficiencies

- **Iron**
  - 47% of preschool-age children (293 million); 42% of pregnant women (56 million); 25% of the total population (1.6 billion) are anemic

- **Vitamin A**
  - 1/3 of preschool-age children (190 million) are vitamin A deficient

- **Iodine**
  - Nearly 2 billion people have insufficient iodine intakes


**Iodine**

**HISTORY**

I am satisfied. I have seen the principal features of Swiss scenery — Mount Blanc and the goiter — and now for home.

*Mark Twain, 1880*
Sources of Iodine

- Concentration in food reflects the soil in which plants are grown or on which animals graze
- Plentiful in the ocean
- Needed in tiny amounts, but this amount is critical

Dietary Iodine

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Recommended Iodine Intake (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td></td>
</tr>
<tr>
<td>0-6 months</td>
<td>110*</td>
</tr>
<tr>
<td>7-12 months</td>
<td>130*</td>
</tr>
<tr>
<td>Children</td>
<td></td>
</tr>
<tr>
<td>1-8 years</td>
<td>90</td>
</tr>
<tr>
<td>Males &amp; Females</td>
<td></td>
</tr>
<tr>
<td>9-13 years</td>
<td>120</td>
</tr>
<tr>
<td>14+ years</td>
<td>150</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>220</td>
</tr>
<tr>
<td>Lactating women</td>
<td>290</td>
</tr>
</tbody>
</table>

Institute of Medicine

Functions of Iodine

- An essential part of thyroxin
- Thyroxin is a hormone produced in the thyroid gland
- Thyroxin stimulates basal metabolism, oxygen use and heat production
- Essential for function and development of the brain and nervous system

Hypothalamic Pituitary Thyroid Axis

- Use of iodophor sanitizing agents for udder washes, teat dips, and cleaning milking equipment (not mandatory)
**HYPOTHYROIDISM**  
Cold intolerance  
Bradycardia (slow pulse)  
Constipation  
Fatigue  
Weight gain

**HYPERTHYROIDISM**  
Heat intolerance  
Tachycardia (fast pulse)  
Increased defecation  
Anxiety, Tension  
Weight loss

**Thyroid Function**

**Iodine Intake and Thyroid Function**

**Iodine Deficiency**
- Median Urinary Iodine (<100 µg/L)
  - Iodine excreted primarily through urine
  - Indicator of iodine intake, not thyroid function

<table>
<thead>
<tr>
<th>Median Urinary Iodine (µg/L)</th>
<th>Iodine Intake</th>
<th>Iodine Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>Insufficient</td>
<td>Severe iodine deficiency</td>
</tr>
<tr>
<td>10-49</td>
<td>Insufficient</td>
<td>Moderate iodine deficiency</td>
</tr>
<tr>
<td>50-99</td>
<td>Insufficient</td>
<td>Mild iodine deficiency</td>
</tr>
<tr>
<td>100-299</td>
<td>Adequate</td>
<td>Iodine sufficiency</td>
</tr>
<tr>
<td>&gt; 300</td>
<td>Excessive</td>
<td>Marked iodine excess</td>
</tr>
</tbody>
</table>

**Fetal Effects**
- Maternal iodine deficiency
  - Decreased placental transfer of thyroxine
  - Impaired brain development
    - (cretinism, poor motor/cognitive performance)
Iodine and Evolution

The Geographical Review

Iodine Deficiency

**Physiological Groups**

<table>
<thead>
<tr>
<th>Iodine Deficiency</th>
<th>Health Consequences of Iodine Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allages</td>
<td>Cold</td>
</tr>
<tr>
<td></td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td></td>
<td>Increased susceptibility to nuclear radiation</td>
</tr>
<tr>
<td>Preterm</td>
<td>Spontaneous abortion</td>
</tr>
<tr>
<td></td>
<td>Jaundice</td>
</tr>
<tr>
<td></td>
<td>Congenital anomalies</td>
</tr>
<tr>
<td></td>
<td>Prematurity</td>
</tr>
<tr>
<td>Neonates</td>
<td>Encephalopathy, including mental deficiency with a mixture of mutism, spinal diplegia, retinitis pigmentosa, and short stature</td>
</tr>
<tr>
<td></td>
<td>Infant mortality</td>
</tr>
<tr>
<td>Child and adolescent</td>
<td>Impaired mental function</td>
</tr>
<tr>
<td></td>
<td>Delayed physical development</td>
</tr>
<tr>
<td></td>
<td>Iodine-induced hyperthyroidism (ISM)</td>
</tr>
<tr>
<td>Adults</td>
<td>Impaired mental function</td>
</tr>
<tr>
<td></td>
<td>Iodine-induced hyperthyroidism (ISM)</td>
</tr>
</tbody>
</table>

Vulnerable Groups

- Nearly 2 billion people worldwide have insufficient iodine intake
- Single greatest preventable cause of mental retardation
- Serious consequences of deficiency:
  - People have impaired mental function, less vigorous, harder to educate & motivate
  - Mild maternal deficiency can ↓ child's IQ by 10-15 points
  - Implications on economic productivity

Global Burden

Pregnancy and Lactation

- Iodine Supplementation for Pregnancy and Lactation: Recommendations of the American Thyroid Association
  - "... the American Thyroid Association recommends that women receive 150 µg iodoine supplements daily during pregnancy and lactation and that all prenatal vitamin/mineral preparations contain 150 µg of iodine"
Interventions

- Fortification of salt:
  - Universal Salt Iodization
- Iodized oil capsules for pregnant women in areas with a high prevalence of iodine deficiency & access to iodized salt is limited

Why Fortification?

- Salt is consumed by everyone and generally stable throughout the year
- Safe and inexpensive
- Accessible fortification technology
- Limited number of producers
- Sensory/cooking properties
- Ease of program implementation

Change (1995-2008)

Source: UNICEF Global Database, Nov 2009

SELENIUM

History

- Discovered in 1817 by Jons Jacob Berzelius
- Schwarz and Foltz in 1957
  - Dietary Se prevents liver necrosis in rats
- 1960s-70s
  - Identified as a critical component of a number of enzymes
Sources of Selenium

- Plants take up selenium from the soil & incorporate into selenomethionine (Se is incorporated in place of S during methionine biosynthesis, dependent on Se/S ratio in soil)

\[ \text{Methionine} \rightarrow \text{selenomethionine} \]

- Selenomethionine is incorporated non-specifically in plant proteins in place of methionine

Selenomethionine

\[ \text{C}_5\text{H}_{11}\text{NO}_2\text{Se} \]

Functions of Se

- Selenoproteins contain Selenocysteine (Sec) and mediate Se function
- Knocking out the Sec gene is lethal to the fetus
- 25 Selenoproteins have been identified

Glutathione Peroxidases

- GPx 1-4, 6
- Destroys Hydrogen Peroxide
  - \( \text{H}_2\text{O}_2 \) generates free radicals, which can damage DNA, lipids, and proteins
  - GPx 4 is a structural protein necessary for the integrity of the sperm midpiece
  - Se deficiency can lead to male infertility


Iodothyronine Deiodinases

- Family of 3 selenoenzymes
- Needed for the peripheral conversion of thyroid hormone to its active form

Thioredoxin Reductases

- Provide reducing equivalents for ribonucleotide reductase
- Needed for DNA synthesis
- Over-expressed in many cancers

Selenoprotein P

- Probably protects the cardiovascular system against oxidant damage
- Very efficient at binding heavy metals

Selenium Status

- Hair
- Toenails
- Plasma levels (99% US adults have Se levels < 95 ng/ml)
- Glutathione peroxidase activity

Selenium in the US
Regions of SE Deficiency

- China
- New Zealand
- Central Africa
- Finland
- Western Europe
- Northwestern US

Se Deficiency

- Kashin-Beck Disease
  - Degenerative Osteoarticular disorder - still occurs in parts of China, Korea, and Siberia
  - Se supplementation does not eliminate this disease - likely due to concomitant iodine deficiency
- Keshan Disease
  - Endemic cardiomyopathy - largely been eliminated
- Total Parenteral Nutrition
  - General muscle wasting, flaky skin, problems walking

Se Deficiency

- Epidemiological studies show that Se may be linked to:
  - Cancer
  - Bronchopulmonary disease and Sudden Infant Death Syndrome in Premature Infants
  - Impaired immunity - reduced T-cell counts and impaired lymphocyte activity
  - HIV disease progression
- Thyroid Disease
  - Se deficiency can lead to Goiter
  - Combined Se and I deficiency - Myxedematous Cretinism

Se and Coxsackie Virus

- Coxsackie virus in selenium deficient mice mutates from an avirulent to virulent strain because of a 6 bp change in its genome.
- Se deficiency - Low GPx - More oxidative damage from free radicals
- Similar phenomena occurs with influenza in Se-deficient mice

Se and Cancer

- Observational Studies
  - Death from Lung, Colorectal, and Prostate Cancers lower among people with higher blood levels or intake of Se
- SUVIMAX in France
  - Supplement (vitamins A and C, beta-carotene, zinc, and Se) lowered risk of Prostate CA by half in those who had normal PSA at baseline
- SELECT (Se and Vitamin E Cancer Prevention Trial) in the US
  - Se and/or vitamin E did not prevent prostate cancer
Se and HIV

- Associated with increased risk of disease progression and death
- Trial in Tanzania among HIV-infected women

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean Placebo</th>
<th>Mean Change Selenium Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count (cells/mm³)</td>
<td>486±178</td>
<td>1 (22, 19)</td>
<td>0.72</td>
</tr>
<tr>
<td>CD3 cell count (cells/mm³)</td>
<td>1635±520</td>
<td>10 (38, 58)</td>
<td>0.86</td>
</tr>
<tr>
<td>CD8 cell count (cells/mm³)</td>
<td>1048±439</td>
<td>12 (21, 44)</td>
<td>0.91</td>
</tr>
<tr>
<td>Viral load (log)</td>
<td>4.12±1.03</td>
<td>0.02 (0.11, 0.06)</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Source: Kupka, AJCN 2008;87:1802

Se Toxicity

- Dr. Gregory House: You idiot.
- Dr. Samira Terzi: Who are you calling an idiot?
- Dr. Gregory House: Whoever knew that John was stationed in Brazil, not Bolivia.
- Dr. Samira Terzi: Brazil?
- Dr. Gregory House: [House turns and faces Agent Smith] Well, then, I guess, I'm talking to you, idiot.
- CIA Agent Smith: It's the same region. It's the same parasite, same diseases.
- Dr. Gregory House: But not the same language. In Bolivia, chestnuts are chestnuts. Brazil, on the other hand, has Castanhas-do-Pará, literally, "Chestnuts from Pará." Because it would be stupid for people from Brazil to call them Brazil Nuts.
- CIA Agent Smith: So he ate Brazil Nuts. Big deal.
- Dr. Gregory House: No, he ate a lot of Brazil Nuts, which is a big deal, because they contain selenium. Which, in high doses, causes fatigue, vomiting, skin irritation, discharge from the fingernail beds, and hair loss. Any of this sound familiar?

http://www.imdb.com/title/tt1123416/quotes

Selenosis

- Se toxicity
- GI upsets, hair loss, white blotchy nails, garlic breath odor, fatigue, irritability, and mild nerve damage


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