Effect of over supplementation of vitamins and nutrients

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Lecture Outline

• Interactions of vitamins and pharmaceutical drugs
• Hypervitaminosis → example with Vitamin D
• Over Supplementation
  • B-vitamins
  • Vitamin E
  • Choline
• Canada Food Guide
• Omega 3 and 6 recommendations
• Intermittent fasting
• Future Learning Resources
  • Nutrition
  • Neuroscience
Interactions of vitamins and pharmaceutical drugs

https://www.youtube.com/watch?v=qovaZNiOsfsM
Micronutrients: Vitamins

Can be categorized as:

1) FAT SOLUBLE
2) WATER SOLUBLE
Fat Soluble

- Vitamins A, D, E and K
- Soluble in fats
- Stores in body tissues
- They are absorbed by fat globules and moved into circulation (intestine)

- BOTTOM LINE: vitamin stays in your body
Water Soluble

Vitamins B and C
- Require continuous supply to your body
- Steady daily intake required
- Take too much, then your body removes it (e.g. pee it out)
Upper Limit (UL)

• Fat-soluble vitamin has a tolerable upper intake level, or UL, which
  • the maximum amount you can take in each day with no adverse health effects.
• intake above the UL, the higher your risk of developing a toxicity
• The ULs for
  Vitamins A: 3000ug
  Vitamin D: 4000 IU (Health Canada reference)
  Vitamin E: 40 IU (Health Canada reference)
  Vitamin K: not determined (Health Canada Reference)
Health Canada Recommendations

Dietary Reference Intakes

Table 1 - Reference Values for Vitamins

<table>
<thead>
<tr>
<th></th>
<th>Vitamin A</th>
<th></th>
<th>Vitamin D</th>
<th></th>
<th>Vitamin E</th>
<th></th>
<th>Vitamin K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit</td>
<td>µg/day (RAE)</td>
<td>IU/day (RAE)</td>
<td>µg/day</td>
<td>IU/day</td>
<td>mg/day</td>
<td>µg/day</td>
<td></td>
</tr>
<tr>
<td>EAR</td>
<td>RDA/AI</td>
<td>UL</td>
<td>EAR</td>
<td>RDA/AI</td>
<td>UL</td>
<td>EAR</td>
<td>RDA/AI</td>
</tr>
<tr>
<td>Infants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 mo</td>
<td>ND</td>
<td>400*</td>
<td>600</td>
<td>ND</td>
<td>1333*</td>
<td>2000</td>
<td>ND</td>
</tr>
<tr>
<td>7-</td>
<td>ND</td>
<td>500*</td>
<td>600</td>
<td>ND</td>
<td>1667*</td>
<td>2000</td>
<td>ND</td>
</tr>
</tbody>
</table>

Hypervitaminosis

- refers to a condition of abnormally high storage levels of vitamins, which can lead to toxic symptoms
Symptoms of Hypervitaminosis

- Cloudy urine
- Frequent urination
- Increased urine amount
- Dryness, cracking lips (due to chronic overdose)
- Eye irritation
- Increased sensitivity of the eyes to light
- Irregular heartbeat
- Rapid heartbeat
- Bone pain
- Joint pain
- Muscle pain
- Muscle weakness
- Confusion, mood changes
- Convulsions (seizures)
- Fainting
- Fatigue
- Headache
- Mental changes
- Irritability
- Flushing (reddened skin) from niacin (vitamin B3)
- Dry, cracking skin
- Itching, burning skin, or rash
- Yellow-orange areas of skin
- Sensitivity to sun (more likely to sunburn)
- Hair loss (from long-term overdose)
- Intestinal bleeding (from iron)
- Appetite loss
- Constipation (from iron or calcium)
- Diarrhea, possibly bloody
- Nausea and vomiting
Example: Hypervitaminosis D

• Vitamin D toxicity is usually caused by megadoses of vitamin D supplements — not by diet or sun exposure.

• Body regulates the amount of vitamin D produced by sun exposure, and even fortified foods don't contain large amounts of vitamin D.
Hypervitaminosis D: Cause

• Taking 60,000 international units (IU) a day of vitamin D for several months has been shown to cause toxicity.
• Recommended Dietary Allowance (RDA) for most adults of 600 IU and 800 (> 70 years old) of vitamin D a day
Hypervitaminosis D: Cause

• Higher doses than the RDA are sometimes used to treat medical problems such as vitamin D deficiency
  • given only under the care of a doctor for a specified time frame
  • blood levels should be monitored while someone is taking high doses of vitamin D.
Hypervitaminosis D: Symptoms

- buildup of calcium in your blood (hypercalcemia)
- causes nausea and vomiting, weakness, and frequent urination
- symptoms might progress to bone pain and kidney problems
  - formation of calcium stones
Hypervitaminosis D: Treatment

• stopping vitamin D intake
• restricting dietary calcium
• doctor might also prescribe intravenous fluids and medications, such as corticosteroids or bisphosphonates
VIDEO: 10 surprising dangers of vitamins and supplements

Supplements of Vitamins and Nutrients

• Individual differences (e.g. diseases)

• Environment (e.g. North America)

• Government regulation
B-vitamin over supplementation
Fortification in Canada

Since 1998 the Government of Canada has required that folic acid be added to all white flour and enriched pasta and cornmeal products sold in Canada.

Health Canada, 2008
## Fortification

Table 1. Levels of folic acid fortification in countries with mandatory fortification programs.

<table>
<thead>
<tr>
<th>Country</th>
<th>Fortification level</th>
<th>Date of implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States [25]</td>
<td>140 μg/100 g</td>
<td>1998</td>
</tr>
<tr>
<td>Canada [33]</td>
<td>150 μg/100 g</td>
<td>1998</td>
</tr>
<tr>
<td>Costa Rica [34]</td>
<td>180 μg/100 g</td>
<td>1998</td>
</tr>
<tr>
<td>Chile [35]</td>
<td>220 μg/100 g</td>
<td>2000</td>
</tr>
<tr>
<td>South Africa [36]</td>
<td>150 μg/100 g</td>
<td>2003</td>
</tr>
</tbody>
</table>

Crider et al., 2011
Grain Fortification Legislation

84 countries require fortification of wheat flour, maize flour, and/or rice

August 2015. Source: Food Fortification Initiative.
To request data, e-mail info@ffinetwork.org
Fortification in Canada Results

A 7-province study showed a reduction of 46% in the overall rate of neural tube defects (NTDs), including live births, stillbirths and cases detected prenatally in pregnancies that were subsequently terminated.

Health Canada, 2008
Over supplementation of folic acid

• mandatory fortification has lead to increase in folate levels in general population
• longer term effects of high folate levels not known
• ~ 8-10 studies in pregnant Canadian women reporting increased levels of folic acid and metabolized folic acid
• effects of maternal folic acid supplementation on offspring health unknown
Over supplementation of folic acid

• Maternal folate supplementation in rats, results in small fetuses and poor protein utilization in late gestation (Achon et al., 1999)
High Dietary Folate Supplementation Affects Gestational Development and Dietary Protein Utilization in Rats, Achon et al., 1999

**TABLE 2**

<table>
<thead>
<tr>
<th>Dams</th>
<th>n</th>
<th>Live Fetuses/Litter</th>
<th>Fetal Body Weight</th>
<th>Fetal Vertex-coccyx Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplemented</td>
<td>11</td>
<td>$11.4 \pm 1.16$</td>
<td>$3.15 \pm 0.10^{**}$</td>
<td>$3.5 \pm 0.05^{**}$</td>
</tr>
<tr>
<td>Control</td>
<td>9</td>
<td>$11.6 \pm 0.74$</td>
<td>$3.49 \pm 0.22$</td>
<td>$3.7 \pm 0.09$</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM. **Significantly different from control group, $P < 0.001$. 

25
Maternal Over supplementation of Folic Acid

Folic Acid: 2 mg/kg 40 mg/kg

10.5 embryos

Pickell et al., 2010
Maternal Over supplementation of Folic Acid: Memory

Bahous et al., 2017
Maternal Over supplementation of Folic Acid: Acetylcholine

Bahous et al., 2017
Questions?
Break!
B-vitamin supplementation in the elderly
Neurodegeneration Progression

**Mild Cognitive Impairment**
- Duration: 7 years
- Disease begins in Medial Temporal Lobe
- Symptoms: Short-term memory loss

**Mild Alzheimer's**
- Duration: 2 years
- Disease spreads to Lateral Temporal & Parietal Lobes
- Symptoms include: Reading problems, Poor object recognition, Poor direction sense

**Moderate Alzheimer's**
- Duration: 2 years
- Disease spreads to Frontal Lobe
- Symptoms include: Poor judgment, Impulsivity, Short attention

**Severe Alzheimer's**
- Duration: 3 years
- Disease spreads to Occipital Lobe
- Symptoms include: Visual problems
Folate supplementation in Elderly

Study Background
- 2004-06
- Patients with Mild Cognitive Impairment (MCI) & controls
- Treatment, 2 years; Folic Acid and Vitamin B12

Smith et al., 2010
Folate supplementation in Elderly

Smith et al., 2010
Folate supplementation in Elderly

Placebo

Treated

Smith et al., 2010
Effect of B-vitamin supplementation on grey matter volume in patients with Mild Cognitive Impairment

Objective: investigate whether Alzheimer's disease related gray matter atrophy can be reduced via B-vitamin supplementation

-Patients: Mild Cognitive Impairment
-2 Years of B-vitamin supplementation
-MRI
Results

B-vitamin supplementation for 2 years reduces brain shrinkages by 7-fold
Results

Treated individuals with the highest levels of homocysteine benefited most from B-vitamin supplementation
Grain Fortification Legislation

84 countries require fortification of wheat flour, maize flour, and/or rice

August 2015. Source: Food Fortification Initiative.
To request data, e-mail info@ffinetwork.org
Too much folate

• Exacerbate neurological consequence of vitamin B12 deficiency

• Methyl trap
  • Vitamin B12 deficiency, disguised as folate deficiency

• Safe upper limit of 1.0mg/day
Folate and Cancer

• Plays 2 roles in cancer: protecting against cancer initiation and facilitating progression
• > (greater than) 0.004mg/day, 20% increase in breast cancer
• High blood folate concentrations, increase risk of prostate cancer in males 59 and older
Other examples of over supplementation
Choline over supplementation

• Side effects
• dizziness
• lightheadedness
• high doses of choline can lower your blood pressure.
• excessive sweating and salivation, fishy body odor caused by byproducts of choline metabolism in your body
• Long-term effects unknown
Vitamin E over supplementation

- can increase risk of bleeding
- long-term, this may increase risk of bleeding in the brain and stroke
- can be particularly harmful to people on blood thinners and other medications.
Vitamin over supplementation video


Article referenced in video:
https://jamanetwork.com/journals/jama/article-abstract/2672264
New
Canada’s food guide recommendations

Make water your drink of choice

Eat protein foods

Have plenty of vegetables and fruits

Choose whole grain foods

Older

Source: Health Canada
Definitions of Recommendations

- **Recommended Dietary Allowance (RDA)**
  - average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals
  - often used to plan nutritionally adequate diets for individuals

- **Adequate Intake (AI)**
  - Intake at this level is assumed to ensure nutritional adequacy
  - established when evidence is insufficient to develop an RDA
Definitions of Recommendations

• **Estimated Average Requirement (EAR)**
  • average daily level of intake estimated to meet the requirements of 50% of healthy individuals
  • used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them
  • can also be used to assess the nutrient intakes of individuals
Recommendations for Omega-3 & 6

Table 1: Adequate Intakes (AIs) for Omega-3s [5]

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 months*</td>
<td>0.5 g</td>
<td>0.5 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7–12 months*</td>
<td>0.5 g</td>
<td>0.5 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 years**</td>
<td>0.7 g</td>
<td>0.7 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years**</td>
<td>0.9 g</td>
<td>0.9 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years**</td>
<td>1.2 g</td>
<td>1.0 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years**</td>
<td>1.6 g</td>
<td>1.1 g</td>
<td>1.4 g</td>
<td>1.3 g</td>
</tr>
<tr>
<td>19–50 years**</td>
<td>1.6 g</td>
<td>1.1 g</td>
<td>1.4 g</td>
<td>1.3 g</td>
</tr>
<tr>
<td>51+ years**</td>
<td>1.6 g</td>
<td>1.1 g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*As total omega-3s
**As ALA

https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/#h2
Intermittent Fasting (IF)

Information from
https://neurotrition.ca/blog/intermittent-fasting-better-brain-health
Intermittent Fasting (IF)

What is it?

• eating pattern that involves short periods of fasting
• it does not recommend what to eat, but more so when to eat
Intermittent Fasting (IF)

Hard to do?

• Many people actually find IF easy to follow
• Eating fewer meals in a shorter time frame can simplify their life
• If you have blood sugar issues don’t want any hypoglycemia (i.e. low blood sugar) or subsequent
Intermittent Fasting (IF) & Brain

1.) Intermittent fasting for more brain proteins
   • increasing brain-derived neurotrophic factor (BDNF)
   • BDNF grows new neurons (nerve/brain cells), allows them to talk to one another, and is a natural antidepressant
   • animal studies, BDNF also helps neurons stay healthier longer and helps them resist common brain diseases (like dementia) and injury (from strokes)
   • maintains proper neuron structure and function.
Intermittent Fasting (IF) & Brain

2.) Intermittent fasting actually helps to grow new nerve cells
   • brains grow new nerve cells when intermittently fasting
   • help with brain aging, brain damage from strokes, and epilepsy
Intermittent Fasting (IF) & Brain

3.) Intermittent fasting for better brain aging
• Intermittent fasting seems to keep our brains staying younger
• may even protect against neurodegeneration
• small study, showed that IF improved cognitive ability (ability to think) in people with cognitive impairment. Ten people with early signs of Alzheimer’s started several lifestyle improvements including a 12-hour fast each night. Within 3-6 months, nine of the ten patients had improved cognition
• preclinical animal studies also show that IF may delay the onset, or reduce severity of Alzheimer’s, Parkinson’s, and Huntington’s diseases
Intermittent Fasting (IF) & Brain

4.) Intermittent fasting to protect against brain damage from strokes

• Studies show that animals who get strokes have less brain damage if they’ve been intermittently fasting
  • more BDNF along with antioxidant and anti-inflammatory brain compounds.

• fewer of them died because of the stroke
Intermittent Fasting (IF) & Brain

5.) Intermittent fasting for epilepsy
• studies show that when a brain uses less of its main fuel, carbohydrates
• as it does in the fasting state (and the ketogenic diet)
• the number of epileptic seizures reduces
Intermittent Fasting (IF) & Brain

• most studies conducted in rodents or really small samples with humans
• blood sugar is stable, might be worthwhile to try
Future learning: Nutrition & Neuroscience
More information on vitamin toxicity

Gale Encyclopedia of Medicine, 3rd ed.
https://www.encyclopedia.com/medicine/diseases-and-conditions/pathology/vitamin-toxicity
Future learning: Nutrition

• The Institute of Holistic Nutrition: Ottawa campus
  • http://www.instituteofholisticnutrition.com

• Neurotrition
  • https://neurotrition.ca/

Text Books Available on Amazon:

Whole: Rethinking the Science of Nutrition
by T. Colin Campbell, Howard Jacobson

The China Study: The Most Comprehensive Study of Nutrition Ever Conducted and the Startling Implications for Diet, Weight Loss and Long-term Health
by T. Colin Campbell

Introduction to Human Nutrition 2nd Edition
by Michael J. Gibney, Susan A. Lanham-New, Aedin Cassidy, Hester H. Vorster
Future Learning: Neuroscience

YouTube Channel: Neuro Transmissions
https://www.youtube.com/user/neurotransmissions

Alzheimer's disease blog (for non-scientists)
https://alzscience.wordpress.com/

List of Neuroscience Blogs:
http://www.prymd.com/blog/the-best-brain-blogs-neuroscience-for-the-non-scientific/
More questions?

E-mail me at nafisa.jadavji@carleton.ca

Please fill out course evaluations!