Discussion of Research Recommendations: Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline

Dietary Reference Intake Research Synthesis Workshop

DRI Report on B Vitamins and Choline

Issues

- New knowledge
- Common genetic variations influence DRIs
- Metabolomics and DRIs

<table>
<thead>
<tr>
<th>Steven Zeisel</th>
<th>Patrick Stover</th>
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<tbody>
<tr>
<td>Choline</td>
<td>Folate</td>
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<tr>
<td>Thiamin</td>
<td>B12</td>
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<tr>
<td>Riboflavin</td>
<td>B6</td>
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<tr>
<td>Niacin</td>
<td>Biotin</td>
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<td>Pantothenic acid</td>
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Thiamin

- Major gaps – Requirements of children, pregnant and lactating women and elderly; indicators on which to base Thiamin requirement.
- Gaps – adverse effects of high dose thiamin

No substantial progress since 1998 (PubMed and Roger Butterworth).

Riboflavin

- Major Gaps – requirements in children, pregnancy and lactation, elderly.
- Gaps – functional test to augment FAD dependent glutathione reductase, effects of physical activity.

Progress since 1998 (PubMed)
Public Health Nutr. 4:1069-79, 2001 Ireland, mean daily intake of riboflavin was below the EAR in 12.5% and 20.6% of men and women, respectively.
J.B.C. 275:1471-1478, 2000. Some flavoenzymes contain both FAD and FMN
Arch Opthamol. 123:517-26, 2005 Riboflavin Rx prevents cataracts.

Niacin

- Major Gaps – Increased niacin needs secondary to oxidant damage, blood niacin method rather than urinary method currently used.
- Gaps – requirements of children, pregnancy and lactation, enhanced nutrient databases that separate food content from fortification.

Some progress since 1998 (PubMed and Joel Moss (NIH)).
Public Health Nutr. 4:1069-79, 2001 Ireland, 20.8% of men and 6.3% of women exceeded the UL for pre-formed niacin.
JAMA 2000; 284: 1263–70. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease. The ADMIT study: a randomized trial.
Pantothenic acid

- Major gaps – human requirements esp. children, toxicity, bioavailability from foods, food composition databases.


Choline

- Major gaps – role in chronic disease, refine estimates of human requirements (and infant-child requirements, pregnancy lactation), bioavailability, toxicity, metabolic effects, need for functional biomarkers, interrelationships with B12, B6, methionine and folate metabolism

- Gaps – effects of chronic high intake, food composition tables

Choline

*New human data
Estrogen induces endogenous synthesis
80% men, postmen women require choline
44% premen women require it
**Choline**

**BASELINE**
Day 1 – 10 (10 days)
500 mg choline per 70 kg bwt. daily

**DEPLETION**
Day 11 – 52 (42 days)
< 50 mg choline per 70 kg bwt. daily

**REPLETION**
Day 53 – 92 (40 days)
100% choline
550 mg/70 kg
75%
50%
25%
100% choline
550 mg/70 kg

The baseline diet also contains 400 mg folate, while the Depletion and Repletion diets have 100 µg folate. On Day 11, subjects are randomized to 100 µg folate (placebo) or 400 µg (folic acid) for the remainder of the study.

**Choline**

Liver damage

<table>
<thead>
<tr>
<th>Mean ALT (U/L)</th>
<th>Normal Diet</th>
<th>Depletion</th>
<th>Repletion</th>
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<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>75</td>
<td>50</td>
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<td>25</td>
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<td>50</td>
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Muscle damage

<table>
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<th>Mean CPK Level (U/L)</th>
<th>Normal Diet</th>
<th>Depletion</th>
<th>Repletion</th>
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<tbody>
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<td>50</td>
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*Liver damage*
Choline

Diet plus endogenous synthesis

**Phosphatidylethanolamine** — *N*-methyltransferase (PEMT)

Estrogen induces PEMT gene

- S-adenosylmethionine
- *phosphatidylcholine* PtdEthanolamine
- *phosphatidylcholine* PtdEthanolamine

**Choline**

- New human data
- Estrogen induces endogenous synthesis
  - 80% men, postmen women require choline
  - 44% premen women require it

SNP in PEMT promoter makes women susceptible to choline deficiency
- Women with PEMT -774G>C OR=25
- 18% were CC, 56% GC, and 26% GG (FASEB J, in press)
**Choline**

- **New human data**
  - Estrogen induces endogenous synthesis
  - 80% men, postmen women require choline
  - 44% premen women require it
  - SNP in PEMT promoter makes women susceptible to choline deficiency
  - Women with PEMT -774G>C OR=25
    - 16% were GG, 36% GC, and 48% CC (FASER J, in press)
  - Premen Women with MTHFD1 1958G>A OR=85
    - 11% were AA, 52% GA, and 37% GG (PNAS 102:16025-30, 2006)

- **Choline-betaine inversely relate to plasma homocysteine in humans**

  - Food composition data now available
Choline – Summary of progress

- Major gaps – role in chronic disease, refine estimates of human requirements (and infant-child requirements, pregnancy lactation), bioavailability, toxicity, metabolic effects, need for functional biomarkers, interrelationships with B12, B6, methionine and folate metabolism
- Gaps – effects of chronic high intake, food composition tables