How much calcium and vitamin D do children need?

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Disclosures
• Conflicts: I am a member of the Scientific Advisory Board for MilkPep, The Milk Processor Educational Program
• There are no discussion of off-label products
• I don’t have any idea what my 25-OHD level is and I don’t take a vitamin D or calcium supplement

Learning Objectives
By the end of the presentations, the audience will:
1. Understand the basis for establishing dietary guidelines for calcium and vitamin D.
2. Recognize limitations in markers of vitamin D status
3. Appreciate needs for future research related to bone minerals in children.

Bones through the lifespan: Osteoporosis as a pediatric disease

Peak Timing of Skeletal Calcification

Weaver et al. Osteoporos Int 2016

Age related changes in calcium absorption

Bronner and Abrams; J Nutr 1998;128:1474-80
Calcium intake

- Evidence supports average need for 800-1200 mg/day after early childhood
- Intakes of 1200-1400 mg/day provide a safety margin, most important during limited time period of peak adolescent growth
- Some young adult catch-up is possible, may be more difficult with intakes <600-800 mg/d
- Intakes in US are low, but probably not a "crisis" level for most children due to adaptation to low intakes

2015 Dietary Guidelines for Americans Advisory Committee Report (DGAC)

- Recommendations for dairy products in the American diet have been largely driven by contribution of calcium
- Dairy products also provide other key nutrients:  
  - Protein, potassium, magnesium, phosphorus, zinc, selenium, vitamin A, riboflavin, thiamine, vitamin B12, and vitamin D (when fortified)
- Dairy Group: Fluid milks, soy milk, cheese, yogurt, milk-based meal replacements, ice cream  
  - Almond milk and rice milk are not included

Calcium Bioavailability

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving Size</th>
<th>Calcium Content</th>
<th>Fractional Absorption</th>
<th>Servings needed to equal 1 cup milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>240 g</td>
<td>300 mg</td>
<td>32%</td>
<td>1</td>
</tr>
<tr>
<td>Yogurt</td>
<td>240 g</td>
<td>300 mg</td>
<td>32%</td>
<td>1</td>
</tr>
<tr>
<td>Cheddar cheese</td>
<td>42 g</td>
<td>303 mg</td>
<td>32%</td>
<td>1</td>
</tr>
<tr>
<td>Tofu</td>
<td>126 g</td>
<td>258 mg</td>
<td>31%</td>
<td>1.2</td>
</tr>
<tr>
<td>Kale</td>
<td>85 g</td>
<td>61 mg</td>
<td>49%</td>
<td>3.2</td>
</tr>
<tr>
<td>Broccoli</td>
<td>71 g</td>
<td>35 mg</td>
<td>61%</td>
<td>4.5</td>
</tr>
<tr>
<td>Pinto beans</td>
<td>86 g</td>
<td>45 mg</td>
<td>27%</td>
<td>8.1</td>
</tr>
<tr>
<td>Spinach</td>
<td>85 g</td>
<td>115 mg</td>
<td>5%</td>
<td>16.3</td>
</tr>
</tbody>
</table>

Other Calcium Sources

- Insect Protein (g) Calcium (mg) Vitamin (mg)
  - Giant Water Beetle 19.8 43.5 13.6
  - Red Ant 13.9 47.8 5.7
  - Dung Beetle 17.2 30.9 7.7
  - Cricket 12.9 75.8 9.5
  - Grasshopper 20.8 35.2 5.0

Osteopenia of Prematurity/Rickets

| Px follows similar pattern, at about half the intake (mg:mg) and total amounts retained. In TPN usually target about 1:1 Ca:P on mmol/mmol basis. (Ca is 40 mg = 1 mmol and P is 31 mg = 1 mmol)
**Recommendations**

<table>
<thead>
<tr>
<th>Calcium (mg/kg/day)</th>
<th>Phosphorus (mg/kg/day)</th>
<th>Vitamin D (IU/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrams SA and Committee on Nutrition, AAP, Pediatrics 2013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koletzko et al (2014)</td>
<td>120-200</td>
<td>60-140</td>
</tr>
<tr>
<td>Tsang et al (2005)</td>
<td>100-220</td>
<td>60-140</td>
</tr>
<tr>
<td>Klein (2002)</td>
<td>150-220</td>
<td>100-130</td>
</tr>
<tr>
<td>Agostoni (2010)</td>
<td>120-140</td>
<td>65-90</td>
</tr>
<tr>
<td>AAP Clinical Report (2013)</td>
<td>150-220</td>
<td>75-140</td>
</tr>
</tbody>
</table>

a Text says “from milk + supplement”
b Text says “aim to deliver 400 IU/day”
c 90-125 IU/kg (total amount is shown for 1.5 kg infant)

*Abrams SA and Committee on Nutrition, AAP, Pediatrics 2013
Koletzko et al, Nutritional Care of Preterm Infants, 2014*

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**Details of AAP Recommendations for Preterm Infants**

- When infants reach a body weight >1500 g and tolerate full enteral feeds, vitamin D intake should generally be approximately 400 IU/day, up to a maximum of 1000 IU/day.
- Serum APA >800 to 1000 IU/L or clinical evidence of fractures should lead to a radiographic evaluation for rickets and management focusing on maximizing calcium and phosphorus intake and minimizing factors leading to bone mineral loss.
- A persistent serum P concentration < about 4.0 mg/dL should be followed, and consideration should be given for P supplementation.

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**Does Vitamin D Deficiency Cause Symptomatic Hypocalcemia?**

- Maternal vitamin D deficiency can cause symptomatic neonatal hypocalcemia
  - Probably rare in US but limited data
  - Recent case series of 19 babies in Qatar*
  - Symptomatic hypocalcemia (13 seizures, 5 jittery, 3 stridor), mean age about 9 days
  - Serum 25-OHD mean of 9 ng/mL (range 3 to 18 ng/mL), in mothers was 6 ng/mL (range 4 to 12 ng/mL)

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**Vitamin D: Definitions of dietary requirements**

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**Vitamin D: IOM guidelines 2011**

<table>
<thead>
<tr>
<th>Age</th>
<th>Vitamin D (IU/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated average requirement</td>
</tr>
<tr>
<td>0-6 months</td>
<td>–</td>
</tr>
<tr>
<td>6-12 months</td>
<td>–</td>
</tr>
<tr>
<td>1-3 years</td>
<td>400</td>
</tr>
<tr>
<td>4-8 years</td>
<td>400</td>
</tr>
<tr>
<td>9-18 years</td>
<td>400</td>
</tr>
</tbody>
</table>

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**Vitamin D: A cure for rickets?**

- The strength of the product can be tested on animals whose rickets has been experimentally produced to show that it is potent.
- The cure of infantile rickets was achieved, a remarkable accomplishment by a young scientist.

*Sept 1931*
Can’t please everyone of course

Once more the chemists are trying to prove the usefulness of vitamins by asserting that they prevent rickets in rats. That does not sound like a very good argument. Who cares if rats have rickets? For that matter, would it not be better if all rats had rickets, or even fallen arches? Chemists ought to be forbidden by law to go around making rickets rats well.

The Spokesman Review - Aug 2, 1997

Values of 25(OH)D in children

- Remains very contentious issue.
- AAP, IOM and ESPGHAN target at least 20 ng/mL in all pediatric populations.
- Other groups support higher values, usually 30-32 ng/mL as minimum target.
- High rates of lower values common amongst African-Americans, obese, very low sunshine exposure and those with chronic illnesses.
- Clinical effects of lower levels uncertain with inadequate database regarding monitoring.


Vitamin D levels as indicator of status

<table>
<thead>
<tr>
<th>Vitamin D Status</th>
<th>25(OH)D Level, nmol/L (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe deficiency</td>
<td>≤12.5 (5)</td>
</tr>
<tr>
<td>Deficiency</td>
<td>≥12.6 (5)</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>≥37.5-50.0 (15-20)</td>
</tr>
<tr>
<td>Sufficient</td>
<td>50-250 (20-100)*</td>
</tr>
<tr>
<td>Excess</td>
<td>&gt;250 (100)*</td>
</tr>
<tr>
<td>Intoxication</td>
<td>&gt;775 (150)**</td>
</tr>
</tbody>
</table>

* Adult data indicate that a level of >80 nmol/L (>32 ng/mL) is desirable.
** An arbitrarily arbitrary designation.


Bone outcomes?

- Cochrane/systematic review: No overall benefit
  - Very small effect in those with 25-OHD <14 ng/mL
- Authors conclusions: “These results do not support vitamin D supplementation to improve bone density in healthy children with normal vitamin D levels, but suggest that supplementation of deficient children may be clinically useful”

Note that deficient is defined by review as <14 ng/mL and that RDA of 600 IU/day will bring >97.5% of children to a level above 20 ng/mL

Winzenberg et al., BMJ, 2011

60 caps of 5000 IU for $30-47 (12/2016). Compare to Walmart about $4.88 (12/2016) for 100 capsules of same thing.

www.vitamindcouncil.org
and articles.mercola.com

Misra et al. for LWPES, Pediatrics 2008
At what level does 25-OHD regulate calcium absorption in children?

**Diagram:**

- **Graph:** A scatter plot showing the correlation between serum 25-OHD levels and calcium absorption in children. The regression line is described by the equation \( R = 0.16, P = 0.001 \).

**Reference:**


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**Issues: Should all children be tested?**

- Sunshine exposure, even in Southern US is variable, esp. south of Atlanta and with sunblock.
- Effects of subclinical rickets uncertain – more research needed to determine short and long-term effects.
- Cost of testing would be high. No evidence in healthy population of cost/benefit reason for it.
- Currently there is no routine testing in first months of life for healthy breast-fed infants/mothers. Is 25-OHD important enough to be an exception?

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**A few weeks in the life of Google searches for vitamin D: Does it cure everything?**

- **Problems with Vitamin D Research: Confounding**
  - Individuals who have higher vitamin D intakes or 25-D levels are also more likely to:
    - Not be obese
    - Exercise and spend more time outdoors
    - Consume dairy products and other vitamins
    - Have other indicators of healthier lifestyle
    - Have higher socioeconomic status
  - Many association studies suggested cardiovascular and mortality benefits of estrogen replacement and antioxidant use
    - Benefits were not found in the subsequent clinical trials

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**Real genius requires chocolate**

- **Diagram:** A scatter plot showing the correlation between chocolate consumption and intelligence, illustrated by a graph with data points distributed across a range of chocolate consumption levels.

**Reference:**


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**Are there limitations to this approach?**

- **Diagram:** A graph showing the relationship between chocolate consumption and traffic accidents, illustrating a trend that suggests higher chocolate consumption is associated with a decrease in traffic accidents.

**Reference:**

Can you get too much vitamin D? Risk of death in elderly according to baseline serum 25OHD in the Longitudinal Aging Study

Recommended Dietary Allowances (RDAs) have been established as a target... for intake by an individual... individuals whose usual intakes are above the RDA are likely to be meeting their individual requirements

The RDA is not a useful reference standard for assessing an individual's intake. Intakes below the RDA cannot be assumed to indicate that an individual's intake is inadequate. The RDA, by definition, exceeds the actual requirements of all but 2 to 3 percent of the population

Calcium and vitamin D supplementation continue to be recommended to prevent and treat osteoporosis despite evidence of lack of benefit, say Andrew Grey and Mark Bolland. They examine why change is difficult and call for advocacy organisations, academics, and specialist societies to abandon industry ties

Vitamin D supplementation for prevention of cancer in adults

The age range of the participants was 47 to 97 years and on average 81% were women. The majority of the included participants did not have vitamin D deficiency......We did not find firm evidence that vitamin D supplementation decreases or increases cancer occurrence in predominantly elderly community-dwelling women.
Other conditions

- MS: “The role of high-dose vitamin D supplementation in MS treatment and prevention remains unclear. Canadian Agency for Drugs and Technologies in Health; 2016 Mar.
- We identified seven RCT and found that the summary estimates were not statistically significantly associated with a reduction in the risk of ARI or the rate of hospital admission due to respiratory infection in healthy children (RR 0.95, 95% CI 0.72, 1.26). Our findings indicate a lack of evidence supporting the routine use of vitamin D supplementation for the prevention of ARI in healthy children. Br J Nutr. 2015 Oct 14;114(7):1026-34. Epub 2015 Aug 27. Vitamin D supplementation for the prevention of childhood acute respiratory infections: a systematic review of randomised controlled trials.

What’s ahead?

- Study (pill taking) ends Dec. 2017, analysis continues into 2019

What’s the problem here?

- Excessive focus on a highly flawed marker of status (25-OHD), not outcomes
- Biological outcomes in children except frank rickets are poorly defined
- Marketing and other social forces have overwhelmed scientific discussion
- Research using controlled trials is difficult, expensive and not being done with adequate sample sizes

What to do

- Calcium and Vitamin D requirements as set by the IOM should be met
- Need policy to provide WIC or other support for supplement purchase
- Research on dose-serum 25-OHD relationship is decreasingly useful in health or disease
- Bugs have calcium: Eating three crickets gives you the same amount of calcium as a glass of milk
- Caution about toxicity of high doses, costs of screening, high supplement intakes
Best practice:
Vitamin D containing Beer (mid 1930s)