The Vitamin D Dilemma

Cindy Reuter, ND, LAC, RD
Providence Integrative Medicine Program
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A bit of perspective

Vitamin D has a historical public relations problem:

- Long thought to be "only about bones," but bone health dialogue historically focused on calcium, mostly ignored Vitamin D and other key players (Vitamin K, potassium, protein intake, sodium, trace minerals, weight-lifting)
- Paranoia (or at least over-concern) about toxicity because D is fat-soluble
- Presumption that people exposed to sun will make enough, or get enough from minute amounts in milk (wrong historically!)
- No clear "metabolically driven" lab ranges (more on this later)

A bit of perspective

15 years ago we couldn’t imagine what we know today:

- There is probably such a thing as too much supplemental calcium. More calcium does not necessarily build better bones.
- Moderate intake of fat is good for us, as long as it’s good fat
- What we know about Vitamin D may be wrong

Nutrition is an evolving science, and littered with false steps:

- Low fat diets (probably make us fat and give us insulin resistance)
- Vitamin E supplements to prevent heart disease (actually appear to increase risk of all-cause mortality)
- "Supplemental Vitamin C is safe, it’s water soluble" (may increase risk of cataracts in women)

Vitamin D Review

- Fat soluble vitamin
- Poorly distributed in food supply
- Historically, most “intake” came from humans making it after sun exposure of the skin
- Humans have physiological "wiring" to support fairly high levels of circulating D made from sun exposure

Vitamin D Review

- Dark skinned people need more sun to make D, especially in more northern latitudes tend to have lower levels
- Body fat sequesters D, so obese people tend to have lower levels of D
- Some nutrients that can be measured in blood (K+, Na+, Ca++) have well-defined lab cutoffs above or below which physical symptoms will rapidly appear
Vitamin D Review

- Vitamin D is more similar to Vitamins like B12 – wide range of so-called normal, slow and non-specific development of symptoms when levels drop too low
- As Vitamin D levels change, may see changes in blood calcium, parathyroid hormone, alkaline phosphatase
- D absorption poorer: older age, bowel diseases, gut surgery, some drugs (anti-seizure, long-term steroids)

Vitamin D Review

Forms of Vitamin D:
1. Vitamin D2 (ergocalciferol)
2. Vitamin D3 (cholecalciferol)
   - This is the desired form in supplements & fortified foods
   - D-only supps probably D3, read multivitamin labels carefully
3. 1, 25-(OH)2 Vitamin D (1,25 dihydroxy Vitamin D, AKA Calcitriol, active form)

Vitamin D Review

Vitamin D = more than bones!
- Calcium balance/absorption/parathyroid function
- Helps cells differentiate (turn into their mature form)
- Helps regulate insulin (hormone that takes sugar out of blood) and blood pressure
- Muscle activity and cellular energy pathways
- Cancer Risk - colon, prostate, breast
- Parkinson’s Disease, cardiovascular disease
- Diabetes, multiple sclerosis
- Role in immune function: immune cells have Vitamin D receptors, promotes innate/“natural” immunity, prevents autoimmunity (eg Type 1 DM)

http://bc.kseredtona.edu/collections/tutorials/cheml/trace/mpl.11.2011.06-2.268-274

Vitamin D & Health

Vitamin D & Adult Health
- People with D deficiency often have NO or VAGUE symptoms: fatigue, mood issues, muscle weakness
- Inadequate D = Osteomalacia (soft bones, pain, low blood calcium, osteoporosis (loss of bone density), greater risk of falls and bone fractures
- Heart disease 50% more likely in people with high blood pressure AND low vitamin D levels <10ng/ml, Wang. Circulation 2008;117:503-11
- Fewer deaths in people taking vitamin D (400-2000IU/d), compared to those using placebo  - Auer, Arch Intern Med 2007;167:2175-87

Houghton. Am J Clin Nutr 2006;84:694
Armas, J Clin Endo Metab. 2004;89:5387-91
Is historical reliance on D2 part of current Vitamin D issues?
Maternal Health

Boston study:
- **36% of mothers** and **58% of infants** D deficient at time of birth
- Median levels: 17.2 ng/mL infants, 24.8 ng/mL mothers
- Lower infant levels: winter birth, black mothers, Maternal BMI >35
- PNV use lowered risk to infants, but > 30% of mothers using PNV still deficient at delivery

**Increased risk of cesarean with lower D levels:** <37.5 nmol/l = 4 times more likely to have C-Section


Lactation

**Vitamin D levels in breastmilk**
- 45.6–78.6 IU/L in women receiving 400 IU Vitamin D daily
- Increased from 82 to 873 IU/L in women receiving 6400 IU Vitamin D daily
- Babies had similar increase in their own levels via oral supplementation or breastmilk from 6400 IU/d moms


Vitamin D & Kids

- Rickets in children – bone deformities (bowing of leg bones, “beading” of ribs, abnormalities in skull shape)
- With D deficiency: more obesity and faster weight gain and increase in waist circumference over 30 months


Wheezing/Asthma

- Some risks for Vitamin D and deficiency and asthma similar (non-white race, obesity)
- Low Vitamin D intake linked to increased risk of wheezing symptoms at 3 & 5 yo


Vitamin D & Breast Cancer

- Fewer cases of breast cancer in women who take vitamin D

- Increasing serum Vitamin D levels from 29 to 38 ng/ml reduced incidence of new cancers in women by 75% over 4 years RCT
  - Lappe Am J Clin Nutr 2007;85:1586-91

- Low vitamin D levels in women with breast cancer associated with worse survival
  - Goodwin P ASCO 2008
Lab Reference Ranges
- Standard lab is 25OHD – 25-Hydroxy Vitamin D – this reflects dietary intake, internal metabolism and synthesis from sun exposure.
- Calcium absorption is best when blood levels of D are between 20-30 ng/mL. 

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Problems With Lab Reference Ranges
- D levels naturally change with seasons - this may not be bad!
- Some labs set cutoffs based on levels found in healthy people in the same region – potential for error/sampling bias.
- Acceptable range should be based on interaction of Vitamin D and parathyroid hormone levels (which may go up to above-normal levels as D level drops below 30 ng/mL).
- Sadly, there is not a neat correlation between parathyroid hormone levels and D levels.

Vitamin D Sources

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving Size</th>
<th>Vitamin D Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish (cod) liver oil</td>
<td>1 teaspoon</td>
<td>1-400 IU</td>
</tr>
<tr>
<td>Pink salmon, canned</td>
<td>3 ounces</td>
<td>530 IU</td>
</tr>
<tr>
<td>Sardines, canned</td>
<td>3 ounces</td>
<td>231 IU</td>
</tr>
<tr>
<td>Salmon, fresh</td>
<td>3 ounces</td>
<td>600-800 IU *</td>
</tr>
<tr>
<td>Egg Yolk</td>
<td>1</td>
<td>25 IU</td>
</tr>
<tr>
<td>Unfortified Milk</td>
<td>1 cup</td>
<td>1-3 IU</td>
</tr>
<tr>
<td>Fortified milk</td>
<td>1 cup</td>
<td>~100 IU</td>
</tr>
<tr>
<td>Fortified Orange Juice</td>
<td>1 cup</td>
<td>~100 IU</td>
</tr>
</tbody>
</table>

Vitamin D Supplements
- Supplement s probably my first choice vs. cod liver oil.
- Get decent D levels with cod liver oil, however lots of controversy about safety of Vitamin A.

<table>
<thead>
<tr>
<th>Brand</th>
<th>Potency</th>
<th>Price</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country Life</td>
<td>1000 IU</td>
<td>$6.49</td>
<td>100</td>
</tr>
<tr>
<td>Carlson</td>
<td>1000 IU</td>
<td>$5.49</td>
<td>100</td>
</tr>
<tr>
<td>Carlson</td>
<td>2000 IU</td>
<td>$8.99</td>
<td>120</td>
</tr>
<tr>
<td>NOW</td>
<td>1000 IU</td>
<td>$7.99</td>
<td>180</td>
</tr>
<tr>
<td>NOW</td>
<td>2000 IU</td>
<td>$7.99</td>
<td>120</td>
</tr>
</tbody>
</table>
Fish (Cod) Liver Oil Comparisons

<table>
<thead>
<tr>
<th>Brand</th>
<th>Serving Size</th>
<th>Vitamin D (IU)</th>
<th>Vitamin A (IU)</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nordic Naturals Cod liver oil</td>
<td>1 teaspoon</td>
<td>1-20 IU</td>
<td>1500-2950</td>
<td>$22.95/8 oz</td>
</tr>
<tr>
<td>Nordic Naturals Cod liver oil With D</td>
<td>1 teaspoon</td>
<td>400 IU</td>
<td>1500-2950</td>
<td>$23.95/8 oz</td>
</tr>
<tr>
<td>Carlsons</td>
<td>1 teaspoon</td>
<td>400 IU</td>
<td>700-1200</td>
<td>$22.99/8.4 oz</td>
</tr>
<tr>
<td>TwinLab</td>
<td>1 teaspoon</td>
<td>462</td>
<td>4615</td>
<td>$9.99/12 oz</td>
</tr>
<tr>
<td>Spectrum</td>
<td>1 teaspoon</td>
<td>4</td>
<td>1250</td>
<td>$15.99/8 oz</td>
</tr>
</tbody>
</table>

Prescription Vitamin D Preparations

Oral Ergocalciferol (D2)
- Dosing: 5000-50,000 (or more) units by mouth daily
- One typical dosing regimen: 50,000 IU weekly x8 weeks
- Needs rx and monitoring by HCP

Clinically I see a nice, prompt increase in D levels, with rapid drop when rx is finished. Most people need subsequent supplementation with a D3 supplement to maintain levels

Clinical Issues with Vitamin D

Vitamin D: Clinical Issues
- Fortified milk probably won’t provide adequate Vitamin D intake to support normal levels, even at large intakes
- Dairy products other than milk usually do not have Vitamin D added, check the ingredient label to be sure

Vitamin D: Clinical Issues
- There is no agreed upon standard indication for Vitamin D testing, and no agreement on widespread screening
- That said, many physicians now will test levels proactively, or based on clinical picture (esp cancer, diabetes, musculoskeletal issues, depression etc)

Vitamin D: Clinical Issues
- Reasonable: get baseline D level, supplement if low, recheck 8-12 weeks
- Also reasonable to supplement without testing, if cost of testing will be an issue (~$100-150 for D level + phlebotomy fee)
Vitamin D: Clinical Issues

- Refer to PCP for D discussion: history of kidney stones, parathyroid disease, granulomatous disease (problem with immune system cells)

- What about recommending sun exposure?

- Tanning beds = Vitamin D + melanoma risk, especially bad idea for young people

2010 Institute of Medicine Report

The good

- Increased recommended intake to 600 IU daily (kids, adults to 70 yo)
- Revised tolerable upper limit to 4000 IU daily for adults

The bad

- Set 20 ng/mL as the acceptable low target blood level, implying that levels over this are harmful

2010 Institute of Medicine Report

The controversy

- Recommendations still too low
- Leading researchers believe non-bone data mostly ignored in report. Discussion about conflicts of interest among panel participants
- 20 ng/mL target recommendation is in direct contradiction to published research recommending 40–60 ng/mL to prevent cancer (see Lappe article especially)

Vitamin D: My general approach

- Eat foods rich in D, especially fatty fish – good for you in other ways
- Sun: 15 minutes 3 times weekly on arms and legs (no sunscreen) [Note that issue of sun & skin cancer is important and outside the scope of our discussion today]
- General Supplement Dosages: People up to 65 years old: 1000 IU of D3 daily, people over 65 years old: 2000 IU of D3 daily

Vitamin D: My general approach

- If you use cod liver oil – keep the Vitamin A to less than 5000 IU daily, and use no other supplements with Vitamin A
- Higher doses if clinically indicated & monitored
- Target blood level: >30 ng/mL for most (I aim for 40 ng/mL), > 50 ng/mL if cancer

Cautionary Notes

• Vitamin D is hot right now!

• We are in the infancy of our “new understanding” of the role Vitamin D plays in health – there is a lot we don’t know

• Much of the Vitamin D science is observational or retrospective, the real value will come from properly-done intervention studies

Cautionary Notes

• Until we know more, presume that some is probably good, but a lot more is not better

• There is little long-term study of doses >1000 units daily.

• We don’t yet understand impact of seasonal variations (eg high-levels year-round may be harmful in ways we don’t yet recognize)

Questions & Close