

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

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 D2 Ergocalciferol

- Historically predominant form in prescriptions, supplements & milk fortification
- Made by irradiating ergot mold ergosterol
- More unstable, leading to irregularities in potency, may not be stable in oil
- Less active biologically, greater risk for toxicity
Houghton. Am J Clin Nutr 2006;84:694
- About 30% potency of D3
Armas, J Clin Endo Metab. 2004;89:5387-91
- Is historical reliance on D2 part of current Vitamin D issues?

Vitamin D & Health

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://doi.org/10.1093/ajph/101/11/2000>; Rosen NEJM 2011 364:3. 248-254

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
Dawson-Hughes Osteoporosis 2005;16:713-6
- 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 Autier, Arch Intern Med 2007;167:1730-37

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

Merewood. Pediatrics. 2010 Apr;125(4):640-7. Epub 2010 Mar 22.

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

Merewood. J Clin Endo Metab. 2009 Mar;94(3):940-5. Epub 2008

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

Wagner CL. Pilot study, 6 mo. Breastfeed Med. 2006 Summer;1(2):59-70.

Vitamin D & Kids



Inadequate 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

Gilbert-Diamond AJCN 2010;92:1446-51, Lenders. AJCN 2009 Sep;90(3):459-67. Epub 2009 Jul 29.

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

Devereaux Am J Clin Nutr 2007;85:853-9, Camargo Am J Clin Nutr 2007;85:788-95

Vitamin D & Breast Cancer

Fewer cases of breast cancer in women who take vitamin D

Anderson, L. et al. Am J Clin Nutr 2010 doi:10.3945/ajcn.2009.28869

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

Vitamin D Labs

Lab Reference Ranges

- Standard lab is 25OHD – 25-Hydroxy Vitamin D – this reflects dietary intake, internal metabolism and synthesis from sun exposure Heaney RP. J Steroid Biochem Mol Biol. 2005 Oct;97(1-2):13-9. Epub 2005 Jul 18.
- Calcium absorption is best when blood levels of D are between 20-30 ng/mL Chapuy Osteoporos Int. 1997;7(5):439-43, Rosen NEJM 2011 364:3, 248-254

Approximate Reference Ranges - many labs have different cutoffs

- < 20 ng/ml – deficient
- 20-30 ng/mL – insufficient
- 30- 100 ng/mL sufficient

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

Vitamin D: Food Sources

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

Adapted from <http://sci.oregonstate.edu/infocenter/vitamins/vitaminD/>

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
- I use capsules primarily, liquid is probably ok, though some debate about stability of D in liquid/oil carriers
- Time of day not important, but need food for optimal absorption
- **Take Vitamin D supplements with the largest meal of the day, preferably one containing fat**
- Once weekly dosing for chronic pill forgetters?

Vitamin D Supplements

Brand	Potency	Price	Count
Country Life	1000 IU	\$6.49	100
Carlson	1000 IU	\$5.49	100
Carlson	2000 IU	\$8.99	120
NOW	1000 IU	\$7.99	180
NOW	2000 IU	\$7.99	120

Fish (Cod) Liver Oil Comparisons

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

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)

Life Stage Group	Calcium			Vitamin D		
	Estimated Average Requirement (mg/day)	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)	Estimated Average Requirement (IU/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
Infants 0 to 6 months	*	*	1,000	**	**	1,000
Infants 6 to 12 months	*	*	1,500	**	**	1,500
1-3 years old	500	700	2,500	400	600	2,500
4-8 years old	800	1,000	2,500	400	600	3,000
9-13 years old	1,100	1,300	3,000	400	600	4,000
14-18 years old	1,300	1,300	3,000	400	600	4,000
19-30 years old	800	1,000	2,500	400	600	4,000
31-50 years old	800	1,000	2,500	400	600	4,000
51-70 year old males	800	1,000	2,000	400	600	4,000
51-70 year old females	1,000	1,200	2,000	400	600	4,000
>70 years old	1,000	1,200	2,000	400	600	4,000
14-18 years old, pregnant/lactating	1,100	1,300	3,000	400	600	4,000
19-50 years old, pregnant/lactating	800	1,000	2,500	400	600	4,000

*For infants, Adequate Intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.
**For infants, Adequate Intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.

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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
Crew. Cancer Prev Res 2009. Garland. Ster Biochem Mol 2007, Goodwin JCO 2009.

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