



Vitamin D deficiency: the cause of everything?

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Health problems linked to vitamin D deficiency:

- Type 1 and 2 diabetes
- Multiple sclerosis
- Rheumatoid arthritis
- Osteoarthritis
- Periodontal disease
- Increased susceptibility to infection
- Osteoporosis
- Low birth weight infants
- Low seizure threshold
- Cancers: breast, prostate, colon, pancreas, ovary, Non-Hodgkin's lymphoma
- Hypertension
- Myocardial infarction
- Stroke, congestive heart failure
- Wheezing in childhood
- Falls in the elderly
- Muscle strength in the elderly

Current DRI's for vitamin D

- ◆ Birth to age 50: 200 IU
- ◆ Age 51-70: 400 IU
- ◆ Over age 70: 600 IU
- ◆ Institutionalized & homebound: 800 IU
- ◆ UL (upper limit): 2000 IU



A call to action:

“We call for international agencies such as the Food and Nutrition Board and the European Commission's Health and Consumer Protection Directorate-General to reassess as a matter of high priority their dietary recommendations for vitamin D, because the formal nationwide advice from health agencies needs to be changed.”

Vitamin D intakes in USA: food and supplements

- ◆ Children age 1-8 and Caucasian males age 9-50 had the best intakes (75% \geq DRI)
- ◆ Vitamin D intakes were significantly lower in females and African Americans
- ◆ Older adults (50+) had the lowest intakes (30% \geq DRI)



Sources of vitamin D

- ◆ UVB exposure
- ◆ Foods: Fatty fish, mushrooms, egg yolks
- ◆ Fortified foods: milk, breakfast cereals, soymilk, butter
- ◆ Supplements: fish liver oils, multivitamins, vitamin D



Cantharellus cibarius
(Chanterelles)

UVB: Check your shadow

'Vitamin D winter' begins when your shadow, even at high noon, is longer than you are



<http://zardoz.nilu.no/~olaeng/fastrt/VitD.html>

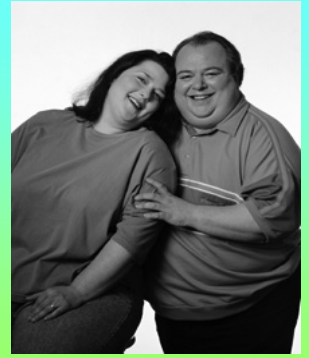
Who is at increased risk of vitamin D deficiency?





Obesity

Obese people are more likely to be vitamin D deficient and vitamin D deficiency seems to predispose people to obesity



The elderly

People aged 62-80 synthesize one third the amount of vitamin D as a person aged 22-30 after the same sun exposure



Darker skin types

- ◆ Melanin is an excellent sunscreen
- ◆ On average, African Americans have levels of 25(OH)D that are half that of Caucasian Americans



Complete clothing coverage



Breast fed infants

Vitamin D levels in breast milk reflect adequacy of vitamin D stores in the mother



Malabsorption

- ◆ Inflammatory bowel disease
- ◆ Celiac disease
- ◆ Cystic fibrosis
- ◆ Pancreatic insufficiency



Medications

- ◆ Anticonvulsants- Dilantin, Phenobarbital
- ◆ Bile acid sequestrants- Cholestyramine
- ◆ Cimetidine, Ranitidine
- ◆ Corticosteroids
- ◆ Antacids
- ◆ Calcium channel blockers
- ◆ Mineral oil, Orlistat

VDR polymorphisms

- ◆ 'bb' genotype: ↑ colon and prostate cancer
- ◆ 'ff' genotype: ↑ Graves' disease and Hashimoto's thyroiditis
- ◆ 'SS' genotype: RR of 3.2 for breast cancer in Latina women



Antarctic researchers

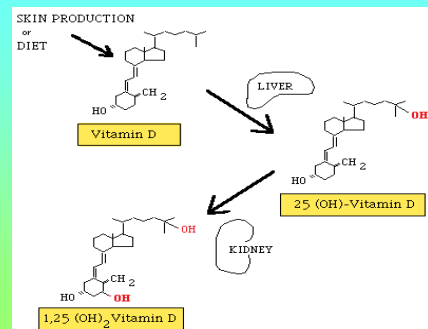


Emerging research on vitamin D

Most vitamin D research has been based on laboratory studies, animal studies and observational human studies.



Vitamin D physiology





Physiology: step 1

- ◆ UVB light converts 7-dehydrocholesterol in the skin to previtamin D3 → vitamin D3 binds to DBP → circulation
- ◆ Dietary vitamin D is primarily absorbed in the proximal small bowel → lymphatics → circulation

Steps 2 and 3: hydroxylation

- ◆ Circulating vitamin D is extracted by hepatocytes → 25(OH)D (calcidiol)
- ◆ In the kidney 25(OH)D → 1,25-dihydroxyvitamin D (calcitriol), the hormonally active form of vitamin D



Extrarenal production of 1,25(OH)₂ D

Hormonally active vitamin D is synthesized in many other body tissues: skin, colon, prostate, mammary tissue, adrenal medulla, brain, lymph nodes, placenta, endothelium, monocytes



Vitamin D has many roles

- ◆ Calcium homeostasis
- ◆ Cell growth, differentiation, apoptosis
- ◆ Immune modulation
- ◆ Antioxidant/anti-inflammatory activity



Vitamin D and calcium balance

- ◆ Falling plasma calcium causes increased parathyroid hormone which increases production of 1,25(OH)₂D in the kidney
- ◆ Vitamin D is necessary for active transport of calcium through the intestinal mucosa
- ◆ Level of 25(OH)D for optimal calcium absorption is ≥ 80 nmol/l



Bone health, muscle strength, fractures and falls

- ◆ Hip fractures: decreased by 26% (700-800 IU)
- ◆ Optimal fracture prevention at ~ 100 nmol/l
- ◆ Bone density is higher in each subgroup of serum 25(OH)D from 22.5-94 nmol/l
- ◆ Muscle strength: walking, sit to stand, improvement continued up to 94 nmol/l
- ◆ Falls in the elderly: decreased by 46% with 700IU vitamin D + 500mg calcium



Vitamin D and osteoarthritis

- ◆ Vitamin D stimulates the synthesis of proteoglycans by mature chondrocytes
- ◆ Dietary intake of vitamin D in OA patients has been found to be 80% below RDI
- ◆ Framingham Study: risk of OA progression was 3x higher in middle/low groups for vitamin D intake and serum vitamin D



Cancer protection

- ◆ Total cancer risk varies directly with latitude and with serum 25(OH)D
- ◆ Cellular effects of VDR signaling include growth arrest, differentiation and/or induction of apoptosis.
- ◆ Vitamin D also inhibits angiogenesis and stimulates adherence of cells



Vitamin D and breast cancer

- ◆ 9/13 studies show less sunlight and/or less vitamin D increases breast cancer risk
- ◆ Women in lowest quartile of vitamin D had 5x higher breast cancer than women in highest quartile
- ◆ In breast tissue, the VDR functions to oppose estrogen driven proliferation and maintain differentiation



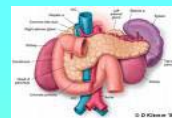
Vitamin D and colon cancer

- ◆ Colon cancer death rates are higher in areas with low solar radiation
- ◆ Intakes ≥ 1000 IU/day or serum level ≥ 82 nmol/l have 50% lower risk



Vitamin D and prostate cancer

- ◆ Sunlight exposure = lower risk
- ◆ Low 25(OH)D levels = higher risk
- ◆ Finland: Men below the median 25(OH)D had a 1.7x higher risk compared to men with levels above the median. These men also got prostate cancer at a younger age and had more aggressive disease.



Vitamin D and type II diabetes

- ◆ Vitamin D is necessary for insulin secretion
- ◆ \uparrow insulin resistance and \downarrow insulin secretion are associated with low vitamin D
- ◆ D deficiency-animal studies: 1st phase, then second phase insulin secretion impaired, then severe failure of insulin secretion
- ◆ Nurses Health Study 800 IU/d \downarrow 23% lower risk of developing type II diabetes



Vitamin D and heart disease

- ◆ Vitamin D deficiency is associated with an increased risk of:
 - hypertension
 - stroke
 - myocardial infarction
 - heart failure
- ◆ Anti-inflammatory effects may play a role



Vitamin D and mood disorders

- ◆ 25(OH)D and 1,25 (OH)₂D are lower in depression and schizophrenia
- ◆ Vitamin D increases “winter well being”
- ◆ Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults

Vitamin D and type I diabetes

- ◆ Large, well designed prospective study of >12,000 children followed for 30 years
- ◆ Children given 2000 IU/day vitamin D had a RR of 0.22
- ◆ Children with possible rickets had a RR of 3.0



Multiple sclerosis

- ◆ 1,25(OH)₂D₃ can completely prevent EAE (autoimmune encephalitis) in mice
- ◆ More common in populations with low concentrations of vitamin D or low UV exposure (higher latitudes)
- ◆ Nurses Health Study: highest vitamin D intake (≥ 400 IU) had 40% ↓ risk of M.S.
- ◆ JAMA: Healthy young adults with highest 25(OH) D had a 62% reduction in MS risk



Vitamin D deficiency

- ◆ Definition is controversial. Reference ranges and measurement methods vary from lab to lab
- ◆ #1 Deficiency is the level at which index diseases such as rickets and osteomalacia appear
- ◆ #2 Deficiency is when the PTH level begins to rise to maintain serum calcium

Symptoms & signs of vitamin D deficiency

- ◆ Mild/moderate may be asymptomatic
- ◆ Diffuse musculoskeletal pain
- ◆ Deep bone pain, fractures
- ◆ Proximal weakness, instability, difficulty with gait, climbing stairs
- ◆ Rickets, osteomalacia



Vitamin D deficiency: 25(OH)D

- ◆ Deficient < 25 nmol/L
- ◆ Relative insufficiency 25-70 nmol/L
- ◆ Optimal 70-250 nmol/L
- ◆ Toxic > 250 nmol/L

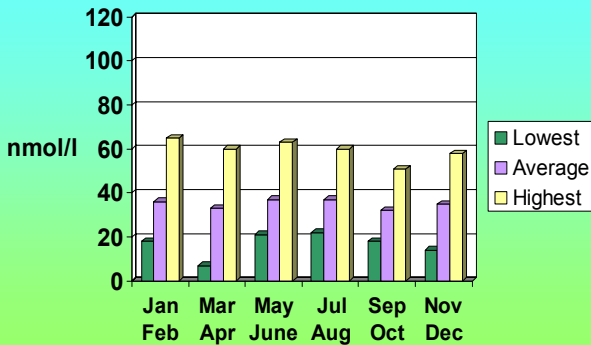


Optimum levels of 25(OH)D for prevention of chronic disease

Based on the available evidence, 25(OH)D level should be at least 75 nmol/L (30 ng/ml)



25(OH)D levels in Saskatoon, Canada



Treatment

- ◆ Higher dose therapy to correct deficiency
- ◆ Follow with maintenance dose
- ◆ Oral vitamin D3 (cholecalciferol) is treatment of choice in most patients
- ◆ To correct deficiency: D3 4000 IU/day with meals



Precautions

- ◆ Liver or kidney problems
- ◆ Sarcoidosis
- ◆ Primary hyperparathyroidism
- ◆ Thiazides
- ◆ History of kidney stones
- ◆ Any condition where there is a risk of hypercalcemia (metastatic cancer)



- ◆ There are widespread health benefits to maintaining an optimum vitamin D intake throughout life.
- ◆ Consider annual screening, particularly for those at increased risk of deficiency