Vitamin D Deficiency

It is not just about bones anymore
In fact, it is about virtually every tissue

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Vitamin D mechanism of action

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Why Deficiency?

Equatorial Africa—? 100,000 years ago
To northern latitudes / less skin pigment

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High latitude; November to March no UVB in Vermont sunlight.

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20-25yo — 65-75yo: 75-80% less Vitamin D synthesis

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Increased risk for low Vitamin D: pigment, smog, sunscreens, clothing, obesity, indoor work, hepatic failure, fat malabsorption, QFR <30, breast-fed infants, glucocorticoids, anti epileptic meds, Cytoschrome P450 Induction / Inhibition.
Vitamin D
Definitions of Deficiency

25 OH D =
40 ng/ml = 100 nmol/liter
0-19 = deficient
<10 = Severely deficient
20-29 = Insufficient
30-45 = minimally sufficient
30-50, 40+ = preferred
50-60 = optimal
80-120 = safe
>150 = toxicity

Vitamin D Testing for 2007

Prevalence of Deficiency

- 92% of adolescent girls <20 ng/ml (deficient)
- Of those 37% <10 ng/ml (severely deficient)
- 37% of elderly woman <20 ng/ml (deficient)
- Of those 17% <10 ng/ml (severely deficient)
- 42% of African American woman <15 ng/ml

In England (45yo men and women)
- During winter and spring months:
  - 47% were deficient, (67% <30, 47% <10, 15% <10)
- During summer and fall:
  - 13% were deficient (5% <30, 15% <30, 3% <10)
Prevalence (cont.)

- 73% pregnant woman <20ng/ml
- 80% of newborns <20ng/ml
- 40-150% of European elderly men and women living in the community are deficient
- More than 30% of post menopausal women taking medication for osteoporosis <30ng/ml ("sub optimal")
- 52% Hispanic and Black adolescents in Boston = <20ng/ml
- 48% white preadolescent girls in Maine <20ng/ml
- 42% of black girls and women in the US (end of winter) <20ng/ml
- 32% of med students, staff MD's and residents deficient despite multi vitammin and glass of milk daily and salmon at least weekly.
- 93% of persons 10-65yo at ER with muscle aches and bone pain (diagnosed as Fibromyalgia, Chronic Fatigue Syndrome, Depression) deficient in vitamin D.

Neuromuscular/Skeletal

Decreased vitamin D leads to
Decreased dietary calcium and phosphorus absorption

Higher risk for:

- Osteomalacia
- Muscle weakness / pain
- Impaired balance
- Slowed reaction time
- Gait disturbances
- Falls

Musculoskeletal

Women drinking >300mg of caffeine (18oz coffee) per day have more bone loss from spine than <300mg.

(? Interference with Vitamin D receptor)

Frailty in older persons: >30ng/ml decreases risk of nursing home admissions
Maximum bone density @40ng/ml or >.
Musculoskeletal

- DJD knees have 3x rate of progression with lowest vitamin D levels
- DJD hip is increased with low vitamin D
- 700 - 800u per day: 26% less hip fractures
- Increasing vitamin D improves balance and muscle performance, growth, and strength.
- Faster 8 step walking / getting out of chair

Malignancy

Lack of vitamin D increases rates of:
- Breast, Colon, Prostate, Ovarian, and Pancreatic Carcinomas
- Hodgkin’s and Non Hodgkin’s lymphomas.

AND DECREASES SURVIVAL RATES

Colon Cancer / UVB in 1980 Paper
Els Czeizler and Frank Gerland

- Ovarian cancer in Norway/Iceland is 5x greater compared to equatorial regions
- Melanoma death rates increase 60% by stopping sun exposure

COLON CANCER RATES
Malignancy

- Death rate from breast/cancer/colon/prostate carcinoma = 30x more than others
- Breast: Highest Vitamin D quintile: 50% vs lowest 10 or < versus 49 or > ng/ml (~4000 units per day)
- Gene GADD45-alpha causes growth arrest in cells with abnormal DNA and directs tumor cells to become more differentiated
- Apoptosis (cell suicide)
- Blocking Angiogenesis
- Increased UVB has been associated with reduction of 13 different cancers; the 7 above plus:
  - Esophagus, larynx, stomach, uterus, vulva, gallbladder,
  - urinary bladder, lung, kidney, testis, and rectum.

Autoimmune Disorders

Decreases: Inflammation / Autoimmune Disease,
Multiple Sclerosis, Crohn's Disease, Rheumatoid Arthritis,
Diabetes, Asthma, Lupus

Low Vitamin D leads to increased Interleukin 10 and CRP

Patients with skin cancer 50% MS rate
Nurses with most Vitamin D 1/3 less MS,
Fish consumption associated with less MS.
Infections

- Vitamin D → DNA Antimicrobial Peptides
  (Cathelicidin, Defensin Beta 2)
- Decreased infections: bacterial, viral, fungal
  "The Antibiotic Vitamin"
- Human Immune cells + bacterial cell walls →
  Increased VDR proteins and 1 alpha hydroxylase
- Vitamin D <20 → decreased macrophage function and
  increased tuberculosis, influenza and seasonal
  infections.
- Ethiopia: Kids with Rickets: 13x incidence of Pneumonia

Antimicrobial Peptides

- Decreased at Vitamin D levels 0-19ng/ml
- Knott Technique (1920's - 1950)
  Irradiation of blood for infections
- TB: January, 1871: "It seems very sad......to think of so many young girls
taken away by consumption....around the vicinity of Plainfield and Barre."
  Sanatoriums

Other relationships of low Vitamin D

- Excess in winter
- Coronary Artery Disease
- Cerebral Vascular Disease
- Peripheral Vascular

- Decreased myocardial contractility (CHF)
- Hypertension (Renin)
- Pre-eclampsia
- Asthma
- Age related macular degeneration

- Type I Diabetes: Hgb A1C
  Insulin resistance
  Insulin production
  Metabolic syndrome
  Triglycerides

- Gangrene/periodontal disease
- "Fibromyalgia"
- Initable bowel syndrome
- Depression (rate limiting enzymes for serotonin)
  Cognitive Decline
Deficient Maternal Vitamin D
Severe deficiency in young women:
Black 12%, White 0.5%

- Pre-pregnancy Obesity Predicts Poor Vitamin D Status: BMI 22–34 Doubles Risk
- Possible permanent brain damage in offspring
- Summer born children have more:
  neuro-developmental problems
  learning disabilities
  dyslexia

Intake Recommendations
Newborn: 1000u, 50-70, 400u, >70, 800u
2000u, "tolerable upper intake level" but

Adult woman, summer, t-shirt 20 minutes: 10,000u
40% skin exposed 10-15 minutes: 2,000 - 5,000u

The best diet will only provide ~250u without sun / supplements.
Supplements: 400u, serum level by 3-5ng/ml
1700u, serum level from 20-32 (12nmol)

50% of US Adults need 1000u to reach 30ng/ml
Pregnant woman: 6400u serum levels plateau @ 40ng/ml
(40 units = 1 microgram)

Reported Effects of Supplements
- "small" differences (3-4ng/ml) may lead to significant changes in risk
- Lower maternal vitamin D intake: increased wheezing in 3yo
  100u more maternal intake = 0.8 risk ratio
- Highest quintile (724u mean): 40% of the risk of the lowest quintile (356u mean) intake.
- 17% lower risk for all cancers (46% lower GI cancers) for each 10ng/ml increase of vitamin D serum level
Reported effects of supplements

- Nebraska women 55yo and >11000 UI/day
  - Year 1: 20% reduction new cancers (95% CI = 40% - 90%)
  - Year 2: 49% reduction new cancers
- 7000 UI/D Vitamin D >40 vs 25 or less
  - 62% reduced NH risk
- Finnish infants first year of life 3000 UI Vitamin D daily = 31 year 68% lower incidence of Type I Diabetes
- 800 IU (plus 400 IU) 2x daily 72% reduction in rate of nursing home residents >70yo
- 7000 IU Vitamin D with 500mg Calcium for 3 years 60% less tooth loss in middle aged women
- Protective effects vs colon cancer begin @ 20ng/ml vs 10ng/ml begins @ 20ng/ml
- **if all Americans levels were at least 55ng/ml we would have 60,000 less colon cancers, 50,000 less breast cancers yearly**

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So What Do We Do?

2,000 units per day leads to mean 40ng/ml
4,000 units per day: 97% @40ng/ml or >

Sunlight? Forget about it!
(40% skin exposure daily for 15 min in warm weather?)
Milk = 20 - 40 glasses per day
or
Supplements: 2,000 - 4,000u per day