Epidemic of Vitamin D Deficiency and Health Hazards

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Objectives

- List the main sources of vitamin D
- Describe the endocrine changes associated with vitamin D deficiency
- Know disease risks associated with vitamin D deficiency
- Know how to diagnose and treat vitamin D deficiency
Mechanisms of Calcium Regulation

- PTH
- 1,25 dihydroxy Vit. D
- Calcitonin
- Calcium sensor receptor
- Calcium effects
Biological pathway

- From diet: D2, D3
- 7-dehydrocholesterol (skin) → UV light from sun
- 25-hydroxylase: 25 OH D3, 25 OH D2
- 1,a-hydroxylase: 1,25(OH)2 D3, 1,25(OH)2 D2
- To target tissues: BIOLOGICALLY ACTIVE FORMS
Control of Serum Calcium

Low concentration of calcium in blood

Release of parathyroid hormone

Efflux of calcium from bone
Decreased loss of calcium in urine
Enhanced absorption of calcium from intestine

Increased concentration of calcium in blood
Calcium Regulation of PTH

![Graph](image)

- Parathyroid hormone release (Percent of maximum)
- Normal human serum Ca++

Extracellular Ca++ (mM)
Main causes of hypocalcemia

1) loss of calcium from the circulation
2) hypoparathyroidism including pseudohypoparathyroidism
3) Magnesium deficiency
4) vitamin D deficiency.
PTH-Calcium Nomogram
Treatment of Hypocalcemia

- Hypoparathyroidism, primary or secondary
  - Oral calcium for mild cases plus vitamin D or calcitriol
  - Intravenous calcium if the symptoms are severe
- Vitamin D deficiency
  - Vitamin D plus supplemental calcium
- Magnesium deficiency
  - Magnesium
Vitamin D Deficiency Without Hypocalcemia

Secondary Hyperparathyroidism
Osteomalacia
Osteoporosis
25 OH Vitamin D and Vitamin D₃ Dose

Heaney et al. Am J Clin Nutr 77:204-10, 2003; Note 40 IU=1ug D₃
Vitamin D production in the skin

• 10000 - 20000 IU maximal daily production
  - i.e. 1 minimal erythema dose (MED)
  whole body exposition

• provitamin D3 is photolabile and will be converted to vitamin D3 after some time of deposition in the skin
Minimal Erythema Dose (MED)

- Amount of UVB that produces redness 24 hours after exposure
- Learn your MED to avoid Sunburns
UV-induced Vitamin D

- 90-95% of vitamin D demand is fulfilled by UVB-radiation
- the daily demand is about 1000 IU
- i.e. 25% wholebody exposition with ¼ MED (minimal erythema dose)
Prudent Use of Sunlight

- sunexposition of 18% body surface with 1/3 - 1/2 MED 2-3 x per week from spring to autumn at high noon according to the skin type for 5-20 min
  - face and arms
  - or lower arms and lower legs
- whole body exposition 1/4 MED (2-5 min)
- UVB therapy in medical light cabin 1 x per week with 1/2 MED
Variable Skin Characteristics

**Skin Type I (2%)**
- Red/red-blond hair, freckles
- Always sunburned, no tanning of the skin
- 5-10 minutes to develop erythema

**Skin Type II (12%)**
- Blond, fair/light colored eyes
- Often sunburned, weak tanning of the skin
- 10-20 minutes to develop erythema

**Skin Type III (78%)**
- Brunette, light or dark eye color
- Rarely sunburned, good skin pigmentation
- 20-30 minutes to develop erythema

**Skin Type IV (8%)**
- Dark hair, Mediterranean type
- Never sunburned, dark tan
- Approximately 45 minutes to develop erythema
## Optimal and Normal Vitamin D-25OH Concentrations

<table>
<thead>
<tr>
<th>Optimal 25-hydroxyvitamin D values are:</th>
<th>25-hydroxyvitamin D lab values are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-60 ng/mL</td>
<td>Insufficiency 20-30 ng/mL</td>
</tr>
<tr>
<td>Toxicity &gt;100 ng/mL</td>
<td>Deficiency &lt;20 ng/mL</td>
</tr>
</tbody>
</table>
Measurement Total Vitamin D 25 OH

- Vitamin D3 25 OH animal sources
- Vitamin D2 25 OH Plant sources
- Mass Spec can measure both forms and provide a total value
- RIA can measure total from both sources
- No known advantage to measure both forms
1,25 DihydroxyVitamin D or Calcitriol

- Circulating Mainly made in the kidney
- Stimulated by PTH and hypophosphatasemia
- Renal failure and PTH deficiency can cause a deficiency and hypocalcemia
- Used to diagnose hypercalcemia
- Monitor therapy of renal failure
Extrarenal Synthesis of Vitamin D 1,25 (OH)\(_2\) D\(_3\)

- Autonomous production 1,25 (OH)\(_2\) D\(_3\)
- Colon
- Prostate
- Mammary gland
- Many other tissues

Lechner et al. Molecular and Cellular Endocrinology 263: 55-64, 2006
How is the optimal serum concentration of Vitamin D 25 OH Determined?
Relationship between PTH and Serum Vitamin 25(OH)D

Thomas, NEJM, 338:777-83
Vitamin D Concentration and Calcium Absorption

- Postmenopausal women
- Increase vitamin D 25 OH from 20 ng/ml to 32 ng/ml increased intestinal calcium absorption 65%.
- This led to defining vitamin D insufficiency as a 25(OH)D concentration of 21–29 ng/ml

Vitamin D 25OH and Osteoid

Priemel et al. J BMR 25: 305-12, 2010
How Frequent is Vitamin D Deficiency?

- About 58% of assays for Vitamin D 25 OH at ARUP in 2008 and 2009 were less than 30 ng/mL
- ng/mL=2.5 nMol/L
Vitamin D 25OH

<table>
<thead>
<tr>
<th>Total #</th>
<th>&lt;10 ng/ml</th>
<th>10-19 ng/ml</th>
<th>20-29 ng/ml</th>
<th>30+ ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>143685</td>
<td>1656</td>
<td>10432</td>
<td>49363</td>
<td>66766</td>
</tr>
<tr>
<td></td>
<td>1.2%</td>
<td>7.3%</td>
<td>34.4%</td>
<td>46.5%</td>
</tr>
</tbody>
</table>
Seasonal changes

[nmol/l]

***

*  

25-OH-D₃

Summer  Fall  Winter  Spring

Priemel et al. JBMR 25: 305-12, 2010
Watching Television

- >4 hours daily 38% Vitamin D < 15 ng/mL
- No TV 2% Vitamin D < 15 ng/mL
Vitamin D Transport Blood

- Vitamin D binding protein (DBP)-4-8 mM
  - 85-88%, only about 2% saturated
  - 25OH, Ka=5x10^8 M
  - 1,25(OH)2D, Ka=4x10^7 M

- Albumin
  - 12-15%

- Free Vitamin D
  - 25OHD-0.03%
  - 1,25(OH)2D-0.4%
Why has Vitamin D Deficiency Increased?
Sun Exposure

- UV triggers Vitamin D synthesis
- Influenced by
  - Season
  - Geographic latitude
  - Time of day
  - Cloud cover-reduces 50%
  - Smog
  - Sunscreen-SPF 8 or > blocks vitamin D
  - Sunlight-10-15 minutes adequate time for vitamin D synthesis
Hypovitaminosis D

Causes of Vitamin D deficiency

- Dietary
- Sunscreen
- Limited sun exposure
- Malabsorption
- Decreased 25 hydroxylation in the liver
- Kidney can’t convert Vitamin D 25 to 1, 25 dihydroxyvitamin D
Who needs supplemental Vitamin D

- Breast feed infants
- Older adults
- Persons with limited sun exposure
- Darker skin people
- Persons with fat malabsorption
- Anticonvulsants
Vitamin D

- Osteoporosis-silent contributor
- Cancer protection-colon, prostate
- Corticosteroids-decrease vitamin D absorption
- Caffeine-may decrease Vitamin D absorption
Food Sources of Vitamin D

- Milk fortified with Vitamin D, 400 IU/Qt
- One cup supplies
  - 50% recommended for adults 19-50 yrs
  - 25% for 51-70 yrs
  - 15% for 71 and older
- Cheese and Ice cream are not fortified
Table 1. Dietary, Supplemental, and Pharmaceutical Sources of Vitamins D₂ and D₃.※

<table>
<thead>
<tr>
<th>Source</th>
<th>Vitamin D Content</th>
<th>Fortified foods</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natural sources</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh, wild (3.5 oz)</td>
<td>About 600–1000 IU of vitamin D₃</td>
<td>Fortified milk</td>
</tr>
<tr>
<td>Fresh, farmed (3.5 oz)</td>
<td>About 100–250 IU of vitamin D₃ or D₂</td>
<td>Fortified orange juice</td>
</tr>
<tr>
<td>Canned (3.5 oz)</td>
<td>About 300–600 IU of vitamin D₃</td>
<td>Infant formulas</td>
</tr>
<tr>
<td>Sardines, canned (3.5 oz)</td>
<td>About 300 IU of vitamin D₃</td>
<td>Fortified yogurts</td>
</tr>
<tr>
<td>Mackerel, canned (3.5 oz)</td>
<td>About 250 IU of vitamin D₃</td>
<td>Fortified butter</td>
</tr>
<tr>
<td>Tuna, canned (3.6 oz)</td>
<td>About 230 IU of vitamin D₃</td>
<td>Fortified margarine</td>
</tr>
<tr>
<td>Cod liver oil (1 tsp)</td>
<td>About 400–1000 IU of vitamin D₃</td>
<td>Fortified cheeses</td>
</tr>
<tr>
<td>Shiitake mushrooms</td>
<td></td>
<td>Fortified breakfast cereals</td>
</tr>
<tr>
<td>Fresh (3.5 oz)</td>
<td>About 100 IU of vitamin D₂</td>
<td></td>
</tr>
<tr>
<td>Sun-dried (3.5 oz)</td>
<td>About 1600 IU of vitamin D₂</td>
<td></td>
</tr>
<tr>
<td>Egg yolk</td>
<td>About 20 IU of vitamin D₃ or D₂</td>
<td></td>
</tr>
<tr>
<td>Exposure to sunlight, ultraviolet B radiation (0.5 minimal erythermal dose)†</td>
<td>About 3000 IU of vitamin D₃</td>
<td></td>
</tr>
<tr>
<td><strong>Supplements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescription</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D₂ (ergocalciferol)</td>
<td>50,000 IU/capsule</td>
<td></td>
</tr>
<tr>
<td>Drisdol (vitamin D₂) liquid supplements</td>
<td>8000 IU/ml</td>
<td></td>
</tr>
<tr>
<td>Over the counter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivitamin</td>
<td>400 IU vitamin D, D₂, or D₃‡</td>
<td></td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>400, 800, 1000, and 2000 IU</td>
<td></td>
</tr>
</tbody>
</table>

Holick NEJM 357:266-281, 2007
Sun Exposure Scale and Serum 25(OH)D

Thomas, NEJM, 338:777-83
Tanning Bed Effects on 25(OH)D, Calcium and PTH

10 min. 3 times/week for 6 months

Holick Curr. Opin. Endo Diab. 9:87-98, 2002
Effect of Sunscreen and Aging on Serum 25(OH)D

Holick Curr. Opin. Endo Diab. 9:87-98, 2002
Serum 25(OH)D in Long-term Sunscreen Users

Matsuoka, Arch Derm
124:1802-04, 1988
What are the health consequences of Vitamin D deficiency?
Vitamin D deficiency Studies in Mice

Mimics Deficiency in Humans and Health Risks
Vitamin D Receptor (VDR) Null Mice

- VRD or vitamin D deficiency
- Immune system is grossly normal
- Increased sensitivity to autoimmune diseases, such as inflammatory bowel disease or type I diabetes after exposure to predisposing factors
- More prone to oncogene or chemocarcinogen-induced tumors
Vitamin D Receptor (VDR) Null Mice

- Increased
  - High renin hypertension
  - Cardiac hypertrophy
  - Thrombogenicity
  - Increased prevalence of diseases in humans
Vitamin D and the Endocrine System

- Fertility decreased in males and females
- Reduced sperm number and motility
- Increased LH and FSH
- Hypergonadotrophic hypogonadism
- These are from studies in mice and human studies need to be done.
Health Consequences of Vitamin D Deficiency in humans
## Disease Incidence Prevention by Serum 25(OH)D Level

| Serum 25(OH)D, ng/ml | 6 | 8 | 10 | 12 | 14 | 16 | 18 | 20 | 22 | 24 | 26 | 28 | 30 | 32 | 34 | 36 | 38 | 40 | 42 | 44 | 46 | 48 | 50 | 52 | 54 | 56 | 58 | 60 | 62 | 64 | 66 | 68 |
|----------------------|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| **Studies of Individuals** |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Cancers, all combined |   |   |    |    |    |    |    |    |  30% |  35% |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Breast Cancer |   |   |    |    |    |    |    |    |  12% |  17% |  83% |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Ovarian Cancer |   |   |    |    |    |    |    |    |  31% |  38% |  60% |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Colon Cancer |   |   |    |    |    |    |    |    |  12% |  18% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Non-Hodgkins Lymphoma |   |   |    |    |    |    |    |    |  25% |  50% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Type 1 Diabetes |   |   |    |    |    |    |    |    |  72% |  50% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Fractures, all combined |   |   |    |    |    |    |    |    |  25% |  50% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Falls, women |   |   |    |    |    |    |    |    |  33% |  46% |  54% |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Multiple Sclerosis |   |   |    |    |    |    |    |    |  30% |  37% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Heart Attack (Men) |   |   |    |    |    |    |    |    |  23% |  49% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| **Natural Experiments** |   |   |    |    |    |    |    |    |  50% |  99% |    |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

Chart prepared by: Garland CF, Baggerly CA
## Age-, Sex- and Race-adjusted Prevalence and ORs of Select CV Disease Risk Factors between the First and Fourth Quartiles of Serum 25(OH)D Levels

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Prevalence of CV risk factor</th>
<th>OR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st quartile (&lt; 21 ng/ml)</td>
<td>4th quartile (≥ 37 ng/ml)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>20.46</td>
<td>15.10</td>
<td>1.30</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.85</td>
<td>3.38</td>
<td>1.98</td>
</tr>
<tr>
<td>Obesity</td>
<td>24.69</td>
<td>11.50</td>
<td>2.29</td>
</tr>
<tr>
<td>Triglyceride level ≥ 150 mg/dl</td>
<td>32.86</td>
<td>23.84</td>
<td>1.47</td>
</tr>
<tr>
<td>ACR ≥ 200 for males / ≥ 300 for females</td>
<td>1.59</td>
<td>0.76</td>
<td>2.54</td>
</tr>
</tbody>
</table>

*Martins D et al., Arch Intern Med 2007; 167: 1159-1165*
Obesity and Vitamin D 25 OH Insufficiency

- Common
- Is the vitamin D insufficiency of obesity causally related to health hazards?
  - Diabetes
  - Cardiovascular disease
  - Cancer
  - Gonadal dysfunction
### Table 2.
25OHD concentrations (ng/ml) of 90 women separated by ethnicity and body mass

<table>
<thead>
<tr>
<th></th>
<th>25OHD (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 90)</td>
</tr>
<tr>
<td>All BMI</td>
<td>30.1 ± 13.0 (6.7 – 69.6)</td>
</tr>
<tr>
<td>Lean (BMI &lt; 25)</td>
<td>34.3 ± 13.8* (15.2 – 69.6)</td>
</tr>
<tr>
<td>Overweight (BMI ≥ 25)</td>
<td>24.6 ± 9.5 (6.7 – 46.0)</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD and (range).
*Indicates a significant difference between lean and overweight subjects (P <0.001)
† Indicates a significant difference between Hispanics and Caucasians (P = 0.002)
‡ ANOVA analysis indicates no statistical difference between Hispanics and Caucasians when adjusted for BMI (P = 0.09)
$r = -0.35, P = 0.001$

Kremer et al. J CEM 93, 2008
Vitamin D Concentrations and Cancer Risk

- Inverse association between vitamin D 25 OH and colorectal cancers
- Mixed results with association of Vitamin D 25 OH and prostate and breast cancer
Vitamin D and the Immune System

- Vitamin D deficiency associated with
  - Increased susceptibility to infections
  - Autoimmune disease such as type I diabetes
Vitamin D and the Endocrine System

- Vitamin D deficiency
- Impairs
  - Insulin secretion
  - Glucose tolerance
- Increases risk of metabolic syndrome
- Increases cardiovascular risk
- Decreased muscle mass, strength and predisposition to falls in the elderly
Vitamin D and Type 2 Diabetes

- Vitamin D 25OH score and T2D
  - Framingham Study-133 T2D cases over 7 years
  - Highest quartile vitamin D score compared to lowest quartile at baseline had 40% lower incidence of T2D
  - Adjusted for age, sex, waist circumference, prenatal history of T2D, hypertension, low HDL, cholesterol, elevated triglycerides, impaired fasting glucose, and dietary guidelines

Lin et al, Am J Clin Nutr, 2010
Vitamin D-Calcium Effect on Bone Remodeling Markers

Grados, JCEM 88:5175-79, 2003
Figure 2. Forest Plots Comparing the Risk of Hip and Nonvertebral Fractures Between Vitamin D (700-800 IU/d and 400 IU/d) and Control Groups

Hip Fracture

<table>
<thead>
<tr>
<th>Source</th>
<th>Favors Vitamin D</th>
<th>Favors Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D 700-800 IU/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chapuy et al. 2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chapuy et al. 1994</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trivedi et al. 2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nonvertebral Fracture

<table>
<thead>
<tr>
<th>Source</th>
<th>Favors Vitamin D</th>
<th>Favors Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D 700-800 IU/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfeifer et al. 2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chapuy et al. 2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chapuy et al. 1994</td>
<td></td>
<td></td>
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<tr>
<td>Dawson-Hughes et al. 1997</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trivedi et al. 2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Relative Risk (95% CI)
Myocardial Infarction Risk and Vitamin D 25 OH

Table 3. Estimated RRs of MI by Level of 25(OH)D at Baseline During 10 Years of Follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Plasma 25(OH)D, ng/mL</th>
<th>P Value (Trend)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤15.0</td>
<td>15.1-22.5</td>
</tr>
<tr>
<td>Cases/controls, No. RR (95% CI)</td>
<td>63/87</td>
<td>156/307</td>
</tr>
<tr>
<td>Matching variables</td>
<td>2.42 (1.53-3.84)</td>
<td>1.65 (1.15-2.37)</td>
</tr>
<tr>
<td>MV1a</td>
<td>2.01 (1.22-3.30)</td>
<td>1.45 (0.99-2.12)</td>
</tr>
<tr>
<td>MV2b</td>
<td>2.09 (1.24-3.54)</td>
<td>1.43 (0.96-2.13)</td>
</tr>
</tbody>
</table>

Hazard Ratio (95% CI) Cardiovascular Mortality

Potential Mechanisms of Vitamin D Health Protection
Effect of Vitamin D, 1, 25 (OH)2 on Foam Cells in Diabetic

Oh et al Circulation 120:687-698, 2009
Effect of Vitamin D, 1, 25 (OH)2 on Foam Cells in Diabetic

Oh et al Circulation 120:687-698, 2009
Vitamin D and diabetic cardiovascular disease

- Deletion of vitamin D receptors in macrophages from diabetics accelerated foam cell formation induced by modified LDL.

- Vitamin D receptor signaling is a potential mechanism underlying increased foam cell formation and accelerated cardiovascular disease in diabetic subjects.
FIG. 1. DBP knockout serum increases monocyte responses to vitamin D metabolites. Human monocytes cultured in medium supplemented with 5% serum from DBP\(^{+/−}\) and DBP\(^{-/-}\) mice were treated with 25OH\(_{3}\) (2–200 nM), 1,25(OH)\(_{2}\)\(_{3}\) (0.02–2 nM), or vehicle control (C, 0.2% ethanol) for 6 h. RNA from the resulting cells were then analyzed by RT-PCR for cathelicidin (panel A) and 24-hydroxylase (CYP24A1) (panel B). Data are shown as mean \((n = 3)\) changes in RT-PCR \(\Delta\Delta Ct\) values relative to vehicle-treated cells. *, Statistically different from DBP\(^{+/−}\) serum cells at \(P < 0.001\).
Changes in glucose and insulin concentration during the first phase of insulin secretion (AUC_{1-8}) before and after treatment with alphacalcidol. Values are mean \pm SE. B = before treatment; A = after treatment.

Insulin Sensitivity and Vitamin D 25OH in PCOS

BMI-adjusted WBISI by vitamin D-deficiency status. *, $P$ for difference between groups = 0.047.

Ashraf et al JCEM (4: 3200-06, 2009)
Vitamin D and Endothelial Function

Tarcin JCEM 94: 4023-30, 2009
Vitamin D and Flow Mediated Dilatation

The correlation data of the vitamin D-deficient subjects and the control group showed a positive association between 25(OH)D₃ and FMD values ($r = 0.45; P = 0.001$), also between 25(OH)D₃ and 1,25(OH)₂D levels ($r = 0.57; P < 0.0001$). There was a negative correlation between FMD and TBARS ($r = -0.28; P < 0.05$), also between 25(OH)D₃ levels and TBARS ($r = -0.46; P = 0.001$).
Cancer and Vitamin D

- Randomized control trial in postmenopausal women 1100 IU vitamin D$_3$ plus 1500 mg of calcium daily for 4 years
- Vitamin D group vitamin D 25OH increased 24 nmol/L
- No change in calcium only or placebo
- >60% reduction in all cancers

Vitamin D and Calcium on Cancer Free

FIGURE 1. Kaplan-Meier survival curves (ie, free of cancer) for the 3 treatment groups randomly assigned in the entire cohort of 1179 women. Sample sizes are 288 for the placebo group, 445 for the calcium-only (Ca-only) group, and 446 for the calcium plus vitamin D (Ca + D) group. The survival at the end of study for the Ca + D group is significantly higher than that for placebo, by logistic regression. (Copyright Robert P Heaney, 2006. Used with permission.)

Expression of CYP27B1

- Increased in hyperplastic colon polyps
- Increased in early stage tumors
- Declines in late-stage neoplasia
- CYP24A1 is induced by 1,25 (OH)$_2$ D$_3$
- Tumor cells determine the extent of Vitamin D catabolism

Lechner et al. Molecular and Cellular Endocrinology 263: 55-64, 2006
Fig. 4. Evaluation of the antiproliferative effect of 25-OH-D₃ in colon cancer cell lines by [³H]-thymidine incorporation into DNA. Caco-2, COGA-1 and COGA-13 cells were exposed to 100 and 10 nM of 25-OH-D₃ (25-D) for 48 h. Data are presented as percentage of vehicle control (C; *** P < 0.001).

Lechner et al. Molecular and Cellular Endocrinology 263: 55-64, 2006
Renal and Colon Vitamin D Synthesis and Catabolism

Figure 3. Comparison of colonic and renal vitamin D synthesis and catabolism. Differences in regulation and function are indicated.

Cross and Kallay Futrue Oncol 5: 493-507, 2009
CYP24A1 and CYP27B1 in Normal Colon and Colon Tumor

Lechner et al. Molecular and Cellular Endocrinology 263: 55-64, 2006
Summary of Vitamin 25 (OH)D Deficiency

- Common, particularly in older women
- Generally asymptomatic

Causes
- Decreased dietary intake
- Decreased sun exposure
- Sunscreen

Diagnosis: Serum 25(OH)D <20 ng/mL and Elevated PTH; insufficiency <30 ng/mL

Benefits - CVD, diabetes, cancer, immune

Treatment: Vitamin D
Questions