ESPEN Congress Prague 2007

Key papers in the field of nutrition
Dietitian

Geila S Rozen
Key Papers in the field of Nutrition

ESPEN 2007 – Prague
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Hypovitaminosis D in British adults at age 45y: nationwide cohort study of dietary and lifestyle predictors

E Hypponen & C Power
American Journal of Clinical Nutrition
2007;85:860-8
Hypovitaminosis D in British adults at age 45y: nationwide cohort study of dietary and lifestyle predictors

• “The thinking about the actions of Vitamin D have made an important shift during the past 10 years. In addition to its well-established role in the regulation of calcium metabolism, the active form of vitamin D has been shown to have antiproliferative and immunomodulatory effects that are thought to influence the development of several serious conditions, including diabetes, cardiovascular disease, and cancer”

Pubmed – 220 articles on the subject search Vitamin D deficiency in 2007 alone! (164 papers – studies in humans)
Vitamin D

- A hormone precursor by physiological definition
- Best known effect on bone metabolism
- Vitamin D receptor (VDR) present in several cell types and tissues – lymphocytes & monocytes, brain, heart, pancreas, intestine, placenta
Vitamin D status – 25 (OH) D

- In the past cutoff point for deficiency was indicated according to levels when rickets and osteomalacia accrued

  25 (OH) D ≤ 25 nmol/L
  25 (OH) D ≤ 10 ng/ml

Research concerning osteoporosis and optimal bone health created new standards
Vitamin D – are current ref. ranges correct?

Malabanan A, Veronikis IE, Holick MF 1998 Lancet
Vitamin D status – 25 (OH) D

Measurement of Vitamin D Status

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Insufficiency</th>
<th>Optimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20 ng/ml</td>
<td>20-32 ng/ml</td>
<td>32-65</td>
</tr>
</tbody>
</table>

Current paper, nmol/L: <25 Deficiency; < 40 Insufficiency, 75+ Optimal
Vitamin D status – implications on chronic disease and health

**Deficiency**

- Short latency disease
  - Rickets
  - Osteomalacia

**Insufficiency**

- Long latency diseases:

**Optimal**

- Calcitropic effects:
  - Osteoporosis, Muscle pain & fatigue, Hypertension / CVD

- Antiproliferative effects:
  - Cancer (breast, colon, prostate)

- Immunomodulatory effects:
  - Diabetes, MS, Lupus
Vitamin D deficiency – possible Western epidemic?

Endogenous source – skin synthesis:
- Western lifestyle:
  - working indoors during daylight hours, long cloths, sunscreen
- Residence in northern latitude (42 °), cloudy climate
- Darker skin color (ethnic group)

Exogenous source – diet
- Fatty fish & fish liver oil
- Dairy products (depending on their exposure to sun)
- Eggs, fortifies foods (margarine only in UK)

Changes in metabolic efficiency
- Obesity & overweight
- Old age (longer life span)
- More chronic disease
- Medication use
- Low dose supplements in OTC
Study design

• British birth cohort of March 1958 (England, Scotland, Wales)
• 9,349 (78%) completes questionnaires, 7,591 (81%) also provided blood sample for Vitamin D status
• Weight and height measured, MBI calculated (obesity >30)
• Season classification: winter (Dec-Feb), spring (Mar-May), summer (June-Aug), fall (Sep-Nov)
• Geographic region – according to present residence
• Seriocomic status
• Food Frequency Questionnaire + supplements & cod liver oil
• Sunlight exposure (hours without time of day!)
• Use of sunscreen & clothes
• Skin color (inner arms)
• “Screen” hours
Results

- **Vit D supplement use** – more frequent in woman and non-obese participants
- **Time outdoors** - significantly lower in woman and non-obese participants
- **Oily fish consumption** – more frequent in woman, non-obese, northern regions, SES high classes
- **Sun screen use** – more in woman, and higher SES class (no variation by geographic region)
Results – 25 OH D levels

• Vitamin D levels in serum peaked at end of summer, and declined in winter
• Use of supplements and oily fish were associated with better levels of vit D (especially for lower subgroups)
• Use of fortified margarine showed no association with 25OUD levels
• Time spent outdoors was strongly associated with 25OHD during summer and fall
• Hypovitaminosis was more common in woman (dependent on season – most prevalent during fall)
• Hypovitaminosis was twice as common in obese subjects than non-obese (regardless of season)
• Hypovitaminosis shows gradient by region of living
Public health implications - UK

- Reports of hypovitaminosis D with rickets (deficiency) in the elderly, children & minorities (in UK and other countries)
- Present report shows the problem of insufficiency is widespread (nearly 50% during winter and spring) in middle-aged white population
- Survey results more severe when comparing to Canada (latitude 51°N) and US (mean latitude 32°N)
Public health implications

• With the new cutoff points for 25OHD a substantial public health problem of insufficiency and deficiency exists in UK

• Worldwide there seems to be an epidemic of 25OHD deficiency in healthy population

• The problem exists also in sunny countries
Public health conclusions

• 25OHD insufficiency is associated with short and long term illness – such as diabetes, CVD, cancer and more

• Immediate intervention action is required at a population level rather than at a risk group level
recommendations

• Patients should be screened for risk factors: diet, no sun exposure, obesity
• Blood test for 25OHD levels should be taken whenever insufficiency suspected
• Population should be encouraged to spend 5-15 minutes a day in sunlight during spring & summer between 10 AM and 3 PM
• Sun screen should be recommended for the rest of the time
• US – calls for increased fortification of foods
• Supplements – specific D₃ should be considered
"Anything I can get you son? tea, coffee....vitamin D?"
Winter leaves men in D-cline

Vitamin D might be solution to lack of sunshine
Further reading
A longitudinal study of serum 25-hydroxyvitamin D and intact PTH levels indicate the importance of vitamin D and calcium homeostasis regulation in multiple sclerosis.


BACKGROUND: Past sun exposure and vitamin D3 supplementation have been associated with a reduced risk of multiple sclerosis (MS). There are no previous longitudinal studies of vitamin D in MS.

OBJECTIVES: To compare regulation of vitamin D and calcium homeostasis between MS patients and healthy controls. To study correlation of parameters of vitamin D metabolism with MS activity.

METHODS: We measured 25-hydroxyvitamin D, intact PTH, calcium, phosphate, magnesium, chloride, alkaline phosphatase, albumin and TSH in serum every three months and at the time of relapses during one year in 23 MS patients and in 23 healthy controls. MRI BOD and T2 activity was assessed every 6 months.

RESULTS: Vitamin D deficiency [S-25(OH)D \(\leq 37 \text{ nmol/L} \)] was common affecting half of the patients and controls at some time of the year. Seasonal variation of 25(OH)D was similar in the patients and in the controls, but the 25(OH)D serum levels were lower and the iPTH serum levels were higher during MS relapses than in remission. All 21 relapses during the study occurred at serum iPTH > 20 ng/L (2.2 pmol/L), whereas 38% of patients in remission had iPTH \(\leq 20 \text{ ng/L} \). MS patients had a relative hypocalcaemia and a blunted PTH response in the winter. There was no correlation between serum 25(OH)D and MRI parameters.

CONCLUSIONS: The endocrine circuitry regulating serum calcium may be altered in MS. There is an inverse relationship between serum vitamin D level and MS clinical activity. The role of vitamin D in MS must be explored further.
Low Vitamin D Status despite Abundant Sun Exposure

N. Binkley, R. Novotny, D. Krueger, T. Kawahara, Y. G. Daida, G. Lensmeyer, B. W. Hollis, and M. K. Drozner

University of Wisconsin Osteoporosis Clinical Research Program (N.B., D.K., T.K., M.K.D.), Madison, Wisconsin 53705; Human Nutrition, Food and Animal Sciences (R.N., Y.G.D.), University of Hawaii at Manoa, Honolulu, Hawaii 96822; Laboratory Medicine (G.L.), University of Wisconsin, Madison, Wisconsin 53792; and Medical University of South Carolina (B.W.H.), Charleston, South Carolina 29425

Context: Lack of sun exposure is widely accepted as the primary cause of epidemic low vitamin D status worldwide. However, some individuals with seemingly adequate UV exposure have been reported to have low serum 25-hydroxyvitamin D [25(OH)D] concentration, results that might have been confounded by imprecision of the assays used.

Objective: The aim was to document the 25(OH)D status of healthy individuals with habitually high sun exposure.

Setting: This study was conducted in a convenience sample of adults in Honolulu, Hawaii (latitude 21°).

Participants: The study population consisted of 98 adults (30 women and 68 men) with a mean (SEM) age and body mass index of 24.0 yr (0.7) and 23.6 kg/m² (0.4), respectively. Their self-reported sun exposure was 28.9 (1.5) h/wk, yielding a calculated sun exposure index of 11.1 (0.7).

Main Outcome Measures: Serum 25(OH)D concentration was measured using a precise HPLC assay. Low vitamin D status was defined as a circulating 25(OH)D concentration less than 30 ng/ml.

Results: Mean serum 25(OH)D concentration was 31.6 ng/ml. Using a cutpoint of 30 ng/ml, 51% of this population had low vitamin D status. The highest 25(OH)D concentration was 62 ng/ml.

Conclusions: These data suggest that variable responsiveness to UVB radiation is evident among individuals, causing some to have low vitamin D status despite abundant sun exposure. In addition, because the maximal 25(OH)D concentration produced by natural UV exposure appears to be approximately 60 ng/ml, it seems prudent to use this value as an upper limit when prescribing vitamin D supplementation. (J Clin Endocrinol Metab 92: 2130-2135, 2007)
### Table 1

**Dietary Sources of Vitamin D*\)**

<table>
<thead>
<tr>
<th>Item</th>
<th>Vitamin D (IU)</th>
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<tbody>
<tr>
<td>Herring (pickled)</td>
<td>680</td>
</tr>
<tr>
<td>Beef liver (fried)</td>
<td>12</td>
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<tr>
<td>Beef kidney (simmered)</td>
<td>12</td>
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<tr>
<td>Beef tallow</td>
<td>19</td>
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<tr>
<td>Beef tripe (raw)</td>
<td>12</td>
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<tr>
<td>Blue crab (steamed)</td>
<td>4</td>
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<tr>
<td>Butter</td>
<td>56</td>
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<tr>
<td>Catfish (steamed or poached)</td>
<td>500</td>
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<tr>
<td>Chicken livers (simmered)</td>
<td>12</td>
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<tr>
<td>Cod liver oil</td>
<td>10,000</td>
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<tr>
<td>Crayfish/crawdads (steamed)</td>
<td>4</td>
</tr>
<tr>
<td>Eastern oysters (steamed)</td>
<td>642</td>
</tr>
<tr>
<td>Egg yolk (fresh)</td>
<td>148</td>
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<tr>
<td>Lamb liver (braised)</td>
<td>20</td>
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<tr>
<td>Lard (pork fat)</td>
<td>2,800</td>
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<tr>
<td>Mackerel (canned/drained)</td>
<td>450</td>
</tr>
<tr>
<td>Northern lobster (steamed)</td>
<td>4</td>
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<tr>
<td>Pork liver (braised)</td>
<td>12</td>
</tr>
<tr>
<td>Shrimp (canned/drained)</td>
<td>172</td>
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<tr>
<td>Skinless sardines (water packed)</td>
<td>480</td>
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<tr>
<td>Small clams (steamed/cooked moist)</td>
<td>4</td>
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<tr>
<td>Smoked chinook salmon</td>
<td>320</td>
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<tr>
<td>Sturgeon roe</td>
<td>232</td>
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</tbody>
</table>

*International units of vitamin D in 100 g or approximately 3.5 oz.

### Table 2

**Cells with Cytosolic or Nuclear and/or Membrane-Bound Vitamin D Receptors<sup>1-3</sup>**

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Liver cells</th>
<th>Muscle cells</th>
<th>Neurons</th>
<th>Osteoblasts</th>
<th>Ovarian cells</th>
<th>Parathyroid cells</th>
<th>Prostate cells</th>
<th>Pituitary cells</th>
<th>Placenta cells</th>
<th>Skin fibroblasts</th>
<th>Transformed B-cells</th>
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<tbody>
<tr>
<td>Activated T-cells</td>
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<td>Aortic endothelial cells</td>
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<td>Chondrocytes</td>
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<td>Circulating monocytes</td>
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<td>Colon enterocytes</td>
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<td>Distal renal tubules</td>
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<td>Endocrine cells, stomach</td>
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<td>Keratinocytes, skin</td>
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</tbody>
</table>

1. Yadhu N. Singh U.S. Pharm. 10:66-72;2004
Bone disease
Calcium, Vitamin D and PTH

Hypocalcemia / Hyperphosphatemia → PTH Secretion

Bone → Resorption / Demineralization

Kidney → Urinary Phosphate, Urinary Calcium, 25(OH) D → 1,25(OH)2D

Intestine → Calcium Absorption, Phosphate Absorption

↑ Serum Calcium

Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 2004