Update in Vitamin D Deficiency

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Case: Assessment

- Type 2 Diabetes
- Hypertension
- Metabolic Dyslipidemia
- Obesity
- Depression
- Osteopenia
- Vitamin D Deficiency?

Vitamin D Metabolism

7-dehydrocholesterol  UV light skin  Cholecalciferol (Vitamin D3)  Liver  Calcitriol (1,25-dihydroxy Vitamin D)

Diet/Supplements  Ergocalciferol (Vitamin D2)  Calcidiol (25-hydroxy Vitamin D)

Intestinal Ca Absorption  Bone Resorption  Renal Ca and Phos Excretion

Calcitriol (1,25-dihydroxy Vitamin D)  PTH

Kidney
Vitamin D Deficiency Disorders

- Primary or Congenital Vitamin D Deficiency
- Acquired Vitamin D Deficiency:
  - Poor intake or Malabsorption
  - Inadequate sunlight
  - Liver disease
  - Renal disease
  - Hypoparathyroidism
  - Obesity
  - Medications

Factors Affecting Cutaneous Vitamin D Production

- Skin Pigmentation
  - Darker skin associated with lower vitamin D levels (higher incidence of vitamin D deficiency) and less conversion in response to sun exposure.
- Age
- Sunscreen use
- Season of the year and time of day

Factors Affecting Vitamin D Production: Sunscreen

Seasonal Variation of Vitamin D levels

What is Vitamin D Deficiency?

• Definition has changed of the last 20 years
• No consensus on optimal levels
  >20? >30? >40?
• There is consensus that levels < 15 ng/dl represent true deficiency
• Severe deficiency (Levels < 8 ng/dl) is associated with rickets in children and osteomalacia in adults
  • Should probably be "worked up"
• Levels of < 20-30 are considered "subclinical" deficiency or "insufficiency"
  • Even mild deficiency is associated with bone loss
• Broad-based screening, however, is not recommended - should individualize

Vitamin D Deficiency
Secondary Hyperparathyroidism
The Majority of American Women Are Not Receiving Adequate Intake of Vitamin D

- NHANES III (3,444 women > 50 yr): over 70% of women 51-70 years did not meet adequate guidelines for vitamin D intake based on diet and supplements (400 IU).
- Nearly 90% of women older than 70 years did not meet guidelines (600 IU).

NHANES = National Health and Nutrition Examination Survey.

Low Vitamin D Levels Are Prevalent in Postmenopausal North American Women Receiving Therapy Indicated For Osteoporosis

Cutoff Points for 25(OH)D Level
N = 1,536

C = confidence interval.

Osteoporosis Treatment
Calcium and Vitamin D

RCT: 3270 healthy elderly women (mean age: 84 yr.)
Calcium (1,200 mg) + Vitamin D (800 IU) vs. Control over 18 mo.

What about vitamin D deficiency and "non-bone" disease?
Vitamin D and Type 2 Diabetes

- **Observational studies:**
  - Worse glycemic control in the winter
  - Inverse relationship between Vit D levels and glycemic control
  - Inverse relationship between Vit D levels and prevalence of diabetes, metabolic syndrome, and insulin resistance

- **Prospective studies:**
  - Inverse relationship between Vit D intake and incident type 2 diabetes

- **Biology:**
  - Vitamin D has a direct effect on insulin secretion
    - Vit D receptors found in beta cells
    - Vit D deficiency leads to impaired insulin secretion
    - Improved insulin secretion with Vit D replacement
  - Vitamin D is associated with insulin resistance and replacement improves peripheral insulin action
  - Vitamin D reduces systemic inflammation
  - Link between Vitamin D Receptor gene polymorphisms and type 2 diabetes

- **Intervention studies:**
  - Paucity of data
  - Some evidence of improved glucose tolerance in treatment of severe vitamin D deficiency
  - Mixed results from treating individuals with IGT or T2D with vitamin D
  - No benefit in individuals without vitamin D deficiency
Vitamin D and Type 1 Diabetes

- Correlation between latitude and sunlight exposure and incidence of type 1 diabetes
- Vitamin D supplementation in infants associated with decreased risk of type 1 diabetes
- Vitamin D supplementation during pregnancy is associated with decreased risk of insulin antibodies
- Immunomodulatory effects of Vitamin D
  - Vitamin D prevents beta cell damage

Vitamin D and Cardiovascular Disease

- Inverse relationship between vitamin D levels and CVD/mortality
  - especially when Vit D < 30 ng/ml
- Vitamin D deficiency associated with endothelial dysfunction and supplementation improves it
- Vitamin D suppresses renin gene expression
- Vitamin D modulates smooth muscle cell proliferation, inflammation, and thrombosis
- Supplementing deficient vitamin D is associated with reduced CVD risk?


Vitamin D Deficiency and Other Diseases

- Cancer: Colorectal, Prostate, Breast
- Autoimmune Disorders: MS, T1DM, RA
- Hypertension
- Obesity
- Dental Health
- Infectious Diseases
- Mental Health
Treatment of Vitamin D Deficiency

### Dietary Sources of Vitamin D

<table>
<thead>
<tr>
<th>Source</th>
<th>Vitamin D Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh, wild (15 μg)</td>
<td>About 400 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fresh, farmed (5 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Canned (20 μg)</td>
<td>About 800 I.E. of vitamin D</td>
</tr>
<tr>
<td>Butter, canned (1 μg)</td>
<td>About 40 I.E. of vitamin D</td>
</tr>
<tr>
<td>Milk, canned (1 μg)</td>
<td>About 20 I.E. of vitamin D</td>
</tr>
<tr>
<td>Tuna canned (3 μg)</td>
<td>About 120 I.E. of vitamin D</td>
</tr>
<tr>
<td>Cod liver oil (5 μg)</td>
<td>About 1000 I.E. of vitamin D</td>
</tr>
<tr>
<td>Chicken, dark meat (5 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Turkey breast (5 μg)</td>
<td>About 100 I.E. of vitamin D</td>
</tr>
<tr>
<td>Eggs (1 μg)</td>
<td>About 40 I.E. of vitamin D</td>
</tr>
<tr>
<td>Breakfast cereals (1 μg)</td>
<td>About 40 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fortified milk (1 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fortified orange juice (1 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fortified margarine (1 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fortified margarine (1 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
<tr>
<td>Fortified cheese (1 μg)</td>
<td>About 200 I.E. of vitamin D</td>
</tr>
</tbody>
</table>


### Vitamin D and Sun Exposure

- One minimal erythemal dose (MED) while wearing only a bathing suit = 20,000 units
- Fair skinned: 10 min of midday sun exposure in shorts and tank top = 10,000 units
- Exposure to arms and legs for 5-30 minutes b/w 10am and 3pm twice a week is often adequate
- Depends on time of year, latitude, skin color, age
### Vitamin D Preparations

<table>
<thead>
<tr>
<th>Vitamin D</th>
<th>Name</th>
</tr>
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<tbody>
<tr>
<td>D2</td>
<td>Ergocalciferol</td>
</tr>
<tr>
<td>D3</td>
<td>Cholecalciferol</td>
</tr>
<tr>
<td>25 (OH) D</td>
<td>Calcifediol</td>
</tr>
<tr>
<td>1,25 (OH)2 D</td>
<td>Calcitriol</td>
</tr>
</tbody>
</table>

### Vitamin D Treatment

- **Maintenance**
  - Optimal intake: 700-1200 units D3 daily
  - Safe intake: up to 2000 units D3 daily
  - Alternate: 50,000 units D2 monthly
  - Goal 25(OH) Vitamin D level: 30-100 ng/ml

- **Vitamin D Deficiency**
  - 25(OH) Vitamin D <10 ng/ml: 50,000 units BIW x 3 mo
  - 25(OH) Vitamin D 10-20 ng/ml: 50,000 units QW x 3 mo
  - 25(OH) Vitamin D 20-30 ng/ml: 1000-2000 units daily

### Conclusions

- Vitamin D deficiency is common
- No consensus on optimal levels
- Vitamin D deficiency is associated with significant morbidity (and mortality?)
  - Low bone mass and fractures
  - CVD, diabetes and other metabolic disorders?
  - Mental health disorders?
- Vitamin D ‘sufficiency’ is associated with reduced fractures
- Broad-based screening, however, is not recommended