Vitamin D: All You Need to Know

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Vitamin D: All You Need to Know

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Outline of Vitamin D

• Basics: structure and production
• Prevalence of vitamin D deficiency
• Consequences of low vitamin D status
  – Skeletal and Non-Skeletal diseases
• Toxicity due to vitamin D
• How to replace /supplement vitamin D
Historically, Humans Obtained Vitamin D from the Sun

UVB (~280–315 nm) Produces Vitamin D

7-DHC → Pre D₃ → Vitamin D₃
A marked seasonal variability of 25D levels is observed since UV light exposure is essential for vitamin D biosynthesis in the skin. Only during the months of July, August and September were 25(OH)D levels sufficient for most patients.

Vitamin D$_2$ versus D$_3$?

Differ only in side chain structure
(c22-23 double bond and c24 methyl group)

Cholecalciferol
Vitamin D$_3$

Ergocalciferol
Vitamin D$_2$

Wimalawansa, SJ; “Vitamin D: All you need to know”
Vitamin D: All you need to know

Vitamin D → 25-hydroxyvitamin D → 1,25-dihydroxyvitamin D

Liver: 25-hydroxylase activity is unaffected

Kidney: 1α-hydroxylase is inactive

Calcidiol: pro-hormone
Calcitriol: active hormone
7-dehydrocholesterol (7-DHC) is a vitamin D precursor. In the skin, exposure to UVB rays converts 7-DHC to pre-vitamin D₃. Pre-vitamin D₃ is then converted to cholecalciferol (D₃) by the skin. Cholecalciferol (D₃) is converted to 25-hydroxyvitamin D₃ by the liver and then to 1,25-dihydroxyvitamin D by the kidney. This final compound interacts with the vitamin D receptor to produce physiological effects.
Generation of Vitamin D

Vitamin D$_3$ 

25(OH) D 
Storage form of vitamin D

Vitamin D$_2$ 
Dietary vitamin D

Vitamin D$_3$ 
Skin-derived vitamin D

Serum Calcium

Vitamin D precursor

7-dehydro-cholesterol

Wimalawansa, SJ; “Vitamin D: All you need to know”
Major Physiological Regulatory Mechanisms in Calcium Metabolism

Diet

Vitamin D

Calcitriol 1,25(OH)2D3

Parathyroid hormone (PTH)

PTH

Calcitonin

Wimalawansa, SJ; “Vitamin D: All you need to know”
Vitamin D Deficiency

- The most common disorder in the world
- With supplements, it is easy to correct vitamin D deficiency
- Deficiency:
  - in children leads to rickets
  - in adults leads to osteomalacia
- Is associated with increased falls, osteoporosis and fractures
- Also associated with many other diseases
Vitamin D Facts and Figures

• Vitamin D is essential for survival
• Major portion of our vitamin D requirement is made in the skin
• Most common cause of vitamin D deficiency is lack of exposure to sunlight
• Measurement of serum vitamin D levels makes the diagnosis
Measurement of Serum 25(OH)D is the Way to Assess Vitamin D Status

The Vitamin D Continuum

Deficiency ~20 ng/mL (50 nmol/L)
Insufficiency 30 ng/mL (75 nmol/L)
Optimal

Wimalawansa, SJ; “Vitamin D: All you need to know”
<table>
<thead>
<tr>
<th>Age</th>
<th>Calcium</th>
<th>Vitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 to 8</td>
<td>800 mg</td>
<td>800 IU</td>
</tr>
<tr>
<td>9 to 18</td>
<td>1,300 mg</td>
<td>1,000 IU</td>
</tr>
<tr>
<td>19 to 50</td>
<td>1,000 mg</td>
<td>1,000 IU</td>
</tr>
<tr>
<td>≥ 50</td>
<td>1,200 mg</td>
<td>1,000 IU</td>
</tr>
<tr>
<td>Pregnancy/Lactation</td>
<td>1,300 mg</td>
<td>2,000 IU</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>1,300 mg</td>
<td>1,000–4,000 IU</td>
</tr>
</tbody>
</table>
Main Sources of Vitamin D

• Sun-light
• Food that contain high content of vitamin D
  – Fortified milk and cereal
  – Mushroom
  – Oily fish; salmon, sardines, mackerel, tuna
  – Cod-liver oil
Nutrition and Bone Health

Fats, Oils & Sweets
Use sparingly

Milk, Yogurt, & Cheese; 2 - 3 servings

Fish, Meat, Eggs, Chicken & Nuts; 2 - 3 servings

Eating for Better Heath (USDA guidelines)
Prevalence of Vitamin D Insufficiency

Wimalawansa, SJ; “Vitamin D: All you need to know”
Prevalence of Vitamin D Insufficiency by Ethnicity

Percentage (%)

Average  African American  Hispanic  Asian  Whites

Prevalence of Vitamin D Insufficiency by Ethnicity
“In a person with a lighter skin, exposure to sunshine for 15 minutes can prevent vitamin D deficiency.”
Solar UVB Exposure in Decline

10-15 minutes twice a week

SPF > 10
Potential Beneficial Effects of Vitamin D

Improve
- Immunity
- Calcium Metabolism
- Muscle Function
- Endocrine
- Cardiovascular

Prevent
- Cell Cycle
- Cell Proliferation
- Tumorigenesis

25(OH)D
Vitamin D
1,25(OH)2D

Wimalawansa, SJ; “Vitamin D: All you need to know”
Beneficial Effects of 25(OH) Vitamin D

Classical effects:
- Calcium metabolism (Calcium absorption, bone mineralization, etc.)

Non-classical functions:
- Neuromuscular functions
  - Balance and muscular coordination/reflexes
  - Prevention of falls/fractures
- Immune system and immunity
- Prevention of diseases
- Reproduction and sexual functions
Potential Benefits of Vitamin D

• **Skeletal effects:**
  - Calcium homeostasis
  - Gastrointestinal absorption of calcium
  - Bone mineralization
  - Avoidance of rickets and osteomalacia
  - Prevention of osteoporosis

• **Non-skeletal effects:**
  - Immune system
  - Nervous system
  - Cancer prevention
  - Balance and muscular system (sarcopenia)
  - Type 2 diabetes
  - Improved survival
W Coastal Wimalawansa, SJ; “Vitamin D: All you need to know”
Summary of Disease Incidence Reduction

50%-70% Reduction In Incidence

- Breast Cancer
- Type 1 Diabetes
- Multiple Sclerosis
- Colon Cancer
- Heart Disease
- High B.P.
- Falls
- Fractures
- URI’s

Good Evidence of Reduction

- Prostate Cancer
- Endometrial Cancer
- Lymphoma
- Lung Cancer
- Malignant Melanoma
- Eczema
Vitamin D and Diabetes?

“A major practical conclusion on vitamin D and diabetes is:

Vitamin D deficiency is undesirable, not only for calcium absorption and bones, but also for glucose metabolism.”

Mathieu et al., *Diabetologia*, 2005; 48:1247-1257
Vitamin D and Diabetes?

- Beta cells contain the vitamin D receptor
- $1,25(OH)_2D$ stimulates insulin release
- Insulin release is reduced in vitamin D-deficient animals
- $1,25(OH)_2D$ prevents development of diabetes in the NOD mouse
- Recent meta-analyses associate low vitamin D status with increased risk of type 1 and type 2 diabetes
Incidence of Diabetes by Serum Vitamin D Levels

Incidence of type 1 Diabetes by Latitude

Mohr, Diabetologia 2008
Vitamin D Supplementation Reduces the Incidence of Type 1 Diabetes by 25%
Effect of Vitamin D on the Renin/Angiotensin System

Physiological levels of vitamin D, decrease blood pressure and improve vascular functions

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Vitamin D and Vascular Disease?

- Vitamin D decreases inflammation
- CVD death rate increases with latitude
- Higher CVD deaths in winter months
- Vitamin D receptors in myocytes
- Vitamin D impacts renin-angiotensin and blood pressure
Vitamin D and Muscle

- Myocytes possess vitamin D receptors
- D deficiency associated with myopathy
  - 32-year-old woman with progressive muscle weakness and diffuse bone pain
  - Fat malabsorption; s/p bowel resection
  - 25(OH)D = 2.4 ng/ml
- Treated with 1,25(OH)$_2$D$_3$

“After 3 weeks she could walk again, and muscle weakness and bone pain disappeared.”

Boonen et al., *Calcif Tissue Int*, 78:257-270, 2006
Vitamin D Reduces Cancer Risk

1179 women avg age 67 years; 4-year study placebo, calcium 1500 mg or calcium + vitamin D 1100 IU

25(OH)D increased from 28 ng/ml to 38 ng/ml

“.. improving vitamin D nutritional status substantially reduced all-cancer risk in postmenopausal women.”

Those with Vitamin D Insufficiency or Deficiency Need Supplemental Vitamin D Therapy

There are Several Ways of Replacing Vitamin D
Treating Vitamin D Insufficiency / Deficiency

- 50,000 IU of Vit.D once a week, for 8-12 weeks
- Followed by 50,000 IU Vitamin D every 2-4 weeks
- Or 2,000 IU Vitamin D every day
- The dosage will raise 25OH D level to sufficient levels 30-50 ng/ml with no adverse effects
- Vitamin D dose in multivitamin ~ 400 IU. Too low to raise 25 OH D level

Wimalawansa, SJ; “Vitamin D: All you need to know”
Two simple and practical therapeutic regimens for supplementation of vitamin D

**Regimen A:**

Serum vitamin D below 10 ng/mL, administer 50,000 IU three times a week; between 11 and 20 ng/mL, administer 50,000 IU twice a week; and between 21 and 29 ng/mL, administer 50,000 IU once a week for 12 weeks;

**Regimen B:**

A loading therapeutic dose of vitamin D (one time high dose, or 50,000 IU 1 to 5 times/week), followed by 50,000 IU, once or twice a week (Table 12).
Vitamin D Conclusions

- Vitamin D inadequacy is very common
- No downside to aiming for 25(OH)D ≥ 30 ng/ml
- Need at least 1,000-2,000 IU/day
  - Not everyone needs the same dose
  - Prudent to recommend D₃
  - These “higher” doses are safe
- “Casual” sun exposure is not enough
- Vitamin D may not be the fountain of youth
- Vitamin D adequacy will reduce osteoporotic fractures, falls, cancer, and potentially a multitude of other diseases
Triad of Negativity

Diabetes
Obesity

Vitamin D Deficiency

Metabolic Syndrome
Osteoporosis Osteomalacia

Wimalawansa, SJ; “Vitamin D: All you need to know”
Conclusions

• Important public health implications
  – Vitamin D and calcium insufficiency are common
  – Both interventions can be implemented easily and inexpensively

• Vitamin D and calcium homeostasis seem to play a role in development of type 1 and type 2 diabetes and cardiovascular diseases (based on observational studies)
Conclusions

• Supplementation with vitamin D (and calcium) may have a role in the prevention of type 1 and type 2 diabetes and reduction of cardiovascular deaths in high-risk individuals.
Reducing the Risk of Osteoporosis and Fracture, Falls, and Cancer is Good Enough for me to Treat My Patients with Vitamin D
Vitamin D Deficiency

Perhaps the most cost-effectively preventable disease in the world
The doctors of the future will also be magicians, so they'll be able to check your bones without x-rays.
Thank you..

We have time for Questions

Sunil Wimalawansa
ANKA MEDICAL ASSOCIATION OF NORTH AMERICA
EASTERN REGION INC.
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SLMANA EAST
CHARITY BALL
ANNUAL GENERAL MEETING
&
SCIENTIFIC SESSIONS
ON
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