Vitamin D in Pregnancy and Infancy

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Vitamin D Outline

• Metabolism of vitamin D
• Calcium Balance and Bone Health
  – Pregnancy
    • Vitamin D in the immune system
• Recommended Dietary Allowances
• Sources of Vitamin D
  – Sun, food, supplements
  – Risk Factors for Deficiency
• Beyond Bone Health
  – Evidence for association of vitamin D deficiency with other diseases
Vitamin D Metabolism

Vitamin D is made by exposure to ultraviolet B (UV-B) rays.

7-dehydrocholesterol → Vitamin D₃

Ergosterol → Vitamin D₂
Vitamin D – A Fat-Soluble Vitamin

- Vitamin D$_2$ = ergocalciferol
  - found in plants, fungi (e.g., mushrooms)

- Vitamin D$_3$ = cholecalciferol
  - Synthesized in human skin; animal-source foods
Question

- How can fish contain so much vitamin D$_3$ if sunlight is required for vitamin D synthesis?

Answer: They eat zooplankton which live in very shallow water.
Vitamin D Metabolism and Action

Vitamin D

↓ (liver)

25-hydroxy vitamin D
[25(OH)D]

↓ (kidney*)

1,25-dihydroxy vitamin D = calcitriol
[1,25(OH)$_2$D]
(hormonal form)

Calcitriol binds to vitamin D receptor (VDR) to regulate gene expression

* and immune system, plus other cells (autocrine/paracrine activity)

Calcitriol acts in a cell’s nucleus to regulate gene expression

Target Cell

Vitamin D metabolites are bound to vitamin D binding protein (DBP) in the blood.

Calcitriol from the blood enters a cell, moves to the nucleus, binds to VDR and increases or decreases expression of target genes, such as transport proteins for calcium absorption in the small intestine.

Ch. 11. "Vitamin D" 2nd ed. Elsevier Press.
Do Vitamins D$_2$ and D$_3$ have the same biological activity?

- Yes, they both bind to the VDR and regulate gene expression.
- However, D$_2$ is less effective than D$_3$ in maintaining blood levels of 25(OH)D.
- The only high-dose supplement available to physicians by prescription to treat deficiency is vitamin D$_2$.

Summary

- Vitamin D has a short half-life in the blood and is rapidly converted to 25(OH)D but may persist in fat tissue for months.
- Serum 25(OH)D circulates in the blood (bound to vitamin D binding protein) and is measured to assess status (half-life = 2 wk).
- Calcitriol is produced in the kidney to act on kidney, bone and intestine to regulate calcium balance (half-life = 2 hr).
- Calcitriol is produced in other tissues and has local effects:
  - Immune system
  - Regulation of cellular proliferation/cancer risk
Vitamin D, Calcium Balance, Bone Health and Pregnancy

Question

• What disease of children was epidemic in large industrialized cities of northern Europe during the late 19th century?

1877 Glasgow, Scotland.
Answer

• RICKETS

Rickets – Healthy - Rickets
www.talkorigins.org/faq/horns/rickets.jpg

Systemic Action - Calcium Balance

PTH = parathyroid hormone

Calcitriol and calcium

• Calcitriol does three important things to maintain blood calcium levels
  – Stimulate calcium absorption from intestine
  – Stimulate calcium release from bone
  – Cause calcium retention by the kidney

• Parathyroid hormone
  – Increases when blood calcium is low
  – Stimulates calcitriol synthesis in kidney

Clinical Vitamin D Deficiency

• Rickets (infants and children)
  – Caused by low calcium absorption
  – Results in deformities of weight-bearing bones including scoliosis (curving of spine)

• Osteomalacia, increased fracture risk in adults
  – Failure normal bone remodeling
  – Weakness, muscle or bone pain, tiredness

• Lower calcium in muscle
  – Weakness, seizures in infancy
  – Weakness, tiredness in adults
    • e.g., slower sitting-to-standing time
Question

• How common is rickets in US infants and toddlers?

• ANSWER: Not sure in US as a whole. In a large, urban pediatric clinical population in the northeastern US the prevalence was about 1% patients.
Prevalence of Rickets in Boston

- 380 healthy primary care patients 8-24 m seen from 2005-7 in pediatrics clinic who had blood drawn for clinical reasons
  - hospital based and provides well-child and acute care for 12,000 children annually
  - 80% live in adjacent urban community
  - population is primarily African American and Latino and 25% are immigrants
  - Poverty rate is 22% to 27%

Nutritional factors associated with serum 25OHD in 247 infants at their 9 m visit and 133 toddlers at their 18 m visit

Breastfeeding at 9 m and amount of milk intake at 18 m were the only significant predictors of status; race, ethnicity, sex, season, skin pigmentation, juice and cereal intake were not.

Prevalence of Deficiency

- 44 of 365 infants (12.1%) were deficient (25OHD <20 ng/mL)
- 40 of the 44 had physical exam, x-rays
  - 3 had rachitic changes
    - 7.5% of those with 25OHD <20 ng/mL
    - 0.8% of all subjects had x-ray-defined Rickets
    - One had bowed legs

*Arch Pediatr Adolesc Med. 2008;162(6):505-512*

Pregnancy
Question

• Do pregnant women have higher requirements for vitamin D? Calcium? Both? Neither?

ANSWER

– Not vitamin D.
– Only Calcium.
Calcium Requirements (and Absorption) Increase in Pregnancy

Vitamin D and Calcium in Pregnancy

- Calcium absorption increases for fetal skeletal development but is not dependent on vitamin D
- Vitamin D requirements are thus not higher in pregnancy (though calcium requirements are)
- Vitamin D deficiency in pregnancy does not cause birth defects but may affect post-natal health
- 25(OH)D crosses the placenta
  - infant umbilical cord blood level 75% of maternal level
- Infants born to deficient moms may develop rickets early in infancy, sometimes presenting with seizures before skeletal effects are evident
- Calcitriol levels increase in 3rd trimester but reason for increase is uncertain
  - Immune regulation to prevent rejection of fetus?
Serum 1,25(OH)$_2$D increases during pregnancy, perhaps to regulate the immune response to the fetus.

Innate and Adaptive Immune Responses

**First Week**
- Innate Immunity
  - **Broad Specificity**
    - Portal-of-entry defense
    - e.g., phagocytosis, antibacterial peptides
  - **Cell types:** neutrophil, monocyte/macrophage

**Weeks 1 – 4**
- Adaptive Immunity
  - **Narrow Specificity**
    - Systemic responses against specific pathogens or vaccines
    - e.g., serum antibody
  - **Cell types:** T and B lymphocytes
Vitamin D Has Two Principal Effects on the Immune System

• Vitamin D enhances some innate defenses against bacterial, viral or yeast infections
  – Example: anti-bacterial peptides produced at mucosal surfaces decreased by vitamin D deficiency
• Vitamin D is required for normal “down-regulation” of immune responses
  – Example: vitamin D may decrease inflammation late in an immune response by promoting development of regulatory T cells
  – Calcitriol production by placenta may decrease mom’s adaptive immune response against fetus

Conditions Associated With “Low” Serum 25(OH)D in Pregnancy

• Maternal Outcomes
  – Preeclampsia
  – Bacterial vaginosis
  – Gestational diabetes
  – Pre-term delivery
• Infant Outcomes
  – Skeletal development
  – Intrauterine growth retardation
  – Risk of infections in infancy, early childhood
Preeclampsia and Vitamin D Insufficiency in Pregnancy

- Preeclampsia
  - high blood pressure and protein in the urine after the 20th week of gestation
  - RX: supportive therapy, calcium (i.v.) deliver the baby (if term)
- Cause of preeclampsia may relate to maternal immune response against fetus
  - Normal part of pregnancy that may be compromised by vitamin D deficiency

Risk of small for gestational age babies higher with low and high maternal serum 25(OH)D

Summary

• Clinical vitamin D deficiency
  – Rickets in infants and children
  – Osteomalacia in adults
  – Both include decreased bone mineralization and neuromuscular effects
• Vitamin D requirements not increased in pregnancy
• Vitamin D “deficiency” may have other risks in pregnancy but no conclusions possible with current data

RDA
RDA Set in 2010

- **EAR** – Estimated Average Requirement
  - Based on intake sufficient to achieve 40 nmol/L serum 25(OH)D
- **RDA** – Recommended Daily Allowance
  - Based on intake sufficient to achieve 50 nmol/L serum 25(OH)D
  - Sufficient for 97.5% of the population
- **UL** – Upper Limit where no adverse affects have been seen

CRITERIA for Vitamin D: Optimizing calcium balance and bone health

Conceptualization of integrated bone health outcomes and vitamin D exposure

* Bone Mineral Density

Dietary Reference Intakes for Calcium and Vitamin D. 2011.
Serum 25OHD response to vitamin D intake

Vitamin D Requirements

<table>
<thead>
<tr>
<th>Age</th>
<th>EAR</th>
<th>RDA</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 m</td>
<td>-</td>
<td>400*</td>
<td>1,000</td>
</tr>
<tr>
<td>6 - 12 m</td>
<td>-</td>
<td>400*</td>
<td>1,500</td>
</tr>
<tr>
<td>1 - 5 y</td>
<td>400</td>
<td>600</td>
<td>2,500</td>
</tr>
<tr>
<td>4 - 8 y</td>
<td>400</td>
<td>600</td>
<td>3,000</td>
</tr>
<tr>
<td>9 – 70 y</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>70+ y</td>
<td>400</td>
<td>800</td>
<td>4,000</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>Lactation</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
</tbody>
</table>

*AI, not RDA; 40 IU = 1 μg

Dietary Reference Intakes for Calcium and Vitamin D. 2011.
Serum 25(OH)D and Status

• >250 nmol/L (>100 ng/mL)
  – Possible toxicity
• 75 nmol/L (30 ng/mL)
  – Suggested by some experts
• 50 nmol/L (20 ng/mL)
  – Used for RDA
• 25 nmol/L (10 ng/mL)
  – Rickets and osteomalacia

Adverse Effects

• Excessive calcium absorption may lead to kidney stones, soft tissue calcification and adverse health effects
  – Some studies show increased risk of death at high intakes of vitamin D in elderly but causal links uncertain
• Marker of potential toxicity
  – Increased urinary calcium excretion
Sources of Vitamin D - Sun

UV-B Intensity Affects Vitamin D₃ Synthesis in the Skin

• What factors determine UV Intensity?
  – Latitude: UV intensity is highest near the equator
  – Season: UV intensity is highest in summer
  – Time of Day: UV intensity is highest near noon
Question

• At what time of year is vitamin D status “best” for someone who gets regular sun exposure?
  A. Winter
  B. Spring
  C. Summer
  D. Fall

Question

• At what time of year is vitamin D status “best” for someone who gets regular sun exposure?
  A. Winter - WORST
  B. Spring – GETTING BETTER
  C. Summer – BEST
  D. Fall – GOOD, BUT TAPERING OFF
Skin Pigmentation Affects Vitamin D$_3$ Synthesis


Season and skin pigmentation affect serum 25(OH)D in Boston

Skin Types

Type 1 - light skin; always burn, never tan
Type 2 - Burn easily, hardly tan
Type 3 - sometimes burn, gradually tan
Type 4 - rarely burn, always tan
Type 5 - medium to dark skin; seldom burn, always tan
Type 6 - black skin; never burn, tan darkly

How many minutes of sun (3 - 4 days per week) do you need for “adequate” vitamin D production in Oakland?

<table>
<thead>
<tr>
<th>Skin Type</th>
<th>Winter</th>
<th>Spring</th>
<th>Summer</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>*</td>
<td>12</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Type 2</td>
<td>*</td>
<td>18</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Type 3</td>
<td>*</td>
<td>35</td>
<td>18</td>
<td>35</td>
</tr>
<tr>
<td>Type 4</td>
<td>*</td>
<td>35</td>
<td>22</td>
<td>35</td>
</tr>
<tr>
<td>Type 5</td>
<td>*</td>
<td>50</td>
<td>30</td>
<td>50</td>
</tr>
</tbody>
</table>

*little vitamin D synthesis in Winter

The UV Advantage. Michael Holick
Question

• Which of these women will have greater vitamin D synthesis at the beach today?

The one with the sunburn!
Question

• Should I recommend sun exposure to improve vitamin D status?

Answer: Probably not, though some experts recommend up to 50% of one MED for adults (i.e., if it takes you 30 min to develop sunburn than get no more than 15 min exposure) before applying sunscreen (or covering up).

• RISK: increased chance of skin cancer?
No longer recommend to prevent Rickets

Summary

• Vitamin D₃ is synthesized in the skin from sun exposure
  – Peak daily synthesis occurs at midday
  – Peak seasonal synthesis occurs in the summer
  – Clothing and sunscreen block synthesis
  – High-melanin skin requires 6X more exposure for equal synthesis
Sources of Vitamin D – Food, Supplements and Human Milk

Vitamin D from Food

• Naturally occurring vitamin D
  – Ocean fish and fish oil (but not purified fish oil supplements sold for omega-3 content)
  – Sun-exposed (sun-dried) mushrooms

• Fortified foods (mostly vitamin D$_3$)
  – Milk (100 IU/serving): nearly 100% of liquid milk products are fortified
  – Milk substitutes (e.g., soy “milk”): 50% fortified (sometimes with vitamin D$_2$
  – Breakfast cereals (40 IU/serving): 75% fortified
  – Cheese, juice, spreads: 10% fortified
  – Foods marketed to vegans contain vitamin D$_2$
Question

• What is the principal food source of vitamin D for adolescent girls?

• Answer: Milk!
Predictors of Vitamin D Intake for Girls (9-16 y) from Longitudinal Study

- white girls consume more than black
  - gap narrows as girls get older
- total intake decreases with age
- breakfast-eaters have higher intake
- greater energy intake = greater D intake
## Mean U.S. Vitamin D Intake

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Male Diet</th>
<th>Male Total</th>
<th>Female Diet</th>
<th>Female Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 3</td>
<td>288</td>
<td>364</td>
<td>276</td>
<td>336</td>
</tr>
<tr>
<td>4 – 8</td>
<td>256</td>
<td>372</td>
<td>220</td>
<td>316</td>
</tr>
<tr>
<td>9 - 13</td>
<td>228</td>
<td>300</td>
<td>212</td>
<td>308</td>
</tr>
<tr>
<td>14 -18</td>
<td>244</td>
<td>276</td>
<td>152</td>
<td>200</td>
</tr>
<tr>
<td>19 - 30</td>
<td>204</td>
<td>264</td>
<td>144</td>
<td>232</td>
</tr>
<tr>
<td>31 - 50</td>
<td>216</td>
<td>316</td>
<td>176</td>
<td>308</td>
</tr>
<tr>
<td>51-70</td>
<td>204</td>
<td>352</td>
<td>156</td>
<td>404</td>
</tr>
<tr>
<td>70+</td>
<td>224</td>
<td>428</td>
<td>180</td>
<td>400</td>
</tr>
</tbody>
</table>

*J. Nutr. 140: 817–822, 2010*
Human Milk Contains Little Vitamin D

- Vitamin D content of human milk
  ~ 1 µg/L (~ 40 IU/L)
  To achieve 400 IU intake → 10 L of milk
  Human milk ≤ 10% of formula target level
- Infant formula vitamin D target
  1-2.5 µg/kcal (40-100 IU/100 kcal)
  10 µg/L (400 IU/L)
  To achieve 400 IU intake → 1 L of milk
- Increasing breast milk vitamin D to formula level would require maternal intake of 6,000 IU per day

*Breastfeeding Medicine* Vol1, No 2, 2006

Question

- Why is vitamin D so low in breast milk?
ANSWER: Perhaps because modern humans evolved in Africa where UV exposure allowed adequate dermal vitamin D synthesis by infants as well as adults.

http://anthro.palomar.edu/culture/culture_2.htm

% US Infants Receiving Recommended Vitamin D Intake (400 IU/d)

<table>
<thead>
<tr>
<th>Age (m)</th>
<th>Total</th>
<th>Breast</th>
<th>Mixed</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>5</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>10</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>13</td>
<td>13</td>
<td>37</td>
</tr>
<tr>
<td>7.5</td>
<td>20</td>
<td>11</td>
<td>14</td>
<td>26</td>
</tr>
<tr>
<td>10.5</td>
<td>17</td>
<td>11</td>
<td>13</td>
<td>20</td>
</tr>
</tbody>
</table>

These data are from the national Infant Feeding Practices Study 2 conducted in the US from 2005-2007. 

Pediatrics 2010;125:627–632
Summary

• Principal dietary sources for women
  – Milk, other dairy, fortified foods
  – Low milk intake = low vitamin D intake
• Human milk levels are low and cannot be increased to levels adequate for infant health without exceeding the UL for maternal vitamin D intake
• Supplements (400 IU/d) recommended for exclusively breastfed infants

Risk Factors for Deficiency
Prevalence of Deficiency is Increasing
(National Health and Nutrition Examination Survey: 1988-94 vs. 2001-06)

- Serum 25(OH)D < 50 nmol/L (2001-06)
  - 32% of US population
  - >40% Hispanic/Mexican
  - >70% Non-Hispanic Black
  - Higher risk in children > 11 y
  - Higher risk with lower income
  - Higher risk in winter
  - Higher risk with no use of supplements

- Possible reasons for increase
  - Increasing obesity, decreasing activity
Serum 25OHD in 411 obese and 87 non-overweight subjects (6–16 yr old)

FIG. 1. Serum 25(OH)D concentration in obese vs. non-overweight subjects by season. Error bars denote SEM; error bars are smaller than the symbols for the obese group. P = 0.03 for interaction of group and season by ANOVA of 25(OH)D values.

### Personal Risk Factors for Poor Vitamin D Status

<table>
<thead>
<tr>
<th>Risk factors for low serum 25(OH)D</th>
<th>Women* Breastfed Infants</th>
<th>Infants</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dark skin pigment (e.g., Af. Am.)</td>
<td>+++</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>Sun avoidance and clothing</td>
<td>++</td>
<td>−</td>
<td>+/−</td>
</tr>
<tr>
<td>Low intake from food</td>
<td>++</td>
<td>NA</td>
<td>++</td>
</tr>
<tr>
<td>Lack of supplement use</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Poor maternal vitamin D status</td>
<td>NA</td>
<td>++</td>
<td>+/−</td>
</tr>
<tr>
<td>Low levels of D in human milk</td>
<td>NA</td>
<td>+++</td>
<td>NA</td>
</tr>
<tr>
<td>Obesity</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*including lactation
Beyond Bone Health: Other Conditions Associated with Vitamin D Deficiency

Criteria Used to Determine if Vitamin D Causes a Particular Disease

• Laboratory studies
  – Evidence showing how vitamin D could prevent development of a particular disease at the cellular level

• Human Studies
  – Ecological evidence
    • Is disease risk higher where vitamin D status is poor?
  – Observational studies of individuals
    • Association of intake or blood levels with risk of disease
  – Intervention trials
    • Randomize volunteers to vitamin D or “placebo” to determine if disease is prevented or severity is decreased
Cancer

- Possible mechanisms
  - Inflammation can cause cancer
    - Vitamin D can decrease inflammation (e.g., in large intestine, which is exposed to bacteria)
  - The immune system can attack tumors
    - Vitamin D may enhance anti-tumor immunity
Analyzing Data from Multiple Studies Together
(Meta-analysis of Cancer and Fracture Risk)

Institutionalized

Community-dwelling

Community with fracture history

Overall

12% decrease in fracture risk

Relationships between pre-diagnosis blood 25(OH)D concentrations and risks for cancer in individual case-control studies

Colorectal Cancer  Breast Cancer
Risks of cancer per 10 nmol/L increase in serum 25(OH)D

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Cancer</td>
<td>0.94</td>
<td>0.91-0.97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>1.01</td>
<td>0.99-1.04</td>
<td>0.35</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>0.99</td>
<td>0.97-1.01</td>
<td>0.42</td>
</tr>
</tbody>
</table>

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Hypertension

- Possible mechanisms
  - Vitamin D affects (decreases) renin levels
    - The renin-angiotensin system is an important regulator of blood pressure
  - Vitamin D may affect blood pressure by regulating vascular smooth muscle and endothelial function
Blood 25(OH)D concentration and hypertension: a meta-analysis

- 18 studies, 4 prospective and 14 cross-sectional
- 17% lower risk of hypertension in the highest (>75 nmol/L) vs. lowest (<37.5 nmol/L) category of blood 25(OH)D
- In a dose-response meta-analysis, risk decreased by 16% for every 40 nmol/L increase in 25(OH)D
- Conclusion: Blood 25(OH)D concentration is inversely associated with risk of hypertension

Effect of vitamin D supplements on blood pressure: a meta-analysis

- 11 randomized intervention trials (D₂, D₃, UV-B);
  - 8 with high baseline BP (>140/90 mm Hg) analyzed
- Meta-analysis showed a non-significant ↓ in systolic BP (-3.6 mm Hg; -8.0 to 0.7) and a small, significant ↓ in diastolic BP (-3.1 mm Hg; -5.5 to -0.6) with vitamin D treatment
- Conclusion: weak evidence to support a small effect of vitamin D on blood pressure in studies of hypertensive patients
Heart Disease

Coronary Artery Disease, Heart Failure

• Possible mechanism
  – Vitamin D is required for heart muscle "health" and normal contractile function
    • Related to sudden death due to heart failure?
  – Vitamin D may diminish inflammation related to development of arterial plaque
    • coronary artery disease
• Observational studies support a relationship of low serum 25OHD to increased risk of disease
• Intervention trials are needed to determine if associations are causal
Association between serum 25(OHD) and relative risk of developing heart disease in five longitudinal observational cohorts

QUESTION: These patients are being treated for what disease?
Patients at the J.N. Adam Memorial Hospital, a Tuberculosis sanitarium south of Buffalo, N.Y., 1920s

Image from Edward G. Miner Library, Univ. of Rochester

Tuberculosis
Activation of Alveolar Macrophage by TB Bacterium Triggers Calcitriol Synthesis and Cathelicidin Production
Liu et al. Science 311:1770 2006

TLR2 = innate immune receptor that senses presence of MTB and triggers calcitriol synthesis, which then triggers synthesis of anti-bacterial peptide cathelicidin

Vitamin D and TB

- In the pre-antibiotic area TB was treated at sanitarium with rest, good nutrition and sunshine
  - Artificial UV exposure was a particularly good treatment for cutaneous TB and development of this treatment resulted in the 1904 Nobel Prize in Medicine
- Modern studies: Serum 25OHD found to be lower in TB patients than controls
  - Meta-analysis Odds Ratio = 0.68 (0.43-0.93) for lower 25OHD in cases than controls
- Intervention trials with vitamin D
  - Few have been done and results are negative
    - For clearance of bacteria as adjunct therapy to standard antibiotics
Markers of Inflammation Decreased by Vitamin D Treatment of TB Patients

- Placebo-controlled intervention with high-dose vitamin D in 146 TB patients in London
- Many subjects vitamin D deficient at baseline
- No treatment benefit in total group
- In subgroup of 95 patients fulfilling per-protocol analysis criteria
  - Decreased time to TB clearance (sputum conversion)
  - Decreased levels of inflammation
- Conclusion: Vitamin D cause more rapid (barely) microbiological cure and decreased most markers of inflammation during recovery

Question

- What do I tell a client who asks if taking vitamin D supplements will decrease the risk of getting influenza or a cold this winter?
Question

• What do I tell a client who asks if taking vitamin D supplements will decrease the risk of getting influenza or a cold this winter?

• ANSWER: Maybe it will work (the jury is still out), but don’t exceed the UL.
  – Low serum 25OHD is associated with higher risk of colds and the flu. One study did find that vitamin D supplements decreased risk of influenza in Japanese schoolchildren.

Asthma
Asthma

• Possible mechanisms
  – Risk of asthma is associated with viral respiratory infections in infancy and vitamin D deficiency impairs host defenses against such infections
  – Vitamin D deficiency allows excessive inflammation and impairs recovery from damage due to infection
  – Vitamin D deficiency impairs normal lung function (e.g., lung volume)

• Observational studies support a relationship of low serum 25OHD to increased risk of asthma
• Intervention trials are needed to determine if associations are causal

Autoimmune Disease
Autoimmune Disease

- Autoimmune diseases result from an attack of the adaptive immune system against host cells or, possibly, normal bacterial flora
  - Multiple sclerosis (MS): target = central nervous system cells
  - Inflammatory bowl disease: target = normal gut bacteria
- Possible mechanisms for prevention by vitamin D
  - Increase protection against viral infections, which may trigger the host response to self antigens
  - Decrease inflammatory response to self antigens
- Animal models and observational studies support a relationship of poor vitamin D status to increased risk of some autoimmune diseases
- Intervention trials are needed to determine if associations are causal

Summary: Beyond Bone Health

- Vitamin D may decrease the risk of some cancers, some infectious diseases and chronic diseases caused by excessive inflammation
- The serum 25OHD levels to treat or prevent such conditions may be higher than required for optimal calcium balance
- These benefits are not yet proven and require intervention trials with vitamin D supplements to prove causality
Questions?