WHAT IS ALL THE FUSS
ABOUT VITAMIN D?

NANETTE DENDY, MD

AUGUST 23, 2014
The discovery of Vitamin D and the elimination of rickets has been considered as one of “Medicine’s Greatest Achievements”.
SIR EDWARD MELLANBY

1884-1955

A DIET CHARACTERISTIC OF SCOTLAND!

The son of a shipyard owner, he obtained a medical degree from St. Thomas Hospital in London in 1913.

A lecturer at King's College for Women 1913-1920 where he was charged with investigating the cause of rickets.

He discovered that feeding caged dogs a diet of porridge induced rickets.

He discovered he could cure the rickets with cod liver oil and concluded that rickets was caused by a dietary factor.

He published this finding in the Lancet 1919 in an article titled “An experimental investigation on rickets”.

A professor of Biochemistry at the University of Wisconsin-Madison, where he had graduated in 1916.

In 1923, Harry Steenbock demonstrated that irradiation by UV light increased the vitamin D content of foods and other organic materials.

After irradiating rodent food, he discovered that the rodents were cured of rickets.

Then invented and patented an irradiation technique used for food stuffs, most memorably for milk, to increase the content of vitamin D.

The Quaker Oats company offered him $1 million for his technology, but he believed the money should be returned to the university.

The University of Wisconsin-Madison's Steenbock Memorial Library is still named in his honor.

Published his findings in Science in December 1924, "The induction of growth promoting and calcifying properties in a ration by exposure to light"
THE FUSS IS NOT SO NEW!

Science (Oct. 20, No. 1344)

Bengal Galapagos has been a name with which to conjure up visions of a vast repulsive life, giant turtles, otter penguins, frogs, and snakes uninstructed by man and of a marine life brilliant and rare as only the tropics can produce. Expeditions have come and gone from these volcanic wastes and have reported their biological finds with elaborate technical detail and an over-emphasizing of connotations of interpretation as to the species limits and relationships of the isolated fauna of the various islands of the archipelago. Have for the herpetologist, ornithologist, cactiologist, or other specialist for the scintillating shows of the many problems of evolution, geographical distribution, isolation and animal behavior, these self-elected reports make the rousing in the words of Mr. Basho's, "World's End.'"

This entertaining work is the outcome of an expedition in the private yacht "Sirena" to several islands off this area last September in 1929. In all less than one hundred hours were spent in exploring, mostly on five of the smaller islands of the group, Enez, Gato Funchal, Dagron, Seymour, and Sumo. Excellent use was made of the time, however, and the story of adventure amidst the turbulent breakers, head swell and rough seas, and the voluminous letters home only of interest at the hands of this fast, brilliant and sympathetic interpreter of nature and life.

This reviewer can only attest to the biological problems involved in the adaptations exhibited by the species of animals inhabiting these wastes and desolate desert islands and islets. The mangrove is extending, and the distance of distance to any land or land such as in the balance of nature. Man and the animals introduced by him have been the great disturbing factor in the island's natural history. The giant tortoises are now seen partially exterminated and will not survive unless protected. On the other hand, the absence of mammalian mammals in the native fauna has made the tortoise the subject of the naturalist. If the tortoise can be kept in another sense, it is not a menace. This reviewer is inclined to believe that the tortoise is an endangered species.

Table 2 will show comparisons of the tortoise, but it is not clear that the tortoise should be considered a species endangered or endangered species. The tortoise is not known to exist in the wild, and the tortoise is not always considered a species endangered or endangered species.
THE FUSS IS ONGOING!

Google search for Vitamin D deficiency latest news (for the last 24 hours on July 24, 2014)....>18,000 hits.


WHAT DO WE NEED TO KNOW?

GOALS FOR TODAY:

1. To review the basics of the physiological functions of Vitamin D.
2. To know some of the associations of Vitamin D to problems we encounter in clinical practice today.
   - Heart Disease
   - Depression
   - Malignancy
   - Osteoporosis
3. To review some of the evidence FOR and the evidence AGAINST screening and treatment of Vitamin D deficiency. (What are the guidelines?)
GOAL 1: THE PHYSIOLOGY
WHERE DO WE FIND IT?

It is fat soluble.

It is scarce in the food supply.

Not typically found in plant material except in rare cases of some waxy-leaf varieties (Solanum glaucophyllum).

Found in low quantities in meats and other animal food sources such as fish liver oils.

The major source is produced though in the skin through a photolytic process, where 7-dehydrocholesterol \(\rightarrow\) Vitamin D.
VITAMIN D3

Structure of vitamin D3, or cholecalciferol, and its numbering system.
FIND IT
Vitamin D3 is biologically inert, thus Vitamin D must be hydroxylated to the active form 1, 25-dihydroxyvitamin D.

Vitamin D3 is converted in the liver to 25-hydroxyvitamin D (THE MAJOR CIRCULATING FORM OF VIT D, ALTHOUGH INACTIVE).

25-hydroxyvitamin D is converted in the kidney to 1, 25-dihydroxyvitamin D (THE ACTIVE FORM OF VITAMIN D).
Metabolic activation of vitamin D3 to its hormonal form, 1,25(OH)2D3.

Vitamin D3 → Liver microsomes (mitochondria) → 25-hydroxyvitamin D3 → Kidney mitochondria → 1α, 25-dihydroxyvitamin D3
NOW, ONCE THAT IT IS CONVERTED TO AN ACTIVE FORM, WHAT IS THE PHYSIOLOGICAL FUNCTION OF VITAMIN D?

*In short...main physiological function is to maintain plasma calcium concentrations at a very constant level.*

**HOW?**

1. **Inducing proteins involved in active intestinal calcium absorption**

2. **Mobilizing (along with PTH) calcium from bone**
   - By stimulating osteoblasts to produce a factor (RANKL) that stimulates osteoclastogenesis and activates resting osteoclasts for bone resorption.

3. **Stimulating reabsorption of calcium (along with PTH) at the distal renal tubule**
   - By working together to reabsorb the last 1% of filtered calcium.
   - This is a significant amount, given an average of 7 grams of calcium are filtered daily.
Diagrammatic representation of the role of the vitamin D hormone and the parathyroid hormone (PTH) in increasing plasma calcium concentrations to prevent hypocalcemic tetany (neuromuscular) and to provide for mineralization of the skeleton.
WHAT ARE SOME OF THE ADDITIONAL ACTIONS OF 1,25 (OH)2D?

The vitamin D receptor is present in most tissues and cells in the body. It is already known to have further, diverse biological effects.

- Inhibiting cellular proliferation
- Inducing terminal differentiation
- Stimulating insulin production
- Inhibiting renin production
- Stimulating its own destruction by enhancing the expression of the 25-hydroxyvitamin D-24-OHase
- Etc.

- THESE ALL SUGGEST A POSSIBLE ROLE OF VITAMIN D IN AREAS OTHER THAN THE REGULATION OF BONE MINERALIZATION.
GOAL 2: ASSOCIATIONS?

What is the evidence that Vitamin D is linked to:

1. Heart Disease?
2. Depression?
3. Malignancy?
4. Osteoporosis?

Let’s take a look at some of the data.
HEART DISEASE

1,25 (OH)2 vitamin D is known to regulate the renin-angiotensin system in animal studies. Mice with null Vitamin D receptor or with inborn deficiency of the 1 alpha-hydroxylase gene develop high renin hypertension and cardiac hypertrophy. In vivo, vascular endothelial and smooth muscle cells respond to exposure to 1,25 (OH)2 vitamin D with reduced thrombogenesis and increased fibrinolysis.

So, is there an association?
HEART DISEASE

**10/08 J Clini Endocrinol Metab**  Published cross-sectional study 3299 Caucasian patients referred for coronary angiography b/w 1997-2000.

- Compared patients with 25(OH)vit D levels <25 to patients with 25(OH) vitamin D levels >75.
- A median f/u time of 7.7 years.
- A higher rate of death due to heart failure and sudden cardiac death in patients with levels <25.

**12/08 Am J Cardiology**  Published cross-sectional study using data from NHANES 2001-2004 with 25(OH) vitamin D divided into >30, 20-29, <20.

- Controlled for age, race and gender.
- A statistically significant increased burden of CAD, HF, CVA and PAD in an inverse proportion to vitamin D concentrations.
HEART DISEASE

10-12/11 J Cardiovasc Pharmocol Ther  A comprehensive review of current evidence quoting the prevalence of Low D varying from approximately 80-95% in patients with HF.

”We believe more trials on vitamin D therapy in HF need to be conducted before any conclusions can be drawn.”
HEART DISEASE

*So, is there an association?*......It seems so.
HEART DISEASE

Does intervention make a difference?

3/10 Annals of Internal Medicine Published a systematic review of 13 observational studies and 18 trials.

- "Trials thus far show no consistent, statistically significant effect of vitamin D supplementation on blood pressure or glycemic or cardiovascular outcomes”.

7/11 J Clin Endocrinol Metabol Published a systematic Review and meta-analysis including 51 studies.

- Pooling across studies showed a non-significant and potentially trivial reduction in mortality that was consistent across studies (RR, 0.96; 95% CI, 0.93, 1.00; P = 0.08; I² = 0%) (Fig. 1).
FIGURE 1: FOREST PLOT REPRESENTING THE POOLED RESULT OF MORTALITY, MI, AND STROKE
A retrospective, observational study out of the University of Kansas examined the associations between vitamin D deficiency, vitamin D supplementation and patient outcomes in a cohort of >10,000 patients with known Cardiovascular-related diseases (HTN, CAD, CM, DM).

- Normal vitamin D >30 ng/ml; deficiency <30 ng/ml.
- 3294 patients in the normal range.
- 7665 patients in the deficient range.
- Followed 5 years and 8 months.

Vitamin D deficiency was a strong independent predictor of all-cause death (odds ratios 2.64, 95% confidence interval 1.901-3.662, p<0.0001).

Vitamin D supplementation conferred substantial survival benefit (odds ratio for death 0.39, 95% confidence interval 0.277 to 0.534, p<0.0001).

The authors note that they did not specify dosage amounts.
Figure 1. Survival in vitamin D deficient vs vitamin D sufficient patients.
Figure 2. Survival stratified by vitamin D supplementation in deficient subjects.

Significant differences in survival seen only for the vitamin D–deficient patients ($p < 0.0001$) on repeat separate modeling stratified by deficiency (Figure 2). Nondeficient subjects had no survival advantage with vitamin D supplementation.
HEART DISEASE

Does intervention make a difference?
Presently....limited randomized controlled studies.
DEPRESSION

The vitamin D receptor and the 1-alpha-hydroxylase enzyme that converts Vitamin D to its active form are expressed in the human brain, affecting neuronal proliferation, differentiation, migration and apoptosis.

......So is there an association?
DEPRESSION

10/11 J Psychopharmacol  3369 male patients with a mean age 60 (+/- 11) participating in the European Male Ageing Study were screened using Beck Depression Inventory and vitamin D levels were measured.

- After adjustments for lifestyle and other health factors, there was an inverse association b/w 25 (OH) vitamin D levels and depression.
DEPRESSION

2013 *J Nutr Health and Aging* Performed a meta-analysis of 16 studies.

- Included approximately 55,000 patients.
- 25(OH)D levels were significantly inversely associated with depression in 5 of 11 case-control studies and 2 of 5 cohort studies.
DEPRESSION

*Is there an association?* .... *Yes, there seems to be an association.*
DEPRESSION

Does intervention make a difference?

3/14 J Clin Endocrinol Metab Investigated 6 Randomized Controlled Trials with 1203 patients.

-The classical meta-analysis showed no significant effect of Vitamin D supplementation on post-intervention depression scores. (standardized mean difference = -0.14, 95% confidence interval = -0.41 to 0.13, P = .32; odds ratio = 0.93, 95% confidence interval = 0.54 to 1.59, P = .79).

-The quality of evidence was low.

-Similar results were found when Bayesian meta-analyses were applied.
DEPRESSION

Does intervention make a difference? .......It doesn’t seem so, at this time.
CANCER

*In vitro studies have shown that the active form of Vitamin D can decrease cell proliferation.*

*In animal studies, deficiency of the vitamin D receptor (VDR) predisposes to precancerous lesions of the breast and intestine.*

....So is there an association?
The meta-analysis for the recommendations to US Preventive Task Force on Vitamin D with or without Calcium for Prevention of Cancer and Fractures was published.

- The task force was charged with a number of questions.

What is the association b/w vitamin D status and cancer?

+ 28 observational studies on baseline vitamin D status and risk for total cancer, colorectal, prostate or breast cancer.

+ 1 = good; 17 = fair; 10 = poor quality

+ mean f/u 7-14 years
CANCER

ALL STUDIES OBSERVED HIGHER BASELINE VIT D CONCENTRATIONS WITH INCREASED RISK FOR TOTAL CANCER MORTALITY AMONG MEN, BUT NOT AMONG WOMEN.

*Let’s take a closer look.....*
1. Colorectal cancer.

-Meta-analysis of 9 nested case-control studies showed that each 10 nmol/L increase in pre-diagnosis vitamin D concentration was associated with a 6% reduction in risk.
2. Prostate cancer.

- Meta-analysis of 3 *poor*-quality studies provided insufficient data.
- Some individual studies were mixed.
- Some individual studies had a non-linear relationship.
CANCER

   - 1 poor quality study with insufficient data.
   - 4 studies with higher pre-diagnosis level showed lower risk.
   - 4 case-control studies showed no association.
CANCER

*Is there an association?*......Unclear.
Does intervention make a difference?

12/11 Annals of Internal Medicine Reviewed a total of 6 RCT’s of Vitamin D vs placebo and Vitamin D plus calcium vs placebo.

- Included a wide range of patients across the trials (elderly men, healthy postmenopausal women, studies of the UK, Nebraska and WHI).

->50,000 patients.

- Again, mixed results.

- Example, Vit D vs placebo: “On the basis of the CIs, one cannot rule out the possibility of clinically important effects in risk in either direction. For example, a protective effect of at least 14% reduction in risk or a harmful effect of at least 20% increase in risk.”

- Nebraska trial reported a 60% reduction in risk for total cancer.
## Table 1: Key Questions and Summary of Evidence Reviewed

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<th>KQs and Comparisons of Interest</th>
<th>Outcomes</th>
<th>Studies (Total Sample Size)</th>
<th>Methodologic Quality</th>
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| **KQ 1: What are the effects of vitamin D with or without calcium supplements on the clinical outcomes of cancer and fractures in RCTs? (overarching question)** | Vitamin D supplementation vs. placebo* | Total cancer | 2 RCTs (n = 3577) | 2 fair | 4–5 y | 1 RCT in elderly men and women, aged ≥71 y (n = 2688)  
- Incidence: HR, 1.08 (95% CI, 0.86–1.36)  
- Mortality: HR, 0.96 (CI, 0.77–1.13) | Supplement 1 |
| | | Colorectal cancer | 1 RCT (n = 2686) | 1 fair | 5 y | Incidence: HR, 1.02 (CI, 0.60–1.74)  
- Mortality: HR, 0.62 (CI, 0.24–1.60) | Supplement 1 |
| | | Breast cancer | 1 RCT (n = 2686) | 1 fair | 5 y | Incidence: HR, 0.99 (CI, 0.25–4.0)  
- Mortality: NR | Supplement 1 |
| | | Fracture | 5 RCTs (n = 14 583) | 1 good  
- 3 fair  
- 1 poor | 7 mo–5 y | Meta-analysis of 5 RCTs in elderly men and women (n = 14 583)  
- Overall: RR, 1.03 (CI, 0.84–1.26)  
- Institutionalized: RR, 0.99 (CI, 0.72–1.34)  
- Community-dwelling: RR, 1.06 (CI, 0.72–1.46) | Supplement 2 |
| | **Combined vitamin D and calcium supplementation vs. placebo** | Total cancer | 2 RCTs (n = 37 016) | 1 good  
- 1 fair | 4–7 y | 1 RCT in postmenopausal women, aged ≥55 y (n = 7934)  
- Incidence: HR, 0.40 (CI, 0.20–0.82)  
- Mortality: HR, 0.23 (CI, 0.09–0.60) | Supplement 1 |
| | | Colorectal cancer | 1 RCT (n = 36 282) | 1 good | 7 y | Incidence: HR, 0.98 (CI, 0.91–1.05)  
- Mortality: HR, 0.89 (CI, 0.77–1.03) | Supplement 1 |
| | | Breast cancer | 1 RCT (n = 36 282) | 1 good | 7 y | Incidence: HR, 0.82 (CI, 0.52–1.29)  
- Mortality: HR, 0.96 (CI, 0.86–1.07) | Supplement 1 |
| | | Fracture | 11 RCTs (n = 52 915) | 2 good  
- 5 fair  
- 4 poor | 1–7 y | Meta-analysis of 11 RCTs in mostly (69%) postmenopausal women (n = 52 915)  
- Overall: RR, 0.88 (CI, 0.79–0.99)  
- Institutionalized: RR, 0.71 (CI, 0.57–0.89)  
- Community-dwelling: RR, 0.89 (CI, 0.76–1.04)  
- Community-dwelling with history of fracture: RR, 1.02 (CI, 0.89–1.16) | Supplement 2 |
| **KQ 2: What are the associations between vitamin D status and the clinical outcomes of cancer and fractures in observational studies?** | Dose–response relationship between 25-OH-D concentrations at baseline and risk for cancer | Total cancer | 3 prospective cohort studies (n = 19 503) | 1 good  
- 2 fair | Mean, 7–14 y | Higher 25-(OH)D concentrations were associated with increased risk for total cancer mortality in men, but the ranges of 25-(OH)D concentrations varied across studies  
One study found that baseline blood 25-(OH)D concentration was not associated with risk for total cancer mortality in adult women (n = 8914) | Supplement 3; Supplement 4 |
| | | Colorectal cancer | 9 nested case–control studies (3136 cases) | 8 fair  
- 1 poor | NA | Linear dose–response meta-analysis of 9 studies  
Pooled adjusted OR, 0.94 (CI, 0.91–0.97) per 10-nmol/L increase in 25-(OH)D concentration | Supplement 3 |
| | | Prostate cancer | 11 nested case–control studies (4005 cases) | 4 fair  
- 7 poor | NA | Linear dose–response meta-analysis of 8 studies  
Pooled adjusted OR, 1.01 (CI, 0.99–1.04) per 10-nmol/L increase in 25-(OH)D concentration | Supplement 3 |
CANCER

Does intervention make a difference? .......Unclear.
OSTEOPOROSIS

1, 25 (OH)2 Vitamin D enhances intestinal absorption of calcium and phosphate.

It is important for optimal muscle function and balance.

Low concentrations of vitamin D cause a compensatory risk in PTH, which results in bone resorption.

So, is there an association?
OSTEOPOROSIS

-Known for a century vitamin D deficiency causes rickets.

-Complicated by secondary hyperparathyroidism and calcium insufficiency.
OSTEOPOROSIS

12/11 Annals of Internal Medicine  The meta-analysis for the recommendations to US Preventive Task Force on Vitamin D with or without Calcium for Prevention of Cancer and Fractures was published.

- Examined 16 studies.
- 5 Vitamin D vs placebo.
- 11 Vitamin D + Ca vs placebo.

RESULTS: Combined vitamin D and calcium supplementation can reduce fracture risk.

BUT....the effects may be smaller among community-dwelling older adults than among institutionalized elderly persons.

One RCT showed adverse outcomes associated with supplementation, including increased risk for renal and urinary tract stones.
### Table 1. Key Questions and Summary of Evidence Reviewed

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<td>Fracture</td>
<td>15 studies (3 prospective cohorts and 12 case–control studies) reviewed in the University of Ottawa Evidence-based Practice Center evidence report (B)</td>
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<td>Overall, there is inconsistent evidence for an association between serum 25(OH)D concentrations and the risk for fractures One of 3 cohorts reported an inverse association between blood 25(OH)D concentrations and fracture rates, and 9 of 12 case–control studies found significantly lower 25(OH)D concentrations in cases vs. controls.</td>
<td>Supplement 3</td>
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</table>
OSTEOPOROSIS

Does intervention make a difference?....
GOAL 3: SUMMARY OF THE EVIDENCE

What are the guidelines?

....I’ll give you 2 opinions.

USPTF: Screening for Vitamin D deficiency→Draft→“Evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency”. I Statement.
### VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS-USPTF

<table>
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<th>Population</th>
<th>Men or premenopausal women</th>
<th>Community-dwelling postmenopausal women at doses of &gt;400 IU of vitamin D$_3$ and &gt;1,000 mg of calcium</th>
<th>Community-dwelling postmenopausal women at doses of ≤400 IU of vitamin D$_3$ and ≤1,000 mg of calcium</th>
</tr>
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<tbody>
<tr>
<td><strong>Recommendation</strong></td>
<td>No recommendation. Grade: I statement</td>
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<td>Do not supplement. Grade: D recommendation</td>
</tr>
<tr>
<td><strong>Preventive Medications</strong></td>
<td>Appropriate intake of vitamin D and calcium are essential to overall health. However, there is inadequate evidence to determine the effect of combined vitamin D and calcium supplementation on the incidence of fractures in men or premenopausal women.</td>
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<td>There is adequate evidence that daily supplementation with 400 IU of vitamin D$_3$ and 1,000 mg of calcium has no effect on the incidence of fractures in postmenopausal women.</td>
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<td>There is inadequate evidence regarding the effect of higher doses of combined vitamin D and calcium supplementation on fracture incidence in community-dwelling postmenopausal women.</td>
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<td><strong>Balance of Benefits and Harms</strong></td>
<td>Evidence is lacking regarding the benefit of daily vitamin D and calcium supplementation for the primary prevention of fractures, and the balance of benefits and harms cannot be determined.</td>
<td>Evidence is lacking regarding the benefit of daily supplementation with &gt;400 IU of vitamin D$_3$ and &gt;1,000 mg of calcium for the primary prevention of fractures in postmenopausal women, and the balance of benefits and harms cannot be determined.</td>
<td>Daily supplementation with ≤400 IU of vitamin D$_3$ and ≤1,000 mg of calcium has no net benefit for the primary prevention of fractures.</td>
</tr>
</tbody>
</table>
**VITAMIN, MINERAL, AND MVI SUPPLEMENTS FOR PRIMARY PREVENTION OF CANCER AND CVD-USPTF**

<table>
<thead>
<tr>
<th>Population</th>
<th>Healthy adults without special nutritional needs. This recommendation does not apply to children, women who are pregnant or may become pregnant, or persons who are chronically ill or hospitalized or have a known nutritional deficiency.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong></td>
<td>Multivitamins: No recommendation. Grade: I statement</td>
</tr>
<tr>
<td><strong>Preventive Medications</strong></td>
<td>Evidence on supplementation with multivitamins to reduce the risk for cardiovascular disease or cancer is inadequate, as is the evidence on supplementation with individual vitamins, minerals, or functional pairs. Supplementation with β-carotene or vitamin E does not reduce the risk for cardiovascular disease or cancer.</td>
</tr>
<tr>
<td><strong>Balance of Benefits and Harms</strong></td>
<td>The evidence is insufficient to determine the balance of benefits and harms of supplementation with multivitamins for the prevention of cardiovascular disease or cancer.</td>
</tr>
<tr>
<td><strong>Other Relevant USPSTF Recommendations</strong></td>
<td>The USPSTF has made several recommendations on the prevention of cardiovascular disease and cancer, including recommendations for smoking cessation; screening for lipid disorders, hypertension, diabetes, and cancer; obesity screening and counseling; and aspirin use. These recommendations are available at <a href="http://www.uspreventiveservicestaskforce.org">http://www.uspreventiveservicestaskforce.org</a>.</td>
</tr>
</tbody>
</table>
WHAT ARE THE GUIDELINES REGARDING VITAMIN D?

Based on the Endocrine Society Practice Guidelines published 7/11:

1. Screen only individuals at Risk

J. Clin Endocrinololgy Metab, July 2011
2. Only use the serum circulating 25 (OH) vitamin D for screening.
   - Insufficiency defined as 21-29 ng/ml.
   - Deficiency as <20 ng/ml.
3. Adults aged 19-50 require at least 600 IU/d to maximize bone health and muscle function.
   - May require 1500-2000 IU/d to raise blood level consistently above 30 ng/ml.

4. Adults aged 50-70 require 600 IU/d of vitamin D to maximize bone health and muscle function, but those 65+ are recommended 800 IU/d for the prevention of falls and fracture.
   - May require 1500-2000 IU/d to raise blood level consistently above 30 ng/ml.
GUIDELINES- THE ENDOCRINE SOCIETY

5. Use either Vitamin D2 or Vitamin D3 for the treatment or prevention of Vitamin D deficiency.

- 50,000 IU of Vitamin D2 or Vitamin D3 once a week x 8 weeks
- 6000 IU per day of Vitamin D2 or Vitamin D3 x 8 weeks
- check level to ensure above 30 ng/ml
- place on maintenance therapy of 1500-2000 IU/d
6. In obese patients, patients with malabsorption syndromes, and patients on medications affecting vitamin D metabolism, will need higher dosing (2-3x higher).

- 6000-10,000 IU/d until the level gets over 30 ng/ml.

- then followed by maintenance therapy of 3000-6000 IU/d.
7. It is recommended to prescribe vitamin D supplementation for fall prevention.

8. Currently, there is no recommendation for supplementation to prevent cardiovascular disease, malignancy or in the treatment of depression.
WHAT TO TAKE BACK TO MY PRACTICE?

Goal 1: To know the basics of the physiological functions of Vitamin D.

Main physiological function is to maintain plasma calcium concentrations at a very constant level, but so much more!
Goal 2: To know some of the associations of Vitamin D to problems we encounter in clinical practice.

- Heart Disease
- Depression
- Malignancy
- Osteoporosis

*There are some associations!*
Goal 3: To know some of the evidence FOR and the evidence AGAINST screening and treatment of Vitamin D deficiency. (What are the guidelines?)

*Screen those at risk.*

*Treat those who are deficient.*

*Prescribe to those at risk for falls.*
GET YOUR VITAMIN D