

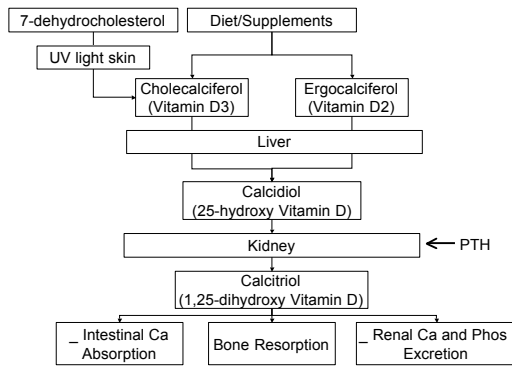
Update in Vitamin D Deficiency

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Case: Assessment

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

Vitamin D Metabolism



Vitamin D Deficiency Disorders

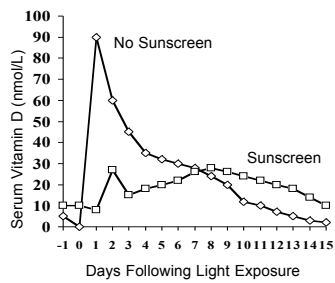
- Primary or Congenital Vitamin D Deficiency
- Acquired Vitamin D Deficiency:
 - Poor intake or Malabsorption
 - Inadequate sunlight
 - Liver disease
 - Renal disease
 - Hypoparathyroidism
 - Obesity
 - Medications

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

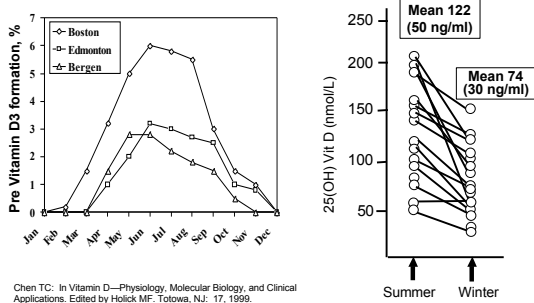
Factors Affecting Vitamin D Production: Sunscreen

Sunscreen with an SPF of 8 inhibits 97.5% of vitamin D production



Matsuoka LY, et al. JCEM. 64:1165-1168, 1987.

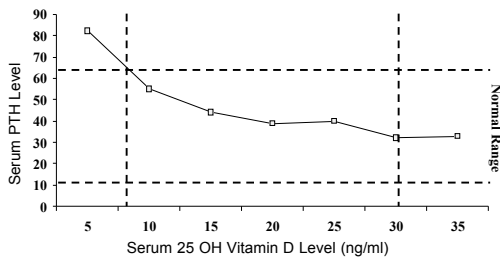
Seasonal Variation of Vitamin D Levels



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

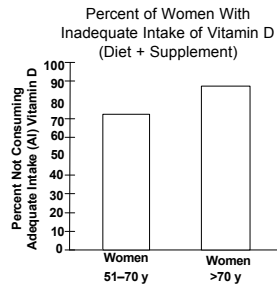
Vitamin D Deficiency Secondary Hyperparathyroidism



Thomas M. N Engl J Med 1996; 338:777

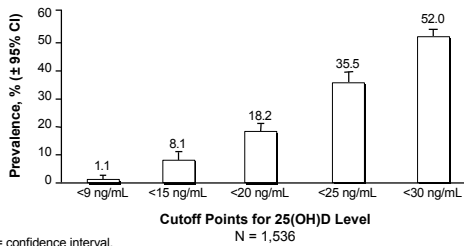
The Majority of American Women Are Not Receiving Adequate Intake of Vitamin D

- 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.
Moore C et al. *J Am Diet Assoc.* 2004;104:980-983.

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

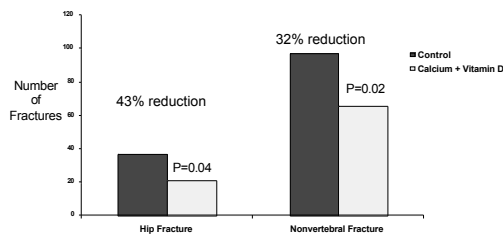


CI = confidence interval.

Holick MF. *J Clin Endocrinol Metab.* 2005;90:3215-3224.

Osteoporosis Treatment Calcium and Vitamin D

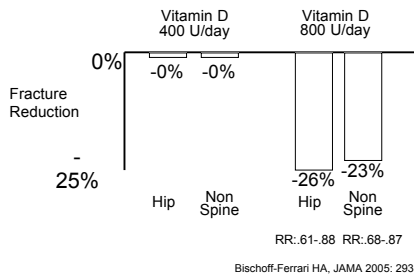
RCT: 3270 healthy elderly women (mean age: 84 yr.)
Calcium (1,200 mg) + Vitamin D (800 IU) vs. Control over 18 mo.



Chapuy M. *NEJM* 1992; 327:1637-42

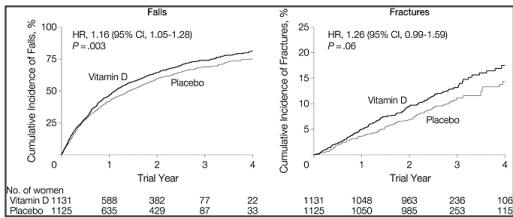
Vitamin D Therapy Fracture Data – Meta-analysis

7 RCTs of Vitamin Supplements in Osteoporotic Patients
Compared to Calcium or Placebo



Vitamin D Therapy Annual High-Dose Oral Vitamin D

500,000 IU of cholecalciferol vs placebo annually
in 2,256 older women (>70yo)



Sanders KM et al, JAMA 2010; 303:1815-22.

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

Pittas et al. *J Clin Endocrinol Metab* 2007;92:2017

Vitamin D and 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

Vitamin D and Type 2 Diabetes

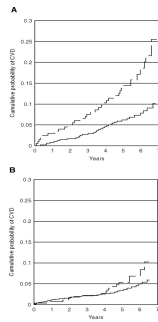
- **Intervention studies:**
 - Paucity of data
 - Some evidence of improved glucose tolerance in treatment of severe vitamin D deficiency
 - Mixed results from treating individuals with IGT or T2D with vitamin D
 - No benefit in individuals without vitamin D deficiency

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?



Wang, T. J. et al. *Circulation* 2008;117:503-511

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

Source	Vitamin D Content
Natural sources	
Salmon	
Fresh, wild (3.5 oz)	About 600-1000 IU of vitamin D ₃
Fresh, farmed (3.5 oz)	About 100-250 IU of vitamin D ₃ or D ₂
Canned (3.5 oz)	About 300-400 IU of vitamin D ₃
Sardines, canned (3.5 oz)	About 300 IU of vitamin D ₃
Mackerel, canned (3.5 oz)	About 230 IU of vitamin D ₃
Tuna, canned (3.6 oz)	About 230 IU of vitamin D ₃
Cod liver oil (1 tsp)	About 400-1000 IU of vitamin D ₃
Shiitake mushrooms	
Fresh (3.5 oz)	About 100 IU of vitamin D ₂
Sun-dried (3.5 oz)	About 1600 IU of vitamin D ₂
Egg yolk	About 20 IU of vitamin D ₂ or D ₃
Exposure to sunlight, ultraviolet B radiation (0.5 minimal erythral dose ¹)	About 3000 IU of vitamin D ₃
Fortified foods	
Fortified milk	About 100 IU/8 oz, usually vitamin D ₃
Fortified orange juice	About 100 IU/8 oz vitamin D ₃
Infant formulas	About 100 IU/8 oz vitamin D ₃
Fortified yogurts	About 100 IU/8 oz, usually vitamin D ₃
Fortified butter	About 50 IU/3.5 oz, usually vitamin D ₃
Fortified margarine	About 430 IU/3.5 oz, usually vitamin D ₃
Fortified cheeses	About 100 IU/3 oz, usually vitamin D ₃
Fortified breakfast cereals	About 100 IU/serving, usually vitamin D ₃

Holick. *N Engl J Med.* 357:266-281, 2007

Vitamin D and Sun Exposure

- One minimal erythmal 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

Vitamin D2	Ergocalciferol
Vitamin D3	Cholecalciferol
25 (OH) Vitamin D	Calcifediol
1,25 (OH) ₂ Vitamin D	Calcitriol

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
