

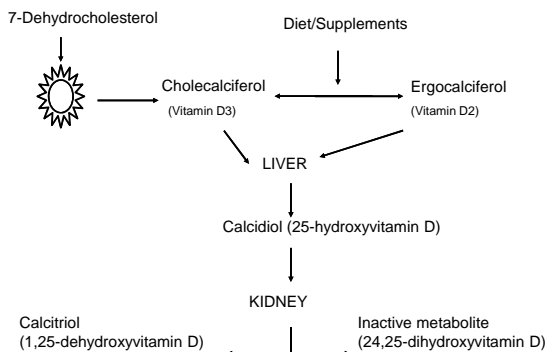
Vitamin D Deficiency

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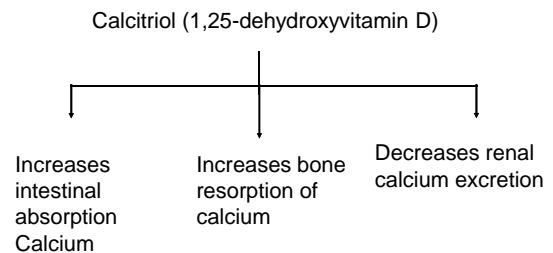
Clinical Case

BD is a 67- year female with PMHx of HTN, hyperlipidemia, OA and varicose veins. She presents for her medicare wellness. She has a negative falls screening. She has a BMI of 28.2 and otherwise negative exam. She had a DEXA at age 65 which showed t-score of -1.1. She has been tired of late with aching muscles and requests for all her vitamins to be checked.

Normal Vitamin D Physiology



Normal Vitamin D Physiology



Definitions of Normal and Deficiency

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- Low <20
- Optimal-???
- 20-40 ng/mL- IOM,
- 30-50 ng/ml- ENDO, NOF, AGS, IOF
- Undetermined safe upper limit
- Racial differences

Definitions of Normal and Deficiency- criteria to define optimal levels

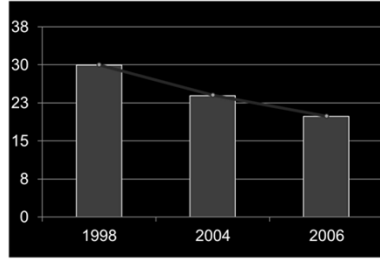
- Maximal suppression PTH
- Adequate intestinal calcium absorption
- Fracture prevention

Definitions of Normal and Deficiency- criteria to define optimal levels

- Maximal suppression PTH= 27.5 to 30 ng/mL
- Adequate intestinal calcium absorption- 4.4 ng/mL
- Fracture prevention- 28-40 ng/mL

Prevalence of Vitamin D

- NHANES data
- Mean Vitamin D 25 (OH) in ng/mL



Symptoms of Deficiency

Symptoms of Deficiency

- Overt:
- Subclinical
- Nonskeletal

Symptoms of Deficiency

- Overt:
 - Hypocalcemia
 - Rickets
 - Osteomalacia
- Subclinical
 - Osteoporosis
 - Muscle pain/weakness, fatigue, falls
- Nonskeletal

Symptoms of Deficiency: Muscle pains

- MayoClinic Proc 2003
- *Prevalence of severe hypovitaminosis D in patients with persistent nonspecific musculoskeletal pain*
- 150 patients presented consecutively between February 2000 and June 2002 with persistent, nonspecific musculoskeletal pain to the Community University Health Care Center, a university-affiliated inner city primary care clinic in Minneapolis, Minn (45° north). Ages 10-65. 6 ethnic groups

Symptoms of Deficiency: Muscle pains

- 93% (140/150) <20 nl/mL in all
- 100% below 20 ng/mL
 - African Americans, East Africans, American Indians
- Levels of vitamin D in men were as deficient as in women ($P = .42$)
- not seasonal

Effects of Deficiency- Nonskeletal

- VitaminD receptor (VDR) - expressed in all nucleated cells
- 3% of human genome is under control of 1,25 dihydroxyvitamin D
- 10 tissues other than kidney express 1-alpha-hydroxylase

Effects of Deficiency- nonskeletal

- Falls
- Cancer
- CV system
- Diabetes
- Immune System
 - MS
 - Asthma
 - URI
 - mortality

**Effects of
Deficiency-
nonskeletal
Falls**

- Several metanalysis decrease risk as high as 20%
- Metanalysis not showing reduction falls in community-dwelling adult

**Symptoms of
Deficiency:
Falls**

- Annual high-dose oral vitamind and falls and fractures in older women: a randomized controlled trial. JAMA 2010;303:1815
- Effect of four monthly oral vitamin D supplementation fracture and mortality in men and women living in the community: randomized double blind controlled study. BMJ 2003;326:469

**Effects of Deficiency-
Cancer**

- Colon Cancer
- Breast Cancer

**Effects of
Deficiency-
Cancer**

- Colon Cancer
- WHO
- for each 4nl/mL increase in pre diagnosis serum 25(OH)D concentration, there was a 6% reduction colorectal cancer risk. ANN INTer Med 2011;155:827
- can elevate risk of pancreatic cancer if >40 ng/ml

**Effects of Deficiency-
Cancer**

- **Breast Cancer**
- **observational studies: inconsistent**
- **Prospective studies: possibly**
- **metanalysis showed inverse relation between cancer risk between 27 and 35 ng/ml in post- but not pre-menopausal women. Medicine(Baltimore) 2013; 92:123**

**Effects of Deficiency-
Cardiovascular**

- **Blood pressure: observational studies show inverse associated between 25 OH D and blood pressure. no effect with supplementation**
- **CV events: Prospective meta-analysis with inverse relationship between 25(OH)D and CVD. no effect with treatment**

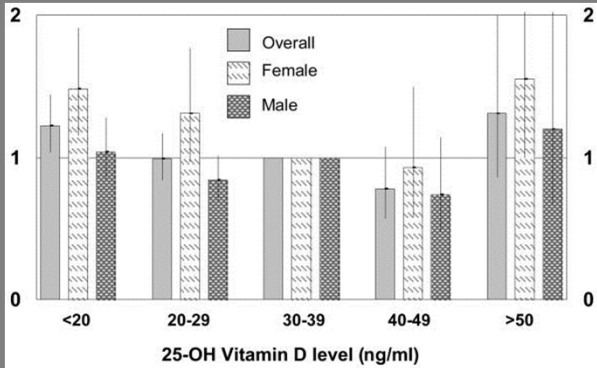
**Effects of Deficiency-
Immune system**

Disease	Prospective studies	Randomized control trials
Multiple sclerosis	+	-
Asthma	?	-
Tuberculosis	+	-
URI	+	-
COPD exacerbation	-	-

**Effects of Deficiency-
nonskeletal
Endocrine**

- **Diabetes type 1: mixed results suggesting link**
- **Diabetes type 2: prospective meta-analysis showed inverse relation between 25 (OH)D and risk of diagnosis. interventional studies negative or limited beneficial effects of supplementation**

Effects of Deficiency- Mortality



Melamed ML, Michos ED, Post W, Astor B. 25-Hydroxyvitamin D Levels and the Risk of Mortality in the General Population. *Arch Intern Med.* 2008;168(15):1629-1637. doi:10.1001/archinte.168.15.1629

High Risk Groups for Deficiency

- darker skin
- obese
- meds that accelerate vitamin d metabolism
- hospitalized on gen med service
- institutionalized
- limited sun exposure
- osteoporosis
- malabsorption

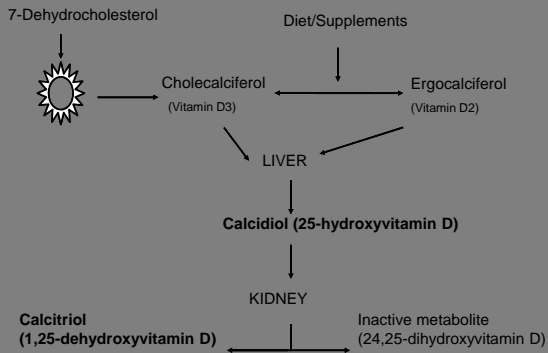
Whom to test

USPSTF 11/2014: in community-dwelling, nonpregnant, asymptomatic adults age 18 years and older, the USPSTF concludes that the current evidence is insufficient to assess the balance of benefit and harms of screening for vitamin D deficiency
High risk groups

Laboratory testing

- Vitamin D 25 (OH)
- Vitamin D 1,25 (OH)
- total Vitamin d= 25 (OH) and 1,25 (OH)

Normal Vitamin D Physiology



Laboratory testing

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

Laboratory testing

- Vitamin D 25 (OH)
- Vitamin D 1,25 (OH)
- if vitamin D25 is less 10=
Calcium, phosphorus, iPTH,
alkaline phosphatase,
BUN/Cr, TTG, DEXA

Treatment

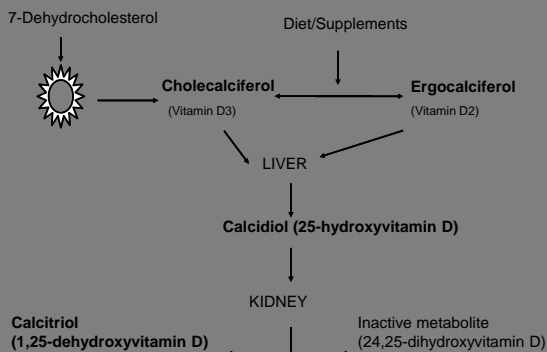
Treatment

- Prevent deficiencies
- Treat deficiencies
- With what?

Treatment

- Vitamin D3/Cholecalciferol
- Vitamin D2/ergocalciferol
- Calcitriol (1,25 dihydroxyvitamin D)
- Calcidiol (25 dihydroxyvitaminD)
- ultraviolet B exposure

Normal Vitamin D Physiology



Treatment-D3 versus D2

- Am J Clinical Nutrition 2012" Comparison of Vitamin D2 and Vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and metaanalysis "

Any randomized intervention trials that involved human adults (men and women) that directly compared the effects of vitamin D2 and vitamin D3 supplementation and used serum 25(OH)D concentrations as a primary outcome were initially included for consideration

3030 studies to 10 studies for systematic review, 7 for met analysis

followup 14 days to 6 months

Systematic review= 8 studies showed d3 with increase in 25 oh measurements. two showed equal effect

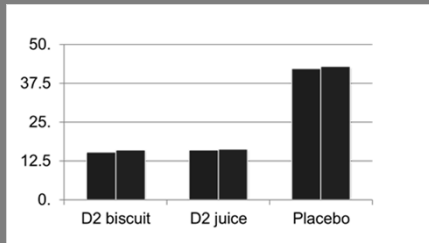
Metanalysis: 15.23 ng/ML increase with D2

Treatment-D3 versus D2

- Daily **food** supplementation with 15ug vitamin d2 compared with vitamin d3 to increase wintertime 25-hydroxyvitamin D status in healthy south Asians and white European women
- America Journal of Clinical Nutrition July 5,2017
- n=335 in Surrey, United kingdom
- given place, supplemented juice or biscuit for 12 weeks

Rate of increase of 25OH vitamin D with D3 supplementation in biscuit and Juice

Treatment-D3 versus D2



Treatment-Prevention

- AGS/NOF: 800-1000 IU
- IOM: adults 600-800 IU of cholecalciferol (vit d3)
 - >18, pregnant=600 IU
 - Older >70=800 IU

Treatment-deficiency

Preparation	DOSAGES AVAILABLE	TYPICAL DOSING	POPULATION
VitD3 cholecalciferol	400,800,1000,2000,5000, 10000, 50,000 IU IM	increased 0.7 to 1.0 for every 100 IU given	Most recommended
VitD2 ergocalciferol	400,50000 IU liquid IM		
Calcitriol	0.25, 0.50 mcg	0.25-0.5 mcg daily to bid	GFR<30 ml/min, type 1 vitamin d- dependent rickets
Calcidiol	25, 50 mcg	50-200 mcg daily	Liver disease
ultraviolet exposure			malabsorption patients

Guidelines

- USPSTF: final recommendation statement on Vitamin D deficiency in adults-screening 2014
- USPSTF: final recommendation statement on vitamin supplementation to prevent cancer and CVD-preventive medication 2014
- Choosing Wisely: Don't perform population based screening for 25-OH vitamin D deficiency 2013
- Choosing Wisely: Don't routinely measure 1,25-dihydroxyvitamin D unless the patient has hypercalcemia or decreased kidney function 2013

Guidelines

- Endocrine Society: clinical practice guideline on evaluation, treatment and prevention of vitamin D deficiency 2011
- ACOG: Committee opinion on vitamin D screening and supplementation during pregnancy 2011, reaffirmed 2015
- North American menopause Society(NAMS): recommendation for clinical care of midlife women 2014

Clinical Case

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Clinical Case

- Vitamin D 25(OH)- 17.7
- What do you recommend?

Summary

- Increasing in incidence
- Do not test all
- Treat with
cholecalciferol
- Monitor for vitamin D
repletion