

# Discussion on VITAMIN D: What you need to know

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# Outline



- Functions in the Body
- Vitamin D and Cancer Research
- RDA
- Sources
- Monitoring
- Replenishment

# Functions in the Body



- Vitamin D is Fat-soluble vitamin
- Vitamin D acquired from food, supplement, and produced in skin from sun. 80% of body's needs come from skin production; Needs 2 hydroxylations before activated in the body: 1<sup>st</sup> in liver form calcidiol, 2<sup>nd</sup> in kidneys to form calcitriol (1,25-dihydroxyvitamin D)

# Functions in the Body



- Essential for calcium absorption in the gut and maintain adequate calcium/phosphate concentration in the blood for proper bone mineralization,
- Prevention of rickets and osteomalacia;
- Supplementation may improve bone mineral density in people with low vitamin d levels

# Functions in the Body (cont'd)



- Used in modulation of neuromuscular and immune function
- Vitamin D works to Reduce inflammation
- Many genes that regulate cell proliferation, differentiation, and apoptosis (all important to control cancer growth) are impacted by Vitamin D

# Symptoms of Deficiency



- Vitamin D deficiency is often asymptomatic. However, severe or prolonged deficiency may cause the following symptoms:
- Bone discomfort or pain in the lower back, pelvis, or lower extremities
- Falls and impaired physical function
- Muscle aches
- Proximal muscle weakness
- Symmetric low back pain (in women)

# Vitamin D and Cancer research



- In regards to cancer mortality (death), vitamin D supplementation significantly reduced total cancer mortality by about 12% in most recent meta-analysis (analysis of all the most recent and relevant studies)
  - Circulating blood levels in study groups reached 54-135nmol/L
  - Reduction in mortality was most significant in daily dosing trials versus bolus dosing

(Keum et al; Annals of Oncology. February 2019 733-743)

# Vitamin D and Cancer research



- In regards to overall cancer prevention, vitamin D supplementation doesn't seem related to incidence
  - Exceptions are reduced risk of colorectal and possibly ovarian
- Studies on cancer risk and specific types of cancers are mixed:

# Vitamin D and Cancer Research



- For breast cancer, some evidence of reduced risk for breast cancer with vitamin D and calcium supplementation (this study used 1,100IU per day of vitamin D3)
- Women's Health Initiative trial supplementation decreased risk of breast cancer in those who didn't already take the supplements;

Grant; Anti-Cancer Research; A Review of Evidence Supporting the Vitamin D-Cancer Prevention hypothesis  
2017; 1121-1136 (2018)

# Vitamin D and Cancer Research



- A analysis study from 2017 of vitamin D and risk of breast Cancer authors concluded protective effect of high blood concentrations in pre-menopausal cases but not as strong in post-menopausal
- Limitations in many studies include different cutoff points, seasonal differences, and types of Vitamin D exposure.

# Vitamin D and Cancer Research



- Prostate Cancer research is mixed suggesting a possible u shaped curve on benefit meaning increased risk with low vitamin D blood levels and very high levels likely related to high vitamin D increasing calcium absorption which is a risk factor for prostate cancer;
- In one study supplement of 4,000 IU vitamin D decreased risk of cancer

# Vitamin D and Cancer Research



- Interestingly when looking at African-American men and risk of prostate cancer vitamin D supplementation could reduce prostate cancer related health disparities considering widespread low vitamin D levels
- It is possible that vitamin D supplementation is more impactful for cancer risk in the African-American population than in general population.

Grant; AntiCancer Research; 1121-1136 (2018)

# Vitamin D and Cancer Research



- Interesting most studies looking at cancer incidence have high population of white participants; in VITAL study that oversampled African-Americans there was a significantly reduced risk of cancer incidence!

(Keum et al; Annals of Oncology. February 2019 733-743)

# Vitamin D and Cancer Research



- In regards to colorectal cancer research, 2019 study found participants at deficient vitamin D concentration ( $<30\text{nmol/L}$ ) were 31% higher risk of colorectal cancer; when levels were  $75\text{-}87.7\text{nmol/L}$  there was a 19% lower risk and when levels were  $87.5\text{-}100\text{nmol/L}$  risk was 27% lower risk; over 100 had no further benefit in this study.

(McCollough et al; Circulating Vitamin D and colorectal Cancer Risk: An International Pooling Project ...; Jour Nat'l Cancer Inst (2019) 111)

# Vitamin D and Cancer Research



- Higher blood concentrations of vitamin D (>50nmol/L) may be associated with better quality of life and less fatigue in colorectal cancer survivors (Koole et. Al, AACR, April 3 2020)
- Some researchers suggest getting 25(OH)D concentration levels certainly over 75nmol/l and maybe in the 100-125 range.

# Mechanisms for Benefit



- Vitamin D influences cellular pro-differentiation, anti-proliferation, and pro-apoptosis (cell death) as well as reduced angiogenesis (blood supply) to cancer cells and inhibits metastasis
- In the colon vitamin D can influence detoxification of the bowel and improve gut mucosal integrity and improve immune function



- For the United States and Canada to reach a goal 50nmol/L blood concentration is: 600 IU/day or 800 IU/day for those 71+
- For osteoporosis recommendation is at least 800 IU/day
- Patients with primary hyperparathyroidism and 25(OH)D concentrations  $<50$  nmol/L =vitamin D doses 600–1000 IU daily aiming to bring 25(OH)D  $\geq 50$  nmol/L at a minimum.
- In primary hypoparathyroidism, it is also recommended to ensure a serum 25(OH)D concentration  $>50$  nmol/L with a suggested supplemental vitamin D dose of 400–800 IU per day

(Pilz et al. Vitamin D Testing and treatment: a narrative review of current evidence. Endocrine Connection. Feb. 2019)

# Sources of Vitamin D



- Sun: exposure to UV B radiation converts 7-dehydrocholesterol to previtamin D3; Season, latitude, time of day, cloud cover, smog, and skin melanin all interfere with UV exposure; Latitude north of 42 degrees is insufficient for production;
- Daily 15 minutes of time in the sun with uncovered extremities and no sunscreen is typically adequate
- Despite importance of sun for Vitamin D production it is still recommended to use sunscreen when exposed to sun and avoid tanning bed radiation as UV rays are carcinogen to skin.

# Sources of Vitamin D



- Food: Salmon, tuna, and mackerel;
- Fish liver oils
- Small amounts in beef liver, cheese, and egg yolks
- Fortified foods like milk, OJ, Cereal

Food	IUs per serving*	Percent DV**
Cod liver oil, 1 tablespoon	1,360	340
Salmon (sockeye), cooked, 3 ounces	794	199
Mushrooms that have been exposed to ultraviolet light to increase vitamin D, 3 ounces (not yet commonly available)	400	100
Mackerel, cooked, 3 ounces	388	97
Tuna fish, canned in water, drained, 3 ounces	154	39
Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup	115-124	29-31
Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)	100	25
Yogurt, fortified with 20% of the DV for vitamin D, 6 ounces (more heavily fortified yogurts provide more of the DV)	80	20
Margarine, fortified, 1 tablespoon	60	15
Sardines, canned in oil, drained, 2 sardines	46	12
Liver, beef, cooked, 3.5 ounces	46	12
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75-1 cup (more heavily fortified cereals might provide more of the DV)	40	10
Egg, 1 whole (vitamin D is found in yolk)	25	6
Cheese, Swiss, 1 ounce	6	2

# Monitoring



- Best lab test is 25-hydroxyvitamin D
- Deficiency <10-11 ng/ml (<25-27.5 nmol/L)
- Inadequate: <10-15 ng/ml (<25-37.5 nmol/L)
- Adequate: >15 ng/ml (>37.5 nmol/L)
- Overall Health: >30ng/ml (>75 nmol/L)\*
- Toxic: >200 ng/ml (>500 nmol/L)

\*recently proposed optimal level for overall health

# Who should monitor?



- Osteomalacia
- Osteoporosis
- Chronic Kidney Disease
- Liver Failure
- Malabsorption syndrome-Cystic Fibrosis, IBD, Crohn's, Bariatric Surgery, enteritis
- Hyperparathyroidism
- Taking steroids, Anti-Seizure meds, AIDS medications, Cholestyramine
- African Americans, Hispanics, and obese individuals
- Older adults with history of falls
- Sarcoidosis, Tuberculosis, Histoplasmosis,
- Lymphoma

# Replenishment



- According to the Endocrine Society Clinical Practice Guidelines for Vitamin D Deficient patients supplementation should occur to bring blood levels to 75nmol/L with recommendation for 6,000IU daily for 8 weeks then maintenance of 1,500-2,000 IU daily (daily Vitamin D3 is the best method to supp. Vs. D2 bolus=more inactive)
- Obese patients, those with malabsorption syndromes, and those on medications affecting vitamin D metabolism should receive a higher dose of 6,000 to 10,000 IU/day to achieve levels above 30 ng/ml. Followed by a maintenance dose of 3,000-6,000 IU/day.

# Replenishment



- It is estimated that for every 100IU increase in vitamin D intake the blood levels increase by 2.5-5nmol/L
- Although there is no clear follow-up recommendations once starting vitamin D it is advisable to wait at least 8 weeks and preferably 12 weeks to recheck the levels

(Pilz et al. Vitamin D Testing and treatment: a narrative review of current evidence. Endocrine Connection. Feb. 2019)

- Of note, there is controversy between the IOM and Endocrine Society on the goal blood levels namely 50 vs 75 nmol/L
- Vitamin D Toxicity is rare

# Take Home Message



- Take Home Message:
  - Know your risk for vitamin D deficiency
  - Know your numbers
  - Replace as needed
  - Incorporate food sources of vitamin D into a plant-based diet and supplement as needed.

Enjoy the Sun carefully to support Vitamin D production without increasing risk of skin cancer!