Benefits of Vitamin D for Cancer and Pregnancy/Birth Outcomes

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Disclosure

• I receive funding from Bio-Tech Pharmacal, Inc. (Fayetteville, AR)
• I serve on the board of directors of VitaminDCouncil.org (San Luis Obispo, CA)
• I am a scientific advisor to GrassrootsHealth.net (Encinitas, CA)
Outline

• Vitamin D pathways
• Cancer: UVB exposure and vitamin D
  – Geographical ecological studies
  – Observational studies
  – Studies of mechanisms
  – Clinical trials
• Pregnancy/birth outcomes and vitamin D
  – Beneficial outcomes found
  – Observational studies
  – Clinical trial demonstrating beneficial effect
Colon Cancer Mortality Rates, White Males 1970-94

Garland et al., Am J Public Health. 2006

The brothers Cedric and Frank Garland published their seminal paper in 1980.
High doses in SW due to thinner stratospheric ozone layer and higher surface elevation.

Data from the NASA Total Ozone Mapping Spectrometer (TOMS)
Higher mortality rates along coast due to fog and clouds.
Breast Cancer Mortality Rates, White Females, 2000-04

Less pronounced geographical variation with respect to solar UVB doses due to less time in the sun, use of sunscreen, increased risk from other factors such as obesity, and improved survival rates.
All less Lung Cancer vs. UVB Index by Occupation in Nordic Countries

28% higher incidence rate for most indoor vs. most outdoor work. For men, the UVB index (lip cancer less lung cancer) was significantly inversely correlated with 14 types of internal cancer.

16 UVB/Vitamin D-Sensitive Cancers from Ecological Studies

- Vitamin D-sensitive cancers with strong support from ecological studies in six mid-latitude plus Nordic countries after accounting for other factors:
  - Gastrointestinal: colon, esophageal, gallbladder, gastric, intestinal, rectal
  - Urinary tract: bladder, kidney
  - Female: breast, cervical, endometrial, ovarian, vulvar
  - Blood: non-Hodgkin’s lymphoma
  - Miscellaneous: laryngeal, lung
Graph of odds ratio for breast cancer incidence vs. 25(OH)D concentration from 11 case-control studies.

The cancer mortality rate for 8 ng/ml is 36% (95% CI, 6%, 74%) higher than for 50 ng/ml.

All-cause and Cancer Survival vs. Baseline 25(OH)D - Norway

Results of a 9-yr study. Significantly reduced cancer-specific mortality rate for 25OHD trend for breast and lung cancer, and lymphoma.
Mechanisms

• Mechanisms whereby vitamin D reduces risk are based on genetic actions of 1,25(OH)$_2$D and include:
  – Cellular – effects on differentiation, proliferation and apoptosis
  – Reduced inflammation
  – Reduced angiogenesis around tumors
  – Reduced metastasis
Creighton University Clinical Trial

• Trial with 2303 postmenopausal women in Nebraska with mean BMI = 30 kg/m², baseline 25(OH)D of 33 ng/ml, given 2000 IU/d vitamin D₃ plus 1.5 g/d calcium or placebo, and followed for 4 yrs.
• By intention to treat, HR = 0.70 (95% CI, 0.47, 1.02, P = 0.06). (one extra case in treatment arm)
• Lappe et al., Effect of Vitamin D and Calcium Supplementation on Cancer Incidence in Older Women: A Randomized Clinical Trial. JAMA 2017
Creighton University Trial: Observational Results

Significantly reduced risk for 25(OH)D >50 ng/ml
All-Cause Mortality Rate vs. 25(OH)D Meta-analysis

Results from 32 studies were included. All-cause mortality rate rose nearly linearly below 38 ng/ml.
Garland et al., Am J Pub Health, 2014
Pregnancy and Birth Outcomes

• Maternal vitamin D deficiency is linked to increased risk of gestational diabetes, pre-eclampsia, primary C-section, preterm birth.
• For the offspring, increased risk of asthma, autism, other neurological disorders, rickets.
Skin Pigmentation

• Skin pigmentation has adapted to where people live for many generations.

• The driving factors are vitamin D production, protection against DNA damage and folate production.


Human Skin Color Distribution
(Chaplin and Jablonski)
Women have lighter skin pigmentation due to vitamin D requirements during pregnancy and lactation.
Primary Cesarean-Section Delivery

Development of Asthma/Recurrent Wheeze vs. Vitamin D Treatment

Kaplan–Meier survival estimates for the effect of vitamin D treatment during pregnancy on the development of asthma/recurrent wheeze by age 3 year analyzed in an intent-to-treat format. Hollis & Wagner, 2017.
Reduced Risk of Preterm Birth

Over 1000 women were enrolled and given free vitamin D supplements with the goal of achieving >40 ng/ml 25(OH)D.

Conclusion

• Optimal serum 25(OH)D₃ concentration is 40 to 60 ng/ml (100 to 150 nmol/l).
• Solar UVB exposure is the most important source of vitamin D₃.
• In absence of UVB exposure, it takes 2000-5000 IU/d (50-125 micrograms/d) vitamin D₃ to reach optimal concentrations.