The Health Benefits of Vitamin D

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Outline

- Types of studies
- Vitamin D and reduction of
  - Dental caries
  - Autism
  - Respiratory infections
  - Diabetes mellitus
  - Cancer
  - Cardiovascular disease
  - Neuroprotection
  - Mortality rates
- Vitamin D recommendations
Types of Epidemiological Studies

- There are four basic types of epidemiological studies used to identify and quantify links between risk-modifying factors and disease:
  - Nested case-control from cohort studies – a defined population followed for years after blood draw;
  - Case-control – blood drawn at time of diagnosis;
  - Cross-sectional – survey of a large population;
  - Ecological – populations are defined geographically or temporally (seasons or longitudinal); both disease outcome and risk-modifying factors are averaged by region or time.
Randomized Controlled Trials (RCTs)

- RCTs are essential for pharmaceutical drugs to demonstrate efficacy and uncover risks.
- There have been a number of successful vitamin D RCTs, including those for hip-fractures, cancer incidence, influenza type A, and all-cause mortality rate.
- However, vitamin D RCTs are often not properly designed and conducted.
- Proper vitamin D RCTs should
  - Have a starting 25(OH)D-health outcome relation
  - Enroll people with low 25(OH)D levels
  - Give those in the treatment arm enough vitamin D3 to raise 25(OH)D levels to the upper region of the outcome relation
  - Measure 25(OH)D levels after supplementation
Higher UVB in the west is due to higher surface elevation and thinner stratospheric ozone layer.
Dental caries are caused by oral bacteria.

Vitamin D, through induction of cathelicidin, reduces concentration of oral bacteria.

This was first shown in a study of vitamin D2 supplementation in 1928 by May Mellanby.

Several recent studies identified cathelicidin as a way to reduce dental caries.

Dental Rank vs. Solar UVB Dose in July, Men Entering WWI and WWII

State-averaged data
Vitamin D has been used to prevent and treat dental caries. The objective of this study was to conduct a systematic review of controlled clinical trials (CCTs) assessing the impact of vitamin D on dental caries prevention. Twenty-four CCTs encompassing 2,827 children met the inclusion criteria.

The pooled relative-rate estimate of supplemental vitamin D was 0.53 (95% CI, 0.43-0.65).

“Animal data has repeatedly shown that severe vitamin D deficiency during gestation dysregulates dozens of proteins involved in brain development and leads to rat pups with increased brain size and enlarged ventricles, abnormalities similar to those found in autistic children. Children with the Williams Syndrome, who can have greatly elevated calcitriol levels in early infancy, usually have phenotypes that are the opposite of autism. Children with vitamin D deficient rickets have several autistic markers that apparently disappear with high-dose vitamin D treatment.”
“Calcitriol down-regulates production of inflammatory cytokines in the brain, cytokines that have been associated with autism. Consumption of vitamin D containing fish during pregnancy reduces autistic symptoms in offspring. Autism is more common in areas of impaired UVB penetration such as poleward latitudes, urban areas, areas with high air pollution, and areas of high precipitation. Autism is more common in dark-skinned persons and severe maternal vitamin D deficiency is exceptionally common the dark-skinned.”

Autism and Vitamin D – Eco Study, U.S. – White American Children

Vitamin D might also reduce the risk or severity of autism through its anti-inflammatory actions, antiautoimmune effects, increasing seizure threshold, increasing T-regulatory cells, protecting the mitochondria, and upregulating glutathione, which scavenges oxidative by-products and chelates (captures and excretes) heavy metals.

Cannell JJ and Grant WB, What is the role of vitamin D in autism? Dermato-Endocrinology, in press
Respiratory Infections

- Vitamin D induces production of cathelicidin, which has antimicrobial properties.
- Higher 25(OH)D levels have been found associated with reduced risk of acute respiratory infections, and pneumonia.
- A randomized controlled trial on schoolchildren in Japan using 1100 IU/d vitamin D3 found a 67% reduction for influenza type A for those not using any other vitamin D supplements compared to 200 IU/d. [Urishama, 2010]
“We measured 25(OH)D in 9841 participants from the general population, of whom 810 developed type 2 diabetes during 29 years of follow-up. Analyses were adjusted for sex, age, smoking status, body mass index, income, physical activity, HDL cholesterol, and calendar month of blood draw.”

“Multivariable adjusted hazard ratios of type 2 diabetes were 1.22 (95% CI 0.85-1.74) for 25(OH)D <5 vs ≥20 ng/mL and 1.35 (1.09-1.66) for lowest vs highest quartile.”
“Finally, in a meta-analysis of 16 studies, the odds ratio for type 2 diabetes was 1.50 (1.33-1.70) for the bottom vs. top quartile of 25(OH)D.”

This study was conducted in Denmark

The first epidemiological study hypothesizing that solar UVB, through production of vitamin D, reduced the risk of cancer was an ecological study published in 1980.

The brothers Cedric Garland and Frank Garland, beginning graduate students at Johns Hopkins School of Public Health in 1974, looked at the map of colon cancer mortality rates in the U.S. and saw a link to solar radiation.
Occupational Study of Cancer Incidence in Nordic Countries

Vitamin D-sensitive cancers with moderate-to-strong support after accounting for other factors:

- Gastrointestinal: colon, esophageal, gallbladder, gastric, pancreatic, rectal
- Urinary: bladder, kidney; Male: prostate
- Female: breast, cervical, endometrial, ovarian, vulvar
- Blood: Hodgkin’s and non-Hodgkin’s lymphoma, leukemia
- Miscellaneous: melanoma
Observational studies provide useful data for determining the serum 25(OH)D concentration-cancer incidence rate relation for breast and colorectal cancer.

Stronger inverse correlations between 25(OH)D concentrations and cancer incidence are found for case-control studies or cohort studies with short follow-up times.
Meta-Analysis of Breast Cancer Risk with Respect to Diagnostic Serum 25(OH)D

Based on five case-control studies from Germany, Mexico, UK, and USA

Mechanisms for Cancer Risk Reduction

- Effects on cellular differentiation and proliferation
- Maintains epithelial cell integrity and tight junctions between cells
- Increased calcium absorption
- Anti-angiogenesis
- Anti-metastasis
Several recent observational studies found that those with lower serum 25(OH)D had higher risk of cardiovascular disease (coronary heart disease and/or stroke) incidence or mortality rate.

The mechanisms appear to include reducing risk of metabolic disease through effects on insulin sensitivity, blood pressure, and arterial calcification, as well as reducing risk of infectious diseases and inflammation.
Meta-analysis of CVD Incidence Rate vs. 25(OH)D Concentration

Data from
Dobnig, 2008;
Giovannucci, 2008;
Ginde, 2009;
Kilkkinen, 2009
“The conflation of in vitro, ex vivo, and animal model data provide compelling evidence that vitamin D has a crucial role in proliferation, differentiation, neurotrophism, neuroprotection, neurotransmission, and neuroplasticity. Vitamin D exerts its biological function not only by influencing cellular processes directly, but also by influencing gene expression through vitamin D response elements.”
This review highlights the epidemiological, neuropathological, experimental, and molecular genetic evidence implicating vitamin D as a candidate in influencing susceptibility to a number of psychiatric and neurological diseases. The strength of evidence varies for schizophrenia, autism, Parkinson's disease, amyotrophic lateral sclerosis, Alzheimer's disease, and is especially strong for MS.

Figure 3. Overall age-adjusted hazard ratios for mortality, all 30 studies combined, 1966-2012; Garland et al., in preparation
List of Vitamin D-Sensitive Diseases A-E

Acne
Acute lower respiratory infection
Alzheimer’s disease
Amyotrophic lateral sclerosis
Anaphylaxis
Anemia
Ankylosing spondylitis
Anxiety
Asthma
Atherosclerosis
Autism
Bacterial vaginosis
Biliary cirrhosis, primary (PBC)
Birth defects
Bones – fractures
Bones - osteopenia

Bones – osteoporosis
Bones – Paget’s disease?
Bones – rickets
Brain injury, traumatic
Bronchitis
Cardiovascular disease
Celiac disease
Cerebrovascular disease
Chronic kidney disease
Chronic liver disease

Chronic, non-specific muscle pain
Cognitive impairment
Common cold
Epstein-Barr virus
Congestive heart failure
Chronic obstructive pulmonary disease
Coronary heart disease
Craniotabies
Cystic fibrosis
Dental caries
Depression
Diabetes, type 1
Diabetes, type 2,
Epilepsy
List of Vitamin D-Sensitive Diseases F-V

Fertility, regular menses  
Fibromyalgia  
Hashimoto's thyroiditis (HT)  
Headache  
Hearing loss  
Hepatitis  
HIV/AIDS  
Hypercalcemia  
Hyperparathyroidism  
Hypertension  
Inflammatory bowel disease  
Influenza, type A  
Insulin resistance  
Ischemic cardiac arrhythmias  
Kidney stones

Lupus  
Macular degeneration  
Meningitis  
Metabolic disease  
Mononucleosis  
Multiple sclerosis  
Muscle strength  
Osteoarthritis  
Pancreatitis  
Parkinson’s disease  
Pelvic floor status  
Periodontal disease  
Peripheral artery disease  
Pneumonia  
Polycystic ovary syndrome  
Post herpetic neuralgia  
Preeclampsia

Premature birth and low birth weight  
Psoriatic arthritis  
Renal failure  
Renal osteodystrophy  
Rheumatoid arthritis  
Respiratory syncytial virus  
Schizophrenia  
Sepsis/septicemia  
Sickle cell disease  
Systemic sclerosis  
Tonsillitis  
Tuberculosis  
Thrombosis  
Uterine leiomyomas (fibroids)  
Vascular dementia  
Vitiligo vulgaris108
Conclusion

There is enough evidence now to conclude that serum 25(OH)D concentrations of at least 40 ng/ml, can significantly reduce the burden dental caries, respiratory infections, diabetes mellitus, many other types of cancer, cardiovascular disease, and cognitive dysfunction, and increase healthy and total life expectancy.

Solar UVB irradiance or vitamin D supplements can be used to reach these concentrations.

It could take 1000-5000 IU/day vitamin D3

Testing serum 25(OH)D recommended.
Additional Resources

- http://www.grassrootshealth.net/
- http://www.healthresearchforum.org.uk/
- http://www.pubmed.gov
- http://www.sunarc.org/
- http://www.vitamindcouncil.org/
- http://www.vitamindwiki.com

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