Vitamin D and Influenza

Warfighter Nutrition: Advanced Technologies and Opportunities”
Uniformed Services University of the Health Sciences
Health Affairs and DARPA co-hosts
Day 2 (16 July 2008)
John Umhau MD MPH
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Standard Form 298 (Rev. 8-98)  
Prescribed by ANSI Std Z39-18
Research associates vitamin D with:

- All cause mortality
- Heart disease
- Diabetes
- Cancer
- Osteoporosis
- Athletic ability
- Depression
Historical studies: cod liver oil prevents respiratory infections

- In the 1930’s, Vitamin A was investigated for its anti-infective properties using Cod liver oil, (which is also abundant in Vitamin D)
- Five studies using cod liver oil, (involving over 7,000 subjects), showed that cod liver oil reduced respiratory infections
- Cod liver oil given to 185 adults for four months reduced colds by 50%; Holmes AD, et al. Journal of Industrial and Engineering Chemistry 1932; 24: 1058-1060.
- In a five year study, cod liver reduced industrial absenteeism caused by colds and respiratory illness; days of missed work was reduced by 30%. (n=3031) Homes AD, et al. Industrial Medicine 1936; 5: 359-361.
Influenza is a seasonal illness

Weekly consultation rates for clinically diagnosed flu

The seasonal and latitudinal distribution of outbreaks of type A influenza in the world, 1964-1975

(WHO Data)
Season influences the effect of inoculated influenza virus

One study evaluated 1248 non-immune males (age 16–18 years) in northern and southern Russia during different seasons of the year.

In the northern group, they found that the inoculated attenuated virus was about eight times more likely to cause fever in the winter than the summer (6.7% vs. 0.8%).

In the southern area, 8% of inoculated subjects developed a fever from the virus in January, but only 0.1% did so in May.

In a replication study, seroconversion (rate of antibody formation) was found to be lowest in summer.

Subjects were more likely to shed the virus in December (40%) than in September (16%), and the quantity of virus shed was lower in summer than winter.

Sub-erythemal doses of UVR (x5) increased polymorphonuclear chemotaxis in healthy volunteers. Csato M et al., British Journal of Dermatology 1984;111: 567-570.

410 athletes who received sub-erythemal doses of UVR (twice a year for three years) had more salivary IgA, IgG and IgM; 50% less respiratory viral infections, 300% fewer absence days and 30% shorter illness than did 446 non-irradiated control athletes. Gigineishvili GR, et al. Voprosy Kurortologii, Fizioterapii, i Lachebnoi Fizicheskoi Kul'tury 1990 May-Jun;(3):30-3.

Dutch children with the most sun exposure were half as likely to develop cough, and a third as likely to develop rhinitis, compared to less sun exposed children. Termorshuizen F, et al. Photoimmunology and Photomedicine 2004; 20: 270-271.
Vitamin D Metabolism

Previtamin D → Vitamin D → 25(OH)D → Kidney

Liver

Milk, Orange Juice, Salmon, or Supplements

Most tissues in the body

1, 25(OH)₂D → Prevent and/or treat:
Viral respiratory disease
Cancer, Osteoporosis
Heart disease, Multiple sclerosis
Diabetes, Hypertension

1, 25(OH)₂D → Maintain calcium economy

John Cannell and Bruce Hollis, Alternative Medicine Review Volume 13, Number 1 March 2008
Humans acquire most of their vitamin D from skin synthesis resulting from casual sun exposure.

Seasonal variations - and vitamin D deficiency – occur in both subtropical and tropical latitudes.

No vitamin D is made in the skin at latitude 52° N (the latitude of London) ~ October to March because atmospheric ozone easily filters out Ultra Violet B radiation unless the sun is high enough in the sky.
Seasonal variation of 25(OH)D levels

Vitamin D modulates the macrophage response, preventing the release of excessive inflammatory cytokines and chemokines. 

Vitamin D promotes macrophage production of specific surface antigens, the lysosomal enzyme acid phosphatase, and the secretion of $\text{H}_2\text{O}_2$ (which is antimicrobial), but vitamin D deficiency decreases these functions. 

Vitamin D stimulates genetic expression of antimicrobial peptides, which have broad-spectrum antimicrobial activity and inactivate influenza virus.
Randomized controlled trial of vitamin D₃ prevent bone loss in African-American women:

- 104 women received placebo and 104 received vitamin D₃.
- Vitamin D₃ dose was increased from 800 IU to 2000 IU after 2 years.
- Patients were followed up every 6 months for 3 years for the occurrence of adverse events, which included reports of cold and influenza.
- RESULTS: The placebo group reported 26 instances of cold and influenza vs. 8 instances in the vitamin D₃ group (P<0.002).
Vitamin D₃ supplements eliminate the winter excess incidence of cold / flu

Number of patients reporting colds / flu

JOHN F. ALOIA AND MELISSA LI-NG, 2007, Epidemiology and Infection
How much vitamin D results from sun exposure?

- Serum 25(OH)D levels indicate the average American gets between 50 and 1000 IU units.
- 5 minutes in a bathing suit in the summer noon day sun provides about 3,000 IU.
- Melanin in the skin reduces production of vitamin D by sunlight, and African Americans have much lower 25(OH)D levels than whites.
- 90% of vitamin D is obtained from the sun.
Fish is virtually the only food naturally rich in vitamin D.

One glass of milk has 100 units, few other products are supplemented significantly.

The current U.S. Dietary Recommended Intake of vitamin D for humans up to age 50 is 200 IU/day.

In the absence of sun exposure, most people will become deficient
How much vitamin D do service members get?

- No one knows.
- War fighters may get sufficient sun exposure, or their protective clothing may effectively keep them out of the sun.
- Dietary intake may be close to 200 IU/day from supplemented milk products.
- The vitamin D status of servicemembers returning from deployment could be easily measured using existing banked serum from the Defense Medical Surveillance System.
Army Rations for troops in WW I supplied ~ 500 IU of vitamin D (and ~1,300 mg of Omega-3)

A "trench ration," especially designed to meet the danger of gas contamination, was developed in 1918; it combined twenty-five rations in a single large metal container:

- 50 cans hard bread
- 10 cans corned beef
- 5 cans roast beef
- 4 cans fish
- 4 cans sardines
- 25 rations sugar
- 25 rations soluble coffee
- 25 rations salt
- Solidified alcohol
- 25 rations cigarettes

8 oz. each
16 oz. each
16 oz. each
4 oz. each
5 lbs. in bulk
18.75 oz.
50 oz.
100 cigarettes

These rations were packed by a Trench Ration Canning Department which was organized at the Chicago Quartermaster Depot and turned out its first million rations (40,000 containers) between June 12 and July 1, 1918. The work was done on a production line basis; the components were placed in a shiny galvanized iron container, somewhat like a wash boiler.
Toxicity

Vitamin D is fat soluble, and accumulation (from diet) in the body can be toxic.

The long-term safe dose of vitamin D is not known, however, 10,000 IU/day is safe in healthy adults.

All known cases of vitamin D toxicity have involved intake of or over 40,000 IU/day.

The LD$_{50}$ in man is unknown – there are no reported deaths from acute toxicity.
In addition to the established long term benefits of vitamin D, it is possible that a short term benefit of adding dietary vitamin D is to maximize readiness by reducing the incidence of colds and flu.

The amount of vitamin D received by warfighters could be easily measured, and such measurement could guide therapy using UV light or through diet.
Warming rays in postwar austerity Britain

Miners at Silverhill colliery in the Nottinghamshire coalfield supplying the vitamin deficiencies inherent in a working life spent underground with a session at the in-house solarium in September 1947. The management at Silverhill pigged itself on rates of pay and perks, which, it claimed, kept its miners contented and the pit strike-free.
Acknowledgements

- Cannell JJ
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A blood calcidiol (25-hydroxy-vitamin D) level is the accepted way to determine vitamin D nutritional status, and shows considerable variation.
How much do we need?

- The dosage depends upon age, latitude, season, skin type, body weight, sun exposure, and preexisting 25(OH)D levels.
- When 25(OH)D levels fall below ~87nmol/L, calcium absorption in the intestine falls with it. That is, calcium absorption is maximized by keeping 25(OH)D levels above ~87nmol/L.
- Approximately 3,000 IU/day of vitamin D is required to assure that 97% of Americans obtain levels greater than ~87nmol/L.
Vitamin D from sunlight affects TB

The 1903 Nobel prize was awarded for the discovery that vitamin D from sunlight could cure cutaneous TB.