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Commentary: Time for public health action on vitamin D for cancer risk reduction

William B Grant[1] and Edward D Gorham[2,3]*

The seminal paper by Garland and Garland[1] continues the tradition of observation and inference leading the way to discovery of new methods for preventing or curing disease. Their paper broke ground by marshalling the evidence for the vitamin D-cancer hypothesis. Their work directly confronted the prevailing paradigms that the main risk factors for colon cancer were deficient fibre intake, excessive fat intake, and/or genetic predisposition.

At that time it was hard to envision that a geophysical characteristic, such as solar ultraviolet-B (UVB) radiation, through photosynthesis of vitamin D, would reduce cancer risk. Solar UVB was considered mainly harmful, and the findings of the paper did not support the paradigms.

In some ways it was not surprising that their hypothesis opposed the conventional wisdom. Many diseases have been eliminated by the epidemiological approach when other approaches have not been successful.

In 1645 a slum-dwelling toddler was taken to a clinic for the poor because he could not walk, his legs being bizarrely weak and twisted. Within a few decades, the feared disease that came to be known as rickets was present in a majority of London children. Early death was common. As with pellagra, the tendency of the disease to run in families led many to regard it as hereditary.

Despite 335 years of recognition of the disease, there had been neither cure nor means of prevention. But when incidence rates worldwide were plotted on a map in 1890, an inverse association was noted with sunlight. Children were soon placed in sunlight or briefly exposed to an artificial source of UVB, and the disease was either prevented or cured in the young.

It took almost 100 years from the discovery that UVB and vitamin D prevented rickets to the realization that they reduced the risk of colon,[1] breast,[2] and ovarian[3] cancers. With unusual speed in biomedical history, a risk-reducing role of UVB and vitamin D was found for prostate,[4] bladder, oesophageal, gastric, pancreatic, rectal, renal, and corpus uteri cancer, and non-Hodgkin's lymphoma.[5] The total number of vitamin D-sensitive cancers determined to date is at least 18.[1–7]

Vitamin D has also been found to improve the prognosis of those with cancer. It was observed that those whose breast, colon, or prostate cancer was diagnosed in summer or fall in Norway, when serum 25-hydroxyvitamin D [25(OH)D] levels are higher, had better survival rates than those whose cancer was discovered in winter or spring.[8] A recent study in Boston found that having lung cancer surgery in summer and high vitamin D intake was associated with twice the 5–10 year survival rate.[7]

The link between UVB and vitamin D and reduced risk for many types of cancer satisfies the criteria for causality in a biological system as postulated by Robert Koch in linking the tuberculosis bacillus to tuberculosis in 1882 and extended by A. Bradford Hill in his Presidential Address to the Royal Medical Society in 1965. The primary criteria are strength of association, consistency among different populations, generally a linear dose–response relation, ruling out confounding factors, and identifying mechanisms to explain the results. These criteria are very well satisfied for UVB and vitamin D and cancer in general except for prostate cancer, for which both low and high values are associated with increased risk in Nordic countries[9] and the US.[10] The reason for this U-shaped curve is still not understood.

While the spectrum of cancers whose risk is reduced in association with vitamin D was rapidly expanded by ecological studies[2–6] and complemented by case–control,[11] cohort,[7–9,11] and laboratory studies, public health action has been virtually non-existent. The greatest advance to date was the designation of 2000 IU/day of oral intake of vitamin D as the No Adverse Effect Level by the US National Academy of Sciences (NAS).

Oral doses currently consumed in the US (an estimated mean of 320 IU/day) are far too low,[11] and the designation of the 2000 IU/day dosage as safe by the NAS provides latitude to the community to increase intakes to levels required to reduce risk of cancer, with essentially no likelihood of adverse effects. It is now increasingly accepted that 0.75 minimal erythemal dose of UVB on 20% of skin area is the equivalent of ~2000 IU of oral intake of vitamin D_3. The duration of solar exposure required for this dosage varies by latitude, season, time of day, and race.

Public health leaders are now in nearly the same position with breast, colon, ovarian, and several other cancers that President Franklin D. Roosevelt was in when he was stricken with polio in 1921. Observation and inference based on its strong seasonality had shown that the disease was infectious, and not primarily genetic. This led to identification of the polio virus in 1908, but no public health action was initially taken apart from isolation of cases and quarantine. Yet FDR realized that action was needed and created the March of Dimes that ultimately led to the development of the Salk vaccine by 1952. The Salk vaccine of that era was 50% effective, which is similar to the effectiveness of 1000–2000 IU/day of vitamin D_3 for prevention of colorectal cancer.

It has been 25 years since the paper by Garland and Garland[1] was published in this journal, and 15 years since evidence of the vitamin D theory was extended to breast[2] and ovarian cancers.[3] The intake of vitamin D is far too low for cancer risk reduction in the US.[11] It is time to act on this research and increase oral intake

[1] Sunlight, Nutrition and Health Research Center (SUNARC), 2107 Van Ness Avenue, Suite 403B, San Francisco, CA 94109-2529, USA.

[2] Department of Family and Preventive Medicine, University of California, San Diego, 9500 Gilman Drive 0631C, La Jolla, CA 92093, USA.

[3] Naval Health Research Center, San Diego, CA 92186-5122, USA.

* Corresponding author. E-mail: Gorham@nhrc.navy.mil

of vitamin D and de-stigmatize moderate exposure to solar UVB. The health benefits of such action will aid in cancer prevention and extend to many other diseases and conditions[12]; the costs are low, the risks are few, and the potential public health benefits are tremendous.

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