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Editor's Corner

# Shining light on the vitamin D

## Cancer connection IARC report

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Recently the International Agency for Research on Cancer released a report on vitamin D and cancer. In response to this report, Dr. Grant wrote a thoughtful and critical review of the report noting not only many deficiencies in the interpretation of the data that the committee members used to base their recommendations on but also noted that the ratio of expertise on the committee favored UV irradiation associated with risk of skin cancer was fourfold higher than expertise and publication record in the field of vitamin D.

As the industrial revolution began to sweep across northern Europe, Whistler, DeBoot and Glisson in the mid-17th century reported the appearance of a new disease that afflicted young children with a constellation of physical signs and symptoms including deformities of the skeleton such as bowed legs, enlargement of the epiphyses at the joints of the long bones and rib cage, deformed pelvis, enlarged head, curvature of the spine, poor dentition and weak and flabby legs.[1,2] The disease had devastating consequences not only by causing growth retardation but also the skeletal abnormalities impaired their ability to function throughout their lives. Women with a deformed pelvis often had difficulty with child birthing with marked increased risk of both maternal and infant morbidity and mortality. Many theories about the cause of this debilitating disease surfaced during the ensuing 250 years including infection, lack of activity, poor nutrition and an inherited disorder.[3] Although cod liver oil appeared to be effective in preventing the disease, it was principally used on the coastlines of the Scandinavian countries and the United Kingdom, but was not widely used elsewhere. The disease continued to plague the industrial centers of the world, and by the turn of the 20th century autopsied studies of children who died of various causes in Leyden, The Netherlands revealed that 80–90% of these children had residual evidence of rickets.

What is remarkable in retrospect is that as early as 1822 the Polish physician, Sniadecki, realized the importance of exposure to outdoors and sunlight for the prevention and cure of rickets.[4] He observed that children living in the inner city of Warsaw, Poland had a high incidence of rickets whereas the children that he saw living in the rural areas rickets was essentially unheard of. He concluded that it was lack of sun exposure for children living in the inner city of Warsaw that was responsible for this bone deforming disease and encouraged direct exposure to sunlight as one of the most efficient methods for the prevention and cure of rickets. However, it was inconceivable to the scientific community at the time how exposure of skin to sunlight could have any impact on the skeleton. Indeed, it would take another 70 years before the British Medical Association in 1889,[5] reported that rickets was infrequently seen in the rural district of the British Islands but was prevalent in large industrialized towns suggesting that it was lack of sun exposure that was responsible for the high incidents of rickets. A year later, Palm[6] collected clinical observations from a number of his colleagues throughout the British empire and the orient and found that rickets abounded in the industrialized centers of Great Britain whereas the improvised cities in China, Japan and India where people lived in squalor and had poor nutrition were spared from this bone deforming disease. Based on this epidemiologic survey, he urged "(a) the establishment of a sunshine recorder in the heart of the city to record the chemical activity of the sun's rays rather than its heat, (b) to remove rachitic children as early as possible from large towns to a locality where sunshine abounds and the air is dry and bracing, (c) the systemic use of sunbaths as a preventative and a therapeutic measure in rickets and other diseases and (d) the education of the public to the appreciation of sunshine as a means of health." However, once again even with the advancements in medicine and science, it was difficult for the scientific community to embrace the concept that the simple remedy of exposure to sunlight could cure this bone deforming disease and little was done to use these insightful observations for the prevention and cure of rickets. By 1900, it was estimated that 80% of the children living in the industrialized cities of northern Europe and northeastern United States were afflicted with this devastating skeletal disease.[1,2] Almost 100 years after the first insightful observation of Sniadecki, Huldschinsky et al.[7,8] reported that exposure to ultraviolet radiation from a mercury arc lamp was an effective method to cure patients with severe rickets. He cleverly demonstrated that the effect of phototherapy was not a direct effect on the skeleton in as much as exposure of one arm had an equal and dramatic effect on the cure of rickets in both arms. This quickly led Hess and Unger[9]

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two years later to expose rachitic children on a roof of a New York City hospital to varying periods of sunshine and reported by x-ray examination marked improvement in rickets in each child.

In the early 1930's, the US government set up an agency that recommended to parents to put their children outside for a reasonable amount of sun exposure in order to prevent this devastating disease.[10,11] Several manufacturers produced ultraviolet lamps that were sold in local pharmacies in the 1930s–1950s to parents who exposed their children to ultraviolet radiation from mercury arc lamps to prevent them from developing rickets.[8,10,11]

In retrospect, it was incredibly unfortunate that the first insightful observation of Sniadecki was not taken seriously by either the scientific or medical communities. As noted by Grant, the IARC report in many ways is reminiscent of how the scientific community responded to and dismissed the observations of Sniadecki, British Medical Association and Palm regarding the beneficial effect of sun for bone health. As noted by Grant, for unclear reasons the IARC committee failed to recognize meta-analyses of data suggesting a strong positive association with either increased exposure to sunlight or vitamin D and reducing risk not only of many deadly cancers but other chronic serious diseases including autoimmune diseases, heart disease and infectious diseases.[12-17] They also failed that when you take out the patients who developed cancer the first year of the four year Lappe et al.[18] study, there was a 77% reduction in overall cancer risk for women taking 1,100 IU of vitamin $D_3$ and 1,500 mg of calcium a day.

The IARC report also raises concern about the possibility that high blood levels of 25(OH)D for long periods of time may have a health hazard. Unfortunately, the committee does not define what high 25(OH)D serum levels are nor do they apparently appreciate the literature regarding the fact that both children and adults exposed to sunlight in the summer or who live near the equator and have a life style where they are outdoors most of the time have circulating blood levels in the range of 40–80 ng/ml.[19,20] There has never been a credible report that either exposure to sunlight or maintaining blood levels of 25(OH)D of between 30–100 ng/ml has ever been associated with a negative health outcome. It also was not recognized by the committee that adults require at least 3,000–5,000 IU of vitamin D/d to satisfy their body's vitamin D requirement.[21] When an adult in a bathing suit is exposed to one minimal erythemal dose, it's equivalent to that person's ingesting between 10,000–20,000 IU of vitamin D.[22,23] It is impossible to get this amount of vitamin D naturally from dietary sources even from diets that have been fortified with vitamin D such as dairy products in the United States, Canada and other practicing countries. Typically, there is 100 IU per serving making it impossible to acquire even 1,000 IU of vitamin D daily. As noted by Grant, for every 100 IU of vitamin D ingested, the blood level of 25(OH)D increases by 1 ng/ml. A recent study reported that healthy adults with an average 25(OH)D of 18 ng/ml taking 1,000 IU of vitamin D/d did not raise their blood level of 25(OH)D >30 ng/ml which many experts in the field of vitamin D believe is necessary not only to maximize intestinal calcium absorption, but also to maximize bone mineral density and muscle strength.[24] Thus, at a minimum, both children and adults should maintain a 25(OH)D >30 ng/ml at least for maintenance of skeletal and muscle health.

The association of excessive exposure to solar ultraviolet B radiation and increased risk of developing non-melanoma skin cancer is well documented.[25] However, the committee sheds little light on the fact that the most deadly form of skin cancer melanoma occurs on the least sun exposed areas and that occupational sun exposure decreases risk of this deadly disease.[25,26]

I agree with Grant that the IARC report generates more heat than sheds light on the role of vitamin D and sensible sun exposure for overall health and well being. Hopefully history will not repeat itself where more than 100 years ago, the scientific and medical communities regarded exposure to sunlight on the skin as a heat producing process and not responsible for any positive photochemical process that would benefit health. Essentially every tissue and cell in the body has a vitamin D receptor, and it has been estimated upwards of up to 6,000 genes are directly or indirectly regulated by 1,25-dihydroxyvitamin D [$1,25(OH)_2D$].[27] To suggest that there is no credible scientific evidence that serum 25-hydroxyvitamin D levels actually prevents any cancer or any other chronic condition ignores the mountain of epidemiologic evidence similar to what was observed by Palm[6] regarding the beneficial effect of sun and vitamin D for health. There continues to be a need for randomized controlled clinical trials regarding the effect of increasing vitamin D intake or exposure to ultraviolet radiation as a means of reducing risk of chronic deadly diseases that hopefully will help enlighten the perspective of the IARC Committee in the future. Sufficient evidence now exists to warrant an increase in the recommended vitamin D intake or production as an effective means of reducing the risk of cancer and other chronic and infectious diseases, and the lack of 100% convincing evidence should not stand in the way.

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