ELSEVIER

Symposium in Print on the Epidemiology of Vitamin D and Cancer

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With this issue, we conclude a set of papers assembled for a Symposium-in-Print on the epidemiological evidence relating vitamin D deficiency with the risk of several major cancers and the role of vitamin D in recurrence, metastasis, and death from cancer.

A review by Mohr (1) describes the scientific discovery that vitamin D and calcium adequacy are associated with lower incidence and mortality rates from colon, breast, ovarian, and several other cancers. Giovannucci (2) examined the association of vitamin D status with risk of cancer in the Nurses Health Study, Physicians Health Study, and Health Professionals Follow-up Study. Methods used for ascertainment of vitamin D status in these cohorts included analysis of 25-hydroxyvitamin D (25(OH)D), the predominant circulating form of vitamin D, in serum collected from healthy individuals before diagnosis of cancer; prospective analyses of oral intake of vitamin D; and modeling of serum 25(OH)D levels based on area of residence, skin pigmentation, and other personal characteristics.

The association of serum 25-hydroxyvitamin D status with the risk of pancreatic cancer, a currently active yet perplexing topic of investigation, was reviewed by Stolzenberg-Solomon (3). Bertone-Johnson (4) reported on the dose–response gradient for prevention of breast cancer, drawing attention to the possibility that there may be subpopulations of individuals who have unrecognized vitamin D resistance due to polymorphisms of the nuclear vitamin D receptor (4). The complex role of sunlight exposure in the risk of melanoma is another area of intense investigation. Because exposure to sunlight is the main source of vitamin D (5) and brief periods outdoors in the sun are often recommended for vitamin D photosynthesis, Egan (6) explores the possible concerns of such recommendations in light of the association of solar overexposure with incidence of melanoma.

Vieth reviewed the extensive literature supporting the low likelihood of toxicity of vitamin D_3 at intakes of 2000–4000 IU/day and reported that toxicity may be unlikely even at doses as high as 10,000 IU/day (7). His review suggests that a serum 25(OH)D target of 60 ng/mL (150 nmol/L) may be optimal for most individuals. Future research on vitamin D and cancer will be informed by Holick's overview of the state of the art of measurement of vitamin D and its metabolites (8). Schwartz described the use of vitamin D-related compounds as components of treatment protocols for prostate cancer, and use of analogues of $1,25(OH)_2D$, known as deltanoids, that have been developed for clinical use (9). Grant and Mohr examined studies that estimated solar and ultraviolet B (UVB) irradiance using NASA satellite-derived data, and the inverse associations of such irradiance with the risk of cancer of the breast, colon, ovary, and several other sites (10). Finally, Garland and colleagues (11) analyzed the global impact of vitamin D deficiency on cancer incidence, and reviewed the results of randomized trials of vitamin D and calcium for cancer prevention. They described the mechanisms for reduction of cancer incidence by vitamin D and calcium, and the amount of incidence reduction that could result from achieving various population serum levels of 25(OH)D.

Measurement issues related to vitamin D are a continued area of intense investigation. The current state of technology and epidemiology, however, suggests a strong inverse relationship between vitamin D status and incidence of breast, colon, ovary, and aggressive prostate cancer. Emerging evidence linking low serum levels of 25 (OH)D with other cancers and major chronic diseases, suggests that the role of vitamin D status in human disease will be a fertile area for future research. All new cohort studies of the general population and randomized trials in cancer patients should collect and freeze serum or plasma at baseline to allow future studies of the role of vitamin D and its metabolites in cancer incidence and survival.

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